Ireland: Pharmaceutical Prices, Prescribing Practices and Usage of Generics in a Comparative Context

Aoife Brick
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The ESRI

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Abbreviations

ACE inhibitor	Angiotensin-converting-enzyme inhibitor
APMI	Association of Pharmaceutical Manufacturers of Ireland
ATC	Anatomical Therapeutic Chemical
DoH	Department of Health
DP	Drugs Payment
EU	European Union
EU-15	Fifteen EU Member States prior to enlargement in 2004 and 2007
EU-27	Twenty-seven EU Member States following enlargement in 2004 and 2007
Euripid	EURopean Integrated Price Information Database
FEMPI	Financial Emergency Measures in the Public Interest Act
GMS	General Medical Services
GP	General Practitioner
HIQA	Health Information and Quality Authority
HSE	Health Service Executive
HTD	High Tech Drug
ICGP	Irish College of General Practitioners
IDTS	Indicative Drug Targeting Scheme
IMB	Irish Medicines Board
IMF	International Monetary Fund
IMO	Irish Medical Organisation
IMS	Intercontinental Medical Systems
Independent Body	Independent Body on Pharmacy Contract Pricing
INN	International Non-Proprietary Name
IPHA	Irish Pharmaceutical Healthcare Association
LTI	Long Term Illness
MMP	Medicines Management Programme
NHS	National Health Service
NCA	National Consumer Agency
NCPE	National Centre for Pharmacoeconomics
NICE	National Institute for Health and Care Excellence
NPS	National Prescribing Service
ODB	Ontario Drug Benefit
OECD	Organisation for Economic Co-operation and Development
OTC	Over-the-counter
PCA	Prescription Cost Analysis
PCRS	Primary Care Reimbursement Service
PCT	Primary Care Trust
PHARMAC	Pharmaceutical Management Agency of New Zealand
PI	Parallel Import
PPI	Proton Pump Inhibitor
PSI	Pharmaceutical Society of Ireland
QALY	Quality-Adjusted Life Year
QOF	Quality and Outcomes Framework
UK	United Kingdom
VAT	Value Added Tax

EXECUTIVE SUMMARY

BACKGROUND

As part of the EU-IMF Programme of Financial Support for Ireland, there was a further (seventh) update of the *Memorandum of Understanding on Specific Economic Policy Conditionality* in November 2012. It states that, '[T]he authorities will conduct a study to compare the cost of drugs, prescription practices and the usage of generics in Ireland with comparable EU jurisdictions'.[1] The Department of Health and the Health Service Executive subsequently commissioned the Economic and Social Research Institute to undertake the study.

PHARMACEUTICAL EXPENDITURE PER CAPITA

One of the facts that motivated the interest of the EU and IMF in pharmaceutical expenditure in Ireland was the rapid rise in the level of such expenditure relative to other OECD countries. In terms of pharmaceutical expenditure per capita, Ireland's position has moved from 20th highest of 27 countries in 2000, to 9th of 31 in 2005, to 3rd of 25 in 2010. If per capita spending in the US, which has consistently the highest expenditure on pharmaceuticals on a per capita basis, was set at 100, then Ireland was 46 in 2000, 58 in 2005 and 70 in 2010.

PHARMACEUTICAL PRICES

New (i.e. single source in-patent) and generic pharmaceutical prices in Ireland are high relative to comparable EU Member States. In contrast, patent-holder or originator pharmaceutical prices are lower in Ireland where a generic pharmaceutical is available. This is a consistent finding across numerous studies and over time. Our own up-to-date research using the latest available data for March 2013 confirms these findings.

GENERIC USAGE

Usage of generic pharmaceuticals in Ireland has traditionally been low in comparison with other Member States. Again, this is a consistent finding across a number of studies and over time. However, in this respect our research for Ireland suggests matters have improved. The market share of generics for the leading GMS Scheme pharmaceuticals with generic competition doubled between 2010 and 2012 to reach 50 per cent. Because, in contrast with much of the EU, generic prices in Ireland tend to be similar to those of the patent-holder, increased generic penetration has not, up until now, led to substantial reductions in pharmaceutical expenditure for either the

[1] EU-IMF (2012, p. 8). No further elaboration is provided.

State or the cash-paying patient. However, this state of affairs is likely to change with the coming into force of the 2012–2015 agreements between the State and the pharmaceutical trade associations and the implementation of the Health (Pricing and Medical Goods) Act 2013, both of which will see the gap between generic and brand name pharmaceuticals widening.

Prescribing Practices

Where prescribers in Ireland have a choice between different pharmaceuticals within three therapeutic sub-groups (statins, ACE inhibitors, proton pump inhibitors) medical practitioners tend to select the most expensive pharmaceutical product. These three groups of pharmaceuticals account for nearly one-fifth of spending by the State under the GMS Scheme, the most important State pharmaceutical reimbursement scheme. In contrast, in the UK medical practitioners often select the lowest priced statin, ACE inhibitor and proton pump inhibitor. Consequently in the UK costs are lower and as pharmaceuticals within the same therapeutic sub-group are generally considered substitutes, quality of care is maintained.

The State We're In: Why?

The status quo in Ireland is a reflection of the series of negotiated voluntary agreements between the State and pharmaceutical representative bodies or trade associations. These agreements benchmark pharmaceutical prices in Ireland against nine Member States, contain provisions for realignment every few years as opposed to annually or biannually (as is done elsewhere), and set the pricing pattern for pharmaceuticals once a generic manufacturer enters the market. There is provision for pharmacoeconomic assessment of a pharmaceutical prior to reimbursement. The agreements also state that the pharmacist will be required to dispense a prescription as written thus prohibiting substitution of a less expensive pharmaceutical product of equal quality.

Reform: Times Past

The State has introduced a series of reforms since the mid-2000s designed to reduce pharmaceutical prices and expenditure. Ex-factory prices are now benchmarked against some lower priced Member States such as Spain. Wholesale mark-ups were halved and retail or pharmacy mark-ups were also reduced. The price of generic pharmaceuticals has fallen faster and further. More information has been provided to prescribers. This record needs to be built upon in order to further reduce prices, increase the use of generics, and improve prescribing patterns.

REFORM: TIMES FUTURE

The Health (Pricing and Medical Goods) Act 2013, which was signed into law on 28 May 2013, holds out the possibility of radically changing the way in which pharmaceutical prices are set in Ireland. The existing agreements between the State and the pharmaceutical trade associations, which are due to expire in 2015, are only one factor that shall be taken into account in setting prices of both new and generic pharmaceuticals. The legislation lists a series of factors that give the HSE a wide discretion in price setting. Pharmacists will also be able to select a lower priced pharmaceutical product than that prescribed for the patient by a medical practitioner for interchangeable pharmaceutical products.

However, lack of clarity and precision as to how prices will be set under the Health (Pricing and Medical Goods) Act 2013 means that it is not possible to predict with any certainty that pharmaceutical prices in Ireland will fall vis-à-vis comparable Member States. Nevertheless, the Act offers the possibility of a decisive break from the past, a structural change in the way in which pharmaceutical pricing takes place in Ireland with consequent benefits for the cash-paying patient and the taxpayer who has to fund the State pharmaceutical reimbursement schemes.

Complementary measures need to be taken to support the initiative of the Health (Pricing and Medical Goods) Act 2013. Price transparency at the retail level is important so that patients are well-informed. Measures need to be taken to ensure that pharmacists have both the ability and incentive to provide such information.

Under the pharmacoeconomic assessment of a pharmaceutical prior to reimbursement, a threshold of €45,000 per quality-adjusted life year (QALY) is set. However pharmaceuticals are being approved for reimbursement in excess of this threshold. This raises certain questions, including:

- Is €45,000 the correct value for the QALY?
- If €45,000 is appropriate, what controls should be put in place to determine when it can be overridden?

A national conversation concerning these questions would bring some clarity in guiding policy makers in this area.

Chapter 1

Introduction

As part of the EU-IMF Programme of Financial Support for Ireland, there was a further update (the seventh) of the *Memorandum of Understanding on Specific Economic Policy Conditionality* in November 2012. It stated that, '[T]he authorities will conduct a study to compare the cost of drugs, prescription practices and the usage of generics in Ireland with comparable EU jurisdictions'.[1] The Department of Health (DoH) and the Health Service Executive (HSE) subsequently commissioned the Economic and Social Research Institute (ESRI) to undertake the study.

Concern over these issues is not new. A series of government-sponsored reports have touched on various aspects of pharmaceutical pricing, prescribing, and dispensing from the ex-factory price through to the price paid by the State or the patient.[2] The issue of pharmaceutical prices and availability continues to be of interest as evidenced by media coverage of issues such as price-setting agreements between government and industry, price comparisons between Ireland and other EU Member States[3], legislation designed to lower prices and encourage greater use of generic pharmaceuticals, and discounting by pharmaceutical suppliers to pharmacies.

In April 2011, the HSE requested the ESRI to undertake a wide-ranging report on virtually all aspects of the pricing, distribution, prescribing and dispensing of pharmaceuticals in Ireland. The report was published in January 2012.[4] In this present report we update and extend aspects of this earlier research to meet the requirements of the EU-IMF mandate. In particular, we consider whether the ex-factory price of pharmaceuticals in Ireland is high in relation to comparable Member States. Recent price comparisons between Ireland and New Zealand are updated.[5] Attention is also paid to the usage of generics and the prescribing practices of medical practitioners.

1 EU-IMF (2012), p. 8. No further elaboration is provided.

2 See Gorecki *et al.* (2012, Appendix A, pp. 147-153) for a summary of earlier reports conducted in Ireland that examined various aspects of pharmaceutical pricing and related issues. In this report our concern is with pharmaceuticals prescribed by a medical practitioner. Hence over-the-counter pharmaceuticals which can be purchased without a prescription are excluded.

3 Hereafter referred to as 'Member States'.

4 Gorecki *et al.*, 2012

5 WHO and EOHSP, 2012; Gorecki *et al.*, 2012

The report is divided into seven chapters including the introduction. Chapter 2 discusses the terms of reference and how we address them. In order to interpret and understand the determinants of the cost of pharmaceuticals, prescription practices and the usage of generics it is necessary to understand the relevant institutional context. This context is discussed in Chapter 3. Comparing the price of pharmaceuticals in Ireland, both over time and with other Member States, is the subject of Chapter 4.

Attention then turns in Chapter 5 to the usage of generic pharmaceuticals in Ireland and, to the extent possible, comparisons with other Member States. The discussion to date is concerned with comparisons made at the level of an individual chemical substance (e.g., omeprazole or lansoprazole). In Chapter 6 the issue of prescribing practices for selected sub-groups of individual chemical substances (e.g., proton pump inhibitors) is presented. The report concludes with Chapter 7 which addresses the issues set out in the terms of reference.

The report represents events as of June 2013.

CHAPTER 2

Mandate, Definitions and Measurement Issues

2.1 INTRODUCTION

In this chapter we first set out the mandate or terms of reference, together with the policy context, in Section 2.2, before clarifying some key definitions in Section 2.3. For example, we concentrate our attention on prices at the ex-factory level (Section 2.3.1) and pharmaceuticals classified mostly at the Anatomical Therapeutic Chemical (ATC) Classification level 5 (Section 2.3.2). We also provide a broad overview of our data sources (Section 2.4). Section 2.5 concludes.

2.2 TERMS OF REFERENCE AND POLICY CONTEXT

2.2.1 Terms of Reference

The terms of reference state that the title of the project will be, *Ireland: Pharmaceutical Prices, Prescribing Practices and Usage of Generics in a Comparative Context*. The report's overall objectives, drawing on the EU-IMF mandate, are '[T]o produce a report that will compare the price of pharmaceuticals, prescribing practices and the usage of generics with comparable European jurisdictions'. A detailed specification of the data required to conduct the research is also included. This is reproduced as Appendix A of this report. The object of such a detailed specification is to ensure that the data underlying our earlier report is comparable with the 2012 and 2013 data supplied by the HSE for this project. This will permit comparisons to be made from 2010 to the present.

The report is being commissioned because of a concern that pharmaceutical prices are too high in Ireland, that prescribing practices could be improved, and that generic usage is too low. The cumulative impact of these three concerns is that the pharmaceutical bill of the State and the prices paid by cash-paying patients (i.e., those not covered by the various State pharmaceutical reimbursement schemes)[1] is too high.[2] By examining whether these concerns are valid, together with an understanding of the reasons for the current state of affairs, this analysis should permit the development of policy options to address any remaining concerns.

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1 These groups are detailed in Gorecki *et al.* (2012), Table 2.1, p. 15. It should be noted that in some instances those covered by a State pharmaceutical reimbursement scheme are also cash-paying because they are responsible for a portion of the pharmaceutical cost. For details see Table 2.1 below.

2 NCA, 2013. This shows that cash-paying patients pay widely varying prices for the same pharmaceutical.

The European Commission's autumn 2012 review of the *Economic Adjustment Programme for Ireland* sets out its concerns under the heading 'More could be done on the cost of Pharmaceuticals', where it states:

> While all EU countries have seen substantial increases in drugs costs since the turn of the century, Ireland's increases have been among the sharpest, nearly tripling from 2000 to 2008 …
>
> In 2010, per capita spending on pharmaceuticals in Ireland was the highest in the EU, 34% above the average, while health outcomes are not better than the average for EU countries over a range of high-level indicators. This suggests a potential for savings well beyond the measures already announced.
>
> High drug prices is an important factor. In particular in the area of generics, prices of the same drugs vary considerably across EU Member States, and with the patents on many branded drugs approaching expiration (the so-called 'patent cliff'), renewed attention could be paid to maximising the benefits of lower cost generics. Cost savings from generics are greatest when the uptake follows quickly from patent expiry. Important savings could be achieved with a reform of the external reference pricing mechanism. At present, Ireland sets prices for drugs based on an average of a basket of reference countries. Significant gains could be made by …[3]

The European Commission then makes a series of recommendations which draw heavily on our earlier work.

More recently the IMF in its April 2013 *Ireland: Ninth Review Under the Extended Arrangement* called for greater provision of information on pharmaceutical expenditure and measures to increase the use of generics. On the former, quarterly reports on pharmaceutical prescriptions and expenditure are to be undertaken. On the latter, the IMF state that the 'authorities will set high level annual targets for increasing the share of generic drug usage in the medium-term. Enabling measures – such as compulsory prescription by International Non-propriety Name (INN) by end 2013, where appropriate – required for the achievement of these targets will be put in place and kept under further review'.[4]

2.2.2 Policy Context

As noted in Chapter 1 the issues raised by the EU-IMF are not new. Indeed, policy measures have been and are being taken by the State to address these issues, independent of the intervention of the EU-IMF. It is thus important to outline, albeit briefly, these measures to contextualise the situation. In several instances more detail is provided in subsequent chapters of the report. This is not to take away, of course, from the important role that the EU-IMF is playing in stimulating discussion of these pharmaceutical cost issues and policy measures to address these problems.

---

3 European Commission (2013), p. 23

4 IMF, 2013, p. 87. See *ibid*, p.90 concerning the provision of information on pharmaceutical expenditure.

Since the mid-2000s the State has followed a systematic policy to reduce the cost of pharmaceuticals. This was driven, in part, by the rapid growth in pharmaceutical expenditure per capita both in absolute terms[5] and relative to other Organisation for Economic Cooperation and Development (OECD) countries. Per capita pharmaceutical expenditure in Ireland, measured in nominal terms, almost doubled between 2000 and 2005. Furthermore, if the OECD countries for which data was available are ranked from highest to lowest in terms of per capita pharmaceutical expenditure, Ireland ranked 20 out of 27 in 2000 but ninth out of 31 in 2005. Measured relative to the US (set at 100), per capita pharmaceutical expenditure in Ireland increased from 46 to 58 between 2000 and 2005.[6]

It is estimated that the State accounts for 85 per cent of overall pharmaceutical expenditure in Ireland, in both the hospital and community sector.[7] In 2010 total pharmaceutical expenditure was €2.2 billion. The State provides free or subsidised pharmaceuticals to patients under various schemes. Details on the most important of these schemes, administered by the Primary Care Reimbursement Service (PCRS) are presented in Table 2.1, with the General Medical Services (GMS) Scheme being by far the most important scheme both in the mid-2000s and today.

The reimbursement price paid by the State under the four schemes operated by the Health Service Executive (HSE) in Table 2.1 can be decomposed into the following components: an ex-factory price (P_{ex}); a wholesale mark-up, currently 8 per cent;[8] and a pharmacy mark-up that is currently 20 per cent for the DP and LTI schemes and zero for the GMS Scheme, and for the HTD there is patient-care fee which is unrelated to the pharmaceutical cost. The price paid by the State under the DP and LTI schemes is (1.20) x (1.08xP_{ex}) under the GMS and HTD schemes, it is (1.08 x P_{ex}). Thus the State can influence the cost of a pharmaceutical at three different but interrelated stages in the process of a pharmaceutical moving from the manufacturer, to the wholesaler and to the pharmacy, where the patient presents a prescription obtained from a medical practitioner.

5 Table 2.2 shows that, for the GMS Scheme between 2000 and 2005, nominal expenditure increased by a factor of 2.5, the number of items by a factor of 1.6, and ingredient cost per item by a factor of 1.5.

6 Pharmaceuticals were defined as pharmaceuticals and other non-medical durables; per capita expenditures were measured in US $ purchasing power parity. The US was selected as a benchmark since it consistently has the highest per capital pharmaceutical expenditure. The data source was the OECD Health Data 2012 [last accessed 8 May 2013].

7 Gorecki *et al.* (2012), p. 16, which is also the source for the €2.2 billion estimate.

8 The mark-up for fridge items is currently 12 per cent.

TABLE 2.1 Four Leading Pharmaceutical Schemes, Eligibility for Free or Subsidised Pharmaceuticals[a]

Scheme/Payment	Description
General Medical Services (GMS)	Persons who are unable without undue hardship to arrange general practitioner (GP) medical and surgical services for themselves and their dependants receive free General Medical Services. Drugs, medicines and appliances supplied under the Scheme are provided through retail pharmacies. In most cases the doctor gives a completed prescription form to a person, who takes it to any pharmacy that has an agreement with the HSE to dispense GMS prescription forms. In rural areas the GP may dispense for those persons who opt to have their medicines dispensed by him/her. All GMS claims are processed and paid by the Primary Care Reimbursement Service. Since 1 October 2010, an eligible person who is supplied a drug, medicine or medical or surgical appliance on the prescription of a Registered Medical Practitioner, Registered Dentist or Registered Nurse Prescriber, by a Community Pharmacy Contractor, is charged per item (€1.50 – January 2013) subject to a limit per family per month (€19.50 – January 2013). The prescription charge is recouped by HSE PCRS from the Pharmacist. Number of Claimants 31 December 2011[b]:1,507,152 (32.8% of population) Total Cost of Prescriptions: €1,196 million,
Drugs Payment (DP)	Under the Drugs Payment Scheme persons who are ordinarily resident in the State and who do not qualify for GMS can benefit if the spend on approved drugs, medicines and appliances for themselves or their family exceeds a monthly threshold (€144 per month January 2013). Number of Claimants 31 December 2011[c]: 429,102 (9.3% of population) Total Cost of Prescriptions (net):[d] €142 million
Long Term Illness Scheme (LTI)[e]	On approval by HSE, persons who suffer from one or more of a schedule of long-term illnesses are entitled to obtain, without charge and irrespective of income, necessary drugs, medicines and appliances under the LTI Scheme. Number of Claimants 31 December 2011[f]**:** 59,274 (1.3% of population) Total Cost of Prescriptions: €118 million
High Tech Drugs (HTD)	High Tech Drugs are generally only prescribed or initiated in hospital and include items such as anti-rejection drugs for transplant patients or medicines used in conjunction with chemotherapy or hormonal therapy. The medicines are purchased by the Health Service Executive and supplied through Community Pharmacies for which Pharmacists are paid a patient care fee. The cost of the medicines and patient care fees are reimbursed by the Primary Care Reimbursement Service. Total Payments to Wholesalers and Pharmacists: €368 million

Notes:
a All figures relate to 2011.
b The number of eligible persons: 1,694,063 (36.9% of population)
c The number of eligible persons: 1,518,241 (33.1% of the population)
d Net of the co-payment by the patient
e Acute Leukaemia, Mental Handicap, Cerebral Palsy, Mental Illness (in a person under 16), Cystic Fibrosis, Multiple Sclerosis, Diabetes Insipidus, Muscular Dystrophies, Diabetes Mellitus, Parkinsonism, Epilepsy, Phenylketonuria, Haemophilia, Spina Bifida, Hydrocephalus, Conditions arising from the use of Thalidomide
f The number of eligible persons: 142,585 (3.1% of the population)

Source: Adapted from HSE (2013); HSE, personal communication, 23 May 2013.

At the ***ex-factory*** or manufacturer level the State, through the HSE and the Department of Health (DoH), reduced ex-factory prices paid for pharmaceuticals, both for new (i.e., single source in-patent) and for those experiencing generic competition (i.e., multiple source off-patent). As we shall see in Chapter 3, it did this for new pharmaceuticals by including in 2006 some lower ex-factory priced Member States, such as Spain, in the basket of countries against which the ex-factory price of a new pharmaceutical in Ireland is benchmarked. Where there is generic competition the ex-factory price of a pharmaceutical is typically set at a discount to the ex-factory price of the new pharmaceutical prior to generic entry. In successive agreements with pharmaceutical representative bodies the discount has been increased, thus reducing the ex-factory prices of multiple source off-patent pharmaceuticals.

In terms of the ***wholesale mark-up*** this was reduced from 17.66 per cent in March 2008 in two stages – July 2009 and June 2011 – to 8 per cent.[9] At the retail level ***pharmacy mark-ups*** for the DP and LTI schemes were reduced in July 2009 from 50 to 20 per cent, although this was to some extent offset by an increase in the dispensing fee. Nevertheless, the reduction in the mark-up reduces, but does not eliminate, the incentive for the dispensing of higher ex-factory priced pharmaceuticals (where the prescription is by INN). Finally, 2013 is likely to see further reductions in the ex-factory price of multiple source off-patent pharmaceuticals with the introduction of reference pricing and generic substitution due to the implementation of the Health (Pricing and Supply of Medical Goods) Act 2013, which is discussed further in Chapter 5.

It is difficult to estimate the impact of all of these measures on the reimbursement prices paid by the HSE for pharmaceuticals (i.e., ex-factory price, plus wholesale and pharmacy mark-ups). Ideally, the patterns of reimbursement prices based on the policies in place in 2006 would be estimated and then compared with the actual reimbursement prices, which would reflect the policy changes outlined above. Unfortunately this is not possible and hence we resort to a much more crude methodology. We present in Table 2.2 the ingredient cost, which is the ex-factory price plus the wholesale mark-up per item (i.e., pack), under the GMS from 2000 to 2013. There is a correlation in some instances between falls in ingredient cost per item and some policy changes, for example, the ex-factory price reductions that commenced on 1 November 2012 and 1 January 2013.

Nevertheless, much more work would need to be done to isolate the relative importance of policy changes as distinct from other determinants of changes in the ingredient cost per item. The patent cliff, for example, may be expected to lead to lower ingredient cost per item as pharmaceuticals no longer have patent protection and begin to experience competition from lower priced generic manufacturers.[10] Furthermore, the ingredient cost might also be expected to be influenced by the deflationary macroeconomic forces experienced with the onset of the recession triggered by the financial crisis in 2008. Finally, the definition of an item is a particular pack size (e.g., 28 pack of atorvastatin 10mg). If the pack size declines (increases) in size over time then, other things being equal, cost per item will also decline (increase). We have not been able to take into account any fluctuations in pack size.

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9 See Gorecki *et al.* (2012), table 2.3 p. 23, for further details.

10 Figure 5.1 shows how the share of single source in-patent pharmaceuticals has been falling between 2010 and 2013 across both the GMS and the DP schemes.

TABLE 2.2 Ingredient Cost per Item and Other Characteristics of the GMS Scheme, 2000–2013

	Prescription Costs[a]	Number of Items[b]	Ingredient Cost per Item[c]	Eligible Patients	Selected Policy Changes[d]
	€ Millions	000's	€	Millions	
2000	328	22,880	11.49	1.15	
2001	422	25,521	12.91	1.20	
2002	538	29,500	14.35	1.17	
2003	637	32,241	15.62	1.16	
2004	748	35,030	16.70	1.15	
2005	816	37,428	17.45	1.16	
2006	925	40,569	18.34	1.22	Ex-factory price reductions of multiple source off-patent pharmaceuticals
2007	1,032	44,358	18.58	1.28	
2008	1,129	48,212	18.28	1.35	Ex-factory price realignment of new pharmaceuticals; ex-factory price reductions of multiple source off-patent pharmaceuticals
2009	1,246	50,722	18.97	1.48	Reduction in wholesale mark-up (17.66% to 10%, July)
2010	1,220	54,308	17.17	1.62	Ex-factory price realignment of new pharmaceuticals
2011	1,196	57,983	15.22	1.69	Reduction in wholesale mark-up (10 to 8%, July)
2012 (Jan – Oct)	-	-	15.08	-	
2012 (Nov – Dec)	-	-	13.55	-	Reduction in the ex-factory price of multiple source off-patent pharmaceuticals and realignment of the ex-factory price of new pharmaceuticals placed on the market prior to 1 September 2006 (1 November)
2013 (Jan – Feb)	-	-	13.43	-	Realignment of the ex-factory price of new pharmaceuticals placed on the market after 1 September 2006 (1 January)

Notes
a Prescription costs include dispensing fees, VAT for non-oral medicines, and the ingredient cost.
b Each item (i.e., a pack) is a separate pharmaceutical. In other words, if a prescription is written for more than one pharmaceutical then each is considered separately for the purposes of this table.
c Ingredient cost is the ex-factory price plus the wholesale mark-up. It is the gross price and hence does not take into account any patient co-payments which were introduced towards the end of the period covered by the table.
d For details of the policy changes see Chapter 3. Reference is made to policy changes that affect either the ex-factory price or the wholesale mark-up.

Source: Based on data supplied by the HSE, personal communication, 22 April 2013.

There are number of other caveats which need to be borne in mind when interpreting the data in Table 2.2. First, other Member States experiencing recession and fiscal austerity, will also have moved to reduce pharmaceutical costs. If these Member States are more successful than Ireland, then pharmaceutical prices in Ireland in comparison with these Member States will have increased. Second, although the discussion applies to the pharmaceuticals purchased by the State under the GMS Scheme, the various schemes operated by the HSE all determine the wholesale price in the same way. However, the ex-factory price and the wholesale mark-up are also used as the basis for pricing to the cash-paying patient.[11]

[11] The cash-paying patients are those that have no access to any of the State pharmaceutical schemes or those eligible for the DP Scheme but whose monthly family expenditure on pharmaceuticals is less than €144. It should be noted that if the

Nevertheless, there can be no guarantee that the pricing regime that applies, for example under the DP Scheme, will apply to the cash-paying patient. Here the pharmacist can charge what market forces dictate. Third, as we shall see in the remainder of this report and as was evident in our earlier report, although substantial progress has been made in reducing the reimbursement price of pharmaceuticals in Ireland, there is still considerable scope for further reductions.

2.3 KEY DEFINITIONS

2.3.1 Defining a Pharmaceutical

We have not, as yet, defined what we mean by a pharmaceutical. The ATC Classification classifies pharmaceuticals. Under the ATC Classification system, 'the active substances are divided into different groups according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties'.[12] There are five levels into which such substances are disaggregated. The finest level, ATC 5, refers to individual chemical entities or substances such as atorvastatin, omeprazole, furosemide, lansoprazole, or rabeprazole. The next level is ATC 4, which consists of different chemical/pharmacological/therapeutic subgroups. For example, proton pump inhibitors are an ATC 4 classification which consists of several ATC 5 substances such as omeprazole, lansoprazole, or rabeprazole. In general when we use the term pharmaceutical we will be referring to ATC 5, with the noticeable exception of Chapter 6.

2.3.2 Defining the Price of a Pharmaceutical

Attention is paid in this report primarily to pharmaceutical prices at the ex-factory level rather than the retail or pharmacy level.[13] The ex-factory price is the base price on which wholesale and pharmacy margins and fees are added in order to determine the price paid by the patient or the State. Prices at the ex-factory level are largely set through agreements between the State (i.e., the DoH and/or the HSE) and representative bodies of different segments of pharmaceutical manufacturing. In other words, these arrangements set up an administrative framework within which maximum prices are set, with only a limited role for the market. It is this agreed ex-factory price that is used for the purposes of the State pharmaceutical reimbursement schemes.

expenditure exceeds the monthly limit then all of the pharmaceuticals of the family are priced according to the DP Scheme reimbursement rules, not just the portion over €144 per month.

12 http://www.whocc.no/atc/structure_and_principles/ [last accessed 14 March 2013]

13 Our earlier report dealt extensively with the issue of pricing at the wholesale and retail (i.e., pharmacy) level. The issues that were raised in that report, especially the introduction of greater competition and price disclosure at the pharmacy level, remain in our view as relevant today as they were in January 2012.

Although attention will be paid to the ex-factory price of a pharmaceutical, attention will also need to be paid to the operation of downstream wholesale and pharmacy markets. Rules that operate concerning generic substitution at the pharmacy level, for example, will influence generic usage. Equally, if there is extensive discounting by pharmaceutical manufacturers to pharmacies off the agreed ex-factory price then this may indicate that the listed ex-factory price is in some sense too high. Hence in order to be able to interpret upstream ex-factory prices, attention needs to be paid to downstream markets closer to the patient.

2.3.3 Measuring Pharmaceutical Prices

In comparing the ex-factory prices of pharmaceuticals between Ireland and other Member States, we need to decide the unit of analysis. Within each ATC level 5 (e.g., atorvastatin), there are multiple products (i.e., doses, pack sizes, etc.), and multiple manufacturers. For single source pharmaceuticals, for which there is one manufacturer on the Irish market, then the solution is more straightforward, although, of course, there are still likely to be different dosage strengths and pack sizes. This situation arises for new pharmaceuticals which are still subject to patent protection. However, even here, as we shall see, there may be more than one pharmaceutical manufacturer. Where sales of a pharmaceutical are low, perhaps because it is off-patent and improved newer pharmaceuticals have replaced it, there is likely to be only one manufacturer. The return to a second manufacturer is too low to merit the investment.

Where there is more than one manufacturer of a pharmaceutical the ex-factory price paid for that pharmaceutical is the weighted average of those manufacturers, where the weights are the quantity supplied. This further complicates price comparisons and measurement. To take a simple example, suppose that there are two manufacturers of a pharmaceutical with ex-factory prices of €0.90 per 10 mg tab from manufacturer 1 and €0.10 per 10 mg tab from manufacturer 2. The total ex-factory bill for that pharmaceutical by the State or patients as whole will depend on the market share of the two manufacturers. If manufacturer 1 accounts for most of the market, the ex-factory price paid for the pharmaceutical will be nine times higher than if manufacturer 2 accounts for most of the market. Hence in determining the ex-factory price paid for a pharmaceutical attention has to be paid to price determination of all manufacturers of a particular pharmaceutical and the rules that determine the market shares of the different categories of manufacturers.[14]

We divide pharmaceuticals into two categories for these purposes, which is summarised in Table 2.3. First, we examine ***single source in-patent*** pharmaceuticals,

[14] These issues are discussed in Chapter 3.

which are also referred to as new pharmaceuticals. These are pharmaceuticals still subject to patent protection and where there is no competition from other manufacturers, except via parallel imports.[15] The EU single market imperative means that firms can import a single source in-patent pharmaceutical (i.e., parallel import) from another Member State for sale in Ireland without the permission of the patent owner.[16] Here the ex-factory price paid for a single source in-patent pharmaceutical is a weighted average of the patent-holder's ex-factory price[17] and that of each of the parallel importers, where the weights are the quantity supplied.[18] Hence in determining the ex-factory price paid for single source in-patent pharmaceuticals we need to consider the price determination process for the patent owner and the parallel importers and the rules and incentives that determine the market shares of these two groups of manufacturers.

TABLE 2.3 Classification of Pharmaceuticals, by Type and Manufacturer/Supplier

Pharmaceutical	Type[a]	Manufacturer/Supplier
Single source in-patent[b]	4. Brand name or proprietary pharmaceutical without a generic equivalent	Patent holder Parallel importer[c]
Multiple source off-patent	1. Unbranded generic (i.e., using the international non-proprietary name (INN))	Patent holder Generic
	2. Branded generic (i.e., generic pharmaceuticals that use a brand name)	
	3. Brand name or proprietary pharmaceutical with a generic equivalent	

Notes
a This four-fold classification by type is that used by the HSE for administrative data purposes.
b Also referred to as a new pharmaceutical.
c Parallel imports are usually single source in-patent pharmaceuticals, but may sometimes be multiple source off-patent pharmaceuticals.

Source: Based on information supplied by the HSE.

Second, ***multiple source off-patent*** pharmaceuticals, where the pharmaceutical patent is no longer valid and the patent holder cannot legally prohibit new entrants, usually referred to as generics, from supplying the pharmaceutical. Generic manufacturers typically enter the market for high-volume pharmaceuticals. Here the ex-factory price paid for the pharmaceutical product is the weighted average of the patent owner's ex-factory price and that of each of the generic manufacturers. Hence in determining the ex-factory price paid for multiple source off-patent pharmaceuticals we need to consider the price determination process for the patent holder and the generic manufacturers and the rules and incentives that determine

15 In some instances off-patent pharmaceuticals are single source for various reasons and in some instances these are captured in the data source as single source in-patent pharmaceuticals. In other words they are included in class 4 in Table 2.3. See note to Table 4.1 in Chapter 4.

16 Of course, all pharmaceuticals can be traded between Member States, irrespective of their patent status or whether or not they are experiencing generic competition.

17 In some cases the patent holder may license a firm to market the pharmaceutical in Ireland, in which case the licensee is assumed to be the patent holder.

18 Clearly if there are no parallel imports then the ex-factory price for the pharmaceutical will be that of the patent holder.

the market shares of these two groups of manufacturers. The stronger the incentives to encourage generic manufacturer market penetration, and given that such manufacturers generally charge a lower ex-factory price, then the ex-factory price paid for the pharmaceutical will be lower than would otherwise be the case.

We will present the following pricing information for leading pharmaceuticals, where price is measured at the ATC 5 level and expressed as the unit ex-factory price per dose (e.g., per milligram):

- The trend in ex-factory pharmaceutical prices in Ireland from 2011 to 2013
- The ex-factory price of the patent owners (for single source in-patent and multiple source off-patent pharmaceuticals) and of generic manufacturers (for multiple source off-patent pharmaceuticals)
- A comparison of ex-factory pharmaceutical prices in Ireland to those in other Member States

The last set of comparisons poses particular challenges which are elaborated in Chapter 4.

The data that generates ex-factory prices for multiple source off-patent pharmaceuticals can also be used to estimate the importance of generic usage by estimating their market share in value and volume terms. The difference between the two measures reflects the price difference between the patent holder and generic manufacturers taken as a whole.

2.3.4 Defining a Comparable Member State?

An examination of the ex-factory pharmaceutical prices in other Member States is one way of measuring whether or not Ireland is paying ex-factory prices that are too high, too low or in some sense just right. Pharmaceuticals are traded goods and typically prices, in the absence of trade barriers, would be expected to equalise across the Member States.[19] If ex-factory prices in Ireland are above those paid by other Member States then this suggests that there are grounds for arguing that prices in Ireland may be too high. The choice of comparable Member States thus becomes critical.

[19] Of course, it could be argued that pharmaceuticals are unlike many other traded goods in view of the substantial degree of intervention by governments in determining the price. Persistent price differences between Member States confirm the existence of such barriers. It thus emphasizes the importance of policy at the individual Member State level in determining pharmaceutical prices.

We use several benchmarks against which to measure ex-factory pharmaceutical prices in Ireland. First, for the comparative analyses in Chapters 4 and 5, we initially use the nine Member States that are contained in the agreement between the DoH/HSE and the Irish Pharmaceutical Healthcare Association (IPHA), which is the representative body of the 'the international research-based pharmaceutical industry in Ireland.'[20] It is these firms that are responsible, by and large, for the introduction of new pharmaceuticals.

As we shall see in Chapter 3, the ex-factory price of new pharmaceuticals in Ireland is set in relation to the ex-factory price in nine Member States: Belgium, Denmark, France, Germany, the Netherlands, Spain, the UK, Finland, and Austria. These are all members of the EU-15, which tend to be the richer Member States, prior to enlargement which saw the EU grow to the EU-27 Member States.[21] The basket of nine might be considered a reasonable benchmark since income per capita is likely to be an important determinant of pharmaceutical prices[22] and hence, other things being equal, prices might be expected to be more similar and comparable across these nine Member States than if the comparison were extended to include those poorer Member States that joined the EU more recently.

Second, it could be argued that the selection of the basket of nine Member States, which reflects the result of negotiation between the State and IPHA, omits some similarly high income per capita Member States. Therefore, instead of confining attention to the basket of nine Member States, it could be argued that it would be more appropriate to include all EU-15 Member States.

Third, the leading Member States from which parallel imports into Ireland are sourced were selected. It appears, based on consultation with the HSE, that these Member States are Greece, the UK and Spain, two of which are already included in the basket of nine. These may be considered comparable in that pharmaceuticals are being imported into Ireland from these Member States and hence these prices are relevant. Essentially the argument here is that pharmaceuticals are traded freely within the EU under the single market imperative and if a pharmaceutical is available from another Member State at a lower price than obtains in Ireland and it is imported into Ireland then this indicates something about relevant prices.

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20 http://www.ipha.ie/alist/about-us.aspx [last accessed 15 March 2013]

21 Croatia becomes the 28th Member State on 1 July 2013. For details see http://ec.europa.eu/enlargement/countries/detailed-country-information/croatia/index_en.htm [last accessed 19 March 2013].

22 There is a positive relationship between pharmaceutical expenditure per capita and GDP per capita across EU Member States. Member States with higher GDP per capita might, for example, be both more willing and able to pay for newer more expensive pharmaceuticals as compared to those Member States with a lower GDP per capita. For details and discussion see Kanavos *et al.* (2011), pp. 19-20; Danzon and Furukawa (2003); and Kanavos *et al.* (2013).

Hence we will have three groups of comparable Member States, plus, as noted in Chapter 1, New Zealand. We will also use other non-EU jurisdictions that are part of the OECD, such as Australia, Canada, and the US. We select New Zealand because it is similar in size to Ireland in terms of population, and assigns responsibility to an independent agency, the Pharmaceutical Management Agency (PHARMAC), to purchase pharmaceuticals designed to get value for money. PHARMAC uses innovative techniques such as tendering in order to secure favourable ex-factory prices while at the same time ensuring security of supply.[23] In addition, the use of New Zealand allows us to compare with previous analyses.

2.4 DATA SOURCES

The main source of data for this report is the pharmaceutical dispensing database administered by PCRS. All data therefore refer to pharmaceuticals dispensed in the community, i.e., we do not analyse the usage of generics or prescribing patterns in the hospital sector. For the ex-factory price analysis we have detailed data on sub-sets of pharmaceuticals at ATC level 5, with the data containing dispensing quantities and ex-factory prices for each distinct product within each ATC level 5. The choice of pharmaceuticals is based on the leading single- and multi-source pharmaceuticals by value on the GMS Scheme in 2010.[24]

Information on ex-factory prices in comparable Member States is sourced from the Euripid database.[25] On this database Member States record the price for each pharmaceutical at the ATC level 5 of all the various products (i.e., doses, pack sizes, etc.), by manufacturers. The price recorded is one or all of the following: ex-factory, wholesale price, and, retail price (i.e., net and gross). No quantities are presented. Access is restricted to Member States. Due to confidentiality issues prices for individual Member States cannot be identified, but by setting prices in Ireland equal to 100 comparative prices can be presented for groups such as the basket of nine or the EU-15.

Aggregated data on pharmaceutical values and volumes for 2010, 2011 and 2012 across the four main schemes, details of which were presented in Table 2.1, is used to analyse trends in generics over time, and across the various schemes (to inform the analysis in Chapter 5). We also use these data for the analysis of prescribing patterns in Chapter 6, by aggregating the data to ATC level 4 for three groups of pharmaceuticals (i.e., proton pump inhibitors, statins, and ACE inhibitors). Further details on the data sources (year, unit of analysis, etc.) are provided in Table 2.4.

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23 For details on PHARMAC see http://www.pharmac.health.nz/ [last accessed 2 April 2013].

24 Value means the total cost to the HSE of a particular ATC 5 pharmaceutical. The market shares of the leading pharmaceuticals selected is detailed in Appendix B, Table B.1.

25 The discussion of the Euripid is based on information supplied by the HSE.

TABLE 2.4 Ireland and EU Pharmaceutical Data Supplied by the HSE

		Value and Volume Data	Price Data
Ireland, Data at ATC Level 5 (Chapters 4, 5 and 6)			
1.	Top 20 single source on-patent pharmaceuticals[a]	2010 2011 2012	01-09-11 01-03-13
2.	Top 20 multiple source off-patent pharmaceuticals[a]	2010 2011 2012	01-09-11 01-03-13
3.	Market share by pharmaceutical type (e.g., unbranded generic, branded generic, proprietary with a generic equivalent, proprietary without a generic equivalent, and parallel imports) on the GMS, DP, LTI and HTD Schemes[b]	2010 2011 2012	-
European Union, Data at ATC Level 5 (Chapter 4)			
4.	Euripid price data for the top 10 single source on-patent pharmaceuticals[c]	-	01-09-11 01-03-13
5.	Euripid price data for the top 10 multiple source off-patent pharmaceuticals[c]	-	01-09-11 01-03-13
Ireland, Data at ATC Level 4 (Chapter 6)			
6.	ATC 4 dispensing quantities: proton pump inhibitors, statins, ACE inhibitors	2010 2011 2012	-

Notes:
a The rankings used data for 2010, where the ranking was based on total cost of a pharmaceutical to the HSE.
b GMS=General Medical Scheme; DP= Drugs Payment Scheme; LTI = Long Term Illness Scheme; and HTD = High Tech Drugs Scheme.
c The sample reflected the leading pharmaceuticals selected in (1) in the table.
- Not available or relevant/applicable.

Source: Based on information provided by the HSE.

2.5 CONCLUSION

This chapter has set out the rationale for the study, key definitions and the major data sources. However, before proceeding to analyse the data on prices, generic usage and prescribing patterns, it is important to set out the context, i.e. how ex-factory prices are set in Ireland. It is only by understanding this process that the trends and comparative patterns in ex-factory prices, usage of generics, and prescribing patterns may be understood.

CHAPTER 3

Context: How Are Ex-Factory Pharmaceutical Prices Set?

3.1 INTRODUCTION

Ex-factory pharmaceutical prices are not set in a vacuum. In order to be able to predict and interpret the data presented in Chapters 4, 5 and 6, it is necessary to understand how ex-factory prices are set in Ireland. What mechanism is used to determine ex-factory pharmaceutical prices? How has it changed over time? Does it take into account the ex-factory pharmaceutical prices in other jurisdictions? How transparent and accountable is the price-setting mechanism? What is the objective used to set prices?

The most important mechanism used to set ex-factory pharmaceutical prices in Ireland is the agreements reached between the State and the representative bodies of different groupings of pharmaceutical manufacturers.[1] In this chapter we begin in Section 3.2 with the agreement between the State and the IPHA with regard to the setting of the maximum price of new pharmaceuticals, which are typically single source and subject to patent protection.[2] The maximum ex-factory price of parallel imports and generic pharmaceuticals are set in relation to the price of new pharmaceuticals.[3]

Next attention turns in Section 3.3 to the setting of the ex-factory price of pharmaceuticals for which the patent has expired and for which there is generic competition. These are multiple source off-patent pharmaceuticals. Here the relevant agreements are not only those between the State and the IPHA, but also that between the State and the representative body of the generic pharmaceutical manufacturers, the Association of Pharmaceutical Manufacturers of Ireland (APMI).

The ex-factory price-setting mechanisms under these agreements follow the same procedure regardless of the type of pharmaceutical,[4] except where the classification changes between agreements (e.g., the pharmaceutical's patent protection expires

1 The State signatories to the agreements have varied. See Table 3.1 for an outline of the signatories to each agreement.

2 It should be noted that once the patent expires the new pharmaceutical price obtains until a generic manufacturer enters the market.

3 Parallel imports largely occur when the patent for the new pharmaceutical is extant; generic pharmaceuticals appear when the patent on the new pharmaceutical has expired.

4 As set out in Table 2.3.

and generic competitors enter the market). A single maximum ex-factory price across hospital and community supply is also a feature of the agreements.[5]

In considering the agreements between the State and the pharmaceutical representative bodies, we consider the influence of the Health (Pricing and Supply of Medical Goods) Act 2013 which was signed into law on 28 May 2013. This Act is concerned with setting the ex-factory price not only of single source in-patent pharmaceuticals but also of multiple source off-patent pharmaceuticals which will be designated as interchangeable by the Irish Medicines Board (IMB). Under the 2012–2015 State/APMI Agreement once the IMB has designated a group of pharmaceuticals as interchangeable, then the ex-factory price declines to 40 per cent of the patent-holder's price prior to generic entry. We will return to the Act in Chapters 5 and 7.

The purpose of the section is to outline the major developments since the mid-2000s. However, it will go beyond that by predicting, based on agreements between the State and the pharmaceutical representative bodies, the likely pattern of price changes, how Ireland compares internationally, and the implications for generic usage and prescribing practices (issues evaluated using the latest data in Chapters 4, 5 and 6).

Unless otherwise specified in this chapter, pharmaceutical price refers to the ex-factory price. Various wholesale and retail pharmacy mark-ups are added to this to derive the price paid by the State under the various pharmaceutical schemes.[6] It should also be noted, however, that the ex-factory price derived from the various agreements between the State and IPHA/APMI should be viewed as a maximum price. Pharmaceutical manufacturers can charge the State a lower price, although there appears to be little incentive to do. The agreed price is also a list price, from which deviations can take place as set out below, when pharmaceutical manufacturers compete for business from pharmacies by offering discounts.[7]

3.2 Setting the Price of New Pharmaceuticals

3.2.1 Introduction

This section is divided into four parts including the introduction. We begin with an examination of the agreements between the State and IPHA in relation to the price charged for new pharmaceuticals by the patent holder or originator, before

5 It should be noted that hospitals are free to negotiate lower prices directly with manufacturers and in fact do so (Gorecki *et al.*, 2012; p.25).

6 These are set out in Gorecki *et al.* (2012), Table 2.3, p. 23.

7 Issues surrounding how these discounts can be captured by the State are discussed in Chapters 5 and 7.

discussing how the price for parallel imports is set. Given that the ex-factory price of a particular new pharmaceutical is the weighted average of the price of the patent holder and the parallel importer, attention turns to the factors that are likely to influence their respective market shares. The section concludes with a discussion of the extent to which the analysis of these agreements and associated arrangements is likely to lead to new pharmaceutical prices that are high or low by reference to other Member States and how prices are likely to have evolved in Ireland.

3.2.2 The State/IPHA Agreements: External Reference Pricing

The agreements between the State and the IPHA in terms of their duration, signatories and reference to the pricing of single-source pharmaceuticals are set out in Table 3.1. Since these agreements use the term new pharmaceutical rather than single source in-patent pharmaceutical we use the two terms interchangeably. The table shows that since 2006 there have been two agreements lasting at least three years and a couple of shorter term or interim agreements between these two longer term agreements.[8] It is the two longer term agreements, particularly the State/IPHA 2006–2010 agreement, that form the basis for the pricing of new pharmaceuticals. These agreements set the price to be charged by the patent holder or originator, which in turn forms the basis of the reimbursement price paid by the State.

TABLE 3.1 Agreements between the State and the IPHA[a]: Duration, Signatories and Reference to the Pricing of New Pharmaceuticals, 2006–2015

Agreement Duration	State Signatories	Pricing Principles
01/09/06–31/08/10	HSE	Extended the basket of Member States used to set prices of new pharmaceutical prices from five to nine. Ex-factory prices were realigned in 2008 and 2010.
01/02/10–01/03/12[a]	HSE	Extension of 2006-2010 State/IPHA Agreement. Presented as Annex 1 to that Agreement. No reference to pricing of new pharmaceuticals in Annex 1.
18/06/12–31/10/12	DoH	Interim arrangements prior to concluding longer term agreement. These arrangements were the subject of emails between DoH and IPHA. No reference to the pricing of new pharmaceuticals in these emails.
1/11/12–31/10/15[b]	DoH and HSE	Mechanism for pricing of new pharmaceuticals unchanged from the 2006–2010 State/IPHA Agreement. Downward only realignment of ex-factory prices on 1 January 2013.

Notes: a It should also be noted that there was an exchange of letters in December 2010 between the State and IPHA which stated that IPHA would generate savings of €140 million in 2011 at the ex-factory level 'either by way of individual product price reductions, or through payment of a rebate or a combination of both'. Most of the savings were achieved by individual product price reductions commencing January 2011.

b The 2012–2015 State/IPHA agreement may be accessed at: http://www.ipha.ie/alist/ipha-hse-agreement.aspx

Source: Based on information supplied by the HSE.

[8] There were, of course, earlier agreements dating back to back to at least 1969. However, an examination of these earlier agreements is beyond the scope of this report. Copies of these earlier agreements were provided to the authors by the HSE.

The price of a new pharmaceutical is determined by four factors:

- The price charged by the patent holder of the new pharmaceutical in a basket of nine other Member States
- A formula for using this price information to set the new pharmaceutical price in Ireland
- The frequency with which the price of a new pharmaceutical is realigned
- A pharmacoeconomic assessment, but only for pharmaceuticals that are likely to have a significant budgetary impact.[9]

This approach to setting the price of new pharmaceuticals, commonly-termed 'external reference pricing', is used extensively across the EU.[10] We consider each of the four factors in turn.[11]

The ***basket of nine EU Member States*** is: Belgium, Denmark, France, Germany, the Netherlands, Spain, the UK, Finland and Austria.[12] These Member States are all part of EU-15 prior to enlargement. They represent some Member States that tend to have high prices for new pharmaceuticals such as Germany, and some that tend to have lower prices such as Spain. The selection of the nine represents a compromise between the buyer, the State, which given its budgetary and other pressures would prefer a basket consisting of lower-priced Member States, and the seller (the IPHA), which given its aim of maximising profits would prefer a basket consisting of higher-priced Member States.

Having agreed on the Member States to be contained in the basket, the next step is to select a ***pricing formula***. In the 2006–2010 State/IPHA Agreement and the subsequent agreements, the price of a new pharmaceutical in Ireland is set as the unweighted average price of the new pharmaceutical charged by the patent holder or originator in the nine Member States in the basket in which the product is available. An alternative approach would have been for the IPHA and the State to have agreed to use the lowest price across the basket of nine Member States, an approach that is followed in most Member States,[13] but not Ireland.[14]

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9 In 2012, 39 new pharmaceutical products were reviewed by the NCPE, of which a pharmacoeconomic assessment was recommended for 27 products. HSE, personal communication, 16 May 2013

10 For details see Kanavos *et al.* (2011) and Carone *et al.* (2012)

11 Gorecki *et al.* (2012), pp. 43–53 discusses the situation in Ireland in greater detail up to January 2012.

12 These nine were first included in the 2006–2010 State/IPHA Agreement and have remained unchanged since that date.

13 Gorecki *et al.* (2012) Table 4.1, p. 40 details the Member States that use the lowest as opposed to the mean or average. These tend to be the new Member States, with only France, Greece, Italy and Spain using the lowest amongst the EU-15.

14 Gorecki *et al.* (2012), p. 43 recommended to the State that the lowest priced Member State be used in setting the price of new pharmaceuticals. The evidence suggested that, based on past experience, substantial price reductions are possible, in the order of 20 to 25 per cent (*ibid,* Table 4.2, p. 45).

The third factor is the ***frequency with which the price of the new pharmaceutical is realigned***. Typically a new pharmaceutical is not marketed by the patent holder simultaneously across all Member States or even the nine Member States in the basket used to set prices in Ireland. Hence the initial price of a new pharmaceutical reflects the average price only in those Member States of the nine where the pharmaceutical is marketed on the date at which the patent holder applies to the HSE for the pharmaceutical to be listed for reimbursement purposes under one of the State pharmaceutical reimbursement schemes. As the new pharmaceutical is marketed across the other nine Member States then the new pharmaceutical price in Ireland is realigned to reflect its wider availability. However, previous evidence has shown that prices of new pharmaceuticals in Ireland are realigned considerably less frequently than in other European countries.[15]

The evidence suggests pharmaceuticals tend to be launched relatively early in Ireland, so most new pharmaceuticals are only available in a small number of Member States in the basket of nine.[16] Furthermore, those Member States that are early adopters of new pharmaceuticals – Denmark, Germany, and the UK – have free or unregulated pricing and as a result relatively high prices.[17, 18] However, as the new pharmaceutical is marketed by the patent holder in the remaining Member States, then the price of the pharmaceutical can be recalculated to reflect its wider availability. Hence the pharmaceutical price is likely to be high, initially at least. However, it is likely to fall through time as the pharmaceutical becomes available in some lower-priced jurisdictions such as Spain.

However, there is only limited realignment under the various agreements set out in Table 3.1. Indeed, the realignments have grown more infrequent under successive agreements. Under the 2006–2010 State/IPHA Agreement there was provision for a Price Monitoring and Review mechanism. This was to occur at two distinct points (2008 and 2010) to take into account currency movements and the availability of new pharmaceuticals in the remaining Member States in the basket. However, there was no adjustment for a year after the date of reimbursement approval from the

15 Gorecki *et al.*, 2012, p. 42

16 Gorecki *et al.*, 2012, p. 42. Indeed, in a small number of instances Ireland appears to be the first Member State in which the new pharmaceutical was launched, as indicated by the fact that at launch there were no prices listed for any of the basket of nine Member States. Based on HSE personal communication, 11 August 2011.

17 Gorecki *et al.*, 2012, p. 42. It appears that Germany introduced a limited form of reference pricing in 2012. For details see Carone *et al.*, 2012, pp. 13-14. In the case of the UK, although the ex-factory price of new pharmaceuticals is unregulated, the returns to pharmaceutical manufacturers are constrained through the operation of the Pharmaceutical Price Regulation Scheme (Office of Fair Trading, 2007).

18 Under free pricing the pharmaceutical manufacturer is able to set a price based on existing market conditions. In contrast, external reference pricing uses the average or lowest ex-factory price across a number of Member States, sometimes including those Member States with free pricing. Hence a pharmaceutical manufacturer has an incentive to charge a high ex-factory price under a free pricing regime, since this price then is often then used to set the price in those Member States using external reference pricing. The evidence suggests that free pricing leads to higher prices than external reference pricing. See, for example, Kanavos and Vandoros (2011), p. 354.

HSE. In other words, once a new pharmaceutical was approved for reimbursement its price was reviewed between one and three years later. [19]

The impact of realignment is set out in Figure 3.1. It sets the price in the first year in which a pharmaceutical is launched at 100 and then measures its price relative to this base for realignments in 2008 and 2010. Hence if the price is €0.60 per unit in 2006, €0.55 per unit in 2008 and €0.50 per unit in 2010, the index would be 100, 92 and 83, respectively. The exercise is conducted for new pharmaceuticals launched in 2006, 2007, 2008, but not 2009 because so few of those launched in 2009 were realigned in 2010. For new pharmaceuticals launched in 2007, we distinguish between those undergoing both the 2008 and 2010 realignments (i.e., 2007(1)), and those undergoing just the 2010 (i.e., 2007(2)) realignment. In each case the average value of all the pharmaceutical products launched in a particular year is presented in the figure.

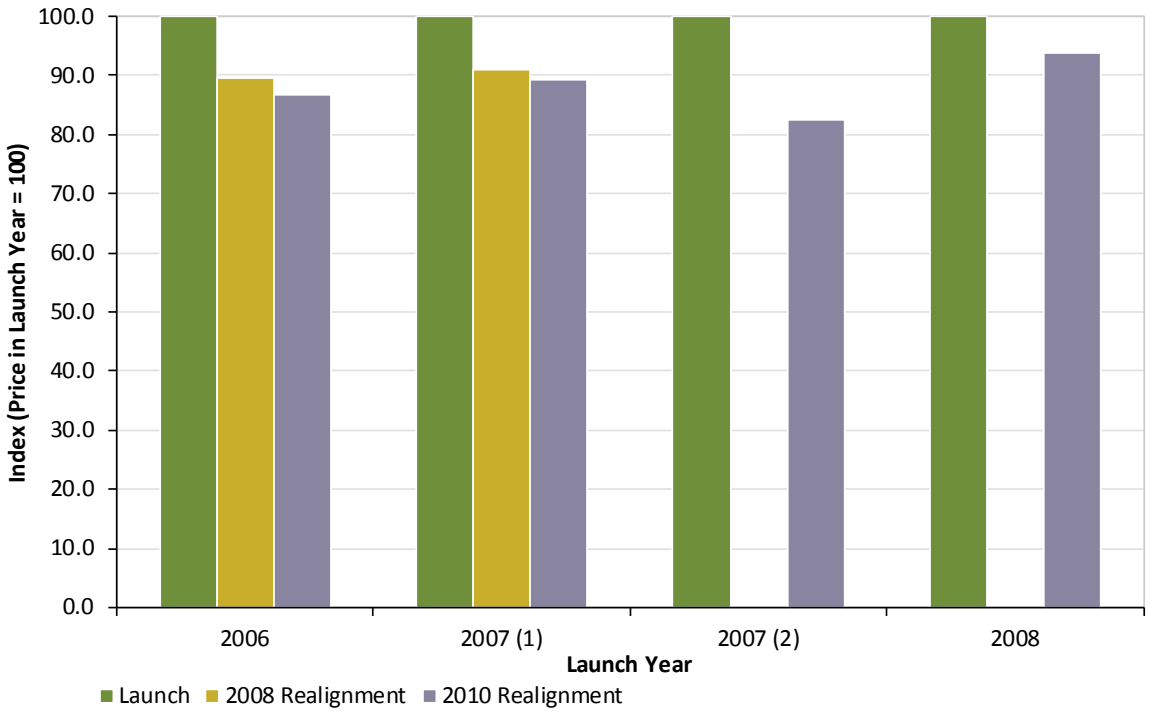
Realignment under the 2006–2010 State/IPHA Agreement led to an initial drop in new pharmaceutical prices of about 10 per cent, with a small decline thereafter. The only exception is for products launched in 2007 which were only realigned once in 2010 where the fall in prices was close to 20 per cent.[20] In part the ex-factory price declines are due to a decline in price in the Member States where price data was available when the pharmaceutical was launched and in part due to the availability of prices from other Member States in the basket of nine. The former influence was especially the case for pharmaceuticals launched in 2007, irrespective of whether or not there were realignments in 2008 and 2010 or just 2010.[21]

[19] For example, if a pharmaceutical was first introduced in late 2007 then it would not be realigned for a year (i.e., in 2008). Hence the first realignment for which it would qualify would be 2010.

[20] These pharmaceutical products only became subject to realignment in 2010 because they were not on the market for a year in September 2008.

[21] For details see Appendix B, Figure B.1, which reproduces Figure 3.1 except that the realignments refer only to the prices in the Member States used to set the ex-factory price when the pharmaceutical was first launched.

FIGURE 3.1 Impact of Realignment on the External Reference Price,[a] Using the Average Price in the Basket of Nine Member States, by Year of Launch, Ireland, 2006–2010



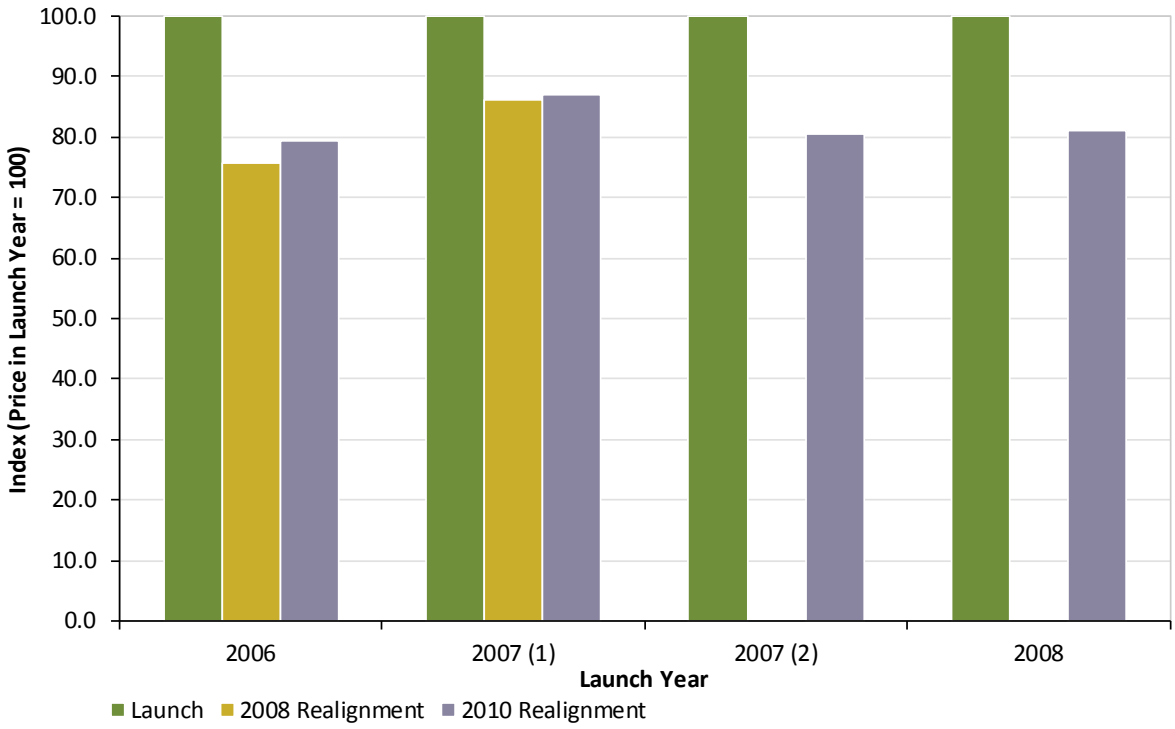
Notes: a The data refers to products launched on the GMS Scheme in 2006, 2007, and 2008. The original data contains information on 464 products launched between September 2006 and July 2011. Products for which data was missing were excluded from the analysis. Only pharmaceuticals for which prices were available at launch from at least some of the Member States in the basket of nine were included. The final analysis is based on 101 pharmaceutical products. There were 15 new pharmaceuticals included in the figure with a 2006 launch with a 2008 and 2010 realignment, 19 with a 2007 launch with a 2008 and 2010 realignment (1), 20 with a 2007 launch with only a 2010 realignment (2), and 47 with a 2008 launch with a 2010 realignment. For each new pharmaceutical product its price is set at 100 at launch and expressed relative to that for the 2008 and/or 2010 realignments. The average was then estimated and presented in the figure.

Source: ESRI calculation from HSE, personal communication, 11 August 2011.

The decline in the price of a new pharmaceutical could have been even greater, however, if instead of using the average price across the nine Member States for which the pharmaceutical was available, the IPHA and the State had agreed to use the lowest price. As noted above the lowest price is used in a number of Member States to set the price of a new pharmaceutical. The results are presented in Figure 3.2 which is the same as Figure 3.1, except for the way the new pharmaceutical price is determined. As can be readily observed the price of a new pharmaceutical declines to a much greater extent when the lowest priced Member State is used than when the average price is used. Instead of a drop of 10 per cent, depending on the launch year, the decline in price reaches approximately 20 per cent.[22]

[22] In Appendix B, Figure B.2 reproduces Figure 3.2, but only for those Member States which were used to set the price of a new pharmaceutical at launch were included. The price declines for those pharmaceuticals launched in 2006 and 2008 in Figure B.2 as compared to Figure 3.2.

FIGURE 3.2 Impact of Realignment on the External Reference Price,[a] Using the Minimum Price in the Basket of Nine Member States, by Year of Launch, Ireland, 2006–2010



Note: a See notes to Figure 3.1. The minimum price is used in all instances, including the year of launch.

Source: ESRI calculation from HSE, personal communication, 11 August 2011.

Since the 2006–2010 State/IPHA Agreement, realignment has become less frequent. No realignment took place under the next two (interim) agreements. However, under the 2012–2015 State/IPHA Agreement there was a once-off price realignment on I November 2012 for single source in-patent pharmaceuticals placed on the market prior to 1 September 2006 and on 1 January 2013 for those single source in-patent pharmaceuticals placed on the market after 1 September 2006.[23] In other words, for all pharmaceuticals placed on the market in Ireland after the latter date, the pharmaceutical price is the average price across those of the nine Member States for which it is available on 1 January 2013. No further realignments are contained in the 2012–2015 State/IPHA Agreement, which expires on 31 October 2015, although the DoH is of the view that the Mid Term Review includes within its remit the realignment of pharmaceutical prices.[24] More frequent realignments were

[23] It should be noted that when the 1 November 2012 and 1 January 2013 realignments took place, only downward realignments were allowed. See Clause 7.3 of the 2012–2015 State/IPHA Agreement. Table 2.2 suggests that this led to a drop in the wholesale price (i.e., ex-factory price plus 8 per cent). It should also be noted that on 1 November 2012 all pre-2006 multiple source off-patent pharmaceuticals also had a price realignment.

[24] There is a provision under Clause 12.1 of the 2012–2015 State/IPHA Agreement for a Mid Term Review to take place in 2014, but no earlier than June. It is confined to the 'governance and operation' of the agreement and hence it is not clear further realignment of ex-factory prices falls within this remit. Nevertheless, the DoH is firmly of the view that price review is covered by this clause, DoH, personal communication, 14 May 2013. In addition, under the Health (Pricing and Supply of Medical Goods) Act 2013, provision exists for the State to review pharmaceutical prices.

found in the 2006–2010 State/IPHA Agreement and in other Member States operating an external reference pricing system.[25,26]

As a result of these arrangements for realigning the price of new pharmaceuticals, high prices for new pharmaceuticals tend to persist longer in Ireland than otherwise would be the case. It is likely that the IPHA would likely prefer the current approach to realignment since the price of a new pharmaceutical remains higher for longer than it otherwise would be not only in Ireland, but also in the 10 other Member States that include Ireland as part as their basket of Member States to set prices of new pharmaceuticals.[27] This aspect of the pricing of a new pharmaceutical was highlighted in a letter from the Chairman and Chief Executive of Abbot Laboratories Ltd, Illinois, US to the Taoiseach dated 23 February 2012 which read in part:[28]

> In common with other pharmaceutical multinational organisations, we find it difficult to reconcile a policy of pursuing inward manufacturing investment with an attempt to drive medicine prices to amongst the lowest in the European Union.
>
> International price-referencing results in pricing in Ireland having a knock-on effect on the pricing of medicines in 11 other European countries and up to an additional 37 countries worldwide.

On the other hand, the State would likely prefer more frequent realignments to get the benefits of the price reductions sooner and thus be in a better position to deal with fiscal austerity. Furthermore, if the lowest price rather than the average price were used to set the new pharmaceutical price the benefits would be even greater.

The fourth element in setting the price of a new pharmaceutical is a ***pharmacoeconomic assessment*** of pharmaceuticals that according to Clause 4.3 of the 2006–2010 State/IPHA Agreement 'may be high cost or have a significant budget impact on the Irish healthcare system'. A similar statement appears in the 2012–2015 State/IPHA Agreement.[29] There are well developed methodologies that are used to conduct a pharmacoeconomic assessment which are designed to ascertain whether or not a particular pharmaceutical delivers value for money. If it is decided that the price yielded by external pricing mechanism as set out above is too high,

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25 See reference in previous footnote.

26 Based on evidence from other countries. Gorecki *et al.* (2012), p. 44 recommended a twice-yearly realignment, but this provision was not included in the 2012–2015 State/IPHA Agreement .

27 This was the case in 2010. For details see Kanavos *et al.* (2011), Appendix 1, pp. 80–81.

28 The letter was obtained by the *Irish Times* under the Freedom of Information Act. The sections quoted are taken from an article by Colm Keena, 'Bitter pill that comes with large drugs sector,' which appeared on 15 December 2012. The article may be found at: http://www.irishtimes.com/debate/bitter-pill-that-comes-with-having-large-drugs-sector-1.3223# [last accessed 2 April 2013]. The fact that the letter refers to 11 countries whereas the source in the previous footnote refers to 10 is likely to reflect the fact that two different dates are being referred to – 2010 and 2012.

29 However, under the 2012–2015 State/IPHA Agreement there is an Appendix on 'Parameters for the Pricing and Reimbursement Process in Ireland' that details some important aspects of the pharmacoeconomic assessment. These include, for example, the maximum time the Assessment should take (90 days, subject to standard clock stopping rules) and that the Quality-Adjusted Life Year (QALY) threshold is €45,000. The 2012–2015 State/IPHA Agreement may be found at: http://www.ipha.ie/alist/ipha-hse-agreement.aspx [last accessed 25 March 2013].

then negotiation does take place between the State on the one hand and the pharmaceutical manufacturer on the other to reach a mutually acceptable price consistent with the pharmacoeconomic assessment.[30]

For pharmacoeconomic assessments, which are conducted by the National Centre for Pharmacoeconomics (NCPE),[31] to work requires that it operate in a transparent and consistent manner. If, for whatever reason the NCPE recommendations are not implemented then the reasons should be carefully laid out for this departure. This makes it easier for decisions to be consistent with the analytical framework applied by the NCPE and less likely to be unduly influenced by patient advocacy groups, manufacturers or other interested parties. However, while the initial NCPE analysis is published, this does not always appear to be the case with subsequent negotiations, as a recent example illustrates.

In the case of a new pharmaceutical, ivacaftor, for which the brand name is Kalydeco, the NCPE assessment concluded that in view of 'the very high drug acquisition cost, the significant budget impact, the absence of long term clinical data and the fact that the company has failed to demonstrate the cost effectiveness of ivacaftor we cannot recommend reimbursement … at the submitted price of €234,804 per patient per annum'.[32] The costs per quality-adjusted life year (QALY) for ivacaftor were well above the €45,000/QALY threshold set in the 2012–2015 State/IPHA Agreement.[33] Box 3.1 explains the meaning and how a cost per QALY is estimated.

30 For a discussion on the background of economic evaluation of reimbursement decisions see Drummond (2012).

31 For further discussion see Gorecki *et al.* (2012), pp. 51-53 and the website of the NCPE, http://www.ncpe.ie/ [last accessed 26 March 2013].

32 NCPE, 2013, p. 4

33 *Ibid*, p. 3. The costs per QALY under different scenarios ranged from €449,035 to €855,437.

BOX 3.1 Measuring effectiveness and cost effectiveness: the QALY

A standard and internationally recognised method to compare different pharmaceuticals/treatments and measure their clinical effectiveness is the quality-adjusted life years measurement (the QALY).

How is this calculated?

Although one treatment might help someone live longer, it might also have serious side effects. Another treatment might not help someone to live as long, but it may improve their quality of life while they are alive.

The QALY method helps measure these factors so that different treatments for the same and different conditions can be compared. A QALY gives an idea of how many extra months or years of life of a reasonable quality a person might gain as a result of treatment.

A number of factors are considered when measuring someone's quality of life, in terms of their health. They include, for example, the level of pain the person is in, their mobility and their general mood. The quality of life rating can range from negative values below 0 (worst possible health) to 1 (the best possible health).

What about cost effectiveness?

Having used the QALY measurement to compare how much someone's life can be extended and improved, cost effectiveness is then considered – that is, how much the pharmaceutical or treatment costs per QALY. This is the cost of using the pharmaceutical or treatment to provide a year of the best quality of life available. Cost effectiveness is expressed as '€ per QALY'.

How a QALY is calculated

Patient x has a serious, life-threatening condition:

- If he continues receiving standard treatment he will live for 1 year and his quality of life will be 0.4 (0 or below = worst possible health, 1 = best possible health)
- If he receives the new pharmaceutical/treatment he will live for 1 year 3 months (1.25 years), with a quality of life of 0.6.

The new treatment is compared with standard care in terms of the QALYs gained:

- Standard treatment: 1 (year's extra life) x 0.4 = 0.4 QALY
- New treatment: 1.25 (1 year, 3 months extra life) x 0.6 = 0.75 QALY

Therefore, the new treatment leads to 0.35 additional QALYs (that is: 0.75 -0.4 QALY = 0.35 QALYs).

- The cost of the new pharmaceutical/treatment is assumed to be €10,000, standard treatment costs €3,000.

The difference in treatment costs (€7,000) is divided by the QALYs gained (0.35) to calculate the cost per QALY. So the new treatment would cost €20,000 per QALY.

Source: Adapted from National Institute for Health Care and Health Excellence. http://www.nice.org.uk/news room/features/measuringeffectivenessandcosteffectivenesstheqaly.jsp [last accessed 16 May 2013]

Ivacaftor was approved for reimbursement by the DoH after discussions between the manufacturer and the HSE led to a mechanism that would reduce its cost, although details were not released.[34]

Confidential negotiated reimbursement contracts, sometimes referred to as patient access schemes,[35] between pharmaceutical manufacturers and payers such as the State are becoming increasingly important in OECD countries for new pharmaceuticals.[36] In part these contracts appear to be motivated by the submission of prices by pharmaceutical manufacturers that are unlikely to satisfy value for money based on a cost per QALY of, for example, €45,000. Lower prices are then obtained by contract negotiations leading to a rebate off the list price. These contracts are typically confidential, with little transparency as to duration, price ex rebate, risk sharing, enforcement mechanisms, contract standards, monitoring procedures, QALY, and so on.

This process raises at least a couple of issues. First, the degree to which the €45,000 QALY is a binding constraint? It appears in the case of the approval of ivacaftor this was not the case. A difficult decision had to be made concerning whether or not the State would pay for this pharmaceutical. The HSE felt that ivacaftor should be approved, but asked the Minister to make a policy decision.[37] In its advice the HSE stated:[38]

> …Although it may be unpalatable to society to acknowledge this, a positive reimbursement decision might ultimately have implications (opportunity costs) for other social services which might be provided (including health services). Some of those other health services could be highly cost effective to support.

It continued:

> The Drugs Group decided that it does not have a formal understanding of societal views to guide it in decision making on such issues. On balance the group felt that society would wish that the medicine be funded given the possibility of significant survival benefits. The group recognises that other international authorities have arrived at the same conclusion.

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34 The announcement was made in a DoH press release, dated 1 February 2013, 'New cystic fibrosis drug ivacaftor (Kalydeco) to be made available for Irish patients'. See http://www.dohc.ie/press/releases/2013/20130201.html [last accessed 26 March 2013]. It appears that the agreement is confidential.

35 See, for example, UK Department of Health, 2012, p. 13.

36 This paragraph is based on Morgan *et al.* (2013). In Ireland one indicator is the increased number of pharmacoeconomic assessments undertaken. The number increased from 12 between 2006 and 2009 (Tilson *et al.*, 2010) to 27 in 2012 (HSE, personal communication 16 May 2013).

37 Letter from Director General Designate, HSE to Minister for Health, 'Re: ivacaftor (Kalydeco) for treatment of Cystic Fibrosis', 31 January 2013. DoH, personal communication, 14 May 2013
See also press reports in the *Irish Times* (http://www.irishtimes.com/news/reilly-approves-costly-cf-drug-1.1254667) and *Irish Health* (http://www.irishhealth.com/article.html?id=21647) [last accessed 26 March 2013].

38 These two quotations are taken from the letter dated 31 January 2013 referred to in the previous footnote.

This suggests that there needs to be greater discussion and guidance provided in making such decisions.

- Is it appropriate for the threshold value of the cost per QALY to be decided as part of a negotiated agreement between the State and the IPHA, rather than the State deciding independently the threshold value?
- Is €45,000 the correct value for the QALY? In the UK, for example, the National Institute for Health and Care Excellence (NICE) uses a range from €23,500 to €35,000, while a recent exhaustive report for NICE suggests a threshold of €21,500.[39]
- If €45,000 is appropriate, what controls should be put in place to determine when it should be overridden?
- What are the implications of disregarding the threshold for other aspects of the health budget which will inevitably suffer – the opportunity cost – as well as for similar negotiations with pharmaceutical manufacturers in the future?[40]

We will return to this issue in Chapter 7.

The second aspect concerns issues surrounding transparency and accountability. No information is available on the mechanism used to determine the cost of ivacaftor, the implied QALY, the long-term monitoring of health outcomes and so on. There is clearly a delicate balance to be struck here. On the one hand the State could decide not to enter into negotiations and therefore base its reimbursement decision on the list price. Indeed, Austria does not use such contracts because they believe secret rebates make it impossible for medical practitioners to be cost-effective when prescribing. On the other hand, entering into such contracts results in lower prices, but at the cost of a loss of transparency and to some degree accountability.

There is likely to be an asymmetry not only in information, in that the pharmaceutical manufacturer will know the rebates granted elsewhere, but also the manufacturer's possess much greater experience in negotiating such contracts across a number of jurisdictions. This should not prevent more information from being published. Examples might include details of the monitoring of health outcomes, details of new pharmaceuticals approved under patient access agreements as compared to the more normal procedures, and a frequency distribution of the cost per QALY of those pharmaceuticals approved under patient access agreements on an annual basis. This should go some way to increase transparency and accountability without compromising the gains from negotiated

[39] These data are taken from Claxton, 2013, pp. v-vi. The exchange rate used is £1=€1.1754, the monthly average for April 2013. It is taken from http://www.centralbank.ie/polstats/stats/exrates/Pages/default.aspx. [last accessed 29 May 2013].

[40] This raises a further question: Is a QALY most appropriately seen as a proxy for the value of life or the opportunity cost of using the resources in their next best alternative?

access to new pharmaceuticals. We are aware, for example, in the case of ivacaftor, that there is Kalydeco Health Outcomes Protocol that has been circulated to relevant health professionals and organisations and sets out clearly a monitoring framework that will be employed.[41]

The above discussion for setting the price of new pharmaceuticals in Ireland for the patent holder suggests that these prices are likely to have declined between 2011 and 2013, the two years for which we have data, due to the realignment of prices on 1 November 2012 and 1 January 2013. In relation to new pharmaceutical prices in other EU Member States, prices in Ireland will initially tend to be based on higher-priced Member States and will fall more slowly due to the timing of the realignment of prices as the pharmaceutical becomes available in more Member States in the basket of nine used to set the price of new pharmaceuticals in Ireland.

3.2.3 Pricing Parallel Imports[42]

The EU Single Market allows firms, whether parallel importers, wholesalers, pharmacies or others, to purchase in-patent and other pharmaceuticals in Member States with lower prices and resell them in Member States where prices are higher without the permission of the patent holder. Parallel imports are identical to the patent-owner's brand of the new pharmaceutical except that they may be packaged differently and may not carry the original manufacturer's warranty. Parallel imports are usually undertaken by specialist firms that must comply with certain regulatory requirements, including those of the Irish Medicines Board, concerning, for example, packaging and labelling.

The price of parallel imports is not part of the State/IPHA or State/APMI Agreements. Instead, the State negotiates an ex-factory price for parallel imports which is at a discount to the price of the new pharmaceutical, the determination of which is set out in Section 3.2.2. However, there is nothing to prevent a higher discount being offered by a parallel importer. As can be readily observed from Table 3.2, the discount has increased over time from 1 per cent to 3 per cent. Hence, if the patent-holder's price of a new pharmaceutical is €10.00 per unit and the discount for a parallel import is 3 per cent, then the price of the parallel import is €9.70 per unit.

41 HSE, personal communication, 20 May 2013

42 This discussion draws heavily on Gorecki *et al.* (2012), pp. 46–49.

TABLE 3.2 Pricing of Parallel Imports, Negotiated Discount Off Ex-Factory Price of New Pharmaceuticals for Patent Holder, 2006–2013

Year	Discount	Year	Discount
2006	=>1%	2010	=>3%
2007	=>1%	2011	=>3%
2008	=>3%	2012	=>3%
2009	=>3%	2013	=>3%

Source: HSE, personal communication, 13 and 27 March 2013; PCO Manufacturing Ltd, personal communication, 15 August 2011

3.2.4 The Price of a New Pharmaceutical

The ex-factory price of a new pharmaceutical, P_{np}, can thus be expressed as:

$$P_{np} = aP_{ph} + bP_{pi} \quad (3.1)$$

a = share of the new pharmaceutical supplied by the patent holder, measured in volume terms

P_{ph} = price of the patent holder as determined through external reference pricing outlined in section 3.2.2

b = share of the new pharmaceutical supplied by parallel importers, measured in volume terms

P_{pi} = price of parallel imports expressed as a negotiated discount off P_{ph} outlined in section 3.2.3

$a + b = 1$

Given that P_{pi} can be written as $(1- c). P_{ph}$ where c is the parallel import discount off the patent-holder's price, equation 3.1 can be rewritten as

$$P_{np} = P_{ph}(a + (1-c)b) \quad (3.2)$$

Thus the price of a new pharmaceutical is a function of the patent-holder's price, P_{ph}, the extent of the discount off this price for parallel imports, c, and the market share of the patent holder, a, and the parallel importers, b.

When the patent holder first markets its product it is likely to account for 100 per cent of the market. As noted above Ireland tends to be an early adopter so that the new pharmaceutical will only have limited availability in other countries. Furthermore sales volume takes time to build to be large enough for a parallel importer to incur the regulatory and other expenses necessary to market a parallel import in Ireland. However, as the patent holder markets the new pharmaceutical more widely across the EU, especially in lower priced Member States, then it may be profitable for parallel imports to develop. This reflects the fact that the parallel importer will pay a lower price than $(1-c)P_{ph}$. This difference or wedge is captured by the parallel importer, less any regulatory, shipping or other costs.

Suppose for example that c were set at .03 and P_{ph} at €10.00 per unit, as in the above example, yielding an ex-factory price for the parallel importer of €9.70. If the price of the new pharmaceutical in (for example) Spain or Greece was €7.50 then in the absence of transaction costs the parallel importer has a mark-up of €2.20 per unit or 29 per cent.[43] This provides an incentive for parallel importers to market such pharmaceuticals in Ireland as illustrated in Figure 3.3.

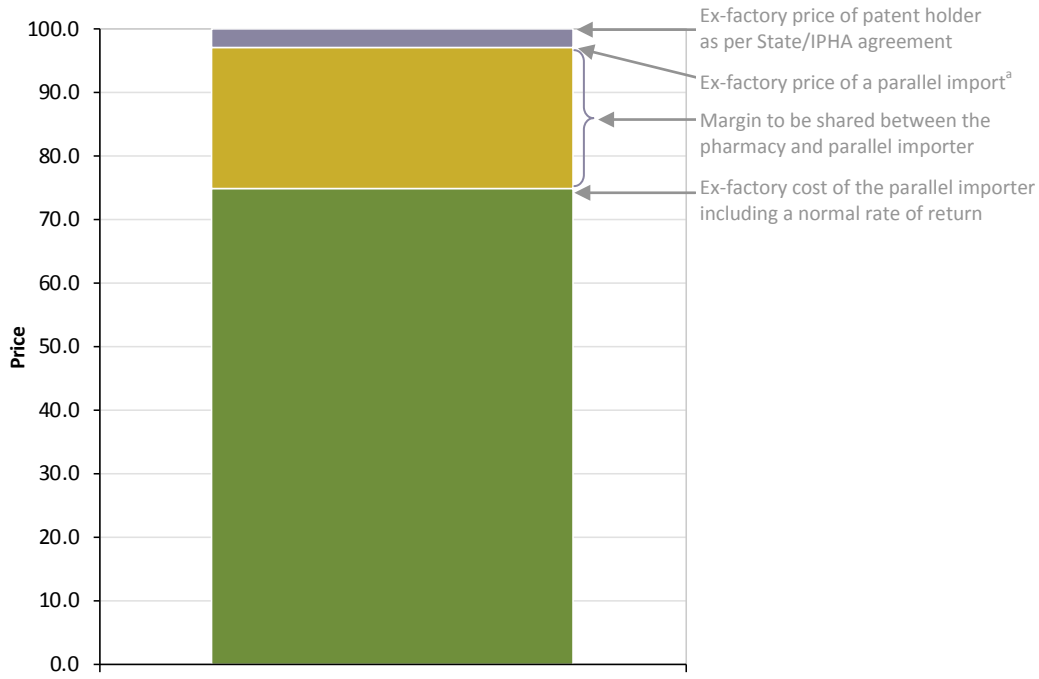
As far as we are aware, parallel imports, provided that they have obtained the relevant regulatory approvals, can be substituted by the pharmacist when presented with a prescription for the brand holder's or originator's product, with no permission required of the patient or the prescriber.[44] The incentive that the pharmacist has to dispense the parallel import is that although he/she is reimbursed on the basis of a price that is set at $(1-c)P_{ph}$, the parallel importer is able to discount off this price with the difference retained by the pharmacy.

The importance of parallel imports will thus depend on the price difference between the ex-factory price of the parallel import, $(1-c)P_{ph}$, compared with the price that the parallel importer actually pays in (say) Greece or Spain. The greater this difference the greater the incentive for parallel imports. However, apart from the 3 per cent discount, the benefit of the remaining price difference accrues to the parallel importer and the pharmacist, not the State.

[43] See note b to Figure 3.3 for details.

[44] One of the authors of this paper has had parallel imports from Greece dispensed with no comment from the pharmacist. The packaging was in Greek, but with labels in English across the package.

FIGURE 3.3 Parallel Imports and the Pricing of a Single-Source In-Patent Pharmaceutical – Illustrative Example



Notes: a This is priced at 3 per cent less than the ex-factory price of the patent holder. The 3 per cent is taken from Table 3.2. This is the ex-factory price used as the basis to reimburse the pharmacist for dispensing the parallel import.

b The ratio of ex-factory price of the patent holder as per the State/IPHA Agreement to the ex-factory price of the lowest price Member State in the basket of nine Member States as recorded in Gorecki *et al.* (2012), Table 4.2, p. 45 is 1.33. It is assumed that parallel importers are able to source the pharmaceutical either from the low-priced Member State in the basket of nine or another low-priced Member State, such as Greece, such that the ex-factory cost of the parallel importer, including a margin to cover costs and a normal rate of return, is 75.

Source: See text and notes.

In any event, as presently constituted parallel imports are unlikely to lead to markedly lower prices. If we take plausible values[45] of a (0.70), b (0.30) and c (0.03) then by substituting in equation 3.2, the price of a new pharmaceutical is $0.99.P_{ph}$. In other words, the price of a new pharmaceutical is essentially the price charged by the patent holder and it this price we will use in discussing pricing in Chapter 4. In our earlier research we suggested mechanisms by which information concerning parallel imports could be used so that some of the price advantage reaped by parallel importers and pharmacists would accrue to the State.[46] However, we understand that the matter is currently before the Courts.

[45] C is based on Table 3.2, while the market shares are based on Gorecki *et al.* (2012), Table 4.3, p. 48 updated. Setting b at 0.30 is at the upper range in the table for the share of parallel imports by volume.

[46] Gorecki *et al.*, 2012, pp. 49–51

3.3 Setting the Price of Multiple Source Off-Patent Pharmaceuticals

3.3.1 Introduction

The price of multiple source off-patent pharmaceuticals is determined through two sets of agreements: the State/IPHA, and the State/ APMI. In each case, however, the price charged by the patent holder, albeit the patent having now expired, and the generic manufacturer are linked to the price of the patent holder prior to the entry of the generic manufacturer. In other words, the external reference price as determined using the basket of nine Member States is the benchmark from which multiple source off-patent pharmaceutical prices are discounted. Hence local market conditions play little if any role in the price determination of these pharmaceuticals.[47]

In this section we first outline the provisions of the State/IPHA Agreements that deal with the pricing of multiple source off-patent pharmaceuticals before moving to the way in which these issues are dealt with under the corresponding agreements with the APMI. Given these two pricing mechanisms the final issue is to determine the price of a multiple source off-patent pharmaceutical. As with the discussion of the pricing of a new pharmaceutical, unless otherwise stated, it is the ex-factory price that is relevant.

3.3.2 The State/IPHA Agreements

Under a succession of agreements between the State and the IPHA, which were detailed in Table 3.1, there is provision for the price to be charged by the patent holder once their patent expires and a generic manufacturer enters the market. Essentially these arrangements, which are detailed in Table 3.3, see the patent-holder's price dropping in response to the entry of a generic manufacturer in a predictable manner. However, as a glance at the table makes clear, the actual mechanics of the price reductions are complex.

[47] In our earlier report we argued that local market conditions should be used to set the ex-factory price of multiple source off-patent pharmaceuticals. Where the volume of such a pharmaceutical is high, tendering was proposed. In the Health Act 2013 there is provision for such a mechanism to be used. It is an issue we will return to in Chapters 5 and 7.

TABLE 3.3 Setting the Patent-Holder's Price for Off-Patent Pharmaceuticals with Generic Competition,[a] Price Agreements between the State and the IPHA, 2006–2015

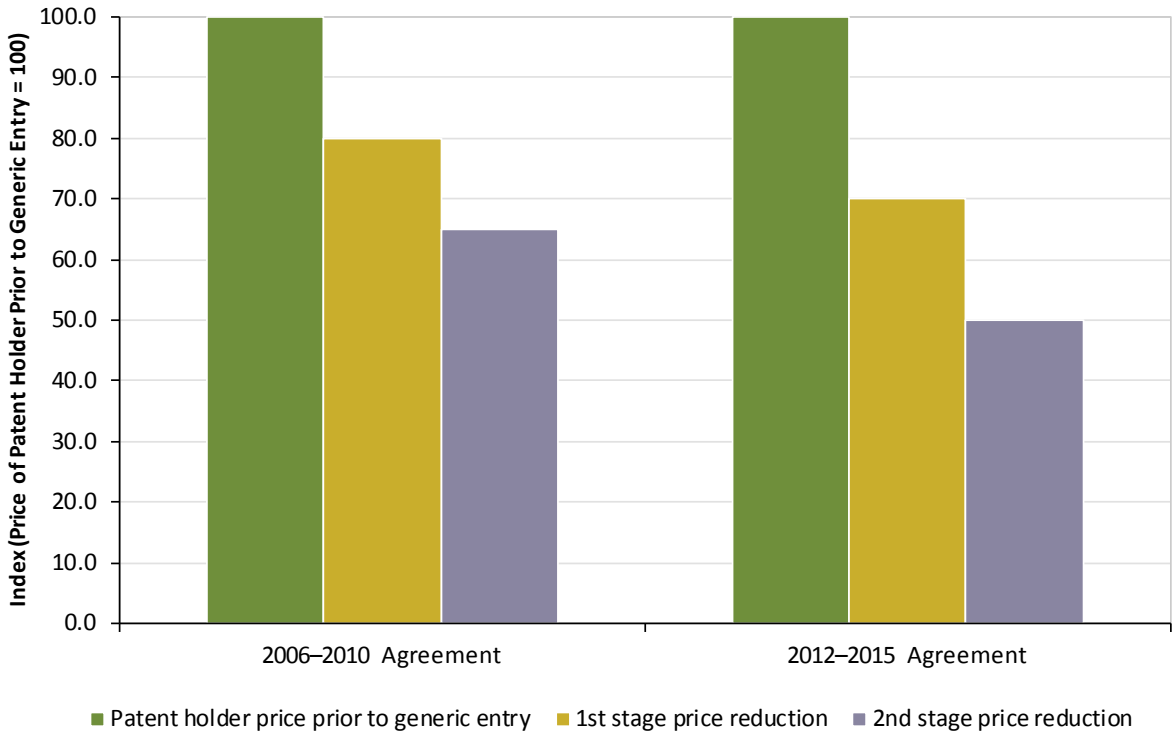
Agreement Duration (State Signatories)	Pricing Principles
01/09/06–31/08/10 (HSE)	*First stage*: six months following the commencement of the State/IPHA Agreement a 20% reduction off the pre-entry price of the patent holder after generic competition first appeared. *Second stage:* 22 months after first stage price reduction, a further 15% reduction off the pre-entry price of the patent holder. *Total price reduction* off the patent-holder's price[b] prior to the entry of the generic, 35%.
01/02/10–01/03/12 (HSE)	For pharmaceuticals where the price reductions were *completed* under the 2006–2010 State/IPHA Agreement by 1/2/10, prices reduced by an additional 40%. *Total price reduction* off the patent-holder's price[b] prior to entry of the generic, 61%.[c] For pharmaceuticals where the *first stage price* reductions under the 2006–2010 State/IPHA Agreement had been made by 1/2/10, prices were reduced by 40 per cent, the subsequent second stage reduction was 9% of the patent-holder's price prior to the entry of the generic. *Total price reduction* off the patent-holder's price[b] prior to the entry of the generic, 61%.[d] For pharmaceuticals that experience generic competition after 1/2/2010, price reductions were in accordance with the pricing principles under the 2006–2010 State/IPHA Agreement.
18/06/12–31/10/12 (DoH)	For pharmaceuticals that are about to or have experienced the *first stage price* reductions under the 2006–2010 State/IPHA Agreement by 18/06/12, an immediate reduction by a further 10%. *Total price reduction* off the patent-holder's price[b] prior to the entry of the generic, 30%.
1/11/12–31/10/15 (DoH and HSE)	For pharmaceuticals where the price reduction is less than 40%, on 1 November 2012 there will be price reduction to 60% of the patent-holder's price[b] prior to the entry of the generic; twelve months later there will be an additional 10% reduction. *Total price reduction* off the patent-holder's price prior[b] to the entry of the generic 50%. For pharmaceuticals that experience generic competition after 1/11/12. *First stage*, immediate price reduction of 30%; *second stage*, twelve months a further 20% price reduction. *Total price reduction* off the patent-holder's price[b] prior to generic competition, 50%.

Notes:
a The table refers to pharmaceuticals which are off-patent (i.e., the patent has expired) and where the identical pharmaceutical form of that pharmaceutical is approved by the Irish Medicines Board or the European Commission and is available for prescription under State schemes, State-funded hospitals and State agencies which normally include the provision of pharmaceuticals. A pharmaceutical meeting these criteria is referred to as experiencing generic competition.
b The patent-holder's price would be set in accordance with the pricing rules for new pharmaceuticals outlined in Section 3.2.
c Under the 2006–2010 State/IPHA Agreement the price reduction was 35%. If the patent holder's price prior to the entry of the generic was 100 then the price was reduced to 65. 40% of 65 is 26, so that the price is now 39 or a reduction of 61% compared to the patent holder's price prior to the entry of the generic.
d Under the 2006–2010 State/IPHA Agreement the first stage price reduction was 20%. If the patent holder's price prior to generic entry was 100, then the price was reduced to 80. 40% of 80 is 32 so the price now falls to 48. The second stage price reduction of 9 per cent off the pre-entry patent holder's price results in a price of 39, so that the price is now 39 or a reduction of 61% compared to the patent holder's price prior to the entry of the generic.

Source: Based on information supplied by the HSE.

At the risk of some oversimplification we present the pricing arrangements for a patent holder under the 2006–2010 State/IPHA Agreement and the 2012–2015 State/IPHA Agreement once generic entry occurs. These are summarised in Figure 3.4. In each case the price reductions occur in two stages. The patent-holder's price declines further under the latter agreement (by 50 per cent as compared to 35 per cent), as well as faster as compared to the earlier agreement. Hence the benefits of generic competition are realised sooner.

FIGURE 3.4 Setting the Patent-Holder's Price for Off-Patent Pharmaceuticals with Generic Competition,[a] Price Agreements between the State and IPHA, 2006–2015



Note: a Under the 2006–2010 State/IPHA Agreement the first stage price reduction was six months after the generic first appeared on the market, the second stage 22 months later. Under the 2012–2015 State/IPHA Agreement the first stage price reduction takes place when the generic first appears on the market, the second stage price reduction 12 months later.

Source: Table 3.3.

3.3.3 The State/APMI Agreements

The State/APMI Agreements parallel those of the State/IPHA Agreements. Typically the agreement with IPHA is concluded first and then agreement with the AMPI is reached. The maximum price of generic manufacturers for multiple source off-patent pharmaceuticals is set in relation to the price of the patent holder, i.e. the price of the patent holder prior to the entry of the generic.

The pricing information concerning the State/APMI Agreements is presented in Table 3.4. The agreements to a large extent mirror those with the State and the IPHA set out in Table 3.3. The picture that emerges from these agreements is that the price of generic manufacturers has declined over time relative to the price of the patent holder or originator prior to generic entry. Under the 2006–2010 State/APMI Agreement the price of generic manufacturers relative to the patent-holder's price prior to entry was discounted by 35 per cent. Under the 2012–2015 State/APMI Agreement the corresponding percentage is between 50 and 60 per cent.

TABLE 3.4 Setting the Generic Price for Off-Patent Pharmaceuticals with Generic Competition,[a] Price Agreements between the State and the APMI, 2006–2015

Agreement Duration (State Signatories)	Pricing Principles
10/09/06–09/09/10 (HSE)	There is no reference in the 2006–2010 State/APMI Agreement to the price charged by generic manufacturers. It appears that the ex-factory price for a generic manufacturer is the same as the patent-holder's price for multiple source off-patent pharmaceuticals as set out in the 2006–2010 State/IPHA Agreement. (Details are provided in Table 3.3 and Figure 3.3.) In other words, the generic manufacturer and the patent holder have the same ex-factory price for multiple source off-patent pharmaceuticals.
01/10/10–01/03/12[b] (HSE)	Effective 1 October 2010: APMI members' *existing* generic prices will be at least 2% lower than the price of the patent holder for the equivalent pharmaceutical; APMI members' *new* generic products, where the patent has expired after 1 February 2010, will be at least 5.6% lower than the price of the patent holder for the equivalent pharmaceutical.
1/11/2012–2015 (DoH and HSE)	On 1 November 2012 the price of generic products were reduced to 50 per cent of the patent-holder's price prior to the entry of the generic.[c] On implementation of the Health (Pricing and Supply of Medical Goods) Act 2013, generic products included ***in*** interchangeable pharmaceutical groups will be reduced by at least 60% of the patent-holder's price prior to the entry of the generic.[c] On implementation of the Health (Pricing and Supply of Medical Goods) Act 2013, generic products ***not*** included in interchangeable pharmaceutical groups will be reduced by at least 52.5% of the patent-holder's price prior to the entry of the generic.[c] The price of all ***new*** generic products will initially be set to at least 50% of the patent-holder's price prior to the entry of the generic. If included in an interchangeable group, these new generic products will reduced by at least 60% of the patent-holder's price prior to the entry of the generic.[c] If not included in an interchangeable group these new generic products will be reduced by at least 52.5% of the patent-holder's price prior to the entry of the generic, when the price of the patent-holder price is reduced to 50% of the price prior to the entry of the generic.[c]

Notes:
a The table refers to pharmaceuticals which are off-patent (i.e., the patent has expired) and where the identical pharmaceutical form of that pharmaceutical is approved by the Irish Medicines Board or the European Commission and is available for prescription under State schemes, State-funded hospitals and State agencies whose normally include the provision of pharmaceuticals. A pharmaceutical meeting this criterion is referred to as experiencing generic competition.
b In December 2010 the State reached an agreement with IPHA that led to reduction in the price of number of pharmaceuticals from January 2011. (See note a to Table 3.1 for details.) The APMI initiated equivalent price reductions, but not until August 2011. (Hence the generic price for a period in 2011 exceeded the patent holder's for the equivalent pharmaceutical.) However, *if* the price reduction by the APMI member necessary to match the patent-holder's price reduction was greater than 30% *and* made the APMI member's product non-viable, a review mechanism was set up that could result in the generic price exceeding the patent-holder's price for an equivalent pharmaceutical. This was only permitted in exceptional circumstances.
c The patent-holder's price would be set in accordance with the pricing rules for new pharmaceuticals outlined in Section 3.2.2.

Source: Based on information supplied by the DoH and the HSE.

The difference between the generic price and the patent-holder's price for a multiple source off-patent pharmaceutical has varied over time. Under the 2006–2010 Agreements between the State and the APMI and the IPHA there was no difference specified in the ex-factory price of patent holder and generic products.[48] In the period 2010 to 2012, due to differences in the timing of the agreements between the State and the IPHA and APMI coming into effect, for periods of time the generic ex-factory price *exceeded* that of the patent-holder's price.[49] Hence over the period 2006 to 2012 there would appear to be little price difference between the generic and patent-holder price for a multiple source off-patent pharmaceuticals.

[48] However, it appears that prior to 2006 that generic products were discounted compared to the equivalent patent-holder pharmaceutical, but that as the patent-holder ex-factory price fell under the 2006–2010 State/IPHA Agreement, the generic did not match the price decline. HSE, personal communication, 21 May 2013

[49] In other words, IPHA reduced ex-factory prices before APMI members. For details see note b of Table 3.4.

Under the 2012–2015 Agreements between the State and the IPHA and APMI the generic/patent-holder price difference depends on whether or not the pharmaceutical is subject to generic competition before or after the implementation of the Health (Pricing and Supply of Medical Goods) Act 2013 and whether or not the pharmaceutical is part of a group of interchangeable pharmaceutical products.[50] The results are presented in Table 3.5.

TABLE 3.5 Patent Holder and Generic Ex-Factory Prices, on Implementation of the Health (Pricing and Supply of Medical Goods) Act 2013, Agreements between the State and the IPHA/ APMI, 2012–2015[a]

	Off-Patent Multiple Source Pharmaceuticals	
	Not Included in an Interchangeable Pharmaceutical Group	Included in an Interchangeable Pharmaceutical Group
Existing	Generic products will be priced at least 5% less than the patent-holder's product.	Generic products will be priced at least 20% less than the patent-holder's product.
New	Initially generic products will be priced 29% less than the patent holder's price[b]; but after a year generic products will be priced at least 5% less than the patent-holder's product.	Generic products will be priced at least 20% less than the patent-holder's product.

Notes: a This table does not capture the position where a reference price has been set.
b This reflects the fact that initially the generic product price is set at 50% while the patent holder's price is set at 70% of the patent holder's price prior to entry. Hence the generic product is 20/70 =28.57% lower in price.
Source: Based on Tables 3.3 and 3.4.

The critical factor in determining the generic/patent-holder price difference is whether or not the pharmaceutical is part of an interchangeable pharmaceutical group, since here the generic price will be 20 per cent less than the patent-holder's ex-factory price. In all other cases the difference in ex-factory price will be small (5 per cent) or substantial, but temporary (29 per cent for a year, 5 per cent subsequently). Thus as the number of interchangeable pharmaceutical groups increases from the summer of 2013, other things equal, overall generic prices will fall relative to those of the patent holder. In the absence of such a designation, differences in generic and patent-holder ex-factory prices for multiple source off-patent pharmaceuticals will, apart from the first year in which the generic enters the market, be five per cent.

[50] The Explanatory Memorandum to the Health Bill 2012 defines an interchangeable pharmaceutical group as 'products that have the same qualitative and quantitative composition in each of their active substances, are in the same pharmaceutical form, and have the same route of administration'.

3.3.4 The Price of a Multiple Source Off-Patent Pharmaceutical

The ex-factory price of a multiple source off-patent pharmaceutical, P_{ms}, can be written as

$$P_{ms} = qP_{phs} + rP_{gs} \quad (3.3)$$

- q = the share of the multiple source off-patent pharmaceutical accounted for by the patent holder, measured in volume terms
- P_{phs} = the price of the patent holder of the multiple source off-patent pharmaceutical as determined under the State/IPHA Agreements outlined in section 3.3.2
- r = the share of the multiple source off-patent pharmaceutical accounted for by the generic manufacturer, measured in volume terms
- P_{gs} = the price of the generic manufacturer of the multiple source off-patent pharmaceutical as determined under the State/APMI Agreements outlined in section 3.3.3

$q + r = 1$.

Both P_{phs} and P_{gs} can be expressed as a function of P_{ph} where P_{ph} is the patent holder's price prior to the entry of the generic as determined under the State/IPHA Agreement (Section 3.3.2) as follows:

$P_{phs} = zP_{ph}$

$P_{gs} = (z-w)P_{ph}$

where z and (z-w) indicate the reduction in the patent holders and generic manufacturers price upon generic entry. For example, for multiple source off-patent pharmaceuticals under the 2012-2015 Agreements between the State and the APMI and IPHA for pharmaceuticals included in an interchangeable product grouping z=0.5 and w=0.1.

We can now substitute into equation 3.3 to yield

$P_{ms} = q(zP_{ph}) + r(z-w)P_{ph}$

$P_{ms} = qzP_{ph} + rzP_{ph} - rwP_{ph}$

$P_{ms} = (q+r)zP_{ph} - rwP_{ph}$, since $q+r = 1$ this simplifies to

$$P_{ms} = (z-rw)P_{ph} \quad (3.4)$$

Equation 3.4 expresses the price of a multiple source off-patent pharmaceutical in terms of the patent-holder's price prior to the entry of the generic (P_{ph}), the reduction in that price due to the 2012–2015 State/IPHA Agreement (z), the success of generic manufacturers in capturing market share (r) and the additional price discount in the 2012–2015 State/APMI Agreement offered by generic manufacturers

(w). When z=0.5 and w=0.1 the equation applies to an interchangeable pharmaceutical group; when w=0.025 it refers to generic pharmaceuticals not included in an interchangeable pharmaceutical group. Our discussion concentrates on the former situation.[51]

It should be noted that both the patent holder *and* the generic manufacturer have an interest in a high pre-entry price being charged by the patent holder. The reasons why the patent holder prefers a high price are set out in Section 3.2.2. For the generic manufacturer a higher pre-entry price means that for a given discount off that price, the return to the generic manufacturer will, other things being equal, be greater. Of course, to the extent that the generic manufacturer has to compete for shelf space in pharmacies, the higher margin due to the high pre-entry price might accrue to a large extent to the pharmacy sector. The generic manufacturer might only earn a normal rate of return.

Prior to the entry of the generic manufacturer the patent holder will account for 100 per cent of the market.[52] For a generic manufacturer to enter the market it has to meet certain regulatory and other requirements, but these are far less onerous than those borne by the patent holder when first introducing the pharmaceutical. As a result, for high volume off-patent pharmaceuticals, the generic manufacturer will likely have costs that are substantially below those of the patent holder. Furthermore the generic manufacturer's costs are also likely to be below the ex-factory price of multiple-source pharmaceuticals as set by the agreements between the State and the APMI (i.e., $(z-w)P_{ph}$). This is consistent with reports of widespread and substantial discounting on the part of generic manufacturers in Ireland,[53] reports of the large difference in the price of generics between the UK and Ireland,[54] and discounting in other Member States.[55]

For the pharmacist, as with parallel imports, discounting by the generic manufacturers results in a wedge developing between the price at which the pharmacist is reimbursed and the price paid to the generic manufacturer (Figure 3.5). However, until the Health (Pricing and Supply of Medical Goods) Act 2013 is commenced pharmacists are required to dispense the prescription as written, which

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51 See Tables 3.3 and 3.4 for details. The values of z and w refer to pharmaceuticals where the generic is new.

52 Save for parallel imports. However, when the generic manufacturer enters the market parallel imports tend to decline.

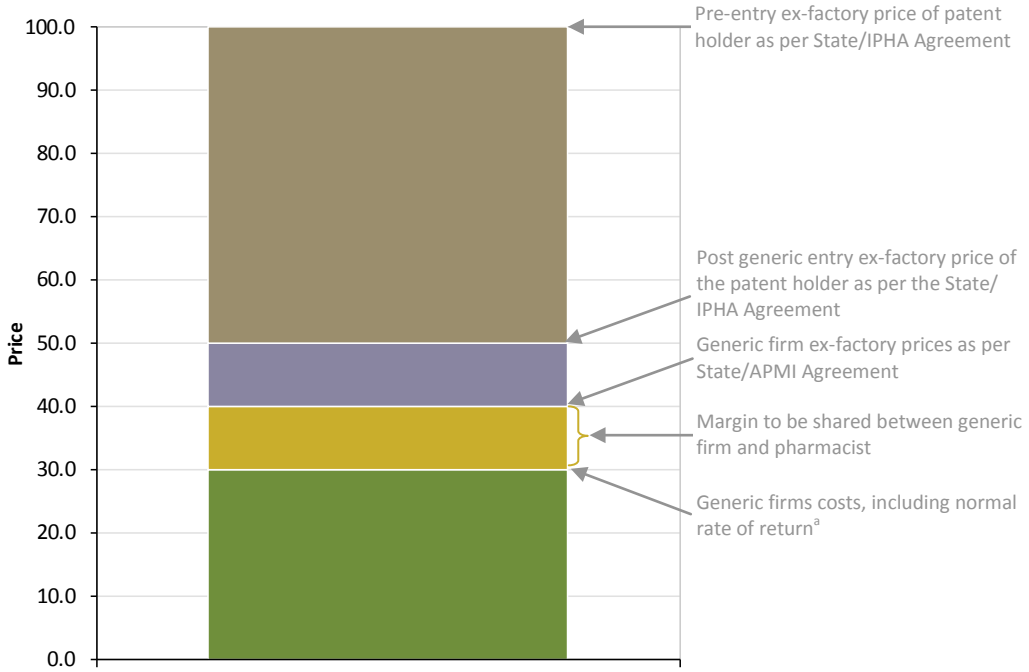
53 For details see press reports in the *Sunday Business Post*, 'Hard to Swallow', by Susan Mitchell, 17 March 2013. See http://www.businesspost.ie/#!search/susan%2520mitchell [last accessed 28 March 2013]. See also Paul Cullen, "Discounts on Generics' Subsidise Pharmacies". *Irish Times*, 18 March 2013. http://www.irishtimes.com/news/ discounts-on-generics-subsidise-pharmacies-1.1329325 [last accessed 29 April 2013].

54 For details see *Sunday Business Post*, 'Patent Rip-Off', by Susan Mitchell, 3 March 2013. See http://www.businesspost.ie/#!search/mitchell%20patent%20rip%20off [last accessed 28 March 2013].

55 Seeley (2008) reports that in France discounts varied between 20 and 80 per cent of the wholesale price, while for the UK discounts off the Drug Tariff exceeded 60 per cent. See also Carone *et al.*, 2012, p. 25, p. 29.

is likely to be typically for the patent-holder's pharmaceutical. However, it appears growing acceptance of generic manufacturers by the public[56] has meant that pharmacists have dispensed increased volumes of pharmaceuticals of generic manufacturers, reaching in 2012, 70 per cent of one pharmaceutical.[57]

FIGURE 3.5 Generic Manufacturers and the Pricing of a Multiple Source Off-Patent Pharmaceutical in an Interchangeable Pharmaceutical Group – Illustrative Example



Note: a This is assumed to be the cost of the generic based on widespread reports of discounting by generic firms.
Source: See text.

If we take interchangeable pharmaceutical product groups for example, then under the most recent agreements between the State and the APMI and IPHA, z=0.5, w=0.1. Let us assume that the generic firms' market share based on 2012 data is approximately 0.50[58] and that P_{ph} is €10 per unit. Then the impact the State/IPHA Agreement is to reduce the price to €5.0. In other words, we estimate equation 3.4 with r=0. The additional impact of the State/APMI Agreement is to reduce the price to €4.50. In other words, equation 3.4 is estimated with r=50. Hence, 91 per cent of the price reduction for multiple source off-patent pharmaceuticals is driven by the State/IPHA Agreement.

56 Discussed further in Chapter 5.
57 See Chapter 5, Table 5.1 for details.
58 See Chapter 5, Table 5.1 for details.

It could, of course, be argued that this is an incomplete and partial picture since the generic manufacturers under the Health (Pricing and Supply of Medical Goods) Act 2013 are likely to gain a much larger market share and hence this conclusion is premature. If the market of generics, r, is increased then the results are as follows:

r= 0.70 P_{ms} = € 4.3

r= 0.90 P_{ms} = € 4.1

r= 1.0 P_{ms} = € 4.0.

It still remains the case that even if the generic manufacturers account for all of the market for a multiple source off-patent pharmaceutical most of the reduction in the price is due to the State/IPHA Agreement.

3.4 Conclusion

The price of new pharmaceuticals in Ireland, which are typically single source in-patent pharmaceuticals, are likely to have declined between 2011 and 2013, the two years for which we have data, due to the realignment of prices on 1 November 2012 for new pharmaceuticals placed on the market before 1 September 2006 and on 1 January 2013 for new pharmaceuticals placed on the market after 1 September 2006 as a result of the 2012–2015 State/IPHA Agreement. This is consistent with the results reported in Table 2.2 for the GMS Scheme. In relation to new pharmaceutical prices in other Member States, prices in Ireland will initially tend to be based on higher-priced Member States and will fall more slowly due to the timing of the realignment of prices as the pharmaceutical becomes available in more Member States in the basket of nine used to set the price of new pharmaceuticals in Ireland. Furthermore, of course, there is no further readjustment of new pharmaceutical prices in Ireland until 2015, although the DoH is of the view that the Mid Term Review includes within its remit the realignment of pharmaceutical prices.[59] Notwithstanding this observation, the pressure for further price reductions is likely to continue in other Member States.

In terms of the price of multiple source off-patent pharmaceuticals this price will likely have declined in Ireland between 2011 and 2013 because of the price declines of both the patent holder and generic manufacturers on 1 November 2012. In terms of price comparisons between Ireland and other Member States the situation is less clear. As demonstrated, the price of multiple source off-patent pharmaceuticals in Ireland is linked to the patent-holder's price prior to entry. Since this is likely to be a high price by EU standards, it seems reasonable to assume that, other things being equal, the price of multiple source pharmaceuticals will also be high, but with a

[59] As already noted there is provision under the 2012–2015 State/IPHA Agreement for a Mid Term Review. However, it does not explicitly mention price in contrast to the 2006–2012 State/IPHA Agreement which referred in clause 5.3 to 'Price Monitoring and Review'.

decline between 2011 and 2013 because of the price realignment in November 2012.

Under the current administrative pricing system based on agreements between the State and the pharmaceutical representative bodies, what drives both the price of new pharmaceuticals and multiple source off-patent pharmaceutical prices is the price of the patent holder as determined by the use of a basket of nine Member States. However, under the Health (Pricing and Supply of Medical Goods) Act 2013 these agreements between the State and the pharmaceutical representative bodies will be only one factor to be taken into account when setting the price of new as well as multiple source off-patent pharmaceuticals.[60] Hence the opportunity arises, for example, under reference pricing, to decouple the price of multiple source off-patent pharmaceuticals from the price of the patent holder prior to the entry of the generic manufacturer. The implications of the Health (Pricing and Supply of Medical Goods) Act 2013 will be explored further in Chapters 5 and 7.

[60] See sections 21 and 23, respectively, of the Health (Pricing and Supply of Medical Goods) Act 2013.

CHAPTER 4

Pharmaceutical Price Trends and Comparisons

4.1 INTRODUCTION

The purpose of this chapter is to examine pharmaceutical prices in Ireland. We concentrate on two aspects. First, we examine changes in prices in Ireland through time. Have pharmaceutical prices fallen or risen between 1 September 2011 and 1 March 2013? The discussion in Chapter 3 suggests the price adjustments in late 2012 and early 2013, under the agreements between the State and the IPHA and the APMI, will have led to pharmaceutical price declines. Second, we compare pharmaceutical prices in Ireland with prices in comparable Member States. Are pharmaceutical prices high or low in Ireland and how has this evolved through time? The discussion in Chapter 3 suggests that pharmaceutical prices in Ireland are likely to be towards the higher end in the EU, but that is likely to be moderated somewhat by the price adjustments noted above. However, with no further explicit realignment of the price of new pharmaceuticals until at least 2015[1] prices in Ireland are unlikely to decrease relative to other Member States.

Although the emphasis is on recent price trends and comparisons it is important to put current prices of pharmaceuticals in Ireland into a longer term perspective. Chapter 3 demonstrated that the price-setting mechanism at the ex-factory level for pharmaceuticals in Ireland has remained largely unchanged since 2006, particularly for new pharmaceuticals. Hence, other things being equal, Ireland's ex-factory prices relative to other Member States should have remained fairly stable. Of course, other things are unlikely to have remained constant, but nevertheless a longer term perspective serves to put the current situation into context.

Although the price-setting mechanism has remained largely unchanged since 2006, there has been a marked increase in the importance of pharmacoeconomic assessments of single source in-patent pharmaceuticals prior to approval for reimbursement. There has also been an increase in patient access agreements under which the price paid for a single source in-patent pharmaceutical is not published. The price comparisons presented in this chapter are likely to omit such pharmaceuticals from the analysis and as such this caveat should be borne in mind when interpreting the results.

[1] Subject to the caveat noted in Chapter 4 that under the 2012-2015 State/IPHA Agreement there is provision for a Mid Term Review.

The chapter is divided into six sections. We start in Section 4.2 with a discussion of the methodological and measurement issues in making cross-country price comparisons. In Section 4.3 we examine ex-factory price trends in Ireland before turning in Sections 4.4 and 4.5 to pharmaceutical price comparisons between Ireland and other countries. In Section 4.4 we draw on a number of recent papers and recast the results setting Ireland as the benchmark, while at the same time presenting some new findings comparing Ireland with New Zealand. The price comparisons are made not only at the ex-factory level but also the wholesale and retail level. In Section 4.5 we use the EURopean Integrated Price Information Database (Euripid) to make comparisons between Ireland and other Member States for 2011 and 2013. Price comparisons are presented at both the ex-factory and wholesale level. Section 4.6 concludes.

4.2 Cross-Country Price Comparisons: Methodological and Measurement Issues

Cross-country comparisons of pharmaceutical prices are complicated and challenging as each country's pharmaceutical market is different. Results can depend heavily on the choice of methodological approach. There are a number of key factors that need to be decided on in making cross-country comparisons of pharmaceutical prices, including:

- What countries?
- What time period?
- What products (i.e., single source in-patent, multiple source off-patent) and how many?
- What price (ex-factory, wholesale, retail, etc.)? What unit (i.e., per pack, per tablet, per dose, per defined daily dose)?
- Should prices be weighted by volume? Should prices be presented in the form of a price index? Should absolute or relative price indices be presented?

While comparisons at the product level (i.e., comparing products that are identical in terms of manufacturer, pack size, strength and dosage form) may be most accurate, decisions have to be made about which products to analyse (e.g., the leading sellers), and as a result the sample may only account for only a small proportion of overall pharmaceutical expenditure. Applying less strict matching requirements enables more representative comparisons, but with a loss of standardisation. Consequently, there is no one correct method of undertaking cross-country price comparisons. The choice of method inevitably involves judgments on sample selection, matching criteria, price indicator and weights (Danzon and Furukawa, 2003).

Chapter 2 deals with the issue of the relevant countries, time periods and prices that we use in this report in analysing pharmaceutical prices in Ireland and other Member States. In terms of the selection of products and the presentation of price data, there are a number of approaches that are used in this report depending on the availability of data and resources.

The first and simplest approach is to compute a price for each country and each product (manufacturer, pack size, strength, dosage form). The advantage of this approach is that it is accurate (i.e., it involves an 'apples-to-apples' comparison). However, the representativeness of the sample may be poor, particularly if products (usually generics) that are not marketed in multiple countries have to be excluded. This is the approach we adopt in our analysis of ex-factory prices in Ireland and New Zealand in Section 4.4.

The second approach attempts to increase the representativeness of the sample of products by matching only on strength and dosage form. While this approach increases the relevance of the analysis by increasing the sample size, this approach assumes that all products of the strength and dosage form are substitutes for each other. This is the approach we adopt for the Euripid analysis in Section 4.5.

The final approach is to compute a single price for each country (i.e., matching only on the pharmaceutical name). This approach has the advantage that prices are easy to compare across countries, but the approach is data-intensive[2], and requires country-specific volume weights. Concerns over substitutability of products are also relevant with this approach. This is the approach used in several papers (Danzon and Chao, 2000; Danzon and Furukawa, 2003; Kanavos and Vandoros, 2011; Kanavos *et al.*, 2013). We did not do this for analysis of New Zealand prices in Section 4.4 and the Euripid analysis in Section 4.5 as we had concerns over using the Irish weights (which were the only ones available) to compute prices for other countries.[3] However, we used this method for the analysis (of Irish prices) in Section 4.3.

[2] Some studies using this approach calculate a price per defined daily dose (DDD). The DDD is the assumed average maintenance dose per day for a pharmaceutical used for its main indication in adults (http://www.whocc.no/ddd/definition_and_general_considera) [last accessed 6 June 2013]. The calculation of DDDs requires specialist knowledge which was not available to us in undertaking the analyses in Sections 4.3, 4.4 and 4.5.

[3] Danzon and Chao (2000) and Kanavos *et al.* (2013) illustrate the considerable difference in results that are generated when different weights (country-specific vs. constant) are used to calculate price indices.

4.3 Trend in Ex-Factory Pharmaceutical Prices in Ireland

4.3.1 Introduction

The measurement of the trend in pharmaceutical prices in Ireland is based on data on the ex-factory price for leading pharmaceuticals under the General Medical Services (GMS) Scheme.[4] This is by far the most important of the various State funded schemes.[5] Furthermore our earlier research recorded similar results for the GMS and the Drug Payment (DP) Scheme, which depending on the year selected is the second or third most important of the State pharmaceutical reimbursement schemes.[6] The price comparisons will all be made at the Anatomical Therapeutic Chemical (ATC) Classification level 5 (e.g., atorvastatin, fentanyl, etc.).

The sample of pharmaceuticals that were used to examine ex-factory pharmaceutical prices in Ireland is the leading single source in-patent and multiple source off-patent pharmaceuticals in the GMS Scheme in 2010 ranked by value. Some of the single source in-patent pharmaceuticals lost their patent protection and experienced competition from generic manufacturers. Hence, price comparisons between 2011 and 2013 are presented for pharmaceuticals divided into three categories: single source in-patent in both years; multiple source off-patent in both years; and those pharmaceuticals that switched from the former to the latter between the two years. Making these price comparisons over a relatively short period does not, of course, capture the longer term substantial price declines for pharmaceuticals introduced some years ago under the various State agreements with pharmaceutical manufacturer representative bodies.

4.3.2 Price Trends for Pharmaceuticals: Methodology

The price for each single source pharmaceutical, whether single source in-patent or multiple source off-patent, is estimated as follows:

$$\sum_{i=1}^{N} a_i P_i \qquad (4.1)$$

where
N= the number of products,[7]

$a_i = (d_i x\ PKS_i x\ NPKS_i)/(\sum_{i=1}^{N} d_i PKS_i NPKS_i)$

where d_i = dose of i^{th} product,
PKS_i = package size of i^{th} product
$NPKS_i$ = number of packs sold of i^{th} product.

4 The HSE record data by pharmaceutical scheme, reflecting the administrative nature of the data sets. The market shares of the leading pharmaceuticals selected is set out in Appendix B, Table B.1.

5 Gorecki *et al.*(2012), Figure 2.1, p. 18. Table 2.1 in this report sets out the eligibility criteria for access to the scheme.

6 *Ibid,* Table 2.1, p. 18

7 Each product has a distinct name, dose (e.g., 2.5 mg tabs) and pack size (e.g., 28 or 30). The same pharmaceutical at the ATC 5 level made by different manufacturers is a distinct product, even if the products use the generic name. As a result there is no double counting.

$P_i = (PPK_i/PKS_i)/d_i$

where

PPK_i = ex-factory price per pack of the i^{th} product, while PKS_i and d_i are defined above.

Essentially equation 4.1 is a weighted average of the price of different products that fall within a given ATC 5, where the weights are the quantity sold of that particular unit, measured as the number of packs sold multiplied by the pack size (e.g., typically 28 or 30), multiplied by the dose (e.g.10 mg). The quantity weights are 2011 for 2011 prices and 2012 for 2013 prices, since we do not have quantity data for 2013.

When equation 4.1 is applied to single source in-patent pharmaceuticals, it will include the prices and quantities of both the patent holder and parallel importer manufacturers. However, as noted in Chapter 3, despite the presence of parallel imports, due to the small price difference between the parallel imported and patent-holder pharmaceutical products, the ex-factory price of a single source in-patent pharmaceutical closely approximates the patent-holder's ex-factory price. When equation 4.1 is applied to multiple source off-patent pharmaceuticals, it will include the prices and quantities of both the patent-holder and generic manufacturers.

An alternative approach to measuring price trends is to select the most popular dosage form and strength of each ATC. For single source in-patent pharmaceuticals the patent holder's product is selected; for multiple source off-patent pharmaceuticals the patent holder and generic products are selected. If there is more than one generic manufacturer then the manufacturer with the largest sales would be selected as representative. While this approach clearly does not capture movements for a given ATC 5 in the relative shares of particular dosage forms and strengths or the change in market share between the patent holder and the generic manufacturers or among generic manufacturers, it nevertheless does provide a somewhat richer picture of patent holder prices as compared to generic manufacturer's price.

In order to check the sensitivity of the results presented in this section we computed price changes for patent-holder and the most popular generic along the lines suggested in the previous paragraph for virtually all of the pharmaceuticals in Tables 4.1 to 4.3. These results, which are presented in Appendix B, Table B.2[8], are consistent with the results presented here. This serves to strengthen the results presented on the basis of equation 4.1.

[8] The sample of pharmaceuticals in Table B.2 does not match exactly those in Tables 4.1 to 4.3 because the analysis was conducted as part of a broader exercise comparing prices in Ireland with those in New Zealand as presented in Section 4.4.5.

4.3.3 Ex-Factory Price Trends for Single Source In-Patent Pharmaceuticals

Prices for single source in-patent pharmaceuticals are expected to decline between 2011 and 2013 due to the downward only realignment in prices for such pharmaceuticals: on 1 November 2012 for those single source in-patent pharmaceuticals reimbursed *prior* to September 2006; and, 1 January 2013 for those single source in-patent pharmaceuticals reimbursed *after* 1 September 2006. As we showed in Chapter 3, when the price of single source in-patent pharmaceuticals were realigned in 2008 and 2010, prices fell, even without any restriction that the adjustment had to be downward only. No realignments took place between 2010 and 2012/13. Given that under the 2006–2010 State/IPHA Agreement no realignment took place for at least a year after a new pharmaceutical was introduced, this means that no realignment has taken place for new pharmaceuticals for three to four years (i.e., 2009–2012/2013). Some variation would be expected in the extent of price reductions of single source in-patent pharmaceuticals if they were initially reimbursed on different dates.[9]

TABLE 4.1 Ex-Factory Price of Leading[a] Single Source In-Patent Pharmaceuticals[b] – GMS Scheme, 2011[c] and 2013[d]

ATC Description	ATC	Price per dose		Price change
		2011 (€)	2013 (€)	%
Escitalopram	N06AB10	0.0759	0.0678	-10.7
Fentanyl[e]	N02AB03	0.0853	0.0540	-36.7
Formoterol and other drugs for obstructive airway diseases	R03AK07	0.1623	0.1603	-1.2
Pregabalin	N03AX16	0.0177	0.0108	-39.0
Salmeterol and other drugs for obstructive airway diseases	R03AK06	0.1608	0.1508	-6.2
Tiotropium bromide	R03BB04	0.2860	0.2657	-7.1

Notes:
a See Appendix B Table B.1 for GMS market share (volume and value) of each ATC in 2010, 2011 and 2012.
b Estimated using equation 4.1
c Price data for 1 September 2011, quantity data for 2011
d Price data for 1 March 2013, quantity data for 2012
e While fentanyl is off-patent, there are a variety of presentations e.g., patches, tablets, lozenges, nasal sprays, sublingual tablets, etc., none of which are directly substitutable. Fentanyl is therefore recorded as a single source pharmaceutical on the HSE database (see also Table 2.3). HSE, personal communication, 15 May 2013

Source: Based on information supplied by the HSE, personal communication, 13 March 2013.

The data in Table 4.1 is consistent with these expectations. Ex-factory prices decline in every case.[10] However, the magnitude varies considerably, from a decline of only 1.2 per cent for formoterol and other drugs for obstructive airway diseases to between 35 and 40 per cent for fentanyl and pregabalin. The table illustrates the gains from more frequent alignments of pharmaceutical prices. It represents the benefits or price reductions that could have been realised if more frequent

9 All of the pharmaceuticals in Table 4.1 were reimbursed prior to 2006 and hence the price adjustment took place on 1 November 2012.

10 These conclusions do not change if 2011 weights are used to estimate prices for both 2011 and 2013, rather than just 2011. The price changes in the final column of Table 4.1 are instead, reading from top to bottom: -10.9%, -33.2%,-1.4%, -39.0%, -6.3%, and -8.5%, respectively.

realignments had been agreed under successive agreements between the State and the IPHA.

4.3.4 Ex-Factory Price Trends for Multiple Source Off-Patent Pharmaceuticals

Next attention turns to those pharmaceuticals that were multiple source off-patent in 2011 and 2013. Equation 4.1 is used to estimate the ex-factory price of these pharmaceuticals, which will include both the patent holder and generic products.[11] As discussed in Chapter 3 the ex-factory prices of both patent holder and generic pharmaceutical products for multiple source off-patent pharmaceuticals were reduced between 2011 and 2012, including on 1 November 2012. Furthermore, as we shall see in Chapter 5, generic manufacturers increased their market share for leading multiple source off-patent pharmaceuticals between 2011 and 2013, resulting in further ex-factory price declines at the ATC 5 level. Hence the expectation is that the prices of multiple source off-patent pharmaceuticals will have declined between 2011 and 2013.

TABLE 4.2 Ex-Factory Price of Leading[a] Multiple Source Off-Patent Pharmaceuticals[b] – GMS Scheme, 2011[c] and 2013[d]

ATC Description	ATC	Price per dose		Price change
		2011 (€)	2013 (€)	%
Amlodipine	C08CA01	0.0336	0.0335	- 0.3
Bisoprolol	C07AB07	0.0227	0.0231	+1.8
Diclofenac	M01AB05	0.0022	0.0015	- 31.8
Esomeprazole	A02BC05	0.0266	0.0228	- 14.3
Lansoprazole	A02BC03	0.0257	0.0151	- 41.2
Omeprazole	A02BC01	0.0230	0.0228	- 0.9
Pantoprazole	A02BC02	0.0117	0.0116	- 0.9
Pravastatin	C10AA03	0.0167	0.0164	- 1.8
Ramipril	C09AA05	0.0295	0.0296	+0.3
Rosuvastatin	C10AA07	0.0578	0.0459	- 20.6

Notes: a, b, c, d. See notes to Table 4.1.

Source: Based on information supplied by the HSE, personal communication, 13 March 2013.

Table 4.2 shows that for six of the ten leading multiple source off-patent pharmaceuticals the ex-factory price remained essentially unchanged, with a price change that varied between +1.8 per cent and -1.8 per cent. In contrast, the remaining four multiple source off-patent pharmaceuticals recorded ex-factory price declines of between 14 and 41 per cent. Hence the a priori expectation of price declines has not been borne out by the data.[12] There are at least three explanations

11 Of course, the major difference is that with the presence of generic manufacturers N in equation 4.1 will be much higher than with a single source in-patent pharmaceutical. For example, if the generic manufacturers replicated the offerings of the patent holder and there were three generic manufacturers N would increase to 4.

12 These conclusions do not change if 2011 weights are used to estimate prices for both 2011 and 2013, rather than just 2011. The price changes in the final column of Table 4.2 are instead, reading from top to bottom: 0.0%, 0.0%, -31.8%, -9.4%, -41.2%, -0.9%, 0.0%, -1.2%, 0.0%, and -14.7%, respectively.

for these results. First, it might reflect strategies by the patent holder to introduce new dosage forms and strengths or formulations and hence facilitate or at least mitigate the anticipated decline in price.[13] Second, some of the price reductions that would have taken place on 1 November 2012 were brought forward under the interim agreements between the State and the industry representative bodies and took place in 2011.[14] Third, most of the price reductions may have already occurred for older pharmaceuticals and hence only a small decline occurred between 2011 and 2013.

4.3.5 Ex-Factory Price Trends for Pharmaceuticals that Switch from Single Source In-Patent Pharmaceuticals to Multiple Source Off-Patent Pharmaceuticals

The final set of ex-factory prices considered are those pharmaceuticals which switched from being single source in-patent to being multiple source off-patent. In other words, the pharmaceutical lost patent protection and generic competitors entered the market. We focus on the three leading pharmaceuticals on the GMS Scheme in 2010 that switched status in this way. We would expect, based on the discussion in Chapter 3, substantial price declines. The price of the patent-holder's pharmaceutical, for example, declines by 30 per cent on the entry of a generic manufacturer under the agreements between the State and the industry representative bodies.[15] However, although the ex-factory price has declined substantially, the decline does not always match the 30 per cent that might have been expected. Again this might reflect successful strategies by the patent holder to mitigate the impact of generic competition, but also the bringing forward of price reductions under the interim agreements between the State and the industry representative bodies that took place in 2011.

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13 For example, the patent holder of atorvastatin changed the size and shape of Lipitor in late 2011 in Ireland prior to the expiry of its patent protection (Gorecki *et al.*, 2012, p. 77). In Ontario in the late 1980s a similar situation occurred. Modified release dosage forms were introduced, it was argued, in order to neutralise generic penetration for immediate release dosage forms (for details see Gorecki, 1992, pp. 102–104). A broad definition of an interchangeable pharmaceutical product is one way in which such strategies can be addressed by the State. Alternatively for minor changes in presentation that are designed to prevent or discourage entry, with no offsetting benefit, the Competition Authority might consider whether this is an abuse of a dominant position since, it could be argued, this does not constitute competition on the merits.

14 The reductions would have taken place prior to 1 September 2011, the date on which prices for 2011 are measured in Tables 4.1 to 4.3. Details of the agreements referred to in the text are discussed in Chapter 3.

15 These conclusions do not change if 2011 weights are used to estimate prices for both 2011 and 2013, rather than just 2011. The price changes in the final column of Table 4.3 are instead, reading from top to bottom: -16.7%, -21.0%, and -28.0%, respectively.

TABLE 4.3 Ex-Factory Price of Leading[a] Pharmaceuticals that Switch from Single Source In-Patent to Multiple Source Off-Patent Pharmaceuticals[b] – GMS Scheme, 2011[c] and 2013[d]

ATC Description	ATC	Price per dose		Price change
		2011 (€)	2013 (€)	%
Atorvastatin	C10AA05	0.0372	0.0295	- 20.7
Olanzapine	N05AH03	0.3327	0.2451	- 26.3
Quetiapine	N05AH04	0.0143	0.0102	- 28.7

Notes a, b, c, d. See notes to Table 4.1.

Source: Based on information supplied by the HSE, personal communication, 13 March 2013.

In sum, the ex-factory prices of leading pharmaceuticals under the GMS Scheme, as expected, have in general fallen between 2011 and 2013. This is particularly the case for single source in-patent pharmaceuticals and those that have changed status from single source in-patent to multiple source off-patent. It is much less the case for multiple source off-patent where a large percentage of the leading pharmaceuticals showed little change in price.

4.4 Price Comparisons: Ireland vis-à-vis Other Member States – A Review of the Literature

4.4.1 Introduction

In this section we draw on a rich and varied set of comparisons of pharmaceutical prices in Ireland with other jurisdictions. These include not only other Member States but also other OECD countries including New Zealand. However, it should be noted that the data sources, reports and studies used to make these comparisons do not always include all of the basket of nine Member States, the EU-15, the EU-27 and so on. Furthermore, the comparisons do not always match the classification used in earlier parts of this report – single source in-patent pharmaceuticals and multiple source off-patent pharmaceuticals – but they are sufficiently close to merit inclusion. In some cases the evidence may appear a little dated, but we believe that when taken together a consistent and coherent pattern is presented of pharmaceutical prices in Ireland as compared to other Member States.

4.4.2 Retail Price of Pharmaceuticals, 2005

The first comparison is for the price of pharmaceuticals at the retail level. It is taken from a survey conducted by Eurostat for 2005 across 33 European countries.[16] These countries include all the twenty-five Members States at that date, plus a number of other European countries. Prices were compared for 181 pharmaceuticals; 75 per cent were patent-holder prices, 25 per cent generic prices. The 181 pharmaceuticals were available across the 33 countries and were designed to be sufficiently representative of what patients bought. The price recorded was the total price,

16 For details see Eurostat (2007).

including not only what the patient paid but any portion paid by government. Hence the price is the cost to society as a whole. It is not clear what weights, if any, were applied to the prices to derive the price index for each country.

Eurostat set the EU-25 as 100 and measure prices in all 33 countries relative to this benchmark. Furthermore, Eurostat divide the 33 countries into six categories. These six categories are reproduced in Table 4.4 together with the distribution of the nine Member States in the basket used to determine ex-factory prices in Ireland from 2006 onwards. The table shows that Ireland, together with Germany and Denmark, was in the second highest category in terms of prices. In contrast, prices were much lower in the UK, France and particularly Spain.[17]

TABLE 4.4 Pharmacy Level Pharmaceutical Prices[a] – Ireland and the Basket of Nine Member States, 2005

Price Level Index EU25 = 100	Distribution of Member States included in the Basket of Nine plus Ireland
160 and above	None
115-160	Germany (128), Denmark (121), Ireland (119)
100-115	Finland (111), Netherlands (109), Austria (107), Belgium (106)
85-100	UK (93), France (91)
60-85	Spain (77)
Less than 60	None

Notes: a Measured at the retail level. Total retail price includes contributions both by the government and the patient.
Source: Eurostat (2007), Chart 1, p. 1

4.4.3 Wholesale Price of Pharmaceuticals, 2010

The second comparison is for prices at the wholesale level of the leading pharmaceuticals for 2010. The comparisons are for 210 of the leading 303 pharmaceuticals in Norway in the first half of 2010 that were sold not only in Norway but also in nine other countries, details of which are provided in Table 4.5.[18] The 210 pharmaceuticals consisted of those that were single source in-patent and multiple source off-patent. The data source was the Intercontinental Medical Systems (IMS)[19] and refers to pharmaceuticals sold via pharmacies. In other words, sales to hospitals are excluded. Pharmaceutical prices were estimated as volume weighted average pharmaceutical price per dose. This is the method set out in equation 4.1 above, where the weights were sales in Norway.

17 It should be noted that only two countries are in the highest category (i.e., Switzerland and Iceland) and one in the lowest category (i.e., Macedonia).

18 In fact of the 303, 21 had to be excluded due to lack of information on patent status, so it is 210 from 282 rather than 303. See Brekke (2011), Table 4.3, p. 27, p. 9.

19 IMS is a leading collector of pharmaceutical data worldwide.
For details see: http://www.imshealth.com/portal/site/ims [last accessed 5 April 2013].

The price comparisons, which are at the wholesale level, set Ireland as a 100. The wholesale price is equal to the ex-factory price plus a wholesale margin. The wholesale margin in Ireland in 2010 had been reduced so that it was much closer to the EU norm and as a result the comparisons in the table at the wholesale level are reasonable proxies for price differences at the ex-factory level.[20] Results are presented in Table 4.5 for all pharmaceuticals, single source in-patent pharmaceuticals and multiple source off-patent pharmaceuticals.

TABLE 4.5 Wholesale Pharmaceutical Prices[a] of Leading Pharmaceuticals – EU and EEA Countries, 2010

Country Grouping	All Pharmaceuticals[b]	Single Source In-Patent Pharmaceuticals[c]	Multiple Source Off-Patent Pharmaceuticals[d]
	Ireland = 100	Ireland = 100	Ireland =100
Basket of Nine Member States			
Austria	77.1	84.3	64.1
Belgium	80.7	84.8	77.3
Denmark	76.4	94.9	44.9
Finland	61.3	81.5	42.7
Germany	90.8	104.5	54.4
Netherlands	61.5	77.5	34.4
UK	55.0	67.0	38.6
Other EU-15			
Sweden	65.6	82.8	37.9
European Economic Area			
Norway	58.1	80.1	41.4

Notes:
a Prices estimated as volume weighted average pharmaceutical price per dose, where the weights are the quantities sold in Norway.
b The price comparisons refer to 210 pharmaceuticals out of the leading 300 in Norway in the first half of 2010 that were sold in all of the countries appearing in the table. Pharmaceutical is defined at the ATC 5 level.
c The price comparisons refer to the 73 pharmaceuticals that were classified as 'substances on patent in all countries (without generic competition in any country)'.
d The price comparisons refer to the 68 'substances off patent in all countries (with generic competition in all countries)'.

Source: Brekke (2011), Table 4.3, p. 27

At the wholesale level, prices in Ireland in 2010 were high compared to the Member States in the basket of nine for which data was available, to other EU-15 Member States (i.e., Sweden), and to an EEA Member (i.e., Norway). The differences are substantial according to Table 4.5. Among the basket of nine Member States, the UK has prices that were 55 per cent of those in Ireland, Finland 61.3 per cent. These differences are driven by much higher prices for multiple source off-patent pharmaceuticals in Ireland as opposed to single source in-patent pharmaceuticals.

It could, of course, be argued that only limited reliance should be placed on the results in Table 4.5. Patterns of pharmaceutical consumption might be quite different in Ireland as compared to Norway. Furthermore, the data refer to 2010 and

[20] The wholesale margin for most products was reduced from 17.66 per cent to 10 per cent in 2009 and subsequently to 8 per cent in 2011 in Ireland (Gorecki *et al.*, 2012, Table 2.3, p. 23). On gross margins for various countries see Indecon (2007), Table 4.1, p. 35.

subsequently changes have taken place in Ireland that mean it could be argued the comparisons in Table 4.5 are of limited relevance. While there is obviously some merit to these arguments, they should not be overstated. First, the result that Ireland had the highest prices for pharmaceuticals in the study on which Table 4.5 is based was robust across a number of different methodologies for measuring price differences as well as different pharmaceutical samples drawn from the leading 300 pharmaceuticals sold in Norway in 2010.[21] Second, as the discussion in Chapter 3 makes clear, there do not have appear to have been any major changes in the way in which ex-factory prices in Ireland have been set since 2010.

4.4.4 Ex-Factory Price of Branded Pharmaceuticals, 2000–2011

The third comparison is for ex-factory prices of branded pharmaceuticals and is based on pharmaceutical consumption patterns in England, which is likely to be much closer to that of Ireland than Norway.[22] It is an annual exercise undertaken by the UK Department of Health. The sample is the leading 250 branded products sold in England in primary care, so that sales to hospitals are excluded. Branded products are defined as those products which are prescribed and dispensed by proprietary brand name.[23] It will thus refer to new pharmaceuticals and those for which the patent has expired but for which there is no generic competitor. The lack of a generic could reflect low sales of the pharmaceutical, that it is difficult and costly to manufacture the pharmaceutical, and/or that for whatever reason generic substitution for the branded product is thought inappropriate. A branded product appears to be measured for each separate pharmaceutical by product, proprietary name, form and strength, similar to equation 4.1.

The UK Department of Health comparison consisted of a series of bilateral comparisons between the prices in England with those for the same product in twelve countries. The median coverage – measured as the degree to which pharmaceuticals were available in each country comparison – for 2010 was 53 per cent. The weights applied the products share of England community prescribing. We present these results annually for 2000 to 2011 in Table 4.6 with Ireland set equal to 100. Since Ireland was excluded from the comparisons for 2003 we omit this year from the table. In view of the fact that availability of bilateral comparisons varies across the sample of 250 branded products the results should be viewed with some caution.

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21 See Brekke *et al*. (2011) for details.

22 The discussion of the UK Department of Health comparison is based on O'Neill (2012) and UK Department of Health (2012), and website of the Prescription Cost Analysis from which the sample is drawn.
For details see: http://www.nhsbsa.nhs.uk/PrescriptionServices/3494.aspx [last accessed 5 April 2013].

23 Hence it excludes: (i) pharmaceuticals prescribed and available generically; and, (ii) pharmaceuticals prescribed generically but only available as a propriety brand name.

The results presented in Table 4.6 suggest that by comparison with the eight Member States in the basket of nine for which comparative data is available since 2006, Ireland has been consistently higher priced than all of the seven Member States except Germany. A comparison with 2000–2005 shows that prices were consistently higher in Germany and the UK than Ireland and somewhat similar to Finland.[24] Hence the main conclusion to be drawn from the table is that compared to the basket of nine Member States for which we have data, prices in Ireland have been consistently high for over a decade.

TABLE 4.6 Ex-Factory Pharmaceutical Prices[a] of Leading Pharmaceuticals[b] – EU Member States and other OECD Countries, 2000–2011[c]

Country Grouping	00	01	02	04	05	06	07	08	09	10	11
Basket of Nine Member States[d]											
Austria	93	92	104	95	93	89	86	83	87	88	93
Belgium	94	92	104	91	92	92	90	91	92	92	100
Finland	100	95	106	97	98	91	88	89	78	79	84
France	96	92	97	85	93	85	82	80	80	78	84
Germany	110	107	114	107	105	100	101	106	117	116	124
Ireland	100	100	100	100	100	100	100	100	100	100	100
Netherlands	97	95	106	93	92	89	88	86	n.a	n.a.	95
Spain	77	76	90	81	81	81	78	81	82	80	82
UK	120	114	120	101	97	95	89	81	69	75	81
Other EU-15											
Italy	95	93	104	91	81	74	74	75	83	85	82
Sweden	n.a.	n.a.	n.a.	n.a.	n.a.	98	94	86	87	98	109
Other OECD											
Australia	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	84	70	87	104	116
US	252	246	351	178	197	179	163	188	173	211	269

Notes:
a Prices estimated as volume weighted average pharmaceutical price per dose, where the weights are the quantities sold in England.
b The leading 250 branded pharmaceutical products in England. Pharmaceutical appears to be defined at the ATC 5 level.
c Ireland was not included in the data source for 2003.
d The basket of nine Member States operated from 2006 onwards to set ex-factory prices in Ireland. Prior to that the basket consisted of only five Member States: Denmark, France, Germany, the Netherlands and the UK.

Source: O'Neill (2012) Appendix 2, p. 10, based on UK Department of Health estimates except for 2011.

[24] The price decline in the UK is likely to reflect in part at least comment and criticism over the way in which the Pharmaceutical Price Regulation Scheme, one of the major ways that the UK DoH controls expenditure on single source in-patent pharmaceuticals, operates (e.g., Office of Fair Trading, 2007) and the creation of the National Institute for Health and Care Excellence in 1999. Exchange rate fluctuations also have played a part, although this varies over time. The €/£ exchange remained relative constant between 2002 and 2007 (0.6287 and 0.6843) yet UK prices fell compared to those in Ireland from 120 to 89. Over that period, the variation in the exchange rate would only have accounted for a fall from 120 to 110. Between 2007 and 2011, while Table 4.6 shows a decline in UK prices relative to Ireland from 89 to 81, exchange rates changes would have only accounted for a decline to 87. Exchange rates were sourced from: http://www.centralbank.ie/polstats/stats/exrates/Pages/default.aspx. [last accessed 17 May 2013]. It should be noted that these comparisons neglect to take into account other factors that account for UK/Ireland price differences of pharmaceuticals.

4.4.5 Ex-Factory Price of Pharmaceuticals, 2013

In this section, we update and extend a comparison of ex-factory prices in Ireland and New Zealand that was carried out for our 2012 report.[25] We choose New Zealand as a case study as PHARMAC, the independent agency that manages the pharmaceutical budget in New Zealand, often employs tendering as a method for setting the ex-factory price of multiple source off-patent pharmaceuticals. Successful manufacturers are granted 'sole supply' status, which means that the manufacturer's brand would be the only one subsidised for a particular formulation for a specified period of time (usually no more than 3 years).

We compare the ex-factory price of the leading pharmaceuticals by value on the GMS Scheme in 2010 (March 2013 ex-factory price) with the equivalent price in New Zealand (April 2013 ex-factory price). For each ATC 5 pharmaceutical, we select the most frequently dispensed branded and generic products. We then calculate the unit ex-factory price and the equivalent unit ex-factory price for the corresponding products in New Zealand. The results are presented in Table 4.7. Products which are supplied via a 'sole supply' agreement in New Zealand are noted.

For most products, the ex-factory price per unit in Ireland is substantially higher than in New Zealand. The differential for atorvastatin is particularly striking, with the ex-factory price per unit in Ireland 21 times greater (for the most popular generic product in Ireland) and 25 times greater (for the most popular branded product in Ireland) than in New Zealand. Atorvastatin is supplied via a 'sole supply' agreement for Zarator in New Zealand and, as such, demonstrates the potential savings that can occur due to the use of tendering. While the price differentials are particularly large where 'sole supply' agreements are in place in New Zealand, large differentials are also evident for some products without 'sole supply' agreements such as olanzapine and donepezil. In some cases in New Zealand, a 'special authority for subsidy' form must be completed by the relevant medical practitioner, meaning that additional restrictions on eligibility for full subsidy are in force.

[25] Gorecki *et al.*(2012), Table 4.4, pp.69–70, which was also updated in WHO and EOHSP (2012), Table 2.16, p. 19

TABLE 4.7 Ex-Factory Pharmaceutical Prices of Leading Pharmaceuticals – GMS Scheme, Ireland and New Zealand, 2013

ATC Description	ATC	IRELAND						NEW ZEALAND							RATIO Irl:NZ
		GMS Product	Dose	% of ATC 2011[a]	Pack Size	Ex-Factory Price Mar 2013[b]	Price Per Unit[c]	Pharmac Product	Dose	Pack Size	Ex-Factory Price Apr 2013	Ex-Factory Price Apr 2013	Price Per Unit	Sole Supply	
						(€)	(€)				($NZD)[b]	(€)[d]	(€)[c,d]		
Alendronic acid	M05BA04	Fosamax Once Weekly	70 mg	36.5	4	13.19	3.30	Fosamax[j]	70 mg	4	22.9	14.63	3.66		**0.9**
		Romax Once Weekly	70 mg	11.7	4	13.19	3.30								**0.9**
Amlodipine	C08CA01	Istin	5 mg	19.0	28	5.53	0.20	Apo-Amlodipine	5 mg	100	2.65	1.69	0.02	Y	**11.7**
		Amlid	5 mg	10.2	28	5.42	0.19								**11.4**
Atorvastatin	C10AA05	Lipitor	10 mg	21.6	28	12.83	0.46	Zarator[e]	10 mg	90	2.52	1.61	0.02	Y	**25.6**
		Atorvastatin Teva	10 mg	3.8	28	10.70	0.38								**21.4**
Clopidogrel	B01AC04	Plavix	75 mg	44.0	28	27.32	0.98	Apo-Clopidogrel	75 mg	90	16.25	10.38	0.12	Y	**8.5**
		Clopidogrel	75 mg	15.1	28	22.77	0.81								**7.1**
Donepezil	N06DA02	Donecept	10 mg	22.2	28	43.30	1.55	Donepezil-Rex	10 mg	90	14.06	8.98	0.10		**15.5**
		Aricept	10 mg	21.3	28	44.18	1.58								**15.8**
Escitalopram	N06AB10	Lexapro	10 mg	40.8	28	19.81	0.71	Loxalate	10 mg	28	2.65	1.69	0.06	Y	**11.7**
Esomeprazole[f]	A02BC05	Nexazole	40 mg	20.8	28	20.61	0.74								
		Nexium	40mg	19.8	28	28.24	1.01								
Fentanyl	N02AB03	Durogesic Dtrans	25 mcg	27.9	5	20.75	4.15	Mylan Fentanyl	25 mcg	5	9.15	5.84	1.17	Y	**3.6**
Formoterol[k]	R03AK07	Symbicort Turbohaler	200/6 mcg	52.4	1	46.40	46.40	Symbicort[j]	200/6 mcg	1	60.00	38.32	38.32		**1.2**
Lansoprazole	A02BC03	Zoton Fastab	30 mg	31.2	28	12.70	0.45	Solox	30 mg	28	2.32	1.48	0.05	Y	**8.6**
		Zotrole	30 mg	15.9	28	12.70	0.45								**8.6**
Olanzapine	N05AH03	Zyprexa	5 mg	13.7	28	35.28	1.26	Zyprexa[l]	5 mg	28	101.21	64.69	2.31		**0.5**
		Olanzapine Actavis	5 mg	5.2	28	29.40	1.05	Olanzine/Dr Reddy's Olanzapine[l]	5 mg	28	3.85	2.46	0.09		**12.0**
Omeprazole	A02BC01	Losec Mups	20 mg	17.5	28	13.16	0.47	Omezol Relief	20 mg	90	3.78	2.41	0.03	Y	**17.5**
		Lopraz	20 mg	13.3	28	12.90	0.46								**17.2**
Pantoprazole	A02BC02	Protium	40 mg	25.7	28	13.02	0.47	Dr Reddy's Pantoprazole	40 mg	28	1.54	0.98	0.04	Y	**13.2**
		Pantoflux	40 mg	12.5	28	12.76	0.46								**13.0**
Perindopril[h]	C09AA04	Coversyl Arginine	5 mg	52.1	30	9.60	0.32	Coversyl[h,i]	4 mg	30	25.00	15.97	0.53		**0.6**
Pravastatin	C10AA03	Lipostat	20 mg	16.3	28	11.52	0.41	Cholvastin[e]	20 mg	30	5.44	3.47	0.12	Y	**3.6**
		Pravitin	20 mg	6.6	30	12.09	0.40								**3.5**
Pregabalin[e]	N03AX16	Lyrica	50 mg	20.2	84	73.29	0.87								
Quetiapine	N05AH04	Seroquel	25 mg	37.8	60	21.59	0.36	Seroquel/Dr Reddy's Quetiapine[l]	25 mg	60	7.00	4.47	0.07		**4.8**
		Quetiapine Actavis	25 mg	10.5	60	18.89	0.31								**4.2**
Rosuvastatin[f]	C10AA07	Crestor	10 mg	34.9	28	16.52	0.59								
		Rosuvastatin Teva	10 mg	13.4	28	11.21	0.40								
Salmeterol[g]	R03AK06	Seretide Evohaler	250 mcg	30.4	1	57.61	57.61								
Tiotropium bromide	R03BB04	Spiriva Combopack	18 mcg	44.2	1	38.57	38.57	Spiriva[j]	18 mcg	1	70.00	44.71	44.71		**0.9**

Notes: The list of pharmaceuticals refers to the leading pharmaceuticals on the GMS Scheme in 2010. For each of the leading ATCs, we chose the most frequently dispensed brand (and where appropriate, the most frequently dispensed generic). We then searched the PHARMAC Online Schedule for the equivalent product in New Zealand. In many cases, only one manufacturer was available due to the existence of a sole supply contract for that ATC. In some cases (noted below), the ATC is not available in New Zealand, or an exact product match could not be found (e.g., due to different doses). In other cases (also noted below), PHARMAC does not subsidise the full ex-factory price of the product (i.e., the patient must pay the difference, plus pharmacy mark-ups that the pharmacy is entitled to charge on products that are not fully subsidised).

a % of ATC refers to the proportion of the total ATC volume accounted for by the particular GMS product.
b Irish prices refer to March 2013, while New Zealand prices refer to April 2013.
c Price per unit refers to price per tablet, capsule, tube, inhaler, etc.
d NZ dollar converted at the Central Bank monthly average exchange rate for March 2013 (€1=NZ$1.5657).
e Accompanied by prescribing guidelines.
f There is no PHARMAC record for this ATC.
g Salmeterol and other drugs for obstructive airway diseases. The 250 mcg version of this product is not available in New Zealand (max is 125 mcg).
h Although this ATC was multiple source in Ireland in 2013, this particular product within the ATC remains on-patent.
i Coversyl Arginine 5 mg tabs are not available in New Zealand. We have therefore chosen Coversyl 4 mg tabs for comparison. PHARMAC subsidy is $4.05 per pack (i.e., the patient must pay the difference between the subsidy and the final price, i.e., the ex-factory price of $25.00 plus relevant pharmacy mark-ups, GST and patient co-payment).
j A Special Authority for Subsidy is required for this product in New Zealand. For the Spiriva and Symbicort inhalers, the unit price refers to the price per pack (the number of doses per pack is the same in Ireland and New Zealand).
k Formoterol and other drugs for obstructive airway diseases.
l In New Zealand, the PHARMAC subsidy for Zyprexa is $3.85 (i.e., the patient must pay the difference between the subsidy and the final price, i.e., the ex-factory price of $101.21 plus relevant pharmacy mark-ups, GST and patient co-payment). Two generic products (Olanzine and Dr Reddy's Olanzapine) are available and fully subsidised at $3.85 per pack.

Sources: ESRI Calculations
Ireland: HSE, personal communication, 13 March 2013
New Zealand: http://www.pharmac.health.nz/ [last accessed 16 April 2013]; PHARMAC, personal communication, 17 April 2013

4.5 Price Comparisons: Ireland vis-à-vis Other Member States – Some New Comparisons

4.5.1 Introduction

We undertook a comparison of pharmaceutical prices across Member States using Euripid, an administrative data source, that was established in January 2010. Individual Member States submit to Euripid, on a monthly basis, details concerning the prices of reimbursed pharmaceuticals in the given Member State. Data is presented for each pharmaceutical at the ATC 5 level by manufacturer, dosage form and strength. Prices can be presented at three levels: ex-factory; wholesale; and/or, retail or pharmacy (i.e., net and gross retail). It was decided to use the wholesale and ex-factory level, given the variety of ways that pharmaceuticals are priced at the retail level and the absence of retail price data for Ireland. We requested data for September 2011 and March 2013 so that we could capture the impact of the changes to pharmaceutical prices in Ireland in November 2012 and January 2013.

The raw data needed substantial cleaning before it could be used to shed light on whether or not pharmaceutical prices are high in Ireland and the impact of the recent realignment in prices. First, certain Member States were excluded from the analysis. These included Italy which did not always update its data; the UK and Portugal, which provided only retail price data[26]; and several Member States which did not appear to provide data to Euripid (i.e., France, Germany, Luxembourg, Malta and Romania). Second, since we were comparing the prices of the most popular dosage form and strength of the leading single source in-patent and multiple source off-patent pharmaceuticals in Ireland in the GMS Scheme in 2010, the patent-holder's brand in each Member State had to be identified. This was not an easy task since the patent-holder's brand name often differed by Member State and there were no EU-wide common identifiers on Euripid. However, the HSE identified the patent-holder's brand in each Member State for the sample of leading pharmaceuticals used for comparative purposes. Third, except for Ireland we were not able to identify parallel imports.

The comparisons we were able to make for the most popular strength of leading pharmaceuticals in Ireland are as follows: for each single source in-patent and multiple source off-patent pharmaceutical the patent holder and non-patent holder ex-factory and wholesale price in 2011 and 2013. We did not have any information on the quantities sold of the pharmaceutical products in other Member States, so we are not able to select the most popular non-patent holder pharmaceutical product or take a weighted average. We therefore decided to use the median to represent the

[26] Ireland did not supply retail price data so that comparisons with the UK and Portugal could not be made.

price of pharmaceuticals in each Member State including Ireland.[27,28] The most popular strength of leading pharmaceuticals in Ireland was derived from volume data on the GMS Scheme in 2012.

In presenting the results we define four groups of countries:

- Ireland plus the nine Member States in the basket used to define the price of new pharmaceuticals are labelled 1 to 10 where Ireland is 1
- Other EU-15 Member States are labelled 11 to 15
- Member States that joined from 2004 (enlargement) are labelled 16 to 27
- Members of the EEA are labelled 28 to 29.

We only present information for the countries for which we have data and do not identify individual countries, except Ireland, for confidentiality reasons.

We take the non-patent-holder price to be the generic price. In each case we are interested in comparing the patent-holder price or the generic price in Ireland with the corresponding observation in the other Member States for which we have data. We set both the patent holders and the generic median price in Ireland equal to 100 in each year, but this does not imply, of course, that there is no difference between the patent holder and the generic price.

Applying this methodology provides, for each single source in-patent pharmaceutical and each multiple source off-patent pharmaceutical, a chart showing the comparative ex-factory and wholesale median prices for 2011 and 2013. These are reproduced in Appendix C, Figure C.1 and C.2, respectively. As will be apparent from these charts there is typically more data points for 2013 than 2011[29] and for wholesale rather than the ex-factory price. This makes comparisons of the trend in prices over the period 2011 to 2013 difficult. As a result we have decided to present and discuss the comparative wholesale prices only for 2013.

27 In other words, the prices of non-patent holder pharmaceutical products of a given dosage form and strength are ranked from highest to lowest and the median price selected.

28 In the case of Ireland we could identify parallel imports, which we excluded when estimating the median. Parallel imports are of little importance for multiple source off-patent pharmaceuticals.

29 This may reflect for single source in-patent pharmaceuticals that Ireland is an early adopter and hence the pharmaceutical is only available in a limited number of Member States.

4.5.2 Single Source In-Patent Pharmaceuticals

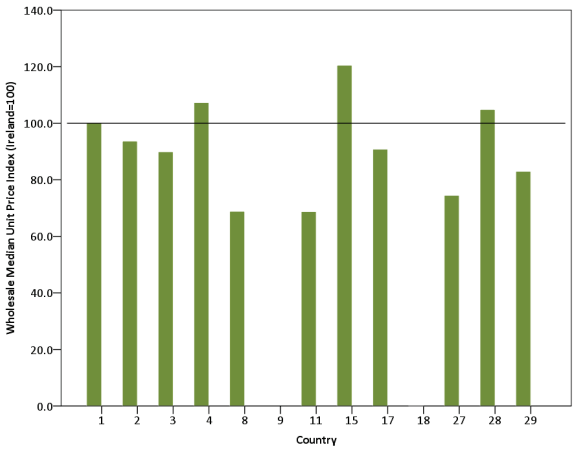
Based on the discussion in Chapter 3 and as set out earlier in this chapter we would typically expect that the wholesale price of single source in-patent pharmaceuticals in Ireland would be higher than other Member States in the basket of nine used to derive the price in Ireland. However, the realignment of the prices of single source in-patent pharmaceuticals, under the 2012-2015 State/IPHA Agreement, in November 2012 and January 2013 is likely to have narrowed the difference. The results are presented for 10 leading pharmaceuticals in Figure 4.1 and summarised in Table C.1. Typically wholesale price data is available for four or five Member States in the basket of nine, although on occasion it drops to one.

The results in Figure 4.1 and Table C.1 are consistent with the expectations concerning the comparative price of single source in-patent pharmaceuticals. The wholesale price in Ireland is high by comparison with Member States that are in the basket of nine. These are labelled 2 to 10. There is typically only one Member State (#4) with a wholesale price that is often above that of Ireland. However, it should be remembered that not all of the basket of nine Member States are included in the comparisons. Germany, for example, which is a high priced Member State, is not included.[30]

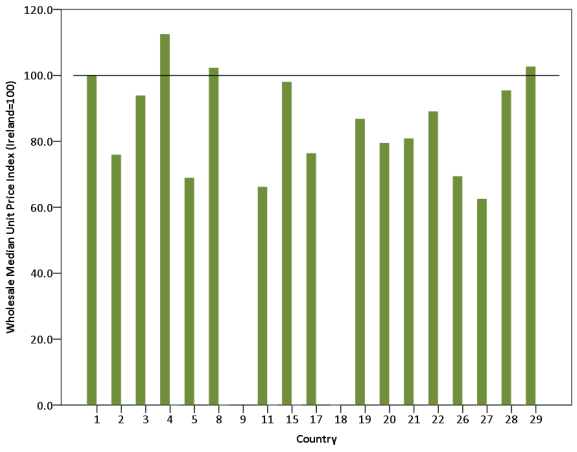
[30] While we have not been able to calculate the average price across the basket of nine for each pharmaceutical, it appears that the average price of pharmaceuticals in the basket of nine countries, based on the price data in Figure 4.1, is lower than the price in Ireland. Under the 2012-2015 State/IPHA Agreement there should be no difference between the average price in Ireland and the basket of nine. There are several possible reasons for this disparity. First, the data in Figure 4.1 refer to the wholesale level whereas the 2012-2015 State/IPHA Agreement refers to the ex-factory price. However, as shown in Figure C.1 where we have price data at both the ex-factory level and the wholesale level, the results are similar. Second, the price reported under the 2012-2015 State/IPHA Agreement is, according to clause 5.2, 'the price to the wholesaler'. However, the Euripid data is based on the reimbursement schemes of the Member States and hence there may be differences due to rebates etc. Third, the methodology used to estimate the price differences may be biased in some way. However, as we show below, when we test the sensitivity of the results to the use of the lowest as opposed to the median price for multiple source off-patent pharmaceuticals, the rankings are unchanged.

FIGURE 4.1 Median Wholesale Unit Price Indices for Single Source In-Patent Pharmaceuticals, 2013 (Ireland (1) = 100)[a]

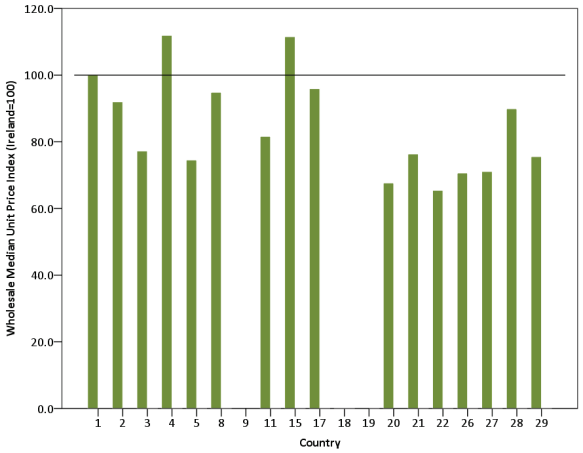
Aripiprazole – ATC N05AX12 – 10mg[b]



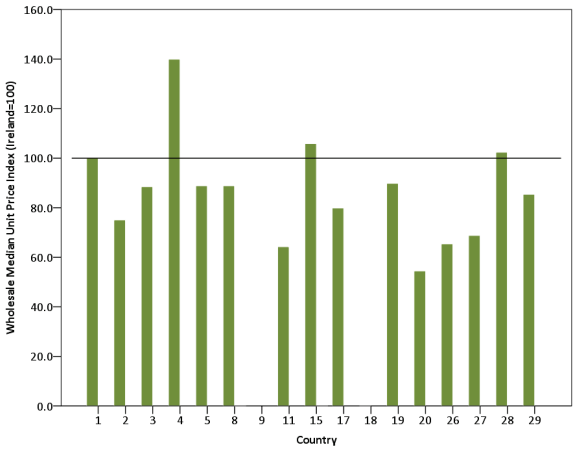
Duloxetine – ATC N06AX21 – 60mg



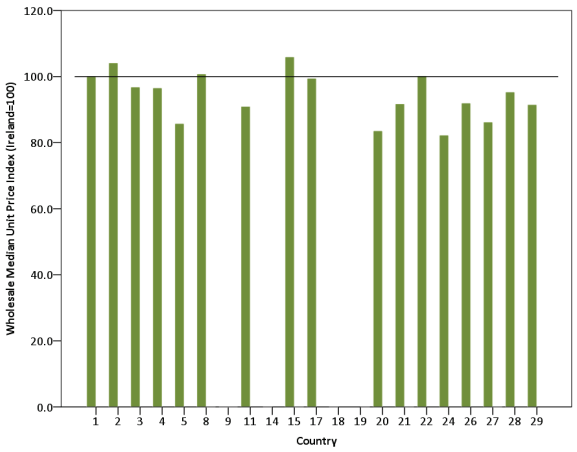
Escitalopram – ATC N06AB10 – 10mg[c]



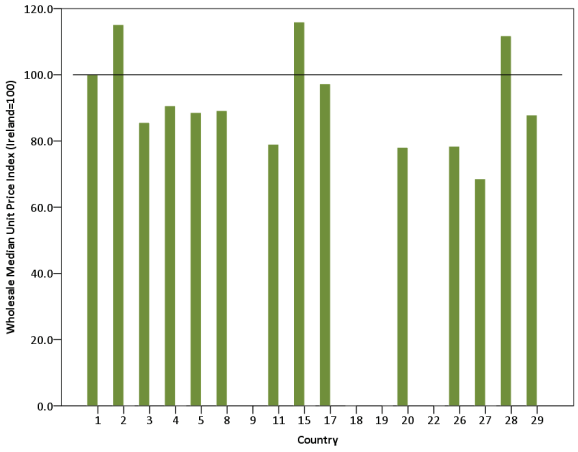
Etoricoxib – ATC M01AH05 – 90mg



Ezetimibe – ATC C10AX09 – 10mg



Memantine – ATC N06DX01 – 10mg[d]



HSE Identified Brand Other

Figure 4.1 Median Wholesale Unit Price Indices for Single Source In-Patent Pharmaceuticals, 2013 (Ireland (1) = 100) (contd.)

Notes:
a See Appendix B Table B.3 for GMS market share (volume) for each dosage strength within each ATC in 2011 and 2012.
b Excludes orodispersible tablets.
c Excludes orodispersible tablets and oral drops.
d Excludes oral solution and oral drops.
e Excludes chewable tablets.

Source: ESRI Calculations. Based on Euripid information supplied by the HSE, personal communications, April 2013.

4.5.3 Multiple Source Off-Patent Pharmaceuticals

In considering multiple source off-patent pharmaceuticals, attention needs to be devoted to expectations concerning both the patent holder and generic manufacturers price in Ireland vis-à-vis other Member States. The analysis in Chapter 3 suggested that there would be very little difference in the prices of these manufacturers in Ireland.[31] Furthermore, as demonstrated in Chapter 3, most of the reduction in the price of multiple source off-patent pharmaceuticals in Ireland was driven by declines in the patent-holder's price. In other Member States it appears

[31] This is consistent with the result reported in Chapter 5 which finds that the market share of generic manufacturers in Ireland is very similar using value and volume measures.

that the patent-holder's price does not always decline when the patent expires and generic competitors enter the market. Indeed, in some cases the patent-holder's price may increase, the so-called generic paradox.[32] In Ireland, in contrast, the decline in price of the generic is from a high pre-entry price when the pharmaceutical was classified as a single source in-patent pharmaceutical so that it may be that generic prices are high in Ireland compared to other Member States. Hence the patent-holder's price for multiple source off-patent pharmaceuticals is likely to be lower in Ireland than in other Member States.

The results are presented in Figure 4.2 and summarised in Table C.1. The comparisons are available for 13 pharmaceuticals. Typically Ireland can be compared to five of the nine Member States that constitute the basket for setting the price of new pharmaceuticals. In most, but not all cases, prices for both the patent holder and generic manufacturers are in evidence, but for some pharmaceuticals such as pravastatin and lansoprazole there are few countries with an equivalent branded product price.

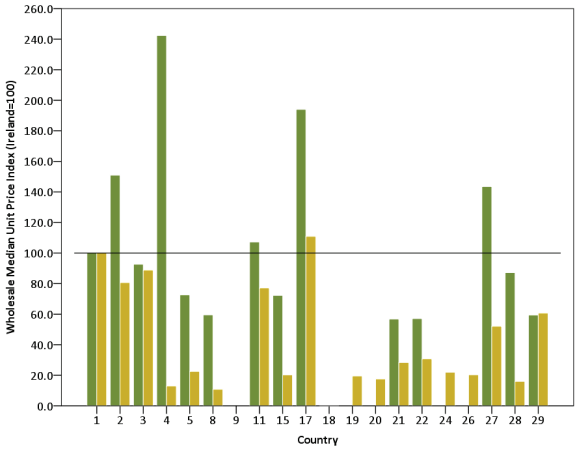
In contrast to single source in-patent pharmaceuticals, the patent-holder's price is less likely to be among the highest across the basket of nine Member States with respect to multiple source off-patent pharmaceuticals. Nevertheless, it is finely balanced with the patent-holder's price being lower in most cases for seven pharmaceuticals (i.e., rosuvastatin, ramipril, omeprazole, diclofenac, bisoprolol, montelukast and quetiapine) but above for five pharmaceuticals (i.e., pantoprazole, esomeprazole, olanzapine, atorvastatin and amlodipine).

In the case of the generic prices these are consistently higher in Ireland than in other Member States in the basket of nine. Generic prices are generally higher in Ireland for atorvastatin, olanzapine, quetiapine, montelukast, amlodipine, bisoprolol, esomeprazole, lansoprazole, omeprazole, pantoprazole, and pravastatin. Only in the case of diclofenac, ramipril, and rosuvastatin are generic prices lower in Ireland. This is consistent with the evidence in Table 4.5 which showed that prices for multiple source off-patent pharmaceuticals were much higher in Ireland compared to Member States in the basket of nine than for single source in-patent pharmaceuticals. As we shall see in Chapter 5 some of these pharmaceuticals have been identified for designation as interchangeable pharmaceutical groups.

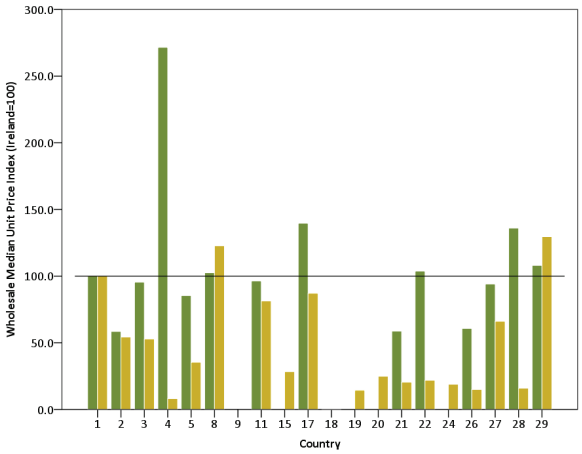
[32] For a discussion see, for example, Vandoros (2008).

FIGURE 4.2 Median Wholesale Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2013 (Ireland (1) = 100)[a]

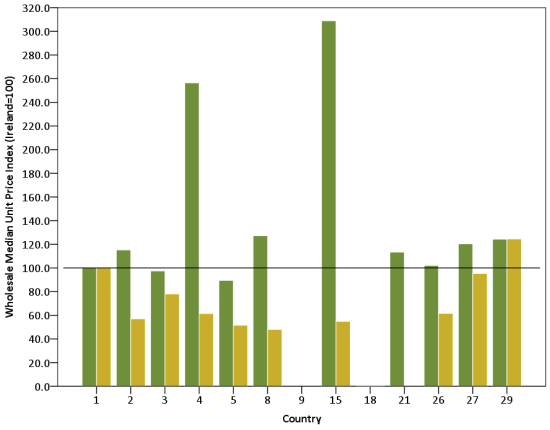
Amlodipine – ATC C08CA01 – 5mg[c]



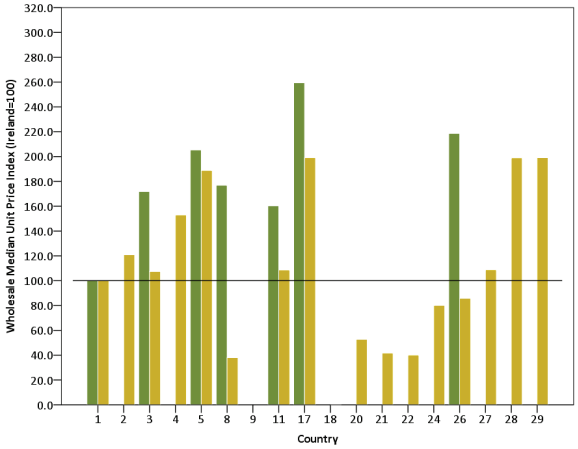
Atorvastatin – ATC C10AA05 – 10mg[b]



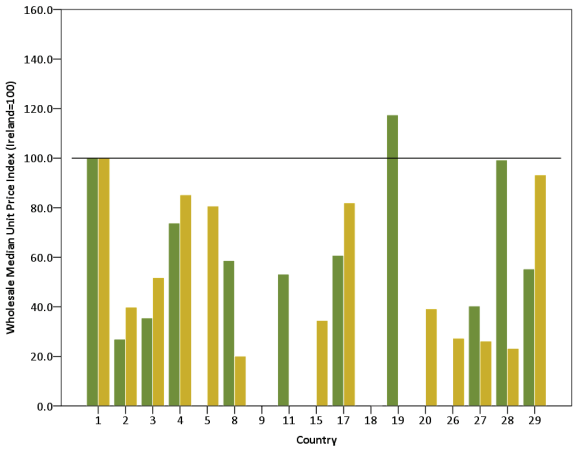
Bisoprolol – ATC C07AB07 – 2.5mg



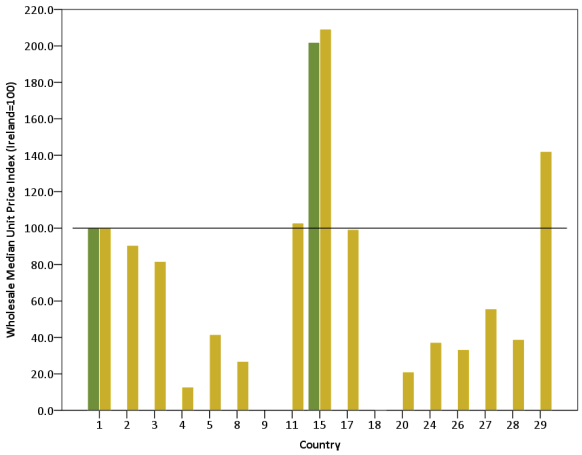
Diclofenac – ATC M01AB05 –75mg[d]



Esomeprazole – ATC A02BC05 – 40mg[e]



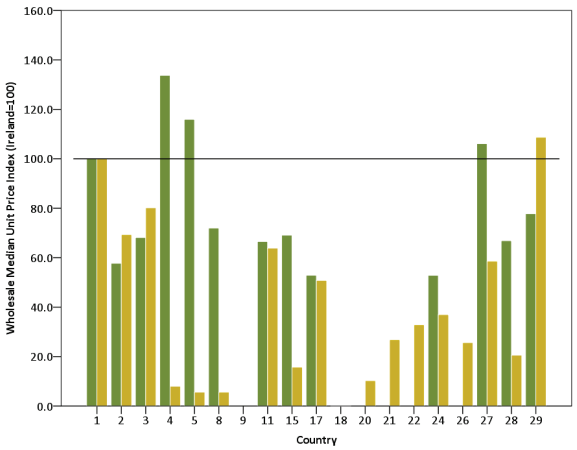
Lansoprazole – ATC A02BC03 – 30mg



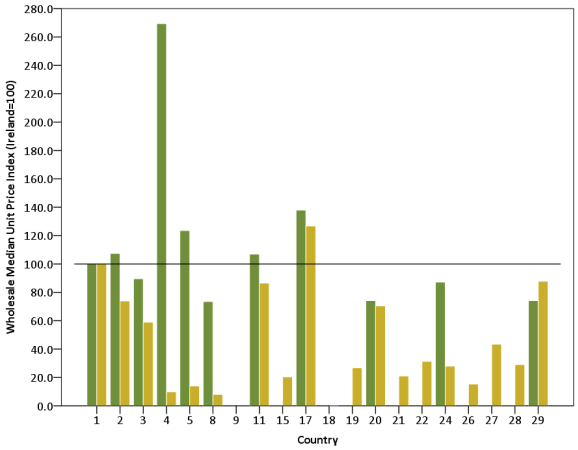
HSE Identified Brand Other

Figure 4.2 Median Wholesale Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2013 (Ireland (1) = 100) (contd.)

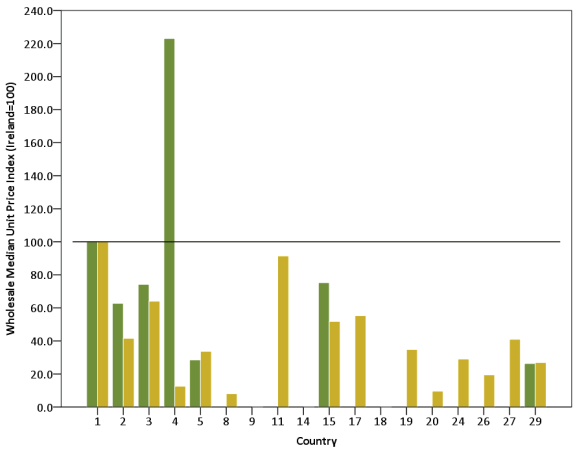
Olanzapine – ATC N05AH03 – 5mg[f]



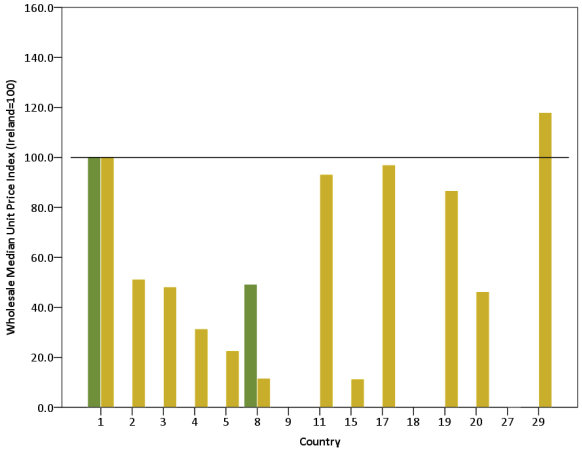
Omeprazole – ATC A02BC01 – 20mg



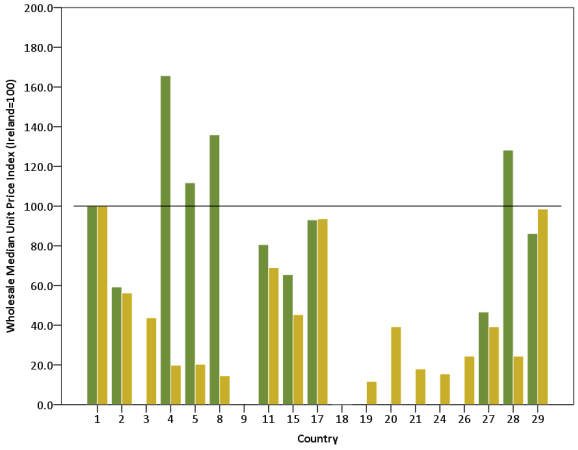
Pantoprazole – ATC A02BC02 – 40mg[g]



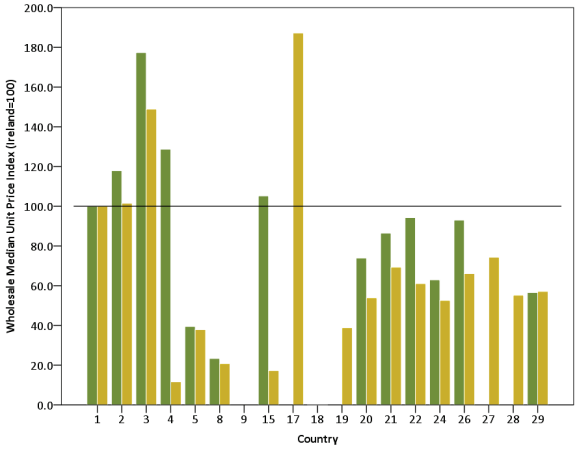
Pravastatin –ATC C10AA03 – 20mg



Quetiapine – ATC N05AH04 – 25mg



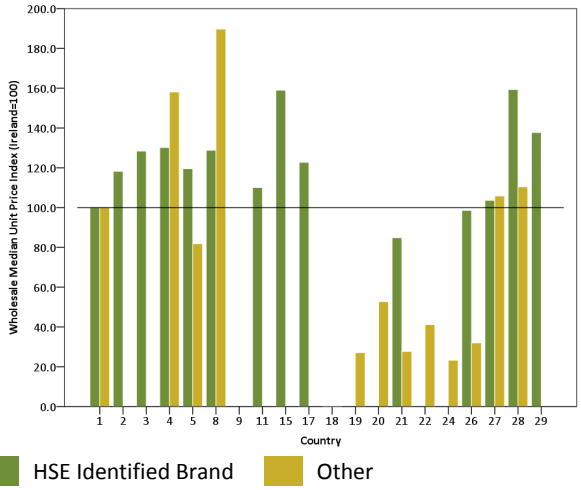
Ramipril – ATC C09AA05 – 10mg



HSE Identified Brand Other

Figure 4.2 Median Wholesale Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2013 (Ireland (1) = 100) (contd.)

Rosuvastatin – ATC C10AA07 – 10mg



Notes:
a See Appendix B Table B.3 for GMS market share (volume) for each dosage strength within each ATC in 2011 and 2012.
b Excludes chewable tablets.
c Excludes orodispersible tablets.
d Excludes solution for injection/infusion.
e Excludes oral lyophilisate and orodispersible tablets.
f Excludes powder for injection/infusion.

Source: ESRI Calculations. Based on Euripid information supplied by the HSE, personal communications, April 2013.

It could be argued that the minimum price should be used rather than the median for the purposes of comparing generic prices for multiple source off-patent pharmaceuticals.[33] What actually matters, it is argued, is the price of the cheapest available generic. Furthermore, any generics priced above the lowest priced are not that relevant. There is clearly merit to this argument since pharmaceutical reimbursement schemes, particularly in times of budgetary pressure, are likely to select the lowest priced product as the reimbursement price, while cash-constrained patients are also likely to favour the lowest price pharmaceutical product. We, therefore, for the purposes of comparison of generic prices, set the lowest priced pharmaceutical product in Ireland as a 100 and then compared it to the lowest priced pharmaceutical product in each of the comparator countries. The results are presented in Appendix C, Figures C.3 and C.4 for wholesale prices for 2013. The evidence suggests that regardless of whether the median or the lowest price is used to make generic price comparisons, prices are higher in Ireland. If anything they are higher using the lowest as opposed to the median price.

33 We should like to thank one of the referees for raising this option.

4.6 CONCLUSION

The evidence suggests that the ex-factory price of single source in-patent pharmaceuticals in Ireland is high when compared with the Member States in the basket of nine countries against which the ex-factory price of these pharmaceuticals in Ireland are benchmarked.[34] This is a robust and consistent finding of a series of reports using a variety of data sets and over time. In terms of multiple source off-patent pharmaceuticals generic prices in Ireland are also high compared to other Member States in the basket of nine Member States. In contrast, the patent-holder's price (once there is generic competition) tends to be lower than other Member States in the basket of nine. These results suggest that savings may be made through the recommendations made in our earlier report, *Delivery of Pharmaceuticals in Ireland.*

[34] See Appendix Table C.1 for a summary of the results.

CHAPTER 5

Usage of Generics

5.1 INTRODUCTION

In this chapter we consider the usage of generics, which are multiple-source off-patent pharmaceuticals where there are manufacturers other than the patent holder. The usage of generics will be a function of at least four factors: the prescribing practices of medical practitioners; the dispensing behaviour of pharmacists; patient preferences; and the reimbursement rules for the various State pharmaceutical reimbursement schemes.[1] We consider each of these influences separately in Sections 5.2.

Attention then turns in Section 5.3 to the extent of usage of generics in Ireland and in a comparison with other Member States. Ideally we would like data on the prescribing and dispensing of pharmaceuticals in Ireland compared to other Member States. However, for Ireland and most other Member States these data relate to what is dispensed by the pharmacist (as these data are typically returned to reimbursement authorities). Nonetheless, it is important to consider the interaction between the prescriber and the dispenser of pharmaceuticals. Chapter 6 discusses the behaviour of prescribers in greater detail. Section 5.4 concludes.

In most of this Chapter we take as given the set of off-patent pharmaceuticals for which there are generic competitors. The importance of generics will be a function not only of whether or not a pharmaceutical has patent protection, but also the regulatory requirements for the generic manufacturer to market a pharmaceutical, the prescribing and dispensing behaviour of health professionals, and the reimbursement mechanisms of State pharmaceutical reimbursement schemes. Thus, although we take as given the set of off-patent pharmaceuticals with generic competition, the discussion in the chapter will have relevance to the presence of generics in particular markets.

Our interest in the usage of generics reflects the fact that the ex-factory price of these pharmaceutical products is typically lower than the corresponding or

[1] Another important influence is the behaviour of both brand and generic firms (including decisions by generic manufacturers to supply the market, and attempts by brand firms to prolong the returns to patent protection by strategies such as 'evergreening', etc.).

equivalent pharmaceutical product of the patent holder. However, as demonstrated in Chapters 3 and 4, the price differences are not large in Ireland. Indeed, for periods in 2010 and 2011 the prices of generic pharmaceutical products were *above*, not below those of the equivalent pharmaceutical product of the patent holder. However, that is no longer the situation. Generic price reductions were triggered on 1 November 2012 under the agreements between the State and industry trade associations.[2] The Health (Pricing and Supply of Medical Goods) Act 2013 is likely to lead to further price reductions for generic pharmaceutical products.

5.2 Determinants of Generic Usage

5.2.1 Introduction

In this section we consider four determinants of generic pharmaceutical use in Ireland: prescriber practice; pharmacist behaviour; patient preferences; and State pharmaceutical reimbursement schemes. Although each will be dealt with separately there are clear inter-relationships between these factors, which we explore. We conclude with a discussion of the Health (Pricing and Supply of Medical Goods) Act 2013, which is likely to affect all four of these determinants and hence the use of generics.

5.2.2 The Prescriber: A Qualified Medical Practitioner[3]

The prescriber, typically the General Practitioner (GP) in an outpatient setting, in response to a patient's condition may decide that the appropriate treatment, in whole or in part, consists of prescribing a pharmaceutical. Once the prescriber has selected the appropriate pharmaceutical they have a choice as to how to write the prescription for the patient to present to the pharmacist. In Ireland, there are currently two options: the prescription is written generically (e.g., one month's supply of atorvastatin 10 mg tabs); or the prescription is written for a particular brand of the pharmaceutical, typically the patent holder, (e.g., one month's supply of Lipitor 10 mg tabs). In countries with generic substitution, a further type of prescription is available, where the prescriber writes a prescription for a particular brand of the pharmaceutical, but with the words 'no substitution' or 'do not substitute' written across the prescription in the prescriber's own handwriting. These will be referred to as generic, brand name and 'no substitution' prescriptions, respectively.

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2 These differences, based on April 2013 prices, include: clopidogrel (17 per cent), esomeprazole (27 per cent), risedronic acid (17 per cent), rosuvastatin (29–30 per cent), tamsulosin (12 per cent) and anastrazole (17–40 per cent). HSE, personal communication, 14 May 2013

3 This section draws heavily on Gorecki *et al.* (2012), Chapter 7, pp. 123–142.

For a generic prescription the decision as to the particular pharmaceutical dispensed is delegated to the pharmacist,[4] for the 'no substitution' prescription the prescriber makes the decision,[5] while for the brand name pharmaceutical prescription the situation will depend on the regulatory environment and financial incentives under which the pharmacist operates. In Ireland pharmacists are required to dispense pharmaceuticals as prescribed.[6] Hence, a brand name prescription is the same as 'a no substitution' prescription, since the pharmacist is required to dispense the prescription as written.[7] Of course, there may be conditions under which the patient influences the particular pharmaceutical prescribed and/or dispensed, an issue also considered further below.

There are few, if any, restrictions on the volume and type of pharmaceuticals that may be prescribed, other than limits on the length of the prescription (maximum six months) and the availability of the pharmaceutical subject to regulatory approval and related conditions. There are no financial incentives for the prescriber to favour one type of prescription over another. Indeed, the representative body for medical practitioners, the Irish Medical Organisation (IMO), argued that since the price difference between the generic and patent holder for a multiple source off-patent pharmaceutical was low in Ireland,[8] it left 'little incentive for physicians to prescribe the generic drug or for patients to request it'.[9]

The Medical Council's *Guide to Professional Conduct and Ethics for Registered Medical Practices* states that medical practitioners 'should be aware of the wider need to use limited health care resources efficiently and effectively'[10] and more specifically encourages medical practitioners to prescribe bio-equivalent medicines where they are appropriate.[11] However, a 1997 study of Irish GPs found that the major deterrent to generic prescribing was a concern over the reliability and quality of generic products.[12] Even though the IMO has come out strongly in favour of

4 In other words, if the prescription was written for atorvastatin the pharmacist makes the decision as to which of the different manufacturers' products of that pharmaceutical is dispensed.

5 This reflects the fact that where legislative provisions exist for such a prescription (typically on clinical grounds), the use of the term 'no substitution' signifies that that brand specified must be dispensed by the pharmacist.

6 This will change with the commencement of the Health (Pricing and Supply of Medical Goods) Act 2013. It is discussed further in Section 5.2.6 below.

7 As noted, such prescriptions are not relevant currently in Ireland. However, that will change with the proposed legislation on reference pricing and generic substitution referred to in the previous footnote.

8 This observation is consistent with the discussion in Chapters 3 and 4 above, but as noted above is not always the case today.

9 IMO, 2010, n.p.

10 Medical Council, 2009, paragraph 49.2

11 *Ibid*, paragraph 49.2.

12 Gorecki *et al*., 2012, p.130

greater generic prescribing,[13] it nevertheless argued that medical practitioners 'are … concerned about the risk pharmaceutical substitution presents to certain patients'.[14]

The consensus is that generic prescribing in Ireland is low,[15] no doubt in part for the reasons set out above. The evidence on the prescribing patterns in Ireland is inferred from the dispensing behaviour of pharmacists, since data is not collected on the types of prescriptions written by medical practitioners. This contrasts sharply with the UK.[16] However, as noted above, since in Ireland the pharmacist is required to dispense the prescription as written, data on dispensing patterns should, in theory at least, provide a reasonable approximation to prescribing patterns.

5.2.3 The Dispenser: The Pharmacist[17]

The pharmacist is responsible for the dispensing of the prescription(s) written by a medical practitioner and presented by a patient. The pharmacist may offer advice to the patient concerning the side effects of the pharmaceutical, when it should be taken, the conditions under which it should be taken, and possible interactions with existing pharmaceuticals and over-the-counter (OTC) products that the patient is taking. On occasion, if the pharmacist considers that the prescriber may have erred in some respect in the prescribing decision, the pharmacist may contact the prescriber for clarification.

The pharmacist's influence over the usage of generics depends on their ability to dispense a generic as opposed to the patent-holder's brand of a pharmaceutical and the incentives that influence the pharmacist's decision. The ability reflects the legal and regulatory position of what a pharmacist can and cannot do in terms of selecting a generic pharmaceutical,[18] as well as the availability of relevant generic products. The incentives the pharmacist faces determine, within the legislated/regulatory choice set, the decision that the pharmacist is likely to make. The incentives may not only be financial but also reflect patient preferences.

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13 The IMO went so far as suggesting that all prescriptions should be written generically i.e., using the international non-propriety name (INN) (IMO, 2010, n.p.).

14 *Ibid.*, 2010, n.p.

15 See, for example, Barry *et al.* (2010) and IMO (2010), p. 243. These sources refer to aggregate market shares of generic pharmaceuticals. It is also consistent with the few studies conducted at a more disaggregated level. For example, a 2009 comparison between a UK National Health Service hospital and a hospital in Ireland found significantly higher rates of generic prescribing in the NHS hospital. For details see Gorecki *et al.* (2012), pp. 129–130.

16 For example, the UK Department of Health reports (for 2008) that 83 per cent of prescription items were prescribed generically, made up of 65 per cent of prescription items that were prescribed as generics that could be dispensed as generics, but the remaining 18 per cent, although prescribed generically, were only available as branded products. For details see UK Department of Health (2012), pp. 14–15.

17 This section draws heavily on Gorecki *et al.* (2012), Chapter 6, pp. 103–122.

18 In some instances the regulatory authorities may issue non-binding guidelines.

As noted above, in Ireland patients present prescriptions to the pharmacist that can be categorised as either generic or brand name. Since pharmacists are required to dispense pharmaceuticals as prescribed, it is only for generic prescriptions that the pharmacist has the ability to decide whether or not to dispense a generic pharmaceutical. The issue is therefore for this subset of prescriptions what incentives or factors are likely to influence the pharmacist's dispensing decision.

In order to answer that question the context needs to be set. As set out in Chapter 4 generic manufacturers compete for pharmacy business by discounting off the wholesale reimbursement price[19] set by the State in its various pharmaceutical reimbursement schemes. To the extent that these wholesale reimbursement prices are used to price a pharmaceutical for the cash-paying patient the same incentives affect all patients, irrespective of who is responsible for funding the pharmaceutical. The discounts off the wholesale price are captured by the pharmacist, not the State or the cash-paying patient.[20] Thus the pharmacist has an incentive to dispense the generic product that offers the highest discount off the reimbursement price.[21]

The incentive for the pharmacist to seek out such discounts and dispense generic products will have increased as the State put increased pressure on the returns to pharmacists (i.e., the retail mark-ups/dispensing fees) from participating in the State pharmaceutical reimbursement schemes. This pressure consisted of regulations made under the Financial Emergency Measures in the Public Interest Act 2009 (FEMPI) which reduced pharmacy mark-ups and switched the basis on which pharmacists were reimbursed under State pharmaceutical reimbursement schemes towards greater reliance on a fixed dispensing fee and less on a percentage mark-up.[22]

These remarks concerning the impact of increased pressure on pharmacy returns on the greater use of generics are consistent with survey evidence.[23] The percentage of patients reporting that the medical practitioner and/or pharmacist had discussed prescription options although initially declining from 21 to 14 per cent between 2008 and 2009, increased to 41 per cent in 2012. Of these patients 38 to 39 per cent

19 The wholesale price is the ex-factory price plus an 8 per cent mark-up for the wholesaling function. The exception is fridge items where the wholesale mark-up is 12 per cent.

20 In part this reflects the lack of information available to patients concerning pharmaceutical prices which leads to wide variation in prices charged to cash-paying patients. Unlike State pharmaceutical reimbursement schemes the pharmacist is free to charge the cash-paying patient whatever the pharmacist deems appropriate. For details of the lack of price transparency at the pharmacy level and proposals to address the situation see Gorecki *et al.* (2012), Chapter 6, pp. 103–122; on the variation in price for the cash-paying customer, see NCA (2013).

21 Under the GMS Scheme there is no retail mark-up allowed for the pharmacist, but under the DP Scheme there is a mark-up which might provide an incentive for dispensing the higher priced patent-holder's product, but this mark-up has declined from 50 to 20 per cent in 2009. For details see Gorecki *et al.* (2012), Table 2.3, p. 23.

22 For details of these changes see Gorecki *et al.* (2012), pp. 23–26.

23 Details of the survey are discussed in the next section.

responded yes in 2008 and 2009 as to whether they ever had been offered a generic alternative when they went to fill in a prescription. However, by 2012 that percentage had increased to 71 per cent.[24]

5.2.4 The Patient

Patient acceptance of generics is likely to be an important factor facilitating their use. If patients are concerned about changes in the identity of the manufacturer of their pharmaceutical, whether from the patent holder to a generic or between generic manufacturers, then that is likely to make generic market penetration difficult. It will also limit the degree to which pharmacists can dispense generic pharmaceuticals. Furthermore, given limited price disclosure by pharmacists, cash-paying patients are unable to accurately trade-off the various aspects of different products (e.g., tablet size, packaging, price, etc.).

The evidence strongly suggests, however, that patients have confidence in generics. A recent survey conducted by Behaviour and Attitudes for Teva Pharmaceuticals Ireland, a leading generic manufacturer, in October 2012, found that 90 per cent of patients felt that generics were as safe as brand name pharmaceuticals.[25] There has been a marked increase in the acceptance of generics. In 2009, 65 per cent of patients would accept a generic if offered one by their medical practitioner or pharmacist, while 30 per cent would refuse; in 2012 the corresponding numbers were 96 per cent and 4 per cent, respectively.[26] This survey evidence is consistent with the press coverage in Ireland which is by and large favourable to greater use of generic pharmaceuticals.[27]

Furthermore, when asked what was the main reason for using a generic, the overwhelming reason cited by patients was cost (54 per cent), followed by pharmacist recommendation (23 per cent), the view that generics provide equal or better value than branded generics (14 per cent), and medical practitioner recommendation (9 per cent).[28] Cost was a factor particularly for younger persons reflecting the fact that these patients would most likely be under the DP threshold[29] and hence paying for the pharmaceuticals as a cash-paying patient.[30] This evidence

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24 Ryan and Clarke (2013), Slide 13

25 Ryan and Clarke (2013), Slide 10. A comparable survey was also carried out for 2008 and 2009. The sample size of the 2012 survey was 1,001 persons aged 16 and over.

26 *Ibid,* Slide 14.

27 It is also consistent with a subsequent Behaviour and Attitudes survey conducted for the IMB, the results of which were summarised in a press release dated 6 June 2013. For details see http://www.imb.ie/EN/News/Irish-consumers-have-increased-awareness-of-Generic-Medicines.aspx. [last accessed 7 June 2013].

28 *Ibid*, Slide 8.

29 Under the DP Scheme patients (including their families) are responsible for the first €144 expenditure of pharmaceuticals per month; above that threshold the State pays 100 per cent of the cost.

30 In contrast, pharmacist recommendation was more likely for older patients.

suggests that patients in Ireland are sensitive to price when purchasing pharmaceuticals and is consistent with reports of residents of Ireland getting their prescriptions filled in Northern Ireland due to lower prices.[31]

5.2.5 State Pharmaceutical Reimbursement Schemes

The influence of the State pharmaceutical reimbursement schemes on the usage of generics has already been alluded to above. At the present time the reimbursement price that a pharmacist receives for dispensing a pharmaceutical varies by scheme. However, common to all schemes is the ex-factory price plus a wholesale mark-up of 8 per cent. The ex-factory price is set as discussed in Chapter 3. Under the GMS Scheme the pharmacist receives no retail mark-up over the ex-factory price plus the wholesale mark-up, just a sliding scale dispensing fee depending on the number of items dispensed by the pharmacy. In contrast, under the DP and LTI schemes the pharmacist receives a 20 per cent mark-up over the ex-factory price and the 8 per cent wholesale mark-up and the same sliding scale dispensing fee as under the GMS Scheme.[32]

These schemes, as noted above, set a wholesale price for generics, which given extensive discounting, is in excess of the actual cost of the generic to the pharmacist for reasons set out earlier in this chapter, but also in Chapter 3. This reflects the fact that the ex-factory price of a generic is a percentage of the patent-holder's price prior to the entry of the generic. It is not linked to the cost of these pharmaceuticals to the pharmacist. As a result, to a considerable extent, the benefits of price competition between generic manufacturers accrue to pharmacies, not to the State or the cash-paying patient.

5.2.6 Health (Pricing and Supply of Medical Goods) Act 2013

The Health (Pricing and Supply of Medical Goods) Act 2013 is designed, amongst other things, to increase the usage of generics and reduce the price of interchangeable pharmaceuticals.[33] This Act, which we will refer to as the Health Act 2013, introduces generic substitution and reference pricing. Generic substitution permits the pharmacist to select a different pharmaceutical product from that prescribed on a brand name prescription, for pharmaceuticals that will be designated as interchangeable by the Irish Medicines Board (IMB).[34] A reference price is a common price for a group of interchangeable pharmaceutical products. The reference price will constitute the reimbursement price for the various State

31 See for example, Dan Keenan, 'Prescription shoppers head North for big savings'. *Irish Times*, 9 April 2013.

32 For further details see Gorecki *et al.* (2012), Table 2.3, p. 23.

33 Other important aspects of the Act will be discussed in Chapter 7.

34 The Health Act 2013 also deals with dispensing a generic prescription using the common name or INN.

pharmaceutical reimbursement schemes, except where the medical practitioner uses a no substitution prescription.[35] The DoH has asked the IMB to prioritise 20 of the leading pharmaceuticals including statins, PPIs, ACE inhibitors and angiotensin II receptor blockers for designation as interchangeable.[36]

Setting the Reference Price. Section 24 (3) of the Health Act 2013 sets out the factors that the HSE or the Executive *shall* take into account when setting the reference price:

a) the ability of suppliers of the relevant listed items to meet patient demand for the relevant listed items,

b) the value for money afforded by the relevant listed items,

c) the equivalent relevant prices (if practicably available) of the relevant listed items in all other Member States where one or more than one of the relevant listed items is marketed,

d) the relevant prices of therapeutically similar listed items,

e) the resources available to the Executive, and

f) the terms of any agreement in place (whether entered into before, on or after the commencement of this section) between the Executive and any representative body of the suppliers of drugs, medicines or medical or surgical appliances where the agreement relates, whether directly or indirectly, to the price of one or more of those items.

The agreements between the State and the IPHA and APMI are only one factor (f) to be taken into account in setting the reference price. This suggests that the reference price will be at or below that specified under these agreements as set out in Chapter 3.[37]

Section 24 does not settle, however, the question of *how* the reference price will be set, what methodology or mechanism will or should be used. Instead, it lists a wide ranging set of six factors that *shall* be taken into account. There are a number of different, but not necessarily mutually exclusive, ways in which the reference price could be set, including:

- tendering system for high volume interchangeable pharmaceuticals[38]

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35 The reference price can only be set once the IMB has designated a group of pharmaceutical products as interchangeable.

36 'IMB FAQ on the Health (Pricing and Supply of Medical Goods) Bill 2012,' 27 February 2013. DoH, personal communication, 14 May 2013. The 20 pharmaceuticals were also listed in a written response to Dáil questions on 16 April 2013. For details see http://oireachtasdebates.oireachtas.ie/Debates%20Authoring/DebatesWebPack.nsf/takes/dail2013041600102#N41. [last accessed 30 May 2013].

37 This was confirmed in discussions with the DoH and HSE held on 22 April 2013.

38 This option would appear to be consistent with Section 24(4) of the Health Act 2013 which states that the HSE 'may use a competitive process to set the reference price for a relevant group of interchangeable medicinal products'.

- benchmarking against the prices charged for the interchangeable pharmaceutical products in other Member States as occurs, for example, with new pharmaceuticals under the 2012–2015 State/IPHA Agreement
- requesting manufacturers of interchangeable pharmaceuticals to submit prices and then using a rule such as the lowest or the median to select the reference price (these prices would almost certainly at least match those set out in the various agreements between the State and the pharmaceutical manufacturer representative bodies)
- a combination of the latter method together with claw backs from pharmacists if there is evidence of a substantial discounting by generic and brand holder manufacturers off the reference price.[39]

There are advantages and disadvantages associated with each option. In our earlier work for the HSE we discussed options and argued in favour of tendering for certain high volume interchangeable pharmaceuticals and something similar to the last of the four options outlined above for other interchangeable pharmaceuticals.[40]

An examination of the June 2012 Regulatory Impact Analysis (RIA) of the Health Bill 2012 does not specify the method by which the reference price will be set,[41] nor does the Explanatory Memorandum that accompanied the Health Bill 2012. A series of presentations in November 2012 on the Health Bill 2012 by the IMB, DoH and HSE, the latter with the title, 'Reference Pricing – Operational Matters,' do not shed any additional light on the way in which the reference price will be set.[42] There are at least three reasons for concern over the lack of detail in how the reference price will be set.

First, the RIA process is an important *ex ante* method for ensuring that regulation in Ireland is thoroughly evaluated. It is a tool used for the structured exploration of different options to address particular policy issues'.[43] Furthermore, the RIA is 'also a means of improving the quality of governance by increasing the transparency and legitimacy of the regulatory process'.[44] It is designed to contribute to achieving 'efficiency by generating more detailed information in relation to cost and allowing

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39 Claw backs are used in the UK. For details see IMS Institute for Health Care Informatics (2012), p. 140. In the province of Ontario, where concerns about discounts off the government reimbursement price to pharmacists from manufacturers date back to the 1970s, numerous attempts have been made to capture the discounts in the form of lower reimbursement prices. For a discussion see Gorecki *et al.*, 2012, Box 4.2, p. 64 and Gorecki, 1992.

40 See Gorecki *et al.* (2012), Chapter 4, section 4.5, pp. 56–79 for details.

41 For details see: http://www.dohc.ie/issues/reference_pricing/RIA.pdf?direct=1 [last accessed 11 April 2013].

42 These presentations, together with one by the IMB may be found at: http://www.dohc.ie/issues/reference_pricing/ [last accessed 27 April 2013].

43 Department of the Taoiseach, 2009, p. 3

44 *Ibid,* p. 3

more extensive analysis of alternative options for achieving policy objectives'.[45] Hence in order to conduct an RIA the alternative options need to be carefully specified to facilitate the RIA analysis, thus improving the quality of decision making and ensuring that the objectives of the regulation are more likely to be attained.

The Health (Pricing and Supply of Medical Goods) Bill 2012 (the Health Bill 2012) RIA states that manufacturers 'of off-patent medicines … currently have little incentive to compete on the basis of price. Price competition can be promoted by the introduction of generic substitution and reference pricing'.[46] At the present time, for multiple source off-patent pharmaceuticals,[47] competition takes place between manufacturers in the form of discounts or price reductions off the reimbursement price set by the State, to the pharmacist, which are not captured by the State. According to the Health Bill 2012 RIA, '[G]eneric substitution and reference pricing are expected to result in greater price reductions over a shorter period of time by promoting price competition between manufacturers of interchangeable medicines'.[48] However, the Health Bill 2012 RIA does not specify the mechanism or mechanisms (i.e., alternative options) by which price competition is likely to lead to lower prices. In other words, the incentives or competitive forces that may result in manufacturers of interchangeable pharmaceuticals lowering their ex-factory price to the State above and beyond that set out in the current agreements with the IPHA and the APMI are not specified.

Second, by detailing, if not in the legislation itself then at least in the supporting documentation, how the reference price is to be determined allows debate over the merits of the various alternatives and also ensures that the legislation is consistent with the preferred option. Although there is little information in the public domain on this issue of setting the reference price, the HSE inform us that there has been extensive consultation with the relevant groups such as patient representatives, pharmacists, medical practitioners, and pharmaceutical manufacturers on this and on generic substitution.[49] Perhaps not surprisingly given the diverse interests and incentives there is no consensus on how the reference price should be set. Some groups want a high reference price, while others want a low price but with security of supply. Many groups do not want tendering, arguing it leads to problems of firms withdrawing from the market. Although such consultation is clearly useful, given the lack of consensus it does not resolve the problem of how the reference price is to be

45 *Op cit,* pp. 3-4

46 Paragraph 1.3 of the Health Bill 2012 RIA.
For details see: http://www.dohc.ie/issues/reference_pricing/RIA.pdf?direct=1 [last accessed 11 April 2013].

47 In other words, the set of pharmaceuticals some of which will be designated groups of interchangeable pharmaceutical products by the IMB under the Health Act 2013.

48 Paragraph 1.5 of the Health Bill 2012 RIA
For details see: http://www.dohc.ie/issues/reference_pricing/RIA.pdf?direct=1 [last accessed 11 April 2013].

49 HSE, personal communication, 16 May 2013

set, nor does it necessarily ensure that the legislation, despite giving the HSE considerable discretion, is consistent with the preferred method(s) of setting the reference price.

One alternative option for setting the reference price is to rely initially on the ex-factory price based on the agreements between the State and the representative pharmaceutical manufacturer bodies.[50] However, where there is evidence of substantial price discounting by pharmaceutical manufacturers off these ex-factory prices, then the State could impose unilateral claw backs by reducing the reference price further.[51] We have been informed that while the State does not intend to use any mechanism of retrospective claw back it expects to use discounting intelligence to assist in prospective price-setting.[52]

Third, detailing how the reference price will be determined permits a shared understanding to develop between the State, on the one hand, and those involved in the delivery of pharmaceuticals, from the manufacturers to the pharmacist, on the other. Based on this shared understanding those involved in the delivery of pharmaceuticals can adjust to the legislative changes. However, if, as is the case here this has not been done, then manufacturers, wholesalers and pharmacists will find it more difficult to be able to anticipate and adapt to change. Furthermore, to the extent that those involved in the delivery of pharmaceuticals have concerns about the reference price mechanism it is not clear how these concerns can be taken into account once the legislative process is complete.[53] Pharmacists, for example, might argue that discounts are essential for their business model and hence any claw back mechanism is likely to jeopardise that model.[54] In any event the discussion above demonstrates the widely differing attitudes towards setting the reference price.

Generic Substitution. The Health Act 2013 sets out the rules concerning the procedure to be followed by the pharmacist in selecting a different brand from that prescribed by the medical practitioner. The Health Act 2013 puts an onus on the pharmacist to offer the least expensive medicine *in stock* to the patient. The pharmacist explains to the patient that the product they are supplying has the same

50 The DoH and the HSE state that this is not an option that they intend to pursue. DoH/HSE, personal communication, 24 May 2013.

51 Reference to the high prices of generics revealed in Chapter 4 would appear to provide grounds under Section 24(3)(c) for such price reductions.

52 HSE, personal communication, 31 May 2013

53 While it is the case that Section 25 and Part 4 of Schedule 1 of the Health Act 2013 set out consultation procedures with respect to individual reference pricing decisions, this is not the same as a consultation exercise on the methodology to be employed in setting the reference price before it is applied in individual cases.

54 See, for example, Paul Cullen, 'Discounts on generics subsidise pharmacies'. *Irish Times*, 18 March 2013. See http://www.irishtimes.com/news/discounts-on-generics-subsidise-pharmacies 1.1329325?mode=print&ot=example .Ajax PageLayout.ot [last accessed 29 April 2013].

ingredients as the previous pharmaceutical but may look different. If a patient has a preference for an interchangeable pharmaceutical that has a higher reimbursement price than the reference price, then the patient will be required to pay the difference in price; if the medical practitioner, for clinical reasons, takes the view a higher-priced interchangeable pharmaceutical is necessary then they may write a no substitution prescription and the State (or the patient)[55] will pay the higher price. Interchangeability will take place at the ATC 5 level.[56] Hence therapeutic substitution (at the ATC 4 level) will not be permitted under the Health Act 2013. It is an issue we return to in Chapter 6.

***Interaction of Reference Pricing and Generic Substitution*.** There is potential difficulty with the proposed interaction of generic substitution and reference pricing, which is illustrated in Table 5.1. Assume that there are four products in a group of interchangeable products, the patent holder and three generics. The generic manufacturers charge different prices, with, in this example, the lowest price being used by the State as the reference price. The table presents four possible options in terms of the pharmaceutical products that the pharmacist stocks. Attention is confined to the case where the patient that presents a prescription is cash-paying and the prescription presented is for the patent-holder's product and the pharmacist in accordance with the Health Act 2013 offers the patient the choice of the least expensive interchangeable pharmaceutical product in stock.[57]

Under Options A and D the pharmacist will offer the patient the lowest priced product which is generic 3. The patient thus pays the reference price should they decide to select the generic. However, under Options B and C the pharmacist does not stock the lowest priced interchangeable pharmaceutical product, but instead stocks the more expensive generic 1 and/or generic 2. In these two options the patient, if they decide to accept a generic, will pay more than the reference price. What choice will the pharmacist make?

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55 This will depend whether or not the patient is eligible for one of the State pharmaceutical reimbursement schemes.

56 Section 5(5)(a) of the Health Act 2013. The meaning of this section was clarified by the HSE, personal communication, 7 May 2013.

57 It is assumed that when a prescription is presented for the patent holder's more expensive pharmaceutical product, under the GMS Scheme or the DP Scheme (where the €144 monthly threshold is exceeded), and the patient accepts an interchangeable pharmaceutical product, that the State pays the reference price irrespective of the pharmaceutical product dispensed within the interchangeable pharmaceutical group. The patient may or may be required to make a contribution depending on whether the pharmacist has in stock pharmaceutical products at or below the reference price. Even if the only pharmaceutical in stock is priced slightly above the reference price it is assumed that there is nothing to prevent the pharmacist, should they so wish, from charging the reference price.

TABLE 5.1 Operation of Reference Pricing and Generic Substitution, Health (Pricing and Supply of Medical Goods) Act 2013 – Illustrative Example

		Price	Pharmacist Stocks			
			Option A	Option B	Option C	Option D
		€	€	€	€	€
A Group of Interchangeable Pharmaceutical Products	Patent Holder Brand[a]	0.50	✓	✓	✓	✓
	Generic 1[b]	0.40	-	✓	✓	✓
	Generic 2[c]	0.35	-	-	✓	✓
	Generic 3[d]	0.30	✓	-	-	✓
	Reference Price[e]	0.30				

Notes
a The patent-holder ex-factory price is 50 per cent of the price prior to the entry of the generic under the 2012–2015 State/IPHA Agreement. It is assumed that this latter price was €1.00.
b Generic 1 sets an ex-factory price that is 60 per cent less than the price prior of the patent holder prior which is consistent with the 2012-2015 State/APMI Agreement. It is assumed that this latter price was €1.00.
c Generic 2 decides to lower the price below generic 1.
d Generic 3 decides to lower the price below generic 1 and 2.
e It is assumed that the State sets the reference price based on the lowest priced interchangeable pharmaceutical product.

Source: Health (Pricing and Supply of Medical Goods) Act 2013, Tables 3.3 and 3.4

A generic manufacturer wants to make their product as attractive as possible to the pharmacist. By pricing somewhat above the reference price, the generic manufacturer is able to offer the pharmacist a higher margin to the cash-paying patient than if the reference price was used. At the same time because generic manufacturer 1 or 2 offers substantial discounts that bring down the actual cost below the reference price the pharmacist is able to accept the reference price for State schemes. Since it is likely that generic manufacturers will have similar costs, the generic price exclusive of discounts and rebates is likely to be quite similar across generic manufacturers. The pricing structure of generic 2 and 3 enables the pharmacist to price discriminate between different classes of patient, cash-paying as compared to those funded by the State.

In our earlier report[58] we argued that under a reference pricing system where the reference price is set based on price quotations (or a similar mechanism) from generic manufacturers[59] and then competition takes place between generic manufacturers for market share, that there will be an incentive for generic manufacturers to submit a particular price. This would be *low* enough to ensure savings for the State compared to the patent holder's price (e.g., the price set in the 2012–2015 State/APMI Agreement); but *high* enough for generic manufacturers to be able to offer discounts/rebates to pharmacists in order to gain market share. There is little incentive for the generic manufacturer to offer a low price for the purposes of reimbursement since other generic firms easily match the lower price and hence it is not at all obvious it will lead to an increase in business for the generic manufacturer initiating the price reduction. This has been the experience in Ontario for the reference pricing system that it has operated for several decades, and there

[58] Gorecki *et al.*, 2012, pp. 63–68
[59] Excluding competitive tendering as a reference price-setting mechanism

is clearly a danger that it might be repeated in Ireland.[60] However, in the absence of details on how the reference price in Ireland will be set it is not possible to state with any precision whether this is likely to occur.

It could, of course, be argued that this reasoning is flawed. Patients can shop around, but they need to be informed as to the reference pricing regime and how it operates as well as requiring an incentive to do so. The HSE and the DoH will provide information on how reference pricing and generic substitution will work, but it is not clear that pharmacists can and will provide information on whether or not they charge the reference price. At present there is little provision of information by pharmacists to influence patient choice, in part because of the approach of the industry regulator, the Pharmaceutical Society of Ireland (PSI). It has not, for example, mandated posting of information concerning prices/fees, as has occurred with respect to dentistry in an initiative of the Dental Council of Ireland, or facilitated the delivery of some services over the internet as has the Medical Council of Ireland.[61] The resulting lack of competition is reflected in the wide variation in price for pharmaceuticals in Ireland for the cash-paying patient,[62] suggesting that the pricing rules set for State reimbursement may not be followed for these patients at the present time. As we argued in our earlier report, there are strong grounds for much greater price disclosure by pharmacists so that consumers can make informed choices.[63] Why, for example, should pharmacists not be required to post, in a prominent place in the pharmacy, the price charged for the leading 20 interchangeable pharmaceuticals that are to be designated by the IMB, together with the reference price? At the pharmacist's discretion this could also be published online.

The DoH and the HSE inform us that the PSI have undertaken to provide guidance for pharmacists in respect of their obligations in relation to reference pricing and generic substitution against the background of the statutory Code of Conduct.[64] The PSI advises that pharmacists should be in a position to provide patients with whatever information or clarification they require about prescribed pharmaceuticals, including information about the pricing of those pharmaceuticals. The PSI is currently examining options to achieve greater price transparency for patients.

Notwithstanding the lack of precision in the Health Act 2013 and the surrounding documentation (e.g., the RIA) as to how reference pricing will operate, this should not take away from the fact that it represents a significant step towards the

60 Gorecki, 1992, 1993
61 Gorecki *et al.*, 2012, pp. 119–122
62 NCA, 2013
63 Gorecki *et al.* (2012), Chapter 6, pp. 103–122
64 DoH/HSE, personal communication, 24 May 2013

possibility of lowering ex-factory pharmaceutical prices in Ireland over and above those measures already agreed between the State and the pharmaceutical representative bodies. The Health Act 2013 permits for the first time generic substitution. It provides the HSE with legislative authority to set a reference price for the purposes of reimbursement based on a wide array of considerations that extend beyond the current agreements with industry representative bodies. Tendering, for example, is an option under the legislation. Unilateral price reductions based on the fact that prices are lower in other Member States is permissible. As a result under the Health Act 2013 the State may succeed in capturing a significant portion of the discounts, kickbacks and deals that currently accrue to other parts of the manufacturing, wholesaling and pharmacy chain. An important corollary of these reforms is ensuring that the cash-paying patient also benefits, which requires more price disclosure and competition at the pharmacy level, issues we addressed in our earlier report but on which progress appears to be slow.[65]

5.3 The Importance of Generics

5.3.1 Introduction

In this section we quantify the extent of the usage of generics in Ireland by examining their market share in 2010, 2011 and 2012. We also make comparisons of generic penetration in Ireland vis-à-vis a number of other Member States, but for 2009 and 2010 only (due to data availability). In some instances we compare generic penetration at the ATC 5 level, while in other cases, particularly in comparison with other Member States, the comparison will be at a higher level of aggregation (e.g., for all prescription products). To the maximum extent possible we will present results both for the market share of generic pharmaceuticals in terms of value and volume since there is likely to be a difference between the two. There will be no difference if generic and brand holder products of a multiple source off-patent pharmaceutical charge the same price, but since the former usually have a lower ex-factory price, the market share of generics will be lower measured in value rather than volume.

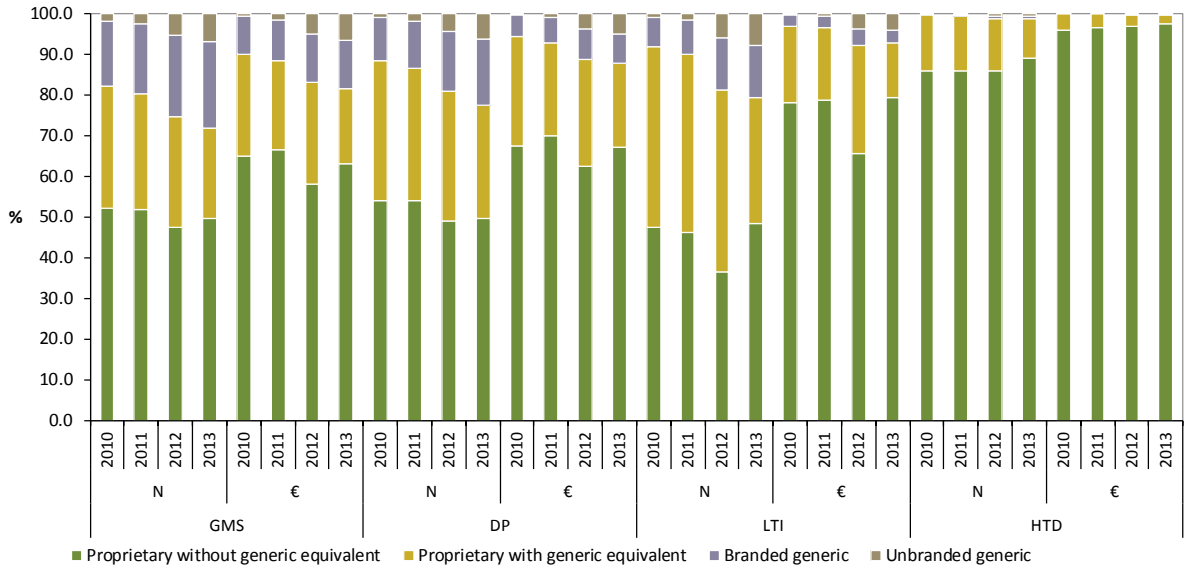
Based on our discussion in Section 5.2, the expectation is that the usage of generics in Ireland will be low. This reflects the likely behaviour of prescribers and the current limitations that pharmacists face with a 'dispense as written' requirement and hence the inability to select a generic pharmaceutical for brand name prescriptions. That is likely to change, of course, with the implementation of the Health Act 2013, but this will not be captured by the data that we present below. The pharmacist's ability to substitute a generic will, in any event, only apply to interchangeable pharmaceuticals.

[65] Gorecki *et al.* (2012), Chapter 6, pp. 103–122

5.3.2 Ireland: Usage of Generics, 2010–2012/3

The aggregate share of generic pharmaceutical products across all pharmaceuticals reimbursed by the State under the four main pharmaceutical reimbursement schemes is presented in Figure 5.1. The figure presents pharmaceutical type using the classification in Table 2.3. Single source in-patent pharmaceuticals are proprietary without a generic. Multiple source off-patent pharmaceuticals are supplied either by brand holder (proprietary with a generic) or generic (branded and unbranded generic) manufacturers. The market shares of these various categories of pharmaceutical type as presented in Figure 5.1 are both in value and volume terms.

FIGURE 5.1 Market Share by Pharmaceutical Type,[a] GMS, DP, LTI and HTD Schemes, by Volume and Value, 2010–2013[b]



Notes a The pharmaceutical type is determined in December of each year, but the value and volume refer to the whole of the year.
b Year-to-date 31 March 2013

Source: ESRI calculations based on HSE, personal communication, 9 April 2013 and DoH, personal communication, 29 May 2013.

It is clear from Figure 5.1 that the importance of the different pharmaceutical types varies by State pharmaceutical reimbursement scheme. To a considerable degree this reflects the pharmaceuticals that are eligible for reimbursement under the different schemes. Pharmaceuticals under the High Tech Drugs (HTD) Scheme, for example, are prescribed or initiated in hospitals and include items such as anti-rejection drugs for transplant patients or pharmaceuticals used in conjunction with chemotherapy or growth hormones. In contrast, pharmaceuticals eligible under the GMS and DP schemes are generally prescribed by a medical practitioner in the community. Nevertheless, there are differences in the importance of different pharmaceutical types as between State pharmaceutical reimbursement schemes where the set of eligible pharmaceuticals is likely to be quite similar. In one such case where this is likely to be the case, between the GMS and DP schemes, we explore the reasons for the differences further below.

Irrespective of the State pharmaceutical reimbursement scheme, the share of single source in-patent pharmaceuticals has fallen between 2010 and 2012, both in volume and value terms. In the case of the GMS Scheme the share of single source in-patent pharmaceuticals has declined from 52.0 per cent in 2010 to 47.4 per cent in 2012 (measured in volume terms). The corresponding percentages for the DP Scheme were 54.1 and 48.9, respectively. With the expiry of patents on leading pharmaceuticals occurring at the present time and in the near future – the so called patent cliff – the importance of single source in-patent pharmaceuticals is expected to decline further. It has been estimated that in eight key markets the pharmaceuticals losing patent protection in 2011, 2012 and 2013 accounted for 8, 6 and 3 per cent, respectively, of the previous year's sales.[66]

Multiple source off-patent pharmaceuticals, taken as a group, have increased their value and volume across all the State pharmaceutical reimbursement schemes in Figure 5.1 between 2010 and 2012. This is of course, a corollary of the decline of single source in-patient pharmaceuticals. However, what is striking is that the patent-holder's market share is much larger than the combined share of generic manufacturers for multiple source off-patent pharmaceuticals. Nevertheless despite this, the importance of generics has increased. In the case of the GMS Scheme in 2010 the patent holder accounted for 63 per cent of all multiple source off-patent pharmaceuticals measured by volume, but by 2012 this had declined to 52 per cent. The corresponding percentages for the DP Scheme were 75 and 63, respectively. In part this may reflect a timing issue. As pharmaceuticals come off patent and generic manufacturers enter, generic market share will be low and build up gradually over time. In order to explore this issue further, and to avoid the complication in interpreting the patterns in Figure 5.1 due to the patent cliff, we switch our attention to the market share of generic pharmaceuticals over time for individual multiple-source pharmaceuticals (i.e., ATC 5).

The market shares of generic pharmaceuticals for 10 leading multiple source off-patent pharmaceuticals are presented in Table 5.2, by volume and value, for the GMS and DP schemes, for 2010, 2011 and 2012. The rankings refer to the leading proprietary pharmaceuticals with a generic equivalent by value in 2010, identified separately for the GMS and DP schemes. There is considerable variability across the different pharmaceuticals in the penetration of generic manufacturers. This will no doubt reflect differences such as in the length of time that the patent is expired and the ability of brand name manufacturers to 'evergreen', and so on. Two broad conclusions can be drawn from Table 5.2.

[66] The eight markets are Canada, France, Germany, Japan, Italy, Spain, UK and US. For details see Sheppard (2010), Figure 12, p. 12.

TABLE 5.2 Generic Market Shares (Branded and Unbranded) of Leading Pharmaceuticals with a Generic Equivalent,[a] GMS and DP Schemes, by Volume and Value, 2010–2012

	ATC Description	ATC	2010		2011		2012	
			Volume	Value	Volume	Value	Volume	Value
			%	%	%	%	%	%
GMS	Alendronic acid	M05BA04	32.2	25.6	41.3	48.5	55.3	55.3
GMS	Clopidogrel	B01AC04	18.4	14.5	34.2	32.7	49.0	46.3
GMS	Esomeprazole	A02BC05	8.2	6.3	34.8	35.2	51.8	49.4
GMS	Omeprazole	A02BC01	57.9	59.9	63.0	62.5	69.2	66.8
GMS	Pantoprazole	A02BC02	34.5	37.2	48.2	46.7	61.0	59.8
GMS	Pravastatin	C10AA03	39.4	46.6	46.2	49.3	55.0	54.8
GMS	Risedronic acid	M05BA07	0.0	0.0	18.7	19.0	31.7	30.2
GMS	Rosuvastatin	C10AA07	2.8	2.0	27.6	25.4	46.7	43.2
GMS	Tamsulosin	G04CA02	26.8	21.3	33.8	31.6	42.1	39.1
GMS	Venlafaxine	N06AX16	20.7	24.4	27.6	29.2	35.7	37.6
DP	Alendronic acid	M05BA04	19.7	15.1	28.1	34.3	41.1	40.7
DP	Anastrozole	L02BG03	0.0	0.0	6.2	4.9	15.8	12.5
DP	Clopidogrel	B01AC04	11.8	9.1	24.0	22.2	38.0	34.2
DP	Esomeprazole	A02BC05	4.6	3.4	22.5	22.8	36.7	34.1
DP	Omeprazole	A02BC01	38.5	40.8	44.6	44.6	53.2	50.2
DP	Pantoprazole	A02BC02	22.6	24.3	36.1	34.0	49.5	47.1
DP	Pravastatin	C10AA03	27.2	33.0	33.4	35.7	41.9	40.5
DP	Risedronic acid	M05BA07	-	-	10.5	10.4	21.4	19.7
DP	Rosuvastatin	C10AA07	1.6	1.1	20.0	18.0	36.2	32.4
DP	Venlafaxine	N06AX16	13.7	16.1	20.3	20.7	28.5	28.4

Note: a Pharmaceuticals are ranked in terms of the top 10 proprietary products with a generic equivalent on the relevant scheme in 2010.

Source: ESRI calculations based on HSE, personal communication, 9 April 2013.

First, the share of generic manufacturers for the leading multiple source off-patent pharmaceuticals is similar in terms of volume and value.[67] In other words, the price of the generic manufacturer for a particular pharmaceutical is quite similar to that of the patent holder. This is consistent with the discussion in Chapter 3 on pricing and with the IMO's observation, quoted above, that there was often little reason for a medical practitioner to prescribe a generic pharmaceutical given the small price difference between the generic and the brand holder's version of a given pharmaceutical. It should be noted, however, that the results in Table 5.2 refer to value and volume over 12 months in 2012 and hence may not capture or reflect for some pharmaceuticals the fact that substantial ex-factory price differences between the patent holder and generic manufacturer have developed since November 2012.[68]

67 It should be noted that, in general, the price of a generic manufacturer is below that of the brand holder, meaning that the market share of generic manufacturers should be less in terms of value than volume. However, this is not always the case for 2010 and 2011. This reflects differences in the timing of price reductions under the agreements between the State with IPHA and AMPI. Typically, as noted in Chapter 3, agreement was reached first with the IPHA and subsequently with the APMI. Hence price reductions agreed with the IPHA may have come into effect before those agreed with the APMI, resulting in the generic price exceeding the patent-holder's price for a multiple source off-patent pharmaceutical for short periods.

68 This is the case for example, with respect to clopidogrel, esomeprazole, risedronic acid, rosuvastatin, tamsulosin and anastrozole (HSE, personal communication, 14 May 2013). Details of the price differences between the patent holder and the generic are provided above. These price differences reflect the fact that when a pharmaceutical no longer has patent protection and experiences generic competition the generic manufacturer's ex-factory price is set at 50 per cent of the patent holder's ex-factory price prior to generic entry, while the patent holder's price is initially set at 70 per cent, falling to 50 per cent a year later. For details see Tables 3.3, 3.4 and 3.5.

The second conclusion to be drawn from Table 5.2 is that the market share of generic manufacturers of multiple source off-patent pharmaceuticals has increased dramatically over the period 2010 to 2012. Indeed, it has more than doubled: for the GMS Scheme, measured in volume terms, from, on average, 24.1 per cent in 2010 to 49.7 per cent in 2012; and, for the DP Scheme, from 14.0 per cent to 36.2 per cent, respectively.[69] These data refer to what is dispensed by the pharmacist and not what is prescribed by the medical practitioner. The increasing use of patient management systems that issue electronically generated prescriptions by medical practitioners and patient preference for generic pharmaceuticals may have led to more generic prescriptions. However, the evidence, albeit somewhat limited, suggests that the change in the importance of generics is also likely to reflect, in part at least, the behaviour of pharmacists.

For reasons set out above, the financial incentive for pharmacists to dispense generic products increased because of the squeeze that the State put on pharmacy returns, while there is no corresponding pressure on medical practitioners that is likely to affect their prescribing behaviour. Also, there are reports of concerns by the IMO[70] that pharmacists are dispensing generic pharmaceuticals for a brand name prescription without the medical practitioner's knowledge. It appears that pharmacists may be anticipating the commencement of the Health (Pricing and Supply of Medical Goods) Act 2013. Furthermore, given the small price differences between the generic and the equivalent patent holder pharmaceutical product patients have little incentive to request the generic. This applies particularly for the GMS Scheme where the State pays the pharmaceutical cost and the recently introduced flat charge (i.e., co-payment) is unrelated to the cost of the pharmaceutical. However, as noted above some difference is beginning to develop for some pharmaceuticals between the patent holder and the generic manufacturers, which is consistent with the 2012–2015 agreements between the State and the pharmaceutical representative bodies set out in Chapter 3.[71]

5.3.3 Ireland: Usage of Generics in a Comparative Context

In this section we compare the usage of generics in Ireland with other Member States as well as countries beyond the EU. Ideally, in interpreting these data we would want to be able to consider the likely factors that influence the market share of generic manufacturers in each country (e.g., whether there is mandatory generic

69 The lower market share of generics in the DP Scheme may reflect the fact that pharmacists receive a retail mark -up over the wholesale price, whereas there is no such retail mark-up under the GMS Scheme. For further discussion see Gorecki *et al.* (2012), pp. 128–129.

70 See, for example, Susan Mitchell, 'Pharmacists are substituting drugs to increase profit, warns IMO'. *Sunday Business Post*, 31 March 2013.

71 In the case of pharmaceuticals that experience generic competition for the first time, the generic will be 29 per cent less expensive than the patent holder. For details see Table 3.5. However, for reasons discussed in Section 4.3.5, in some instances the price reduction might have been brought forward.

substitution on the part of pharmacists or price differences between brand name and generic products, etc.) and hence be in a position to predict the broad ranking across the various jurisdictions. As we have seen in the case of Ireland, a large increase in the market share of generics between 2010 and 2012 in Table 5.2 is unlikely to have resulted in significant savings for the State for these particular pharmaceuticals due to the small price difference between the generic and the patent holder. This is not, of course, to deny that under the various agreements discussed in Chapter 3 that there would have been an initial price decline once the generic manufacturer entered the market. In contrast to Ireland a large market share of generic manufacturers in a jurisdiction that purchased multiple source off-patent pharmaceuticals on a tender basis might be associated with low prices.[72]

We present two sets of comparisons. The first, in Table 5.3, is similar to Figure 5.1, and shows sales by generic manufacturers as a share of the overall retail market for pharmaceuticals for 2010 for various groupings of Member States. Market share is presented by both volume and value. In the case of Ireland the percentages appear to be on the high side, although it is important to point out that the data in Table 5.3 refer to the overall retail market, i.e. including pharmaceuticals dispensed that are not funded through the State pharmaceutical reimbursement schemes.[73] In terms of volume, for example, the market share of generic manufacturers, summed across all the State pharmaceutical reimbursement schemes in Figure 5.1 for 2010 is 16.3 per cent; summed across only multiple source off-patent pharmaceuticals it is 34.3 per cent. This caveat should be borne in mind when considering the next table. Furthermore the same set of pharmaceuticals may not be off-patent in all Member States.

The main conclusion to be drawn from Table 5.3 is that generic penetration in the Irish pharmaceutical market in 2010, whether in volume or value terms, was low by EU standards. This conclusion applies at the EU level where the average penetration of generic was by volume 43 per cent (by value 18 per cent), but for Ireland 33 per cent (13 per cent). The conclusions do not vary much by Member State grouping, i.e. whether it is the Member States that constitute the basket of nine used in setting the Irish ex-factory price of a new pharmaceutical, the entire EU-15, or those Member States that joined with enlargement. Furthermore there is no obvious relationship between pharmaceutical price levels and generic penetration. From Chapter 4 we saw that the UK was a low-priced Member State for pharmaceuticals, while Germany was a high-priced Member State, yet Table 5.3 shows they are amongst the Member States with the highest penetration of generics.

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72 For a discussion see Gorecki *et al.* (2012), pp. 61–81.

73 In the Irish context, this would also include other State pharmaceutical schemes and pharmaceutical consumption by individuals below the monthly DP deductible (currently €144 per family per month).

TABLE 5.3 Generic Market Shares of Overall Retail Prescription Market[a] – EU Member States, by Volume and Value, 2010[b]

	Generic Market Share	
	Volume (%)	Value (%)
Basket of Nine Member States		
Austria	27	16
Belgium	28	13
Denmark	52	15
Finland	43	17
France	42	18
Germany	70	18
Netherlands	57	15
Spain	32	13
UK	60	23
Other EU-15		
Greece	38	16
Ireland	33	13
Italy	34	13
Portugal	37	28
Sweden	48	12
Enlargement		
Cyprus	53	12
Czech Republic	45	30
Hungary	43	28
Latvia	79	38
Poland	50	40
Romania	70	40
Slovakia	45	28
Slovenia	53	31
European Union[c]	**43**	**18**

Notes: a Measured in relation to the total prescription retail market.
b Or most recent data.
c Measured across as the average across those Member States in the table. No information was available for Bulgaria, Estonia, Luxembourg and Malta.

Source: Carone *et al.* (2012), Graph 3, p. 41

Next we turn our attention to the importance of generic manufacturers amongst only multiple source off-patent pharmaceuticals. This is similar to Table 5.2, but aggregated across all such pharmaceuticals. The results are presented in Table 5.4. The data is for 2009, except for Ireland which refers to 2010. This reflects that the data source for the table did not include Ireland. The figures for Ireland represent the market share of generic manufacturers as a share of all sales of multiple source off-patent pharmaceuticals summed across the four main State pharmaceutical reimbursement schemes in Figure 5.1. The data for Ireland is not strictly comparable to that of the other countries in the table which appears to refer to the utilisation of generic pharmaceuticals across both the community and hospital sector, public and private. The market shares are available for volume only.

TABLE 5.4 Generic Market Shares of Multiple Source Off-Patent Pharmaceuticals[a] – EU Member States and Other Countries, by Volume, 2009

	Generic Market Share
	Volume (%)
Basket of Nine Member States	
France	52
Germany	75
Spain	41
UK	71
Other EU-15	
Ireland	34
Italy	40
Enlargement	
Czech Republic	59
Hungary	46
Poland	73
Other OECD	
Australia	50
Canada	81
Japan	24
Turkey	51
US	89
Other	
Brazil	65

Notes: a Market shares for all countries are based on IMS Health data. However, for Ireland we use the data from Figure 5.1 for 2010 not 2009 summed across all four of the State pharmaceutical reimbursement schemes in the figure.

Source: Sheppard (2010), Figure 4, p. 3

The market shares in Table 5.4 are broadly consistent with those in Table 5.3. The market penetration of generic manufacturers is low in Ireland compared not only to various other groupings of Member States, but also to a number of OECD countries such as Australia, Canada and the US. Japan is the only example of a country with a lower market share for generics than Ireland. However, as noted above, it is difficult to draw any policy conclusions from these data, except that there is no reason for the market of generic manufacturers in Ireland not to increase, given the wide spectrum of regulatory and reimbursement schemes that exist in these different jurisdictions.

Of course, it could be objected that the data in Tables 5.3 and 5.4 relate to 2009 and 2010 and hence may not be as relevant today. This, it could be further argued, is particularly relevant in view of the increases in the generic market shares reported in Figure 5.1 and Table 5.2. However, while this is the case, it should be noted that with many countries facing austerity budgets and pressure on health expenditure, generic market shares may also have increased in these jurisdictions.

5.4 CONCLUSION

Ireland has traditionally had a low usage of generics, both in absolute terms and in comparison with other Member States. This reflected a number of factors including: the small price difference between the generic manufacturer and the patent holder; a 'dispense as written' prescription policy that restricted the discretion of the pharmacist to substitute a generic pharmaceutical; limited use of prescription by INN by medical practitioners[74]; and no certification of interchangeable pharmaceutical products. Nevertheless, despite these limitations, between 2010 and 2012 there was a substantial increase in the dispensing of generics for the leading multiple source off-patent pharmaceuticals in Ireland. Indeed, the market share of generics under the GMS Scheme doubled between 2010 and 2012 for this sample of leading pharmaceuticals to reach 50 per cent. It is not clear to what extent this increase in generic usage is due to changing practices by medical practitioners, patient preferences for generic products, and/or the dispensing behaviour of pharmacists.

Notwithstanding the lack of precision in the Health Act 2013 and the surrounding documentation (e.g., the RIA) as to how reference pricing will operate, this should not take away from the fact that it represents a significant step towards the ***possibility*** of lowering ex-factory pharmaceutical prices in Ireland over and above those measures already agreed between the State and the pharmaceutical representative bodies. The Health Act 2013 permits for the first time generic substitution. It provides the HSE with legislative authority to set a reference price for the purposes of reimbursement based on a wide range of considerations that extend beyond the current agreements with industry representative bodies. Tendering, for example, is an option under the legislation. Unilateral price reductions based on the fact that prices are lower in other Member States is permissible. As a result, under the Health Act 2013 the State may succeed in capturing a significant portion of the discounts, kickbacks and deals that currently accrue to other parts of the manufacturing, wholesaling and pharmacy chain.

An important corollary of these reforms is ensuring that the cash-paying patient also benefits, which requires more price disclosure and competition at the pharmacy level, issues we addressed in our earlier report but on which progress appears to be slow. There is no reason why pharmacists should not be required to post, in a prominent place in the pharmacy, the price charged for the leading 20 interchangeable pharmaceuticals that are to be designated by the IMB, together with the reference price. At the pharmacist's discretion this could also be published online.

[74] For details see Gorecki *et al.* (2012), pp. 134–136.

CHAPTER 6

Prescribing Practices

6.1 INTRODUCTION

In this chapter we consider the behaviour of prescribers in the community, i.e. medical practitioners[1] who are licensed to prescribe pharmaceuticals. Prescribers play a key role in driving expenditure on pharmaceuticals as patients must rely on their medical practitioner to make prescription decisions on their behalf. Prescribers use their clinical expertise to decide whether the patient needs a pharmaceutical, and if so, which product is most appropriate.

Apart from clinical needs and the expectations of the patient, prescriber behaviour is influenced by a variety of financial and non-financial factors such as: prescription guidelines; education and information[2]; monitoring and feedback; financial incentives (e.g., the ability to keep a proportion of savings generated from prescription of cheaper interchangeable products); and regulations concerning international non-proprietary name (INN) prescribing. It is also important to note that presciber behaviour in the community is also influenced by the behaviour of medical practitioners in the hospital sector. For example, GPs may be reluctant to change hospital specialist prescriptions.[3] In Section 6.2, we discuss current policy with respect to prescriber behaviour in Ireland and across the EU, while also examining some recent developments in the Irish context.

As noted in Chapter 5, data on prescriber behaviour in Ireland must be inferred from data on dispensing patterns. While other countries such as the UK report data on both prescribing and dispensing patterns[4], there is no such database available for Ireland. However, as there is currently a 'dispense as written' requirement for pharmacists in Ireland, we argue that data on dispensing patterns should provide a good approximation of prescribing patterns.[5]

1 In Ireland, medical doctors, dentists and a small number of nurses and midwives are permitted to prescribe pharmaceuticals. See Gorecki *et al.* (2012), p. 124 for further details.

2 Information on pharmaceutical products is also provided to medical practitioners by pharmaceutical companies as part of their marketing activities.

3 Feely *et al.* (1997) estimated that approximately 38 per cent of GMS prescriptions in the late 1990s were initiated by hospital doctors.

4 In the UK, data on prescribing and dispensing are available in a number of different formats (see Section 6.4).

5 This assumes that patients fill the entire prescription, i.e. they do not choose to exclude certain products for, for example, financial reasons. The issue of adherence (i.e., consuming dispensed pharmaceuticals correctly), while important, is not relevant to the discussion in this report.

In contrast to previous chapters, in this chapter we consider the behaviour of prescribers at the therapeutic sub-group level (i.e., ATC level 4), rather than at the chemical substance level (i.e., ATC level 5). For example, atorvastatin is just one of a group of five statins that are currently available on the Irish market.[6] The analysis in Chapter 5 considered the usage of generics and highlighted that, while the share of generics for particular pharmaceuticals has increased strongly in Ireland over the period 2010–2012, the potential for substantial cost savings in Ireland at present is limited due to the absence of large differences in price between branded and generic products.[7] However, this is beginning to change. Ex-factory price reductions in November 2012, under the agreements between the State and pharmaceutical trade associations, resulted in the price of some generic pharmaceutical products falling substantially compared to the patent holder's price. The commencement of the Health (Pricing and Supply of Medical Goods) Act 2013 will see further declines in the price of generic pharmaceutical products.

Substitution within therapeutic sub-groups, commonly termed 'therapeutic substitution' offers the potential for significant cost savings. It can also mitigate any tendency for pharmaceutical manufacturers to shift demand away from those products that have lost patent protection and are experiencing generic competition to higher-priced in-patent pharmaceuticals in the same therapeutic sub-group. Indeed, a number of countries such as Germany and the Netherlands, as well as the Canadian province of Saskatchewan (with respect to PPIs) implement reference pricing at this level, i.e. recognising that products are substitutable within therapeutic sub-groups.[8] Therapeutic substitution can be contentious. Substitution may have effects on individual patients (e.g., reduced adherence, increased potential for error).[9] It is also more resource-intensive in establishing the specific products (e.g., dosage form and strength) that may be considered therapeutically equivalent across ATC 4 groups. However, there are a number of therapeutic sub-groups where it is accepted that different ATCs may be substituted for one another for the majority of patients (e.g., PPIs, statins, ACE inhibitors).[10]

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6 There are eight statins within the therapeutic sub-group C10AA (HMG CoA reductase inhibitors), of which five are currently available on the GMS Scheme. HSE, personal communication, 9 April 2013 and http://www. whocc.no/ atc_ddd_index/?code=C10AA [last accessed 1 May 2013]

7 As explained in Section 3.3.3, this is largely due to the small size of the discount for generic products off the patent-holder price in the various agreements with the State and the IPHA and APMI up to late 2012. Chapter 3 discusses the provisions in the 2012–2015 IPHA and APMI agreements that are relevant to the pricing of branded and generic products in Ireland in greater detail.

8 Dylst *et al.*, 2012; Gorecki *et al.*, 2012. Other countries implement reference pricing at ATC level 3, i.e. pharmacological sub-group (Dylst *et al.*, 2012).

9 Duerden and Hughes, 2010

10 For patients who are simulataneously taking other products, substitution may not be appropriate. See also Vandoros, 2013.

In Section 6.3, data on dispensing patterns at ATC level 4 (i.e., therapeutic sub-group) for three groups of pharmaceuticals (proton pump inhibitors (PPIs), statins and ACE inhibitors) are used to evaluate the prescribing patterns of medical practitioners in Ireland. The analysis in this section, while illustrating the exent to which generics are used for particular pharmaceuticals, will also help to understand patterns of prescribing/dispensing within therapeutic sub-groups. Together, these three therapeutic sub-groups (PPIs, statins, ACE inhibitors) accounted for 14.2 per cent of all pharmaceuticals by volume and 18.1 per cent of all pharmaceuticals by value on the GMS Scheme in Ireland in 2012.[11] Sourcing comparable data on dispensing patterns for these three therapeutic sub-groups across the EU is difficult, so in Section 6.4 we focus on a comparison with the UK, for which comparable data are available. Section 6.5 concludes the chapter.

6.2 Current Prescribing Policy in Ireland[12]

The Medical Council's *Guide to Professional Conduct and Ethics for Registered Medical Practitioners* lays out the requirements for prescribing on the part of medical practitioners.[13] Currently, medical practitioners have considerable influence over the volume and product mix of pharmaceuticals that are dispensed due to the 'dispense as written' requirement for pharmacists. Prescribers are thus key players in the pharmaceutical market, and their decisions have important consequences for pharmaceutical expenditure. Internationally, policies targeting prescribers may be grouped into those concerning education and information, feedback and monitoring/auditing, financial incentives, and prescribing by INN.[14]

6.2.1 Education and Information

At present, Irish medical practitioners receive advice on prescribing from a variety of sources. The Medical Council advice asks prescribers not to 'rely solely or excessively on promotional literature distributed by pharmaceutical companies for information about particular drugs. You should seek independent evidence-based sources of information on the benefits and risks associated with medicines before prescribing'[15], although the sources of the independent evidence-based information are not specified. The guidelines also note that while medical practitioners have a duty to act in the best interest of their patients, they also 'should be aware of the wider need to use limited healthcare resources efficiently and responsibly'.[16]

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11 ESRI calculations based on HSE, personal communication, 9 April 2013.

12 This section draws heavily on Gorecki *et al.* (2012), ch.7.

13 Medical Council, 2009, section 59

14 Mossialos *et al.*, 2005; Godman *et al.*, 2011; Carone *et al.*, 2012

15 Medical Council, 2009, section 59

16 *Ibid*., section 49

Our earlier research recommended, on the basis of international evidence, that prescription guidelines for both GPs and hospital medical practitioners should be centralised and standardised.[17] As part of the announcement of the 2012–2015 State/IPHA agreement, the DoH announced the formation of a National Task Force on Prescribing and Dispensing. The task force will '... deliver significant cost savings in terms of achieving more cost conscious prescribing. The work of the Task Force will be wide ranging and include providing advice and guidance and support to prescribers and dispensers to help them improve prescribing practices ...'.[18]

In addition, the recently-established Medicines Management Programme (MMP) of the Clinical Strategy and Programmes Directorate of the HSE is concerned with, among other objectives, securing reductions in the State pharmaceutical bill. In April 2013, the MMP announced a 'preferred drugs initiative' for PPIs and statins, which together account for approximately 15 per cent of the HSE's pharmaceutical budget.[19] Lansoprazole (PPI) and simvastatin (statin) were announced as the preferred pharmaceuticals. Medical practitioners are being asked to prescribe the preferred products in order to save money, with potential savings to the State in 2013 estimated at €7.5 million (PPIs) and €8m (statins).[20] There is also a 'Statin Switching Guidance Document' available for prescribers.[21] The HSE also has standardised guidelines in relation to antibiotic prescribing in the community.[22] It is envisaged that the MMP will focus on other therapeutic areas which are considered to be important drivers of expenditure in the community and hospital sectors in the coming months.[23]

6.2.2 Feedback and Monitoring

Our 2012 report also noted the importance of combining policy in relation to prescription guidelines with periodic benchmarking and auditing of prescribing behaviour.[24] Despite the existence of a comprehensive data-set on community dispensing, and with the exception of two specific areas (benzodiazepine and controlled drugs), prescribing by medical practitioners in the community currently is not audited nor do medical practitioners receive standardised feedback on their

17 Gorecki *et al.*, 2012, p.141

18 DoH, 2012, n.p.

19 PPIs and statins accounted for 15 per cent of the HSE pharmaceutical budget in 2012. HSE, personal communication, 22 April 2013

20 Assuming that 50 per cent of all PPI prescriptions are lansoprazole, and 25 per cent of all statin prescriptions are simivastatin. Potential savings for the cash-paying customer are estimated at approximately €300 per annum for PPIs and €130 per annum for statins. Source: www.hse.ie/eng/services/news/medicinesmanagement.html [last accessed 19 April 2013].

21 HSE, 2013

22 HSE, 2011

23 HSE, personal communication, 16 May 2013

24 Gorecki *et al.*, 2012, p.141

prescribing behaviour.[25] However from July 2012, prescribing guidance designed to ensure more cost efficient prescribing was made available to all GPs under contract with the PCRS. The system allows GPs to quantify the savings that are possible from the substitution of cheaper interchangeable products.[26] From July 2013, a pilot Prescribing Guidance System (PGS) will be introduced, which will provide feedback to GPs on prescribing decisions in the form of instantaneous pop-up messages. Messages will focus on issues such as product substitutions (for more cost effective products), quality prescribing (e.g., for prescribing of antibiotics and benzodiazepines) and reimbursement (i.e., whether a patient is eligible for a particular product under the GMS Scheme).[27] It is not clear however how many GPs will access this facility, how often they will do so, and whether GPs' prescribing behaviour will change as a result. The international evidence on feedback and monitoring, in conjunction with education and information, highlights the difficulty in evaluating the effectiveness of such non-financial influences on prescriber behaviour, but it is thought that unless they are accompanied by vigorous implementation and monitoring, their effectiveness is likely to be limited.[28]

6.2.3 Financial Incentives

There are no financial incentives for medical practitioners in Ireland to prescribe more cost effective products.[29] Based on the the weak international evidence on the effectiveness of incentive schemes for medical practitioners in limiting pharmaceutical (and other healthcare) expenditure, our 2012 report recommended that financial incentives to reduce pharmaceutical expenditure should not be introduced for Irish medical practitioners.[30] In particular, the international evidence highlights the possibility of selection and gaming on the part of medical practitioners, as well as the administrative costs associated with such schemes (Delnoij and Brenner, 2000; Croxson *et al.*, 2001; Dusheiko *et al.*, 2003; Nolan *et al.*, 2011). This recommendation was also based on the limited evidence on the effectiveness of an incentive scheme for Irish GPs that was introduced in the early 1990s. From 1993 to 2006, GPs in Ireland were able to participate in the Indicative Drug Targeting Scheme (IDTS). As part of the IDTS, GPs were provided with

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25 The PCRS maintains a record of every claim for reimbursement under the various State pharmaceutical schemes. Information recorded includes the manufacturer name, pharmaceutical name, ATC 5 code, dosage form and strength, route of administration, patient details and GMS number (where appropriate), GP (or other prescriber) details and dispensing pharmacist details. Extracts from this database concerning prices and quantities for 2010, 2011 and 2012 are used in this report (see Section 2.4 for further details).

26 GPs have been able to access electronic information on their prescriptions for the past six years. In 2013, 1,800 GPs accessed the prescribing system. HSE, personal communication, 14 May 2013. The total number of GPs with GMS contracts in 2011 was 2,758 (PCRS, 2012).

27 HSE, personal communication, 23 April 2013

28 However, there is some evidence that feedback may be effective when accompanied by explicit information on alternative treatments, and that academic detailing (i.e., one-to-one counselling) may be effective at changing prescriber behaviour (Soumerai *et al.*, 1989; Figueras *et al.*, 2001; Kanavos, 2008; Gorecki *et al.*, 2012).

29 Of course, financial incentives for prescribers may also be concerned with other objectives such as quality (e.g., ensuring adherence to clinical guidelines, improved reporting).

30 Gorecki *et al.*, 2012, p. 139

prescribing targets, which were adjusted for patient numbers and demographics, and GPs were allowed to retain 50 per cent of any savings achieved. It was estimated that IR£13.5 million was saved in the first year of the scheme and a trend towards increased generic prescribing was reported, with no discernible negative effects on quality of prescribing.[31] Analysis by the Comptroller and Auditor General revealed savings of £18 million over the first four years of the scheme. The rate of increase in pharmaceutical expenditure on the GMS Scheme over the period 1993–1996 decreased to a little over half its rate over the previous four years, with the proportion of substitutable pharmaceuticals prescribed at their lowest cost increasing over the period.[32] However, in common with other incentive schemes internationally, the savings were short-lived.[33]

6.2.4 Generic Prescribing

In Ireland, medical practitioners are not obliged to write prescriptions generically (i.e., using the INN), whereby prescribers use the active ingredient name (e.g., atorvastatin) rather than the brand name (e.g., Lipitor). Apart from the potential for any cost savings[34], generic prescribing is a recognised quality prescribing indicator as it reduces the potential for confusion and error on the part of the prescriber, pharmacist and patient.[35] Medical Council guidelines encourage the prescription of 'bio-equivalent generic medicines where they are safe and effective'.[36]

Chapter 5 provided data on generic market shares in Ireland, both over time, and in comparison with other countries. Comparative data on generic penetration for 2009 and 2010 suggested that Ireland had a low share of generics, but more recent data are not available. An examination of the proportion of generics dispensed for the leading multiple source off-patent pharmaceuticals on the GMS and DP schemes in Ireland indicated that the proportion of generics dispensed has increased strongly over the period 2010–2012.

Our 2012 report recommended that mandatory prescription by INN should be introduced for all medical practitioners to encourage safe and cost-effective prescribing.[37] The winter 2012 review of the Economic Adjustment Programme for Ireland by the European Commission notes that 'the authorites have also agreed to

31 Murphy, 1997

32 Comptroller and Auditor General, 1997

33 Walley *et al.*, 2000; Dunne *et al.*, 2013

34 The analysis in Chapter 4 outlines why a greater share of generics dispensed in the Irish context does not necessarily lead to significant savings.

35 Barry *et al.*, 2009; National Medicines Information Centre, 2009

36 Medical Council, 2009, section 49

37 Gorecki *et al.*, 2012, p. 136. The report noted that this recommendation should also take into account the forthcoming legislation on reference pricing and generic substitution, including interchangeability and no substitution prescriptions. In response to this recommendation, the DoH has said that it is under active consideration. See Appendix D for details.

setting high level annual targets for increasing the share of generic drug usage in the medium-term. Enabling measures required for the achievement of these targests – such as compulsory prescription by international non-proprietary name (INN) by end 2013, where appropriate – required for the achievement of these targets will be put in place and kept under further review'.[38] The Health (Pricing and Supply of Medical Goods) Act 2013 contains provisions in relation to 'no substitution' prescriptions.[39]

6.2.5 Changing Prescriber Behaviour in Ireland?

As described, Irish medical practitioners have considerable discretion in deciding on the type of pharmaceutical to prescribe. Currently, medical practitioners receive information on prescribing from a variety of sources, and there is evidence that their knowledge of the costs of the pharmaceuticals that they prescribe is limited.[40] In addition, there is limited monitoring of behaviour (the exception is for benzodiazepines and controlled drugs). While the new Prescribing Guidance System will allow GPs to monitor their prescribing costs, and the 'preferred drugs' initiative provides specific advice on therapeutic substitution for two therapeutic sub-groups (i.e., PPIs and statins), international evidence suggests that such measures need to be designed carefully to effect change in prescriber behaviour (e.g., incorporating one-to-one counselling).

In many other countries, in contrast, prescriber behaviour is supported by standardised guidelines, closer monitoring and more targeted feedback. In the UK, for example, the NHS has been very proactive in issuing guidance to Primary Care Trusts (PCTs) and Clinical Commissioning Groups on how to achieve more cost-effective prescribing[41], and the Medicines and Prescribing Centre at the National Institute for Health and Care Excellence (NICE) provides a wide range of tools in a single site to support cost-effective prescribing.[42] The Quality and Outcomes Framework (QOF) component of the UK GP contract also contains a number of targets of relevance to prescriber behaviour[43], although the targets do not explicitly deal with issues of cost effectiveness (and as noted, there is limited international evidence on the effectiveness of such financial incentives). More importantly however, generic prescribing on the part of medical practitioners (both in hospital and the community) has been widely practised for many years.

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38 European Commission, 2013, p. 53

39 Section 13 deals with the issue of clinical exemptions to substitution (http://www.oireachtas.ie/) [last accessed 8 May 2013].

40 McGuire *et al.*, 2009

41 DoH, 2010

42 http://www.nice.org.uk/mpc/index.jsp [last accessed 3 May 2013]

43 http://www.nhsemployers.org/PayAndContracts/GeneralMedicalServicesContract/QOF/Pages/QualityOutcomesFramework.aspx [last accessed 3 May 2013]

Given the absence of standardised guidelines, and the only very recent attempts to provide Irish GPs with the tools to monitor their prescribing behaviour, the expectation is that Irish medical practitioners will tend to favour branded products.[44] Chapter 5 outlined the large increases in generic market share that have occurred for the leading multiple source off-patent pharmaceuticals on the GMS and DP schemes in Ireland in recent years. Given the situation outlined above, it is unlikely that the patterns of generic dispensing presented in Chapter 5 are driven only by changing prescriber behaviour in Ireland. Indeed, prescribing by INN has always been a feature of medical education in Ireland, the IMO recommends generic prescribing[45], and the IMB has been actively involved for a number of years in reassuring the public about the safety and efficacy of generic pharmaceuticals[46].

However, increasing use of electronic prescription software[47] in Ireland may mean that medical practitioners are more likely to prescribe by INN. A 2008 survey of Irish GPs in Galway, Mayo and Roscommon found that while over 90 per cent of all practices used electronic medical records, the majority used paper resources to support their prescribing decisions, such as the British National Formulary.[48] The Irish College of General Practitioners (ICGP) has certified five software operators and the HIQA has recently published an overview of electronic prescribing and transmission systems in a number of other European countries, including the UK.[49]

In addition, it is possible that the added publicity surrounding the pharmaceutical budget and the potential role of generics in recent years has influenced the behaviour of Irish prescribers. It is also possible that patients have started to exert more influence on prescriber behaviour. The international literature highlights the importance of patient characteristics, including the financial situation of the patient, in determining prescriber behaviour.[50] As the recession has deepened and household incomes have fallen, consumers are ever more conscious of getting value for money. The previous chapter referred to research which suggests that Irish patients are becoming more comfortable with generics and more aware of the cost savings that are available, and it is possible that patients are becoming more

44 Branded product names tend to be easier to remember. In addition, in comparison to originator or brand name manufactures, manufacturers of generic pharmaceuticals devote fewer resources to marketing of their products (Paraponaris *et al.*, 2004). It has also been suggested (although this study is now out of date) that Irish medical practitioners may be reluctant to prescribe by INN out of concern that pharmacists may legally dispense more expensive branded products for private prescriptions written generically (Feely *et al.*, 1999).

45 IMO, 2010. In 2009, the IMO estimated that annual savings of €30m were achieveable with mandatory generic prescribing in the Irish health system (IMO, 2009).

46 IMB, 2010

47 In the Irish context, electronic prescribing refers to the ability of the medical practitioner to *print* the prescription; in other countries, electronic prescribing refers also to the electronic transmission of prescriptions to the pharmacy.

48 The response rate to the survey was 37 per cent (Hor *et al.*, 2010).

49 http://www.icgp.ie/go/in_the_practice/information_technology/software_companies [last accessed 8 May 2013]; HIQA (2012)

50 Lundin, 2000; Mott and Cline, 2002; Paraponaris *et al.*, 2004; Dalen *et al.*, 2011

influential in determining the type of pharmaceutical prescribed. However, this explanation does not explain why the share of generics also increased over time for the GMS Scheme. As GMS patients pay a fixed fee for each prescription item (i.e., not related to the value of the product), GMS patients should be less likely to question their medical practitioner about the availability of a cheaper alternative.[51] In addition, as noted in Chapter 4, the difference in price between brand and generic products in Ireland is not large, and for part of 2010 and 2011, generic prices exceeded branded prices for many products.[52] However, this is beginning to change. Ex-factory price reductions in November 2012, under the agreements between the State and pharmaceutical trade associations, resulted in the price of some generic pharmaceutical products falling substantially compared to the patent holder's price. The commencement of the Health (Pricing and Supply of Medical Goods) Act 2013 will see further declines in the price of generic pharmaceutical products.

6.3 Current Prescribing Policy in the EU

Table 6.1 presents information on policies across the EU that are specifically targeted at prescriber behaviour. Information is also provided on the current situation in Ireland. It is difficult to evaluate the impact of these various tools for improving prescriber behaviour on cost-containment due to their quantity and variety. Previous literature suggests that, in general, a mix of interventions, such as monitoring and feedback systems combined with group or one-to-one education interventions, have a positive impact, while focussing on information dissemination alone is ineffective.[53]

[51] However, if GPs are coming under increasing pressure from their cash-paying customers to prescribe cheaper alternatives, then this may also influence their prescribing behaviour for GMS patients.

[52] As explained in Chapter 4, this anomaly arose due to the fact that the agreement with the APMI was concluded later than that with the IPHA.

[53] Soumerai *et al.*, 1989; Kanavos, 2008; Carone *et al.*, 2012; Gorecki *et al.*, 2012

TABLE 6.1 Policies Targeting Prescriber Behaviour – Member States

	Number of Member States (out of 27)	Ireland
Monitoring of prescription behaviour[a]	22	Yes
Prescription guidelines[b]	24 (at least)	Yes
Mandatory INN prescribing[c]	5	No
Education and information	All	Yes (variety of sources)
Pharmaceutical budget control[d]	10 (at least)	No
Prescription quota[e]	6 (at least)	No
Financial incentives	11 (at least)	No

Notes:
a For example, payers may monitor individual medical practitioners' prescriptions and benchmark these with prescriptions of their colleagues of the same specialty in a given region or country.
b Prescription guidelines may take the form of clinical prescription protocols for selected pharmaceuticals/conditions. They are mandatory in six member states.
c Indicative, i.e., recommended or allowed, INN prescribing is used in a further 18 member states, and disallowed in four.
d A maximum pharmaceutical budget may be defined per period, region, field of specialty and /or prescriber.
e This may define a target for the percentage of generics to be prescribed, or may target the average cost of prescriptions per prescriber.

Source: Adapted from Carone *et al.*, 2012. Table 13, p.39.

6.4 Prescribing Practices in Ireland

In this section, we examine the prescribing decisions of Irish medical practitioners, as inferred from data on dispensing patterns administered by the PCRS. We focus on three major therapeutic sub-groups of pharmaceuticals (i.e., defined at ATC level 4): PPIs, statins, ACE inhibitors. We use data from the GMS Scheme for the period 2010–2012 inclusively. The HSE has recently designated a 'preferred drug' for PPIs and statins (lansoprazole and simvastatin, respectively), but the impact of this policy will not be captured in the data available here. For many patients, products within these three therapeutic sub-groups may be substituted for one another.[54]

As noted, these three therapeutic sub-groups accounted for 14.2 per cent of all pharmaceuticals by volume and 18.1 per cent of all pharmaceuticals by value on the GMS Scheme in 2012. Table 6.2 illustrates the number of items (volume) and total ingredient cost[55] (value) on the GMS Scheme for each of the three therapeutic sub-groups over the period 2010–2012. Consistent with overall trends, the number of items increased strongly for each therapeutic sub-group, while the total ingredient cost declined over time.

[54] For patients who are simulataneously taking other products however, substitution may not be appropriate. See Vandoros (2013) for a more detailed discussion.

[55] Total ingredient cost refers to the wholesale price, i.e., the ex-factory price plus the wholesale mark-up of 8 per cent.

TABLE 6.2 PPIs, Statins, ACE Inhibitors – GMS Scheme, by Volume and Value,[a] 2010–2012

	2010		2011		2012	
	Volume	Value	Volume	Value	Volume	Value
	n	€	n	€	n	€
PPIs	2.7	81.5	3.0	64.1	3.2	65.4
Statins	3.1	97.9	3.3	73.0	3.5	71.8
ACE Inhibitors	1.6	16.1	1.6	11.7	1.6	11.4
Total PPIs, Statins, ACE Inhibitors[b]	**7.4**	**195.6**	**7.9**	**148.9**	**8.4**	**148.6**
Total [b,c]	**52.3**	**837.7**	**55.7**	**780.5**	**59.4**	**821.3**

Notes: a The number of items is expressed in millions; the value in €m.
b Totals may not add up due to rounding.
c Total refers to all pharmaceuticals on the GMS Scheme in the relevant year.

Source: ESRI calculations based on HSE, personal communication, 9 April 2013.

The consitutent ATC 5 pharmaceuticals that are currently available on the GMS Scheme for each therapeutic sub-group are presented in Table 6.3. The type of pharmaceutical (i.e., whether single or multiple source) is also noted. With the exception of atorvastatin in the group of statins (which lost patent in Ireland in May 2012), and six of the 11 ACE inhibitor ATCs, all ATCs are multiple source off-patent pharmaceuticals, and have been over the period 2010–2012.

TABLE 6.3 Pharmaceuticals within Selected Therapeutic Sub-Groups

PPIS			Statins			ACE Inhibitors		
INN	ATC	Type[a]	INN	ATC	Type[a]	INN	ATC	Type[a]
Esomeprazole	A02BC05	MS	Atorvastatin	C10AA05	MS[b]	Benazepril	C09AA07	SS
Lansoprazole	A02BC03	MS	Fluvastatin	C10AA04	MS	Captopril	C09AA01	MS
Omeprazole	A02BC01	MS	Pravastatin	C10AA03	MS	Cilazapril	C09AA08	SS
Pantoprazole	A02BC02	MS	Rosuvastatin	C10AA07	MS	Enalapril	C09AA02	MS
Rabeprazole	A02BC04	MS	Simvastatin	C10AA01	MS	Fosinopril[c]	C09AA09	SS
						Lisinopril	C09AA03	MS
						Perindopril	C09AA04	MS
						Quinapril	C09AA06	SS
						Ramipril	C09AA05	MS
						Trandolapril	C09AA10	SS[d]
						Zofenopril	C09AA15	SS

Notes: a MS – Multiple Source; SS – Single Source.
b Atorvastatin was single source for 2010, 2011 and part of 2012 (it lost patent in Ireland in May 2012).
c Fosinopril was not reimbursed on the GMS Scheme in Ireland over the period 2010–2012. However, it was reimbursed on the NHS over this period.
d Trandolapril had patent holder products with a generic equivalent in 2010, but for 2011 and 2012 all products were classed as patent holder without a generic equivalent.

Source: HSE, personal communications, 9 April, 25 April and 14 May 2013

Tables 6.4 presents the distribution of each ATC level 5 pharmaceutical within each therapeutic sub-group by volume and value on the GMS Scheme for each of the years 2010, 2011 and 2012. The data indicates that esomeprazole (PPIs), atorvastatin (statins) and ramipril (ACE inbibitors) are the most popular ATCs by volume in each of the three years. Esomeprazole and atorvastatin are also the popular ATCs by

value, while perindopril is the most popular ATC in the group of ACE inhibitors by value in each of the three years.

While esomeprazole has continued to increase its share of the PPI market[56] in Ireland over time, the most popular statin, atorvastatin, has declined in importance, if only slightly. The most popular ACE inhibitor by volume (rampipril) has increased its share of the GMS Scheme ACE inhibitor market market in Ireland over the period 2010–2012.

TABLE 6.4 Distribution of ATCs within Selected Therapeutic Sub-Groups – GMS Scheme, by Volume and Value,[a] 2010–2012

	ATC Description	ATC	2010		2011		2012	
			Volume	Value	Volume	Value	Volume	Value
			%	%	%	%	%	%
PPIs	Esomeprazole	A02BC05	27.7	37.1	29.1	38.3	30.9	41.4
	Lansoprazole	A02BC03	25.2	27.3	24.2	25.1	23.2	23.5
	Omeprazole	A02BC01	24.0	20.6	23.3	20.0	22.9	19.9
	Pantoprazole	A02BC02	18.5	10.5	19.5	12.8	19.6	11.9
	Rabeprazole	A02BC04	4.6	4.5	4.0	3.8	3.4	3.3
	Total PPIs[b]		**100**	**100**	**100**	**100**	**100**	**100**
Statins	Atorvastatin	C10AA05	58.5	71.1	58.0	69.1	57.6	68.8
	Fluvastatin	C10AA04	1.3	0.4	1.1	0.4	1.0	0.4
	Pravastatin	C10AA03	15.7	9.3	14.1	8.3	12.8	7.6
	Rosuvastatin	C10AA07	18.6	16.0	20.9	20.0	22.6	21.6
	Simvastatin	C10AA01	5.9	3.3	5.9	2.2	5.9	1.6
	Total Statins[b]		**100**	**100**	**100**	**100**	**100**	**100**
ACE Inhibitors	Benazepril	C09AA07	0.0	0.1	0.0	0.1	0.0	0.1
	Captopril	C09AA01	3.3	3.1	2.9	3.0	2.5	2.7
	Cilazapril	C09AA08	0.8	1.3	0.7	1.2	0.7	1.1
	Enalapril	C09AA02	3.1	2.3	2.9	2.5	2.7	2.5
	Fosinopril[c]	C09AA09	n/a	n/a	n/a	n/a	n/a	n/a
	Lisinopril	C09AA03	13.8	10.2	13.2	9.4	12.7	8.7
	Perindopril	C09AA04	28.8	47.5	28.5	45.2	28.1	45.9
	Quinapril	C09AA06	1.9	2.2	1.7	2.8	1.6	2.6
	Ramipril	C09AA05	47.9	32.9	49.7	35.2	51.3	36.0
	Trandolapril	C09AA10	0.2	0.2	0.2	0.2	0.2	0.2
	Zofenopril	C09AA15	0.2	0.3	0.1	0.3	0.1	0.3
	Total ACE Inhibitors[b]		**100**	**100**	**100**	**100**	**100**	**100**

Notes a Volume refers to the number of items; value to the total ingredient cost (ex-factory price plus wholesale mark-up).
b Figures may not add up due to rounding.
c Fosinopril was not reimbursed on the GMS Scheme in Ireland over the period 2010–2012.

Source: ESRI calculations based on HSE, personal communications, 9 April and 14 May 2013.

The higher value than volume share for some of the most popular ATC level 5 pharmaceuticals (esomeprazole; perindopril; atorvastatin) suggests that branded or patent holder products are most commonly dispensed for these ATCs.[57] The

[56] Based on data for the GMS Scheme only.

[57] When making comparisons at ATC 4 level, a discrepancy between value and volume could also be due to the differing prices between the constituent ATC 5 pharmaceuticals. For example, the April 2013 ex-factory price for atorvastatin 10mg

exception is ramipril, the most popular ACE inhibitor ATC by volume, where the share by value is substantially lower, suggesting that generic products are most commonly dispensed in this ATC. The data presented in Chapter 5 illustrated substantial increases in the share of generics for the leading pharmaceuticals on the GMS and DP schemes in Ireland over the period 2010–2012. In Table 6.5, we present data on the share of the total ATC (at level 4 and 5, by volume and value on the GMS Scheme over the period 2010–2012) that is accounted for by generic products (both branded and unbranded). Previous analyses of data in Ireland have noted concerns over the high share of products that are dispensed as patent holder products even when a generic is available.[58] Chapter 4 explained why there is often little difference in the ex-factory price between patent holder and generic products in Ireland although this is beginning to change. Nevertheless, a small share of generics for multiple source off-patent pharmaceuticals is a concern as it suggests that Irish prescribers are not prescribing by INN[59], thus increasing the potential for confusion and error on the part of the prescriber, pharmacist and patient.

Across all ATCs, the share of generics has been increasing over time, and the increases are substantial in some cases (e.g., esomeprazole, atorvastatin, rosuvastatin). The rapid entry of generic manufacturers of atorvastatin in 2012 is evident in the data. The second most popular ATC by volume within the class of ACE inhibitors (perindopril) is dominated by patent holder products, thus explaining the large discrepancy in volume and value presented in Table 6.4.

28 pack was €12.83 for the patent holder, Lipitor, while the April 2013 ex-factory price for simvastatin 10mg 28 pack was €3.23 for Zocor (http://www.sspcrs.ie/druglist/search.jsp) [last accessed 15 May 2013].

58 Barry *et al.*, 2009

59 There are two other scenarios that might explain this pattern of dispensing. First, the patient requests the brand when the medical practitioner writes the prescription, and second, the prescription is by INN and the pharmacist decides to dispense the patent holder product. However, given the discussion in Chapter 5 on the incentives facing Irish pharmacists to dispense generics, we argue that the second scenario is less likely in the current context.

TABLE 6.5 Generic Market Shares (Branded and Unbranded) within Selected Therapeutic Sub-Groups – GMS Scheme, by ATC, Volume and Value, 2010–2012[a]

	ATC Description	ATC	2010		2011		2012	
			Volume	Value	Volume	Value	Volume	Value
			%	%	%	%	%	%
PPIs	Esomeprazole	A02BC05	8.2	6.3	34.8	35.2	51.8	49.4
	Lansoprazole	A02BC03	33.0	23.3	38.6	38.2	44.1	42.6
	Omeprazole	A02BC01	57.9	59.9	63.0	62.5	69.2	66.8
	Pantoprazole	A02BC02	34.5	37.2	48.2	46.7	61.0	59.8
	Rabeprazole	A02BC04	0.1	0.1	10.0	9.9	24.2	22.7
	Total PPIs		**30.8**	**24.9**	**43.9**	**41.9**	**54.9**	**51.6**
Statins	Atorvastatin[b]	C10AA05	-	-	-	-	36.7	34.0
	Fluvastatin	C10AA04	4.2	4.5	5.8	6.3	2.5	2.2
	Pravastatin	C10AA03	39.4	46.6	46.2	49.3	55.0	54.8
	Rosuvastatin	C10AA07	2.8	2.0	27.6	25.4	46.7	43.1
	Simvastatin	C10AA01	52.4	59.7	58.9	71.9	71.1	70.6
	Total Statins		**9.9**	**6.6**	**15.8**	**10.8**	**43.0**	**38.0**
ACE Inhibitors	Benazepril[b]	C09AA07	-	-	-	-	-	-
	Captopril	C09AA01	48.5	52.9	59.6	48.8	62.9	47.6
	Cilazapril[b]	C09AA08	-	-	-	-	-	-
	Enalapril	C09AA02	24.4	29.5	25.6	23.8	28.3	26.4
	Fosinopril[c]	C09AA09	n/a	n/a	n/a	n/a	n/a	n/a
	Lisinopril	C09AA03	47.3	54.7	51.2	54.0	56.9	56.5
	Perindopril	C09AA04	2.0	1.4	3.2	2.8	4.2	3.7
	Quinapril[b]	C09AA06	-	-	-	-	-	-
	Ramipril	C09AA05	45.8	52.7	51.0	51.5	57.3	56.5
	Trandolapril[b]	C09AA10	-	-	-	-	-	-
	Zofenopril[b]	C09AA15	-	-	-	-	-	-
	Total ACE Inhibitors		**31.4**	**25.9**	**35.5**	**26.6**	**40.1**	**28.9**

Note: a For a period during 2010 and 2011, generic products were priced above the patent holder. This explains the higher value share of generics for some ATCs in these years. HSE, personal communication, 15 May 2013
b As these ATCs were single-source in the relevant years, no generics were available.
c Fosinopril was not reimbursed on the GMS Scheme in Ireland over the period 2010–2012.

Source: ESRI calculations based on HSE, personal communications, 9 April and 14 May 2013.

While the difference in ex-factory price between patent holder and generic products within an ATC (level 5) may not be large (due to the reasons outlined in Chapter 3, although this is beginning to change)[60], more substantial price differences are evident by comparing across ATCs within therapeutic sub-groups. In Table 6.6 we present data on the ex-factory price of a typical maintenance dose (defined by the HSE) for products within two of these groups, PPIs and statins. The products are selected by the HSE.[61] The ex-factory price refers to March 2013.

In general, the most dispensed ATCs within each sub-group are the most expensive (e.g., esomeprazole has the highest ex-factory price per unit[62] in 2012). Section 6.6 considers possible explanations for this pattern of prescribing. We also conduct a simple exercise to quantify the savings that are possible on the GMS Scheme if all those who are currently taking the maintenance dose of the most popular product in

60 For example, the March 2013 ex-factory price for atorvastatin 10mg 28 pack ranges from €10.69 for the generic version to €12.83 for the patent holder, Lipitor. HSE, personal communication, 13 March 2013

61 See http://www.hse.ie/eng/services/news/medicinesmanagement.html [last accessed 16 May 2013].

62 In this case, unit refers to tablet, capsule, etc.

the most popular ATC (i.e., Nexium 20mg for esomeprazole and Lipitor 10mg for atorvastatin) were to switch to the ATC with the cheapest ex-factory price per unit. We undertake this analysis using information on the number of items dispensed for the particular products on the GMS Scheme in 2012. We find that if all those currently taking the maintenance dose of Nexium (esomeprazole) were to switch to the maintenance dose of lansoprazole (the HSE 'preferred drug'), the annual saving would be €1.2m, while if all those currently taking the maintenance dose of Lipitor (atorvastatin) were to switch to the maintenance dose of simvastatin (the HSE 'preferred drug'), the annual saving would be €3.2m.[63]

TABLE 6.6 Comparative Ex-Factory Prices for Maintenance Dose within Selected Therapeutic Sub-Groups – GMS Scheme, by ATC,[a] 2012

		Product	Ex-Factory Price[a]
			€
PPIs	Esomeprazole	Nexium 20 mg	0.65
	Lansoprazole	Zoton Fastab 15 mg	0.23
	Omeprazole	Losec 20 mg	0.47
	Pantoprazole	Protium 20 mg	0.25
	Rabeprazole	Pariet 10 mg	0.38
Statins	Atorvastatin	Lipitor 10 mg	0.46
	Fluvastatin	Lescol 20 mg	0.17
	Pravastatin	Lipostat 20 mg	0.41
	Rosuvastatin	Crestor 5 mg	0.46
	Simvastatin	Zocor 20 mg	0.20

Note: a The literature on the 'preferred drugs initiative' records the wholesale price, i.e., the ex-factory price plus the 8 per cent wholesale mark-up. Here, the ex-factory price refers to the ex-factory price per unit, i.e., per tablet/capsule. For all ATCs, the pack size is 28 tablets/capsules. The products are selected by the HSE.

Source: ESRI calculations from: http://www.hse.ie/eng/services/news/medicinesmanagement.html http://www.sspcrs.ie/druglist/search.jsp [last accessed 24 April 2013]

6.5 Prescribing Practices in Ireland in Comparative Context

To what extent are these patterns different to those found in other countries? To answer this question, we compare dispensing patterns for PPIs, statins and ACE inhibitors in Ireland in 2012 with those in the UK, also for 2012. The UK is an important comparator when analysing prescriber behaviour (albeit using dispensing data) as Irish and UK medical practitioners may be expected to be similar in terms of medical training, education and culture. UK data are taken from the Prescription Cost Analysis (PCA) database.[64] In the UK, PCA data cover all prescriptions dispensed

63 These are conservative estimates as they estimate only the savings achievable if all those taking the maintenance dose of the most popular product in the most popular ATC were to switch to the 'preferred' ATC product. The savings would be even greater if *all* those taking the maintenance dose of *other* ATCs were considered for switching. The data available to us do not allow us to generate these estimates as we do not have prescribing frequencies for some ATCs (e.g., rapeprazole, simvastatin). The HSE estimates total annual savings of €15m (assuming that 50 per cent of all PPI prescriptions are Lansoprazole, and 25 per cent of all statin prescriptions are Simivastatin). See footnote 22 above.

64 Prescribing data is also available at the level of the individual GP practice in England. The General Practice Prescribing Data collects information on the number of prescription items that are dispensed each month and information relating to costs for all English practices. All prescribed and dispensed medicines (by chemical substance and presentation level), as we all as dressings and appliances are listed for each GP practice. No patient identifiable data are presented. See

in the community.[65] While annual PCA data are available for the four countries of the UK separately (albeit in slightly different formats), we do not use Northern Ireland data as it is not available at ATC level 5, and in any case is not yet available for 2012.[66]

For England, data at ATC level 5 are presented on the number of items (e.g., number of packs), quantity (e.g., number of tablets), ingredient cost, net ingredient cost per item and net ingredient cost per quantity, where net ingredient cost refers to the cost of the product before discounts and does not include any dispensing costs or fees. Information is also available on the number of items that were prescribed and dispensed generically. For Scotland and Wales, data at ATC level 5 are presented on the number of items, net ingredient cost and net ingredient cost per item only.[67]

Using these data, we calculate the share of each sub-group (i.e., PPIs, statins, ACE inhibitors) accounted for by each ATC level 5 by volume (based on the number of items) and value (based on the ingredient cost) for 2012. This is identical to the approach used for the presentation of the Irish data in Table 6.4. The results are presented in Table 6.7.

They indicate that, for PPIs, the most commonly dispensed ATC in England, Scotland and Wales in 2012 was omeprazole (by volume and value). The most commonly dispensed ATC in Ireland, esomeprazole, was only the third most popular ATC in all UK countries, by both volume and value in 2012.[68] Lansoprazole, the ATC which the HSE has designated as 'preferred' within the sub-group of PPIs, was the second most commonly dispensed ATC (by both volume and value in England and Wales; by volume only in Scotland). Its share (by volume) ranged from 27.3 per cent in Scotland to 40.1 per cent in England, in comparison with 23.2 per cent in Ireland.

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http://www.nhsbsa.nhs.uk/PrescriptionServices/3516.aspx [last accessed 19 April 2013]. General Practice Prescribing Data are available for Wales from April 2013. (http://www.wales.nhs.uk/sites3/page.cfm?orgid=428&pid=65866) [last accessed 24 April 2013]. To our knowledge, these data are not yet available in Scotland and Northern Ireland.

65 Prescriptions written by GPs and non-medical prescribers (nurses, pharmacists, etc.) represent the vast majority of prescriptions included. Prescriptions written by dentists and hospital doctors are also included provided that they were dispensed in the community. Prescriptions written in another UK country are included (e.g., prescriptions written in Wales but dispensed in England are captured in the English data, while prescriptions written in England but dispensed in Wales are captured in the Welsh data). The data do not cover items dispensed in hospital or on private prescriptions.

66 See http://www.hscbusiness.hscni.net/services/2266.htm [last accessed 24 April 2013].

67 Scottish cost data refers to gross ingredient cost. http://www.isdscotland.org/Health-Topics/Prescribing-and-Medicines/Community-Dispensing/Prescription-Cost-Analysis/ [last accessed 24 April 2013]

68 The large difference in volume and value share for esomeprazole in England, Scotland and Wales reflects the fact that relatively more expensive proprietary products are often dispensed in this ATC. See also footnote 58 on interpreting volume and value share figures within therapeutic sub-groups.

TABLE 6.7 Distribution of ATCs within Selected Therapeutic Sub-Groups – England, Scotland, Wales and Ireland, by Volume and Value, 2012

	ATC Description	ATC	England		Scotland		Wales		Ireland	
			Volume	Value	Volume	Value	Volume	Value	Volume	Value
			%	%	%	%	%	%	%	%
PPIs	Esomeprazole	A02BC05	2.5	20.1	4.5	33.4	1.9	16.7	30.9	41.4
	Lansoprazole	A02BC03	40.2	26.8	27.3	17.5	37.1	26.7	23.2	23.5
	Omeprazole	A02BC01	54.6	45.2	66.0	44.2	59.0	51.6	22.9	19.9
	Pantoprazole	A02BC02	1.8	1.2	1.4	0.9	1.5	1.1	19.6	11.9
	Rabeprazole	A02BC04	0.9	6.6	0.7	3.9	0.5	3.8	3.4	3.3
	Total PPIs[a]		**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**
Statins	Atorvastatin	C10AA05	21.1	58.5	24.4	72.2	22.5	57.5	57.6	68.8
	Fluvastatin	C10AA04	0.3	0.5	0.2	0.2	0.2	0.4	1.0	0.4
	Pravastatin	C10AA03	4.8	2.5	3.6	1.1	4.7	2.3	12.8	7.6
	Rosuvastatin	C10AA07	3.3	17.5	5.8	15.0	4.2	21.2	22.6	21.6
	Simvastatin	C10AA01	70.6	21.0	66.1	11.5	68.3	18.7	5.9	1.6
	Total Statins[a]		**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**
ACE Inhibitors	Benazepril[b]	C09AA07	n/a	n/a	n/a	n/a	n/a	n/a	0.0	0.1
	Captopril	C09AA01	0.4	2.2	0.5	0.6	0.4	2.5	2.5	2.7
	Cilazapril	C09AA08	0.0	0.3	0.0	0.2	0.0	0.3	0.7	1.1
	Enalapril	C09AA02	5.6	6.1	7.3	7.6	4.1	6.3	2.7	2.5
	Fosinopril[c]	C09AA09	0.2	0.7	0.5	1.0	0.2	0.6	n/a	n/a
	Lisinopril	C09AA03	23.8	19.2	30.1	23.9	24.3	18.8	12.7	8.7
	Perindopril	C09AA04	12.9	17.1	15.9	19.2	15.1	19.1	28.1	45.9
	Quinapril	C09AA06	0.3	0.7	0.4	0.8	0.4	0.8	1.6	2.6
	Ramipril	C09AA05	56.3	51.7	44.9	44.8	55.0	49.5	51.3	36.0
	Trandolapril	C09AA10	0.4	1.9	0.3	1.8	0.5	2.0	0.2	0.2
	Zofenopril[b]	C09AA15	n/a	n/a	n/a	n/a	n/a	n/a	0.1	0.3
	Total ACE Inhibitors[a]		**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

Notes: a Figures may not add up due to rounding.
b Benazepril and Zofenopril were not reimbursed on the NHS in 2012.
c Fosinopril was not reimbursed on the GMS Scheme in Ireland in 2012.

Sources: http://www.nhsbsa.nhs.uk/PrescriptionServices/3494.aspx [last accessed 8 May 2013]; Irish figures from Table 6.4

A similar pattern emerges for the statins. The most commonly dispensed ATC in England, Scotland and Wales in 2012 by volume was simvastatin (atorvastatin when analysed on a value basis). Simvastatin is the ATC which the HSE has designated as 'preferred' within the sub-group of statins; its share (by volume) ranges from 66.1 per cent in Scotland to 70.6 per cent in England, in contrast to just 5.9 per cent in Ireland.[69]

Finally, for the ACE inhibitors, the most commonly dispensed ATC in 2012 was ramipril (in both volume and value terms). Ramipril was also the most commonly dispensed ATC in Ireland by volume in 2012, but in value terms was exceeded by perindopril (which was in third place behind ramipril and lisinopril in England, Scotland and Wales in 2012).

69 NICE has also specified that 'treatment for the primary prevention of CVD should be initiated with simvastatin 40 mg' (NICE, 2010, p.8).

Comparative data on the share of generics by volume and value in 2012 is presented in Table 6.8 (the data are not available for Scotland and Wales).[70] The data indicates that the share of generics was over 90 per cent in volume terms for PPIs, statins and ACE inhibitors in England in 2012, compared with 40–50 per cent on the GMS Scheme in Ireland in 2012. The difference between England and Ireland is particularly striking for perindopril, one of the most popular ACE inhibitors in Ireland (second most popular by volume on the GMS Scheme in 2012). In England, the proportion of generics dispensed for perindopril was 98.8 per cent by volume in 2012, compared with only 4.2 per cent by volume in Ireland in 2012.

TABLE 6.8 Generic Market Shares of Selected Therapeutic Sub-Groups – England and Ireland, by ATC, Volume and Value, 2012

	ATC Description	ATC	England		Ireland	
			Volume	Value	Volume	Value
			%	%	%	%
PPIs	Esomeprazole	A02BC05	89.5	88.8	51.8	49.4
	Lansoprazole	A02BC03	95.4	87.6	44.1	42.6
	Omeprazole	A02BC01	98.4	95.3	69.2	66.8
	Pantoprazole	A02BC02	99.9	98.1	61.0	59.8
	Rabeprazole	A02BC04	16.1	16.2	24.2	22.7
	Total PPIs		**96.3**	**86.7**	**54.9**	**51.6**
Statins	Atorvastatin	C10AA05	69.4	36.5	36.7	34.0
	Fluvastatin	C10AA04	78.2	40.0	2.5	2.2
	Pravastatin	C10AA03	99.8	96.9	55.0	54.8
	Rosuvastatin	C10AA07	0.0	0.0	46.7	43.1
	Simvastatin[a]	C10AA01	100	98.9	71.1	70.6
	Total Statins		**90.2**	**44.7**	**43.0**	**38.0**
ACE Inhibitors	Benazepril[b,c]	C09AA07	n/a	n/a	-	-
	Captopril	C09AA01	98.7	96.7	62.9	47.6
	Cilazapril[b]	C09AA08	13.5	16.8	-	-
	Enalapril	C09AA02	99.4	94.0	28.3	26.4
	Fosinopril[d]	C09AA09	100	99.9	n/a	n/a
	Lisinopril	C09AA03	99.7	99.3	56.9	56.5
	Perindopril	C09AA04	98.8	95.0	4.2	3.7
	Quinapril[b]	C09AA06	98.9	95.6	-	-
	Ramipril	C09AA05	99.9	99.1	57.3	56.5
	Trandolapril[b]	C09AA10	97.8	97.0	-	-
	Zofenopril[b,c]	C09AA15	n/a	n/a	-	-
	Total ACE Inhibitors		**99.6**	**97.8**	**40.1**	**28.9**

Note:
a A small number of simvastatin products are dispensed as patent holder products in England (0.04 per cent by volume; the rounded figure for the share of generics by volume is therefore 100 per cent).
b As these ATCs were single source in Ireland in 2012, no generics were available.
c Benazepril and Zofenopril were not reimbursed on the NHS in 2012.
d Fosinopril was not reimbursed on the GMS Scheme in Ireland in 2012.

Sources: http://www.nhsbsa.nhs.uk/PrescriptionServices/3494.aspx [last accessed 8 May 2013]; Irish data is from Table 6.5

The Irish data that were presented in Tables 6.4 and 6.6 show that for both PPIs and statins, the most commonly dispensed ATCs in Ireland are those that are most expensive. In England, Scotland and Wales in contrast, the ATCs that are dispensed

[70] PCA data underestimate the extent of generic prescribing in the UK, as products which are prescribed generically but only available as branded proprietary products are classed as proprietary products.

tend to be the cheaper ATCs. Table 6.9 presents data on the cost per item per ATC in 2012 for England, Scotland and Wales. We also present data for Ireland, for the GMS Scheme in 2012. Note that the cost per item is not necessarily comparable across ATCs; doses and pack sizes differ across products and ATCs, which may affect the numbers (e.g., if a particular ATC has larger doses and pack sizes than another, then the cost per item will be higher even though the cost per tablet/capsule is not). Nonetheless, the figures are consistent with the data presented in Table 6.6, namely, that in the UK, among ATCs that may be deemed interchangeable, the most commonly dispensed ATCs are those that are the cheapest, while the opposite is generally the case for Ireland. Section 6.6 considers possible explanations for these patterns of prescribing.

TABLE 6.9 Average Cost per Item within Selected Therapeutic Sub-Groups[a] – England, Scotland, Wales and Ireland, by ATC, 2012

			England	Scotland	Wales	Ireland
			£	£	£	€
PPIs	Esomeprazole	A02BC05	24.40	40.10	21.19	27.18
	Lansoprazole	A02BC03	2.05	3.47	1.74	20.50
	Omeprazole	A02BC01	2.55	3.64	2.12	17.55
	Pantoprazole	A02BC02	2.06	3.57	1.78	12.30
	Rabeprazole	A02BC04	23.12	29.76	19.87	19.81
Statins	Atorvastatin	C10AA05	13.06	37.90	11.33	24.18
	Fluvastatin	C10AA04	8.18	12.27	6.64	6.97
	Pravastatin	C10AA03	2.45	3.94	2.12	12.09
	Rosuvastatin	C10AA07	25.13	33.24	22.22	19.38
	Simvastatin	C10AA01	1.40	2.21	1.22	5.47
ACE Inhibitors	Benazepril[b]	C09AA07	n/a	n/a	n/a	16.94
	Captopril	C09AA01	9.88	3.37	9.10	7.25
	Cilazapril	C09AA08	14.06	17.66	11.17	11.51
	Enalapril	C09AA02	1.93	2.63	2.45	6.32
	Fosinopril[c]	C09AA09	7.76	5.49	6.23	n/a
	Lisinopril	C09AA03	1.42	2.02	1.24	4.73
	Perindopril	C09AA04	2.33	3.06	2.01	11.32
	Quinapril	C09AA06	3.83	4.70	3.27	11.17
	Ramipril	C09AA05	1.61	2.53	1.43	4.87
	Trandolapril	C09AA10	8.15	13.30	7.12	5.92
	Zofenopril[b]	C09AA15	n/a	n/a	n/a	18.29

Note: a Scotland cost per item refers to gross cost per item; England and Wales to net; Ireland to wholesale cost per item.
b Benazepril and Zofenopril were not reimbursed on the NHS in 2012.
c Fosinopril was not reimbursed on the GMS Scheme in Ireland in 2012.

Sources: http://www.nhsbsa.nhs.uk/PrescriptionServices/3494.aspx [last accessed 8 May 2013]
HSE, personal communication, 9 April 2013

6.6 Conclusion

At present in Ireland, due to the 'dispense as written' requirement for pharmacists in Ireland, prescribers play a key role in driving expenditure on pharmaceuticals. As noted, data on prescriber behaviour in Ireland must be inferred from data on dispensing patterns. In this chapter, we considered the behaviour of prescribers at the therapeutic sub-group level (i.e., ATC level 4) for three major therapeutic sub-

groups (PPIs, ACE inhibitors, statins), rather than at the chemical substance level (i.e., ATC level 5). The analysis in Chapter 5 considered the usage of generics, and highlighted that while the share of generics for particular pharmaceuticals has increased strongly in Ireland over the period 2010–2012, the potential for substantial cost savings in Ireland at present is limited due to the absence of large differences in price between branded and generic products. However, this is beginning to change. Ex-factory price reductions in November 2012, under the agreements between the State and pharmaceutical trade associations, resulted in the price of some generic pharmaceutical products falling substantially compared to the patent holder's price. The commencement of the Health (Pricing and Supply of Medical Goods) Act 2013 will see further declines in the price of generic pharmaceutical products.Substitution within therapeutic sub-groups, commonly termed 'therapeutic substitution' offers the potential for significant cost savings.

In summary, the analysis of Irish dispensing data for selected therapeutic sub-groups (i.e., ATC level 4) shows that Irish medical practitioners in the community tend to prescribe the most expensive ATCs. For example, the most commonly dispensed PPI on the GMS Scheme in 2012 was esomeprazole, with an ex-factory price per unit of €0.65, in comparison to €0.23 for lansoprazole, the HSE's 'preferred drug' within this therapeutic sub-group. The earlier discussion alluded to some of the factors that might explain current Irish prescribing patterns, such as the lack of standardised guidelines, limited monitoring and feedback, etc. This is the logic behind the HSE's 'preferred drugs initiative' for PPIs and statins. However, as noted, the international literature highlights the ineffectiveness of education and information in the absence of vigorous monitoring and feedback on behaviour.

In the UK, prescribing patterns are quite different. The share of generics is above 90 per cent for PPIs, statins and ACE inhibitors, and given the large difference in volume and value generic shares for particular pharmaceuticals, this undoubtedly translates into considerable cost savings for the NHS. In addition, within the three therapeutic sub-groups examined, the patterns suggest that it is the cheaper products that are more commonly dispensed. Standardised guidelines from the NICE and an acceptance of generic prescribing by both hospital and community medical practitioners are just two of the factors influencing prescriber behaviour that may explain the patterns observed for the UK.

CHAPTER 7

Conclusion

7.1 INTRODUCTION

Since the mid-2000s the State has introduced a series of reforms designed to lower pharmaceutical prices in Ireland. This reflected, amongst other things, a concern over the substantial increase in the size of the pharmaceutical budget, both in absolute terms and in per capita terms relative to other OECD countries. These reforms have affected all stages in pharmaceutical delivery from the pharmaceutical manufacturer, to the wholesaler, to the prescriber, to the dispenser and, finally, to the patient. The ex-factory prices of pharmaceuticals in the 2006–2010 State/IPHA Agreement were benchmarked against an expanded basket of nine Member States that included some lower-priced jurisdictions such as Spain. For the first time under this agreement there was provision for pharmacoeconomic assessment of a pharmaceutical prior to reimbursement.

Since 2006, under successive agreements between both the State and the IPHA and the APMI, the ex-factory price of multiple source off-patent pharmaceuticals, once a generic manufacturer appeared on the market, has fallen faster and to a greater extent than before. The wholesale mark-up was reduced by more than half for most products to 8 per cent by 2011. Pharmacy margins under the DP and LTI schemes were cut from 50 to 20 per cent in 2009 with more reliance on a flat dispensing fee, thus reducing, if not eliminating, the incentive to dispense higher priced pharmaceutical products (for INN prescriptions).

The Health (Pricing and Supply of Medical Goods) Act 2013 (the Health Act 2013), which was signed into law on 28 May 2013, promises further reductions in the price of both single source in-patent and multiple source off-patent pharmaceuticals that will be interchangeable. It offers a radical departure from the current price-setting mechanism for pharmaceuticals based on voluntary agreements between the State and industry representative bodies.[1] Under the Health Act 2013 these agreements

[1] The Health Act 2013 also sets out, among other things, processes for the establishment and maintenance of a reimbursement list, requires the HSE to review everything on the reimbursement list within three years of the commencement of the Health Act 2013, gives the HSE the power to delist an item from the reimbursement list and gives the HSE the power to add conditions to the supply/reimbursement in the interests of patient safety and cost effectiveness, thus maximising appropriate use and using the resources available optimally.

will be only one factor which the HSE must take into account in setting the ex-factory price of a pharmaceutical.

In part because of these reforms, but also other factors such as the patent cliff, under the GMS Scheme the price per item (i.e. ex-factory price plus the wholesale mark-up) in 2013 has declined, in nominal terms, to the level last seen in 2001–2002. Nevertheless, concerns remain about the price of pharmaceuticals, the usage of generics, and prescribing practices. In terms of per capita expenditure on pharmaceuticals across OECD countries, the most recent data is for 2010. It shows that Ireland had the third highest per capita expenditure of the twenty-five countries for which data is available; in 2005 the comparable position was ninth out of thirty-one countries. In relation to the US, Ireland's per capita expenditure on pharmaceuticals increased from 58 per cent in 2005 to 70 per cent in 2010.[2]

In this, the final chapter of the report, we present and discuss our findings with respect to each of the issues raised in the terms of reference: the price of pharmaceuticals (Section 7.2); the usage of generics (Section 7.3); and, prescribing practices (Section 7.4). Sections 7.2, 7.3 and 7.4 follow the same format. First, we consider the facts arising out of our research. Second, we consider reasons or explanations for this state of affairs. Finally, where relevant, we discuss the implications of the Health Act 2013. Section 7.5 discusses a number of recommendations while Section 7.6 presents concluding comments.

7.2 The Ex-Factory Price of Pharmaceuticals

7.2.1 The Facts

The evidence suggests that, despite the reforms noted above, the ex-factory price of single source in-patent pharmaceuticals in Ireland is high compared with other Member States in the basket of nine countries against which the ex-factory price of such pharmaceuticals in Ireland are benchmarked. This is a robust and consistent finding from a series of reports using a variety of data sets and over time. It is also consistent with our work using the latest information from the Euripid database and from New Zealand.[3] It is an important finding since the price of multiple source off-patent pharmaceuticals is currently linked directly to the price of single source in-patent pharmaceuticals. Hence, perhaps not surprisingly, the evidence suggests that Ireland also has consistently high generic prices.

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2 The data source is discussed in Chapter 2, Section 2.2.2.

3 It should, of course, be remembered, as mentioned in Chapter 4, that prices are not available for single source in-patent pharmaceuticals that are subject to patient access agreements. However, it is not clear why Ireland would be able to negotiate price reductions on these pharmaceuticals substantially different from those using the arrangements under the 2012-2015 State/IPHA Agreement, based on the average price across the basket of nine Member States.

7.2.2 Explanation

High prices for single source in-patent pharmaceuticals reflect the fact that Ireland tends to be an early adopter of such pharmaceuticals. The price is therefore set based on its availability in a limited number of Member States. Since these tend to be higher price Member States, the initial price of a single source in-patent pharmaceutical is high. In Ireland however, realigning the price to take into account not only of its wider availability in the other Member States but also of subsequent price falls in the initial set of Member States used to set the price does not occur periodically after short intervals (e.g. six or twelve months) as occurs in other Member States. Under the 2006–2010 State/IPHA Agreement realignment took place between one and three years after the single source in-patent pharmaceutical was introduced. Under the 2012–2015 State/IPHA Agreement no explicit realignment is scheduled to take place between 2012 and 2015, apart from the once-off downward only realignments on 1 November 2012 and 1 January 2013. However, the Mid Term Review of the IPHA agreement in 2014 offers the opportunity to raise this issue.

The question arises as to why this state of affairs exists. The previous paragraph explained the mechanics – the *how* – but did not explain *why* Ireland pays consistently high prices for single source in-patent pharmaceuticals. There are at least six, not necessarily mutually exclusive, possible reasons. We consider each in turn.

First, policy-makers and other decision-makers may be unaware of the facts. This explanation is untenable. The reports referred to in Chapter 4 on the prices of pharmaceuticals are widely available. Policy makers have access to the Euripid database, while they routinely compare prices across Member States when realigning prices, adding new pharmaceuticals to the reimbursement list and negotiating patient access agreements. There is extensive media coverage of the price differences between Ireland and other Member States.

Second, there are no solutions to the problem of high prices. It is sometimes the case that although policy-makers are aware of a problem there is no practical solution. However, once again this is not a tenable explanation. Our 2012 report, *Delivery of Pharmaceuticals in Ireland, Getting a Bigger Bang for the Buck*, following in the footsteps of earlier reports,[4] set out a series of steps that were designed to lower the ex-factory price of pharmaceuticals. These recommendations were closely modelled on practice elsewhere in the EU.

[4] For details see Gorecki *et al.* (2012), Annexe A, pp. 147–153.

Third, there may be concerns over security of supply in the Irish market. Ireland is a small Member State. Pharmaceuticals are traded widely within the EU. If the ex-factory price of single source in-patent pharmaceuticals is set too low in Ireland vis-à-vis other Member States parallel exports are likely to occur.[5] A profit is to be made by buying in a lower priced market and selling in a higher priced market. The net result is that shortages might occur in Ireland possibly denying access to important, potentially life enhancing, pharmaceuticals to some patients. This is clearly an important concern and policy-makers need to take this into account in setting the ex-factory price of a single source in-patent pharmaceutical.

However, this does not explain the practice in successive agreements between the State and pharmaceutical industry representative bodies of waiting several years before realigning the price of pharmaceuticals when this price has already fallen in those Member States that were used to set the initial price of a single source in-patent pharmaceutical. More frequent realignment of prices could thus take place without leading to shortages due to parallel exports.

In our earlier report we suggested that instead of using the average price across the basket of nine Member States to set the price of a single source in-patent pharmaceutical that the lowest should be used.[6] In the unlikely event that this were to lead to shortages then perhaps the average price of the two lowest Member States could be used.[7] In other words, ensuring security of supply is an important objective, but it is not a tenable explanation for the persistently high ex-factory price of single source in-patent pharmaceuticals in Ireland.[8]

Fourth, the presence of a large pharmaceutical sector in Ireland. The multinational pharmaceutical sector makes an important contribution to the Irish economy.[9] In

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5 Equally of course, if prices are set too high in Ireland then there will be extensive parallel imports, which is indeed the situation. For details see Gorecki *et al.* (2012), Table 4.3, p.48.

6 The DoH and HSE sought such a change in the negotiations leading up to the 2012–2015 State/IPHA Agreement, but did not secure agreement on the proposed change. For further details see Appendix D. It should also be noted that under Section 24(3)(c) of the Health Act 2013 that the HSE can set the reference price based on equivalent relevant prices in other Member States, while Section 21(1)(2) permits the HSE to use the same criteria with respect to considering the proposed price or reviewing the price of a pharmaceutical. See also Section 18 on the maintenance of the reimbursement list.

7 Slovakia, for example, recently changed its external reference pricing system because of concerns that low prices were leading to substantial parallel exports. The determination of the reference price was changed from the second lowest price among Member States to the average of the three lowest priced Member States. For details see: http://www.ihsglobalinsight.com/SDA/SDADetail21975.htm [last accessed 17 May 2013].

8 In the face of austerity Greece reduced pharmaceutical prices 20 per cent below the next lowest Member State. This resulted in concerns over shortages due to parallel exports. A temporary ban on parallel exports was imposed by the Greek government since there was a danger to public health. (For details see: http://rt.com/news/greece-list-pharma-parallel-export-debt-574/ [accessed 5 June 2013]). However, the proposals in this report would not see prices in Ireland fall to such low levels.

9 See, for example: a speech delivered by the Minister for Small Business on 23 February 2012. It may be accessed at: http://www.djei.ie/press/2012/20120223b.htm. [last accessed 5 June 2013]; and, a 2012 report by Davy Investment

terms of employment, for example, it is estimated that 24,500 people work in the pharmaceutical sector accounting for 1.25 per cent of employment.[10] Since price is likely to be an important determinant of profitably, efforts to reduce the ex-factory price of single source in-patent pharmaceuticals may adversely affect these multinational pharmaceutical firms. As a result they might decide to reconsider current and future operations in Ireland. However, it is not clear how credible such an argument is in support of high prices.

Ireland accounts for a very small share of the EU market for pharmaceuticals and hence the Irish price is unlikely to impact to any great extent on the profitability of these multinationals.[11] The literature suggests that there are other reasons that explain the location decision of multinationals such as the corporation tax rate, educated labour force, membership of the EU, and so on.[12] Furthermore, the record of the UK, which in the early 2000s had amongst the highest prices for single source in-patent pharmaceuticals in the EU and a large pharmaceutical sector, is instructive. It has reduced the price of single source in-patent pharmaceuticals and aggressively cut the price of multiple source off-patent pharmaceuticals, but still retains a substantial pharmaceutical sector.[13]

Finally, the sorts of reforms that would see more frequent realignment of the ex-factory price of single source in-patent pharmaceuticals, using the lowest priced or a group of the lowest of the basket of nine Member States to set the price of a single source in-patent pharmaceutical and so on, are not radical departures from the EU mainstream in terms of setting the price of such pharmaceuticals. In other words, the adoption of such policies by Ireland should not lead to adverse knock-on effects elsewhere for multinational pharmaceutical firms.

Fifth, failure to adhere to the €45,000 cost per QALY threshold. As noted in Chapter 3 a threshold is set of €45,000 per QALY in pharmacoeconomic assessments of pharmaceuticals prior to reimbursement. However, if the threshold is exceeded then prices will be higher than if this were not the case. The evidence, albeit somewhat

Brokers on Ireland and the patent cliff. This may be found at: http://www.davy.ie/content/pubarticles/patentcliff 20121128.pdf [last accessed 20 June 2013].

10 (IMF), 2013, p. 7

11 It could, of course, be argued that prices in Ireland are used in other Member States to set new pharmaceutical prices. (See, for example, the letter cited in Chapter 3 from Abbott Laboratories to the Taoiseach dated 23 February 2012 on this issue). Hence if prices were reduced in Ireland they would lower the profitability of these multinationals across a number of different markets. However, as these Member States come to realize, through reports such as this one, the impact caused by high ex-factory prices in Ireland, they may well consider excluding Ireland in setting prices for new pharmaceuticals.

12 Siedschlag, 2013, pp. 3–4

13 On employment, for example, this varied between 68,000 and 73,000 between 1998 and 2010, apart from 2002 when it reached 84,000. For details see: http://www.abpi.org.uk/industry-info/knowledge-hub/uk-economy/Pages/uk-pharmaceutical-employment.aspx. [last accessed 4 June 2013].

partial because of the confidential nature of patient access agreements, suggests that pharmaceuticals are reimbursed even though the €45,000 threshold cost per QALY is exceeded. This certainly seemed to be the case for ivacaftor[14] and ipilimumab[15] and earlier for sunitinub where the QALY was €57,280.[16] As noted in the discussion in Chapter 3 there needs to be greater societal recognition that by exceeding the threshold other aspects of public expenditure as well as health care policy are curtailed, even though the benefits may be greater.

Sixth, the current price-setting mechanism for pharmaceuticals. One of the constants with respect to pharmaceutical pricing in Ireland is the agreements between the State and the various pharmaceutical representative bodies. These are voluntary agreements between a buyer, the State, and suppliers, pharmaceutical manufacturers. Reaching agreement is frequently long and drawn out. A successor to the 2006–2010 agreements between the State and IPHA and APMI was not concluded until 2012. Changing the price-setting mechanism might therefore – depending, of course, on the replacement – offer the chance of structural change leading to lower prices for single source in-patent pharmaceuticals, not only for the State but also for the cash-paying patient.

7.2.3 Implications of the Health Act 2013

The Health Act 2013 offers the prospect of a change in the way in which the ex-factory price of single source in-patent pharmaceuticals is set. Section 21, according to the Explanatory Memorandum, 'sets out the criteria to be taken into account when considering the proposed listing of an item'. The criteria are set out in Section 21(2) as follows:

> The Executive [i.e., HSE] shall, when considering the proposed relevant price by the supplier of an item, take into account
>
> a) the equivalent relevant prices (if practicably available) of the item in all other Member States where the item is marketed,
>
> b) the relevant prices of therapeutically similar listed items,
>
> c) the potential therapeutic benefits of the item for patients likely to use the item if it were to become a listed item,
>
> d) the potential budget impact of the item if it were to become a listed item,
>
> e) the ability of suppliers of the item to meet patient demand for the item if it were to become a listed item,
>
> f) the resources available to the Executive, and

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14 For details see Chapter 3.

15 On the basis of the price submitted, the NCPE (2011) calculated a cost per QALY of €147,899 for ipilimumab. Subsequently there was a patient access agreement, but there was no disclosure of the price agreed.

16 Tilson *et al.*, 2010

g) the terms of any agreement in place (whether entered into before, on or after the commencement of this section) between the Executive and any representative body of the suppliers of drugs, medicines or medicinal or surgical appliances where the agreement relates, whether directly or indirectly, to the price of the item.

Section 21(3) provides that the HSE may review and alter the price of a pharmaceutical to take into account any change in the matters listed in Section 21(2). These is no restriction on the timing of such reviews.

The current agreements between the State and the pharmaceutical representative bodies is just one factor to be taken into account when setting price under Section 21(2). As with the discussion in Chapter 5 concerning a similar provision with respect to multiple source off-patent pharmaceuticals, there is a lack of information and analysis as to how this section is to be implemented. Nevertheless, the new Act gives the HSE more discretion in setting the price for single source in-patent pharmaceuticals.[17]

It could be argued that the Health Act 2013 will not in some senses change the facts on the ground. That is too narrow an interpretation. The HSE will have a legal basis for determining the price that is independent of the current agreements with pharmaceutical representative bodies. Pharmaceutical manufacturers might decide either individually or collectively to refuse to supply or possibly boycott any ex-factory price set under Section 21 that was below that specified in the 2012–2015 State/IPHA Agreement. However, a collective boycott or a refusal to supply by an individual manufacturer might well fall foul of not only the Competition Act but also the corresponding provision in EU legislation.[18,19]

17 As such it affords the HSE the opportunity to implement some of the recommendations we made in our earlier report on pharmaceutical delivery. For details see Appendix D.

18 The Competition Authority (2008) takes the view that the Health Service Executive in reaching agreements with pharmaceutical representative bodies in relation to pharmaceutical reimbursement schemes, such as the GMS Scheme, is not subject to the Competition Act.

19 For a discussion of these issues in relation to a boycott see Competition Authority (2009b), pp. 18–19. It could be objected that this discussion refers to competing firms and that IPHA members do not typically compete directly with one another at the ATC 5 level. However, competition may take place at the ATC 4 level, while members of the IPHA may be in competition in developing new pharmaceuticals.

7.3 The Usage of Generics

7.3.1 The Facts

The usage of generic pharmaceuticals in Ireland has increased dramatically. Indeed, between 2010 and 2012 for the leading multiple source off-patent pharmaceuticals under the GMS Scheme, the share of generic pharmaceuticals doubled to 50 per cent, in some cases reaching nearly 70 per cent. However, because the price of generic and brand name pharmaceuticals has been similar this has not translated into substantial savings for the State.[20] Furthermore, as noted above, prices of generic pharmaceuticals are higher in Ireland than for the Member States in the basket of nine used to set the price for new pharmaceuticals. However, this state of affairs is likely to change with the coming into force of the 2012–2015 agreements between the State and IPHA and AMPI and the implementation of the Health Act 2013, both of which will see the gap between generic and brand name pharmaceuticals widening.

7.3.2 Explanation

Based on an analysis of the ex-factory price-setting mechanism and the current regulations concerning prescribing, the usage of generics in Ireland was expected to be low. This reflected a number of factors.

- Medical practitioners had a propensity to prescribe the patent holder's pharmaceutical product.
- A dispense as written policy left the pharmacist with no discretion in selecting the pharmaceutical product.[21]
- There was little difference in the patent holder and generic manufacturer price. Indeed for periods in 2010 and 2011 the generic manufacturer price *exceeded* the patent holder's price for multiple source off-patent pharmaceuticals. Hence there was no incentive for the patient (if they were cash-paying) or the prescriber (if they were concerned about the HSE expenditure on pharmaceuticals) to select a generic manufacturer's product.

Nevertheless, the evidence points to a dramatic increase in the importance of generic pharmaceuticals between 2010 and 2012 for leading multiple source off-patent pharmaceuticals. It is not clear to what extent this increase in generic usage is due to changing practices by medical practitioners, patient preferences for generic

[20] Nevertheless, as noted in Chapter 3, once a generic pharmaceutical is placed on the market the patent-holder's price declines from the pre-generic entry price level. Hence the entry of a generic leads to price reductions, but increased market penetration by the generic has little impact on the price paid for a pharmaceutical. However, as noted in the text, this situation is changing.

[21] Unless it was prescribed using the INN, a generic prescription.

products and/or changing dispensing behaviour of pharmacists. We consider two possible explanations:

- First, the increased use of computer programmes to print prescriptions, makes the selection of the generic option much easier. Brand names tend to be easier to remember and write than using the INN or common name. However, by ticking the generic option on the computer programme that problem is resolved. In addition, survey evidence suggests that patients are favourably disposed to generic pharmaceuticals and hence may request medical practitioners to prescribe generically, especially if the prescription is to be filled in, for example, Northern Ireland or Spain.[22]
- Second, pharmacist behaviour may be changing. Generic manufacturers offer pharmacies substantial discounts off the reimbursement price set by the HSE.[23] Pharmacists' incomes have been hit by a series of cuts under FEMPI since 2009. Bankruptcy for a pharmacist means that they cannot practice under the Pharmacy Act 2007.[24] One way of offsetting the loss of income from regulations made under FEMPI is through increased discounts off multiple source off-patent pharmaceuticals. Such discounts are likely to increase in importance with the patent cliff.

While both of these explanations no doubt play a part in accounting for the increased importance of generics, we are not in a position to assess the significance of each.

7.3.3 Implications of the Health Act 2013

The Health Act 2013 offers the opportunity for the State to capture an increased share of the discounts currently accruing to pharmacists. Increased generic usage might then lead to a lower bill for the State. Under the various agreements between the State and the IPHA and APMI, the price of multiple source off-patent pharmaceuticals is linked to the patent holder's price prior to entry. Up until very recently the generic manufacturer's price was only a small discount to that of the patent holder, although that is destined to change for interchangeable pharmaceutical products, where the generic manufacturer's pharmaceutical will be 20 per cent below the patent holder's price. Furthermore, as noted in Chapter 3, generic pharmaceuticals will be priced at a 29 per cent discount to the patent holder’s price for the first year in which the generic is available, and 5 per cent thereafter. However, these pricing rules take no account of the competitive

22 This explanation is unlikely to be relevant for GMS Scheme patients since pharmaceuticals are supplied free of charge, except for a fixed co-payment per item that is unrelated to the value of the pharmaceutical dispensed.

23 i.e., the ex-factory price, plus an 8 per cent wholesale mark-up

24 For details see Irish Pharmacy Union, 'Pharmacists call for change to bankruptcy restrictions on profession', 28 April 2013. http://ipu.ie/more-news/1581-pharmacists-gather-for-national-conference.html [last accessed 7 May 2013].

conditions in the supply of generic pharmaceuticals and thus may be missing opportunities for further price reductions.

Notwithstanding the lack of precision in the Health Act 2013 and the surrounding documentation (e.g., the RIA) as to how reference pricing will operate, this should not take away from the fact that it represents a significant step towards the ***possibility*** of lowering ex-factory pharmaceutical prices in Ireland over and above those measures already agreed between the State and the pharmaceutical representative bodies. The Health Act 2013 permits for the first time generic substitution. It provides the HSE with legislative authority to set a reference price for the purposes of reimbursement based on a wide array of considerations that extend beyond the current agreements with industry representative bodies.[25] Tendering, for example, is an option under the legislation. Unilateral price reductions based on the fact that prices are lower in other Member States is permissible. As a result, under the Health Act 2013 the State may succeed in capturing a significant portion of the discounts, kickbacks and deals that currently accrue to other parts of the manufacturing, wholesaling and pharmacy chain.

Nevertheless the same objection as made above concerning single source in-patent pharmaceuticals could be made here viz that the Act does not change the facts on the ground. However, again this argument does not appear to be sustainable. Suppose the State lowers, in accordance with the Health Act 2013, the reference price below the price set out in the 2012-2015 State/APMI Agreement. If generic manufacturers were to boycott or refuse to supply the pharmaceutical whose reference price had been dropped, then this co-ordinated conduct between competitors is likely to breach the Competition Act.[26] There are already analogous examples of such behaviour in the health care sector with respect to pharmacists[27] and dentists[28] falling foul of the Competition Act leading to action by the Competition Authority.

7.4 Prescribing Practices

7.4.1 The Facts

Our analysis of prescribing patterns at the therapeutic sub-group level (i.e., ATC level 4) for three groups (PPIs; statins; ACE inhibitors) showed that when medical practitioners in Ireland are confronted with a choice among different PPIs, statins and ACE inhibitors, they generally prescribe the most expensive pharmaceutical

[25] These are set out in Section 7.2.3.

[26] In contrast to the discussion above concerning members of IPHA, generic manufacturers are much more likely to be competitors.

[27] For details see Competition Authority (2009a).

[28] For details see Competition Authority (2006), p.11.

product. In the UK, in contrast, medical practitioners tend to prescribe the least expensive. As products within these therapeutic sub-groups are considered interchangeable for the majority of patients, moving towards the prescription of cheaper alternatives offers the potential for significant cost savings. PPIs, statins and ACE inhibitors accounted for 18.1 per cent of GMS Scheme pharmaceutical expenditure in 2012.

7.4.2 Explanations

Apart from clinical needs and the expectations of the patient, prescriber behaviour is influenced by a variety of financial and non-financial factors (e.g., prescription guidelines; education and information; monitoring and feedback; financial incentives; regulations concerning generic prescribing, etc.). At present, Irish medical practitioners have considerable discretion in deciding on the type of pharmaceutical to prescribe. While information on prescribing is available from a variety of sources, Irish prescribers' knowledge of pharmaceutical costs is limited. In addition, there is limited monitoring of behaviour. In this context, it is unsurprising that expensive, brand name products are more likely to be prescribed. The recent 'preferred drugs initiative' provides specific advice on therapeutic substitution for two therapeutic subgroups (PPIs and statins), but international evidence highlights the lack of evidence on the effectiveness of education and information alone in the absence of vigorous monitoring and feedback on behaviour.

In other countries in contrast, prescriber behaviour is supported by a wider range of standardised guidelines, closer monitoring, and more targeted feedback. In the UK, standardised guidelines from the NICE and the acceptance of generic prescribing by medical practitioners in both the community and hospital sectors are just two of the factors that explain the patterns of prescriber behaviour observed for the UK.

7.4.3 Implications

In Ireland, medical practitioners choice has two adverse effects. First, they needlessly raise State and patient pharmaceutical costs, but with little or no improvement in the quality of care. Second, the medical practitioner choice renders generic substitution and reference pricing which is part of the Health Act 2013 and operates at the level of an individual pharmaceutical – the ATC 5 level – less effective. If there are several PPIs or statins or ACE inhibitors then as soon one loses patent protection the patent holder has much less incentive to promote that pharmaceutical because the benefits will to a large extent be captured by generic manufacturers. In contrast, those PPIs or statins or ACE inhibitors that remain patent protected are likely to continue to attract marketing effort. If medical practitioners partly prescribe on the basis of pharmaceutical manufacturers marketing then, other

things equal, demand will migrate away from the cheaper PPI, statin or ACE inhibitor experiencing generic competition to the more expensive patent protected pharmaceuticals.

One way to address this problem is through extending reference pricing and generic substitution to the ATC 4 level. This occurs, for example, in some Member States[29] and for the province of Saskatchewan in Canada with respect to PPIs.[30] However, the Health Act 2013 will operate only at the ATC 5 level and so this option, at the present time, is excluded. Another is the provision of information, which is that currently favoured by the HSE for two therapeutic sub-groups – PPIs and statins. As noted, closer monitoring of prescribing patterns should be undertaken to ensure information provision is as effective as possible. In Section 7.6 we consider a mechanism to facilitate such information provision to assist in monitoring.

7.5 Policy Recommendations

It is beyond the scope of this report to prepare a detailed set of recommendations. To a considerable extent that is, in any event, superfluous. In our report issued in January 2012, *Delivery of Pharmaceuticals in Ireland, Getting a Bigger Bang for the Buck,* we made a series of 23 recommendations designed to lower the price of pharmaceuticals, increase the usage of generics, and change prescriber behaviour, among others.[31] These recommendations covered not only the ex-factory price but also issues associated with the behaviour of the wholesaler, retailer (i.e., the pharmacist) and the prescriber. We see no reason to change or revise those recommendations which are as relevant today as they were seventeen months ago.

Nevertheless one set of recommendations is worth reiterating and that is the introduction of more price disclosure and competition at the retail level. This is vitally important if the cash-paying patient is to benefit from the introduction of generic substitution and reference pricing. There is no reason why, for example, pharmacists should not be required to post, in a prominent place in the pharmacy, the price charged for the leading 20 interchangeable pharmaceuticals that are to be designated by the IMB, together with the reference price. At the pharmacist's discretion this could also be published online.

The HSE will assist in informing patients by providing information on the reference price for pharmaceuticals in a consumer friendly format. The National Consumer

29 Carone *et al.*, 2012, Table 8, p. 24

30 Gorecki *et al.*, 2012, Box 4.3, p. 80

31 Appendix D lists each of the recommendations together with the progress made in implementing them prepared by the Department of Health.

Agency has shown an interest in pharmaceutical pricing and the use of their expertise would likely make any information campaign more effective.[32] In addition the DoH has approached the pharmacy regulator, the Pharmaceutical Society of Ireland, with a view to ensuring that there will increased price transparency.[33] At the present time there is limited provision of such information.[34]

Since the publication of our 2012 report, it is evident that patient access agreements have become more important as an alternative mechanism for pricing single source in-patent pharmaceuticals. The evidence, albeit somewhat partial because of the confidential nature of patient access agreements, suggests that these single source in-patent pharmaceuticals are reimbursed even though the €45,000 threshold cost per QALY is exceeded. The experience to date with patient access agreements raises a number of policy questions that need to be addressed:

- Is it appropriate for the threshold value of the cost per QALY to be decided as part of a negotiated agreement between the State and the IPHA (as happens at present), rather than the State deciding independently on the threshold value?
- Is €45,000 the correct value for the QALY? In the UK, for example, the National Institute for Health and Care Excellence (NICE) uses a range from €23,500 to €35,000, while a recent exhaustive report for NICE suggests a threshold of €21,500.
- If €45,000 is appropriate, under what conditions should it be overridden?
- What are the implications of disregarding the threshold for other aspects of the health budget which will inevitably suffer – the opportunity cost – as well as for similar negotiations with pharmaceutical manufacturers in the future?

A national conversation concerning these questions would bring some clarity in guiding policy makers in this area.

If there is agreement to adhering to a threshold, then arrangements should be put in place to ensure that such a commitment is credible. Lessons might be learnt from an agency such as New Zealand's PHARMAC, an independent arm's length agency that has been successful in moderating pharmaceutical costs.[35] PHARMAC has a fixed budget and thus carefully considers the opportunity cost of listing any new single source in-patent pharmaceutical. No doubt in part because of this PHARMAC, for

32 NCA, 2013

33 For details see Chapter 5 and Appendix D.

34 For details see Gorecki *et al.* (2012), pp. 115–122.

35 For discussion see, for example, Duckett *et al.* (2013) and Lybecker (2013).

example, refused to cover the cost of ipilimumab,[36] while an application has not been made to PHARMAC for reimbursement for ivacaftor.[37]

While there is a trade-off involved in the confidential nature of patient access agreements (i.e., transparency vs. lower prices), this should not prevent more information from being published, such as details of the monitoring of health outcomes; details of new pharmaceuticals approved under patient access agreements as compared to the more normal procedures; and, a frequency distribution of the cost per QALY of those pharmaceuticals approved under patient access agreements on an annual basis. We are aware, for example, in the case of ivacaftor, of Kalydeco Health Outcomes Protocol that has been circulated to relevant health professionals and organisations and sets out clearly a monitoring framework that will be employed.[38]

7.6 Concluding Comments

The comments and criticisms in Sections 7.2 to 7.4 of this chapter do not take away from the success of the State in lowering pharmaceutical prices since the mid-2000s. However, this success needs to be built upon so as to further reduce prices and expenditure on pharmaceuticals to levels in comparable Member States while at the same time not compromising the quality of care or security of supply. This report, combined with our earlier report, *Delivery of Pharmaceuticals in Ireland, Getting a Bigger Bang for the Buck*, suggests that reforms can lead to these gains being realized. At a time of budgetary restraint it is imperative that the opportunity be seized so that solutions such as increased user charges for patients are not favoured. Policies such as the pharmaceutical co-payment for those on the GMS Scheme affect some of the most vulnerable members of society, and user charges such as these have well-documented negative effects on access to health care.

It is customary for researchers to conclude a report such as this with a call for more research. However, while there are undoubtedly areas where further research is merited, such as the implications of the Health (Pricing and Supply of Medical Goods) Act 2013 for the cash-paying patient, an issue raised in Chapter 5, or the implications of our findings for the hospital sector, or whether €45,000 is the correct value of a QALY, instead we conclude for a call for the release, on an open access basis, of the monthly records of the GMS and DP Schemes. This is already the practice in the UK and without access to such data we would not have been able to conduct the analysis in Chapter 6 which found that UK medical practitioners often select the lowest priced statin, PPI and ACE inhibitor. Furthermore, the UK also releases data

36 HSE, personal communication, 16 May 2013
37 PHARMAC, personal communication, 21 May 2013
38 HSE, personal communication, 20 May 2013

on prescriber behaviour by individual medical practices. If, as at present in Ireland, the income of medical practitioners from the GMS Scheme is released it is difficult to understand why dispensing data should not also be released. The release of GMS and DP Scheme data will allow ongoing research into the issues investigated in this report and hence monitor the success of reforms to lower pharmaceutical prices, increase the use of generics, and change prescriber behaviour. As such it is fully aligned with the move towards more evidence-based policy and evaluation.

APPENDIX A

Terms of Reference

This project will produce a report comparing the price of pharmaceuticals, prescribing practices and the usage of generics in Ireland with comparable European Union Member States. It reflects the terms of the seventh update of the Memorandum of Understanding on Specific Economic Policy Conditionality, which is part of the EU-IMF Programme of Financial Support for Ireland.[1] The report builds on and updates *Delivery of Pharmaceuticals in Ireland: Getting a Bigger Bang for the Buck* which was prepared for the HSE by Paul K Gorecki, Anne Nolan, Aoife Brick and Sean Lyons. It was published in the ESRI Research Series in January 2012.

In terms of comparable European Union Member States we will include, at a minimum, the nine Member States in the basket used to set the price for new pharmaceutical products in Ireland. We will also use, after consultation with the HSE, the leading Member States – if they are not already included in the basket of nine – from which parallel imports into Ireland are sourced.

The project will to a considerable extent draw on the existing literature and on data sources that the HSE either has under its control or is able to gain access to on behalf of the research team. The HSE will renew the data access agreement with the ESRI previously signed in 2011. The data referred in the text and footnotes of this proposal will be provided in the same format as under this earlier agreements as per the attached example.

The report will consist of four inter-related building blocks.

1) In order to understand and place in context pricing and market share information it will be necessary to review recent changes including the agreements between the State and the representative bodies for:
   (i) brand name pharmaceuticals (Irish Pharmaceutical Healthcare Association);
   (ii) generic pharmaceuticals (Association of Pharmaceutical Manufacturers of Ireland); and,
   (iii) parallel importers.

[1] See: http://www.finance.gov.ie/documents/publications/mou/mounov2012.pdf [last accessed 12 February 2013].

2) A comparison of the price of pharmaceuticals in Ireland with other EU Member States and the recent pattern of price changes in Ireland. The price in this context is the ex-factory price rather than the price at the pharmacy or the HSE reimbursement price.

The sample of pharmaceuticals on the General Medical Services (GMS) and Drug Payment (DP) schemes at the Anatomical Therapeutic Chemical Classification (ATC) level 5 (e.g. atorvastatin, fentanyl *etc.*) will consist of:

(i) the top 20 pharmaceuticals *with* a generic equivalent as per Table 4.5 of *Delivering Pharmaceuticals in Ireland* at p. 71, but updated; and,

(ii) the top 10 pharmaceuticals *without* a generic equivalent as per Table 4.3 of *Delivering Pharmaceuticals in Ireland* at p. 48, but updated.[2]

Price comparisons with other European Member States will be made available through, for example, the HSE's access to the Euripid system.[3]

3) A comparison of prescribing practices. Here there is much less comparable data than for either pharmaceutical prices or generic usage across EU Member States. The literature will be reviewed to see if there are any updates since Delivering Pharmaceuticals in Ireland was published. We will also review dispensing claims data made available from the HSE as a proxy for prescribing practices. We anticipate comparisons being made at the ATC level 4 for at least three classifications: proton pump inhibitors: statins: and, benzodiazepines. It is our understanding that other ATC 4 level classifications may be available.

4) The usage of generic pharmaceuticals, which is often considered a reflection of prescribing practices – especially in Ireland where there is a legal obligation to dispense as written – as well as a measure of how successful *national systems are in reducing* pharmaceutical prices.

(i) We will use a sample of the top 10 pharmaceuticals with a generic equivalent measured by value for the GMS and DP as per Table 4.6 of the *Delivery of Pharmaceuticals in Ireland* at p. 73, but updated.

(ii) In addition data will be made available so that Figure 7.2 of the *Delivery of Pharmaceuticals in Ireland* at p.128 can be updated to 2012.

(iii) Various other sources such as the European Generics Medicines Association will be used to get comparative market shares for other EU Member States,

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2 The data should be presented in such a way that parallel importers are separately identified.

3 The method of access will be discussed with HSE in order to minimise overlap and duplication.

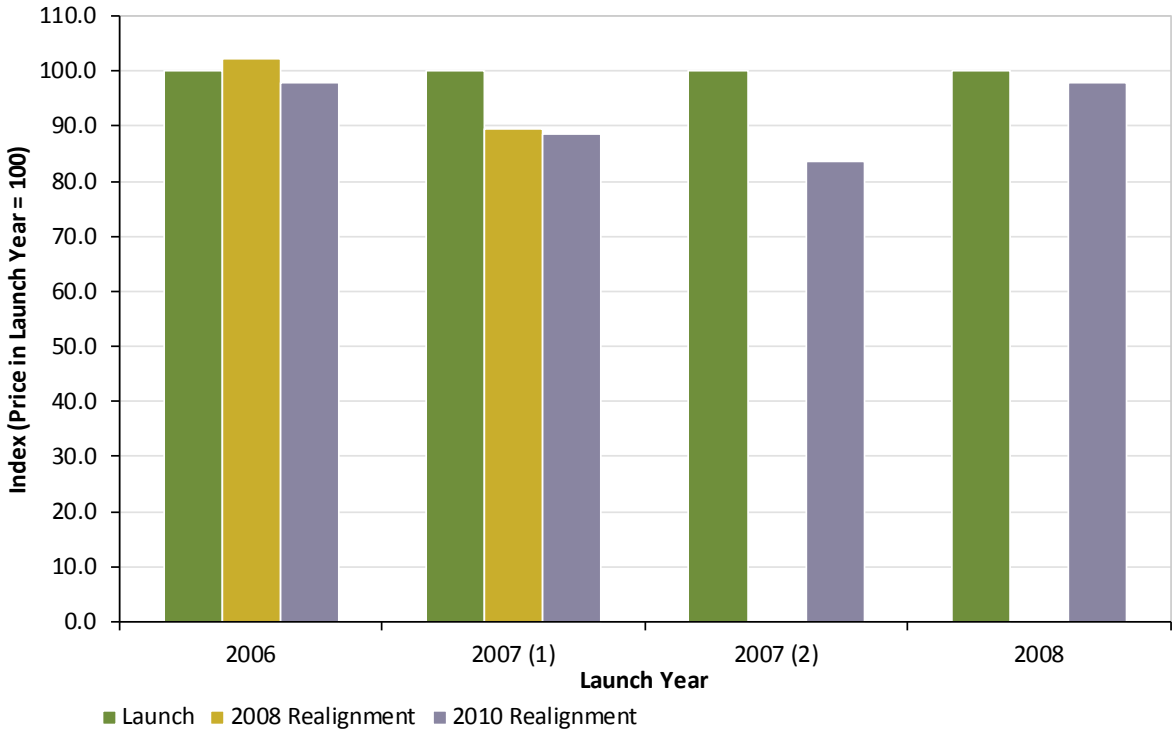
but there does not appear to be any source that provides comparative data on a pharmaceutical by pharmaceutical basis.

It is our understanding that the ranking of the importance of pharmaceuticals in 2) and 4) will be based on the reimbursement value cumulated from January 2012 to the latest month for which data is available in 2012, while the prices will be for January 2013 and for the same date in 2012, 2011, 2010 and 2009.

APPENDIX B

Additional Tables and Charts

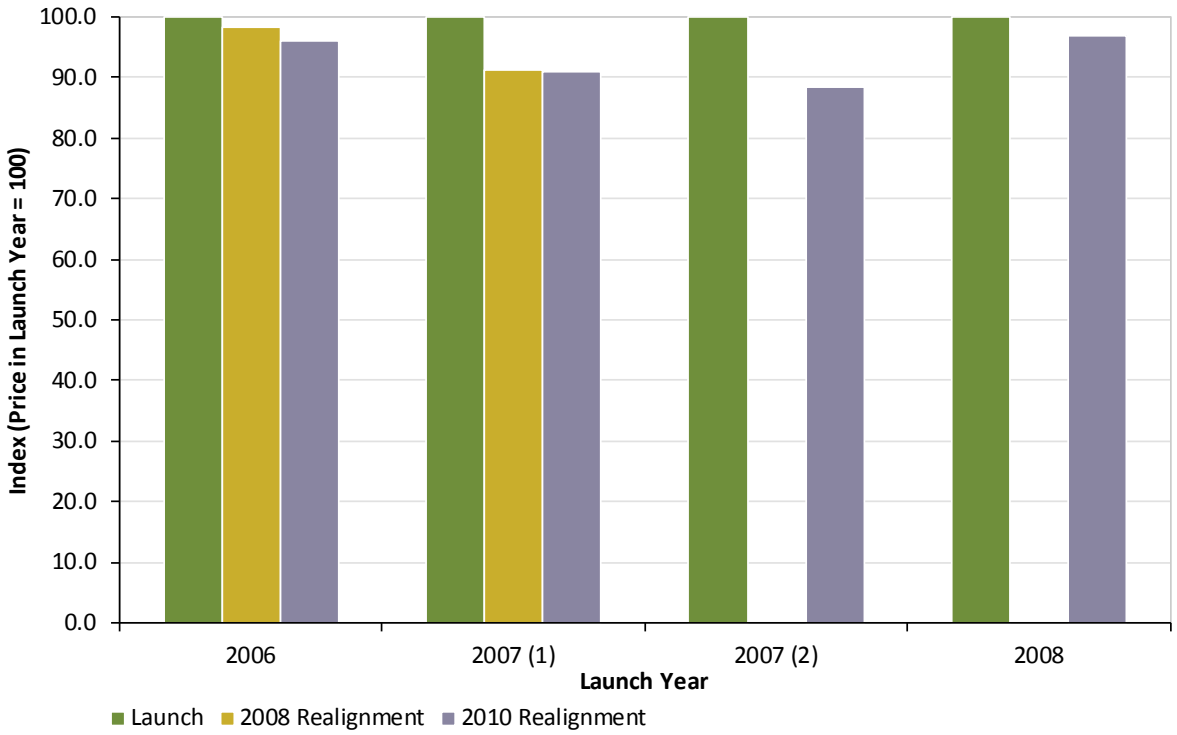
FIGURE B.1 Impact of Realignment on the External Reference Price,[a] Using the Average Price in the Basket of Nine Member States Available at Launch, by Year of Launch, Ireland, 2006–2010



Notes: a The data refer to products launched on the GMS Scheme in 2006, 2007, and 2008. The original data contains information on 464 products launched between September 2006 and July 2011. Products for which data are missing were excluded from the analysis. Only pharmaceuticals for which prices were available at launch from at least some of the Member States in the basket of nine were included. The final analysis is based on 101 pharmaceutical products. There were 15 new pharmaceuticals included in the figure with a 2006 launch with a 2008 and 2010 realignment, 19 with a 2007 launch with a 2008 and 2010 realignment (1), 20 with a 2007 launch with only a 2010 realignment (2), and 47 with a 2008 launch with a 2010 realignment. For each new pharmaceutical product its price is set at 100 at launch and expressed relative to that for the 2008 and/or 2010 realignments. The average was then estimated and presented in the figure.

Source: ESRI calculation from HSE personal communication, 11 August 2011

FIGURE B.2 Impact of Realignment on the External Reference Price,[a] Using the Minimum Price in the Basket of Nine Member States Available at Launch, by Year of Launch, Ireland, 2006–2010



Notes: a See notes to Figure B.1.

Source: ESRI calculation from HSE personal communication, 11 August 2011

TABLE B.1 Market Share of Selected ATCs on the GMS Scheme, 2010–2012

ATC Description	ATC	2010		2011		2012	
		Volume (%)	Value (%)	Volume (%)	Value (%)	Volume (%)	Value (%)
Single Source In-Patent							
Aripiprazole	N05AX12	0.05	0.52	0.06	0.76	0.07	0.87
Duloxetine	N06AX21	0.20	0.45	0.23	0.60	0.27	0.70
Escitalopram	N06AB10	0.87	1.56	0.96	1.87	0.98	1.88
Etoricoxib	M01AH05	0.28	0.51	0.29	0.54	0.28	0.53
Ezetimibe	C10AX09	0.18	0.43	0.19	0.51	0.20	0.54
Fentanyl	N02AB03	0.12	1.03	0.11	1.07	0.11	0.94
Formoterol and other drugs for obstructive airway diseases	R03AK07	0.41	1.39	0.43	1.63	0.44	1.71
Memantine	N06DX01	0.13	0.72	0.16	0.98	0.19	1.18
Montelukast[a]	R03DC03	0.31	0.69	0.32	0.82	0.35	0.88
Pregabalin	N03AX16	0.53	2.81	0.64	3.86	0.75	4.24
Salmeterol and other drugs for obstructive airway diseases	R03AK06	0.92	3.78	0.91	3.81	0.91	3.76
Tiotropium bromide	R03BB04	0.59	1.73	0.61	1.99	0.64	2.06
Varenicline	N07BA03	0.10	0.48	0.10	0.55	0.09	0.47
Multiple Source Off-Patent							
Amlodipine	C08CA01	1.56	0.87	1.52	0.78	1.49	0.76
Bisoprolol	C07AB07	1.84	0.53	1.89	0.44	1.95	0.42
Diclofenac	M01AB05	1.08	0.55	0.99	0.39	0.90	0.31
Esomeprazole	A02BC05	1.44	3.61	1.55	3.15	1.68	3.30
Lansoprazole	A02BC03	1.31	2.66	1.29	2.06	1.26	1.87
Omeprazole	A02BC01	1.24	2.00	1.24	1.64	1.25	1.58
Pantoprazole	A02BC02	0.96	1.02	1.04	1.05	1.06	0.95
Pravastatin	C10AA03	0.94	1.08	0.84	0.78	0.76	0.67
Ramipril	C09AA05	1.46	0.63	1.44	0.53	1.42	0.50
Rosuvastatin	C10AA07	1.11	1.87	1.25	1.87	1.35	1.89
Single-to-Multiple Source							
Atorvastatin	C10AA05	3.49	8.31	3.46	6.47	3.44	6.01
Olanzapine	N05AH03	0.38	2.49	0.40	2.26	0.42	2.17
Quetiapine	N05AH04	0.34	1.22	0.39	1.49	0.43	1.47

Note: a Montelukast went off-patent in Ireland in March 2013.
Source: ESRI calculation from HSE personal communication, 9 April 2013

TABLE B.2 Ex-Factory Pharmaceutical Prices of Leading Pharmaceuticals – Ireland, 2011 and 2013

ATC Description	ATC	GMS Product	Dose	Pack Size	2011				2012				Ex-Factory Price % Change 2011-2013
					Type[a]	Ex-Factory Price Sept 2011	Unit Price	% of ATC 2011[b]	Type[a]	Ex-Factory Price Mar 2013	Unit Price	% of ATC 2012[b]	
						€	€			€	€		
Alendronic acid	M05BA04	Fosamax Once Weekly	70mg	4	3	13.19	3.30	47.3	3	13.19	3.30	36.5	0.0
		Romax Once Weekly	70mg	4	2	13.19	3.30	10.7	2	13.19	3.30	11.7	0.0
Amlodipine	C08CA01	Istin	5mg	28	3	5.53	0.20	23.0	3	5.53	0.20	19.0	0.0
		Amlid	5mg	28	2	5.42	0.19	10.4	2	5.42	0.19	10.2	0.0
Atorvastatin	C10AA05	Lipitor	10 mg	28	3	15.53	0.55	31.6	3	12.83	0.46	21.6	-17.4
		Atorvastatin Teva	10 mg	28	-	-	-	-	1	10.70	0.38	3.8	-
Clopidogrel	B01AC04	Plavix	75mg	28	3	36.43	1.30	56.7	3	27.32	0.98	44.0	-25.0
		Clopidogrel Actavis	75mg	28	1	34.39	1.23	9.7	1	22.77	0.81	15.1	-33.8
Donepezil	N06DA02	Aricept	10mg	28	3	44.18	1.58	27.8	3	44.18	1.58	21.3	0.0
		Donecept Film Coated	10mg	28	2	43.30	1.55	17.2	2	43.30	1.55	22.2	0.0
Escitalopram	N06AB10	Lexapro	10 mg	28	4	20.94	0.75	38.4	4	19.81	0.71	40.8	-5.4
Esomeprazole	A02BC05	Nexium	40mg	28	3	28.24	1.01	27.0	3	28.24	1.01	19.8	0.0
		Nexazole	40mg	28	2	28.24	1.01	20.1	2	20.61	0.74	20.8	-27.0
Fentanyl	N02AB03	Durogesic Dtrans	25 mcg	5	4	35.70	7.14	28.9	4	20.75	4.15	27.9	-41.9
Formoterol[c]	R03AK07	Symbicort Turbohaler	200/6 mcg	1	4	46.40	46.40	51.1	4	46.40	46.40	52.4	0.0
Lansoprazole	A02BC03	Zoton Fastab	30mg	28	4	21.77	0.78	31.4	4	12.70	0.45	31.2	-41.7
		Zotrole	30mg	28	2	21.77	0.78	14.4	2	12.70	0.45	15.9	-41.7
Olanzapine	N05AH03	Zyprexa	5mg	28	3	46.88	1.67	24.9	3	35.28	1.26	13.7	-24.7
		Olanzapine Actavis	10mg	28	-	-	-	-	1	58.81	2.10	5.6	-
Omeprazole	A02BC01	Losec Mups	20mg	28	3	13.16	0.47	19.1	3	13.16	0.47	17.5	0.0
		Lopraz	20mg	28	2	12.90	0.46	10.7	2	12.90	0.46	13.3	0.0
Pantoprazole	A02BC02	Protium	40mg	28	3	13.02	0.46	32.3	3	13.02	0.47	25.7	0.0
		Pantoflux	40mg	28	2	12.76	0.46	8.7	2	12.76	0.46	12.5	0.0
Perindopril[d]	C09AA04	Coversyl Arginine	5 mg	30	4	9.60	0.32	52.3	4	9.60	0.32	52.1	0.0
Pravastatin	C10AA03	Lipostat	20mg	28	3	11.52	0.41	18.8	3	11.52	0.41	16.3	0.0
		Pravitin	20mg	30	2	12.09	0.40	5.9	2	12.09	0.40	6.6	0.0
Pregabalin	N03AX16	Lyrica	50 mg	84	4	122.51	1.46	19.6	4	73.29	0.87	20.2	-40.2
Quetiapine	N05AH04	Seroquel	25 mg	60	3	37.77	0.63	59.2	3	21.59	0.36	37.8	-42.8
		Quetiapine Actavis	25 mg	60	-	-	-	-	1	18.89	0.31	10.5	-
Rosuvastatin	C10AA07	Crestor	10mg	28	3	17.93	0.64	47.3	3	16.52	0.59	34.9	-7.9
		Rosuvastatin Teva	10mg	28	1	16.13	0.58	10.1	1	11.21	0.40	13.4	-30.5
Salmeterol[c]	R03AK06	Seretide Evohaler	250 mcg	1	4	57.61	57.61	30.4	4	57.61	57.61	30.4	0.0
Tiotropium bromide	R03BB04	Spiriva Combopack	18 mcg	1	4	42.55	42.55	44.3	4	38.57	38.57	44.2	-9.4

Notes: The ranking of ATCs refers to 20 leading pharmaceuticals on the GMS Scheme in 2010. For each of the leading ATCs, the most frequently dispensed brand (and where appropriate, the most frequently dispensed generic) were selected.

a Four-fold classification used by the HSE for administrative data purposes. See Table 2.3.

b % of ATC refers to the proportion of the total ATC volume accounted for by the particular GMS product.

c Salmeterol/Formoterol and other drugs for obstructive airway diseases

d Although this ATC was multiple source in 2013, this particular product within the ATC remains on-patent.

Source: ESRI Calculations. HSE personal communication, 13 March 2013

TABLE B.3 Dosage Strength as a Percentage of Total Prescribing Frequency of ATC – GMS, 2011 and 2012

ATC Description	ATC	Dose	Volume (%)	
			2011	2012
Single Source In-Patent				
Aripiprazole	N05AX12	10 mg	39.3	39.4
Duloxetine	N06AX21	60 mg	63.8	62.9
Escitalopram	N06AB10	10 mg	47.6	48.6
Etoricoxib	M01AH05	90 mg	43.5	43.7
Ezetimibe	C10AX09	10 mg	100.0	100.0
Memantine	N06DX01	10 mg	96.3	95.4
Montelukast[a]	R03DC03	10 mg	70.5	69.5
Pregabalin	N03AX16	50 mg	24.0	24.0
Tiotropium bromide	R03BB04	18 mcg	81.1	80.3
Varenicline	N07BA03	1 mg	41.2	43.7
Multiple Source Off-Patent				
Amlodipine	C08CA01	5 mg	62.3	62.9
Atorvastatin[b]	C10AA05	10 mg	42.5	41.9
Bisoprolol	C07AB07	2.5 mg	31.8	32.7
Diclofenac	M01AB05	75 mg	58.1	58.2
Esomeprazole	A02BC05	40 mg	66.6	67.7
Lansoprazole	A02BC03	30 mg	86.0	86.1
Olanzapine[b]	N05AH03	5 mg	31.3	30.9
Omeprazole	A02BC01	20 mg	73.5	70.7
Pantoprazole	A02BC02	40 mg	70.4	70.6
Pravastatin	C10AA03	20 mg	42.1	42.2
Quetiapine[b]	N05AH04	25 mg	59.9	58.3
Ramipril	C09AA05	10 mg	29.6	28.9
Rosuvastatin	C10AA07	10 mg	69.6	66.9

Notes: a Montelukast went off-patent in Ireland in March 2013.

b While atorvastatin, olanzapine and quetiapine are recorded as 'single to multiple source' pharmaceuticals for the analysis of price changes in Ireland over the period 2011–2013 (see Table 4.3) As all three pharmaceuticals were off-patent in 2013, they are regarded as multiple source for the analysis of prices across Member States using the Euripid data (see Figure 4.2).

Source: ESRI calculation from HSE personal communications, April 2013

APPENDIX C

Euripid Analysis

C.1 DATA

The data for the following analysis was provided by PCRS-HSE. The data was sourced from the EURopean Integrated Price Information Database (Euripid)[4] which provides, on a voluntary participation basis of Member States,[5] a platform for immediate price comparisons of reimbursed pharmaceuticals. Euripid contains ex-factory, wholesale and retail prices of the reimbursed pharmaceuticals. All countries do not provide all three prices.

In presenting the results we define four groups of countries:

- Ireland plus the nine Member States in the basket used to define the price of new pharmaceuticals are labelled 1 to 10 where Ireland is 1
- Other EU-15 Member States are labelled 11 to 15
- Member States that joined with and after enlargement are labelled 16 to 27
- Members of the EEA are labelled 28 to 29.

We only present information for the countries for which we have data.

C.2 METHODOLOGY

1) The PCRS-HSE selected 23 leading pharmaceuticals at ATC 5 level on the GMS Scheme in 2010. Ten single source pharmaceuticals, ten multiple source and three that transitioned from single to multiple source over the period were selected.
2) For each of the selected ATCs the PCRS-HSE
    - provided two Euripid data files, one containing 2011 prices and one for 2013 prices
    - identified the *branded* products in each country for which prices were available

[4] Euripid is co-funded by the European Commission and DG Enterprise. The project is coordinated by OEP (National Health Insurance Fund Administration, Hungary) and GÖG/ÖBIG (Gesundheit Österreich GmbH/Österreichisches Bundesinstitut für Gesundheitswesen, Austria) monitored by SUKL (State Institute for Drug Control, Czech Republic).

[5] The database currently contains price and availability data from 22 countries.

- identified dosage forms (e.g. orodispersible tablets) which they deemed not to be comparable with the dosage form of the most popular product in Ireland as selected by the ESRI using prescribing frequency data for 2012 (provided by PCRS-HSE).

3) For Ireland

   a) only the wholesale price was provided on the Euripid database. The ex-factory price was calculated as the wholesale price divided by 1.08[6]

   b) parallel imports of the *branded* products were excluded from the calculations. It was not possible to identify parallel imports in other countries.

4) As information on quantities sold was not available in Euripid, for each ATC the median ex-factory and wholesale prices in each country were calculated for the *branded* and *other* products for 2011 and 2013. It was decided not to look at retail prices as these are the least comparable prices across countries. Certain countries were always excluded from the analysis as they only provide retail prices.

5) An index of the calculated median prices for *branded* and *other* products was created with Ireland equal to 100.

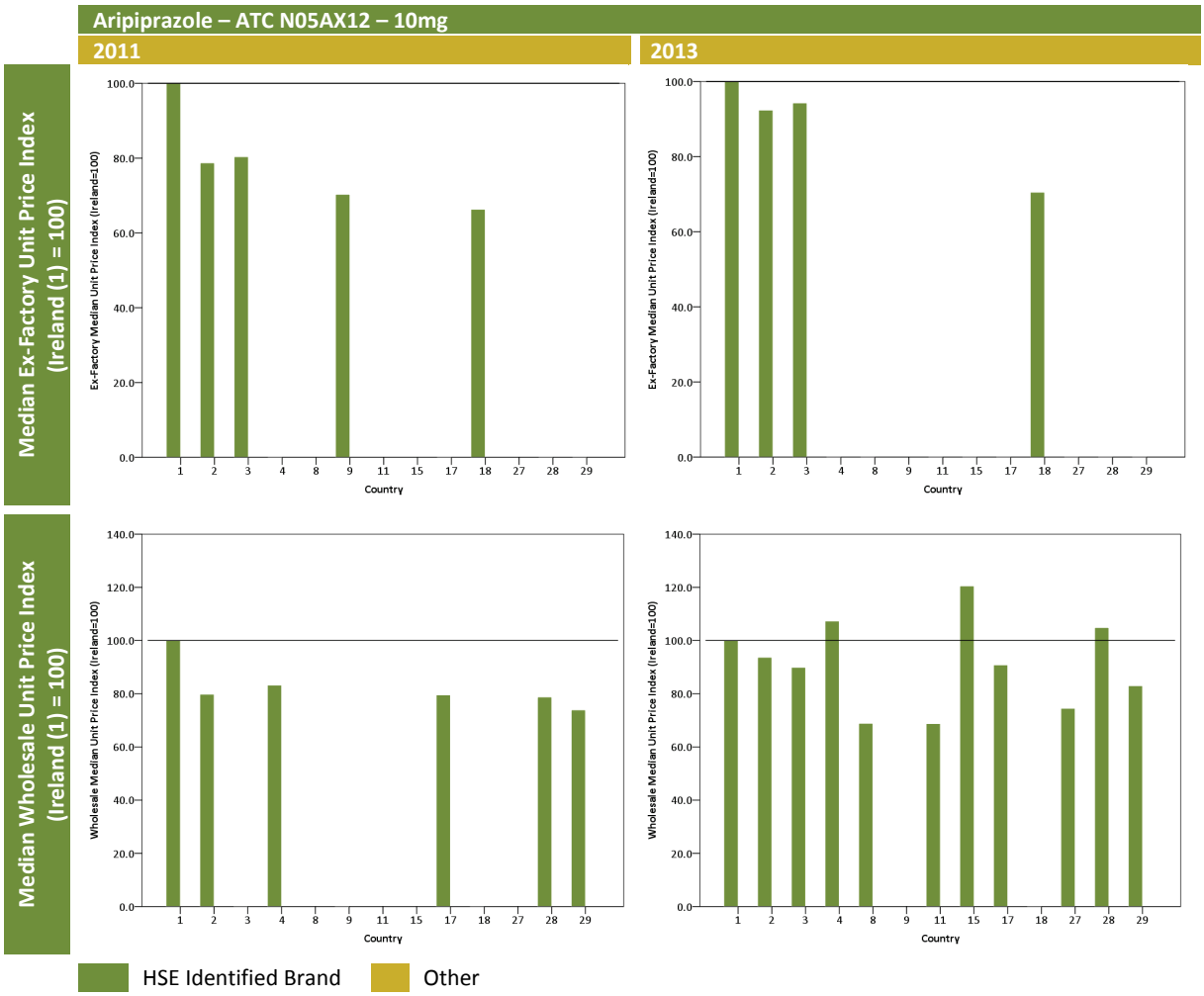
6) Figures C.1 and C.2 present data for single source in-patent pharmaceuticals and multiple source off-patent pharmaceuticals respectively. A set of four charts was created for each ATC, representing ex-factory and wholesale median price indices in 2011 and 2013 for available countries.

7) Figures C.3 and C.4 present minimum and median wholesale unit price indices for *other* products.

8) Table C.1 summarises the results from Figures C.1 to C.2 with respect to wholesale prices for 2013.

[6] See Section 2.2.2.

FIGURE C.1 Median Unit Price Indices for Single Source In-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100)



Note: Excludes orodispersible tablets.

Figure C.1 Median Unit Price Indices for Single Source In-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)

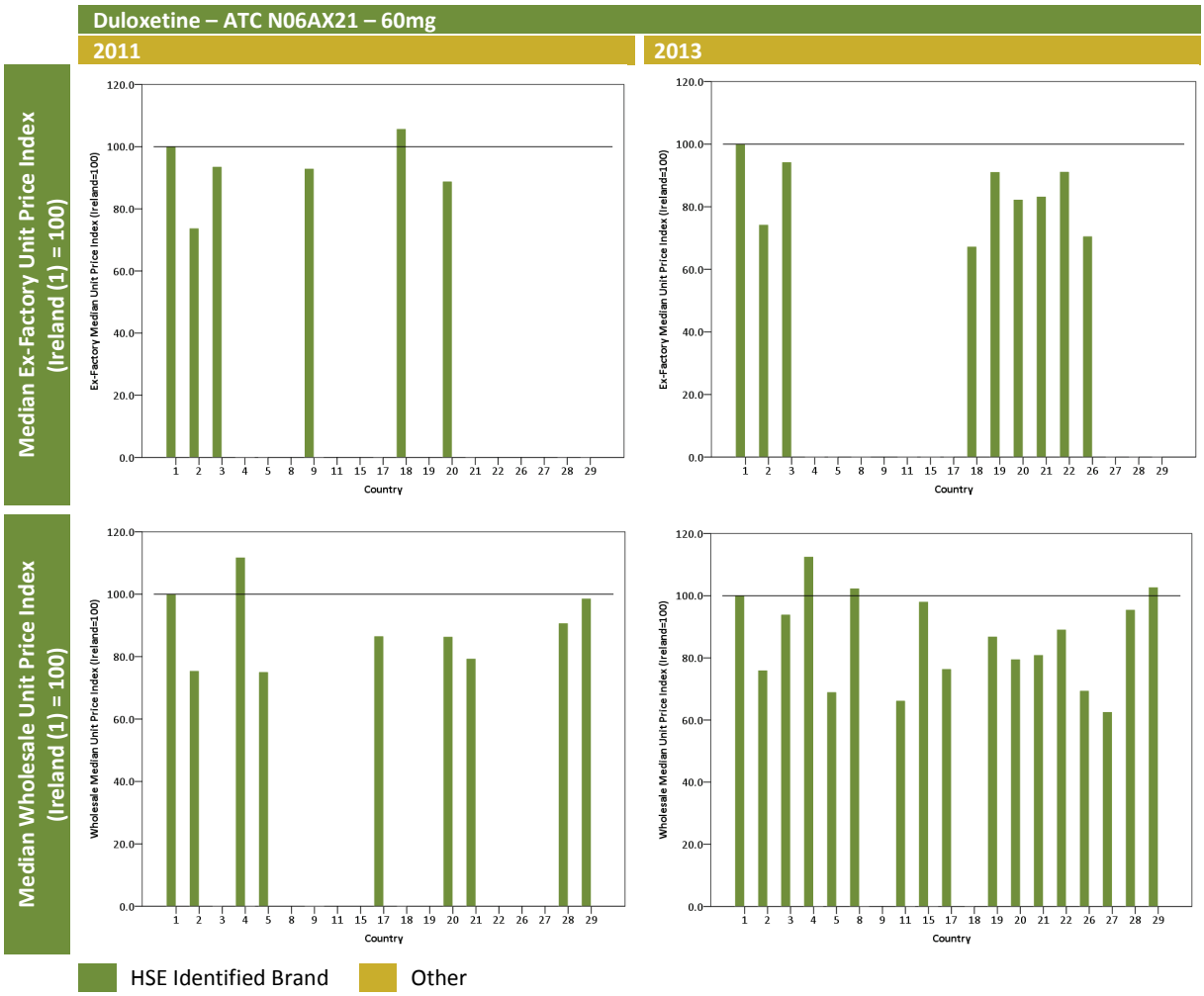
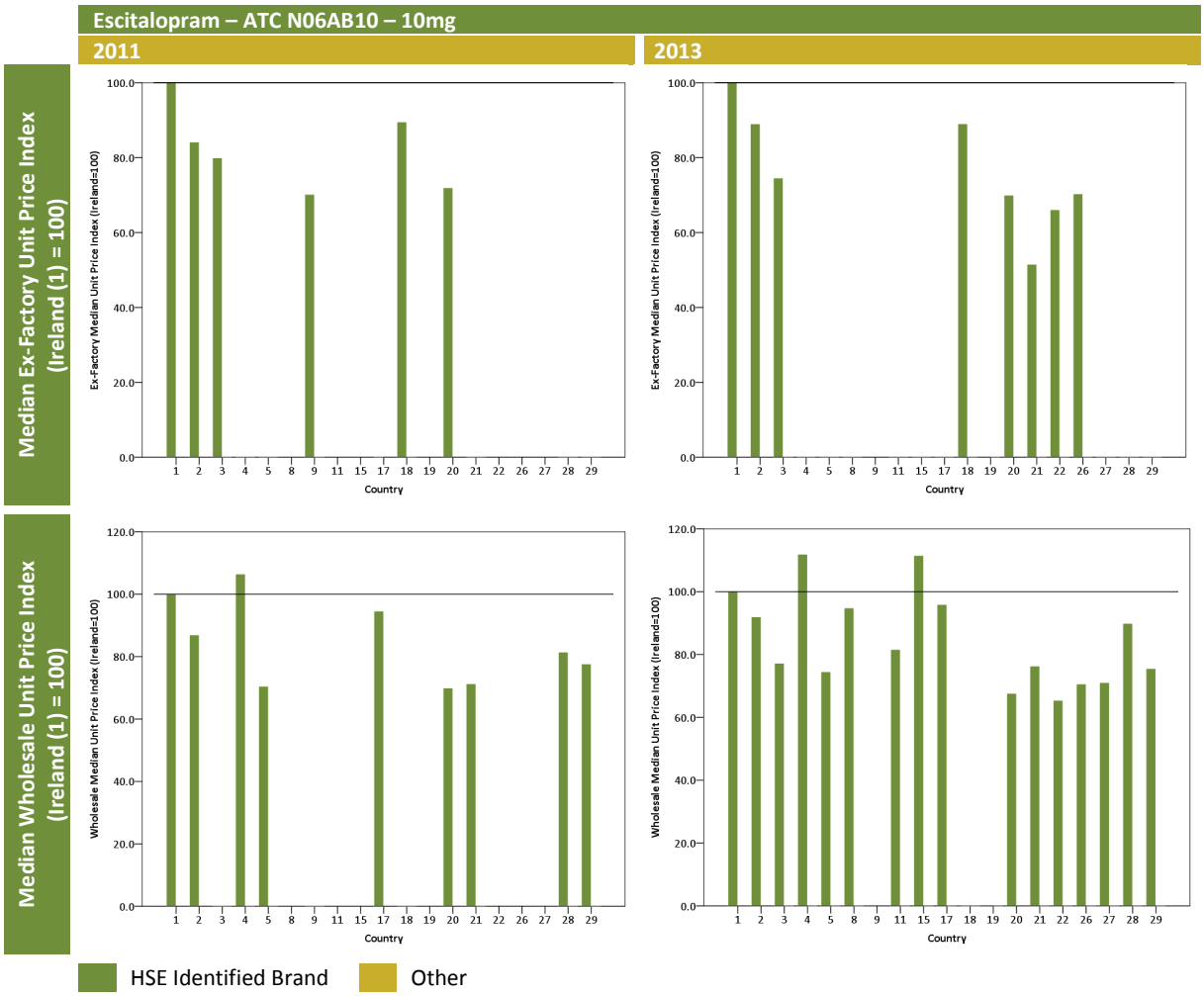


Figure C.1 Median Unit Price Indices for Single Source In-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)



Note: Excludes orodispersible tablets and oral drops.

Figure C.1 Median Unit Price Indices for Single Source In-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)

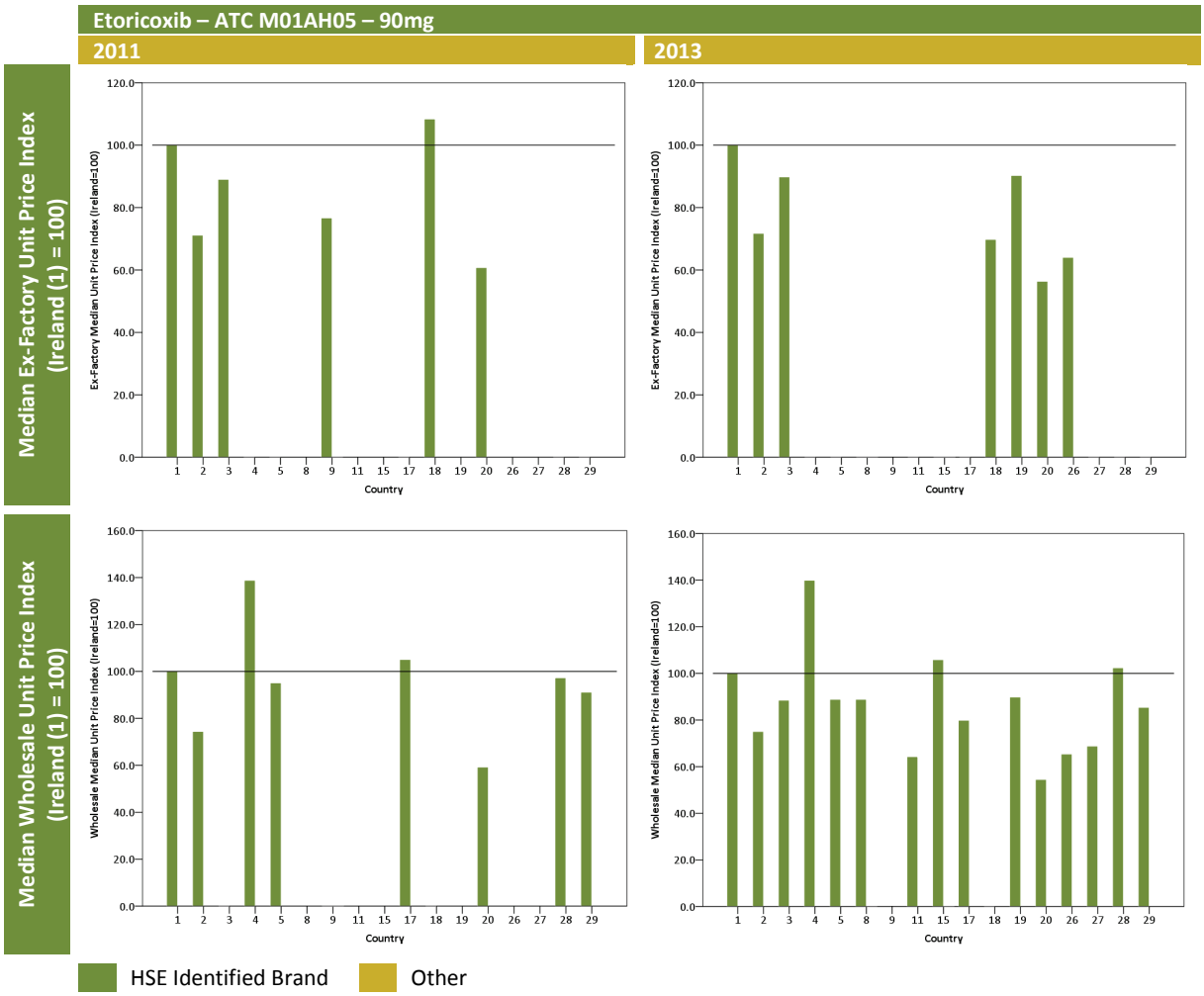


Figure C.1 Median Unit Price Indices for Single Source In-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)

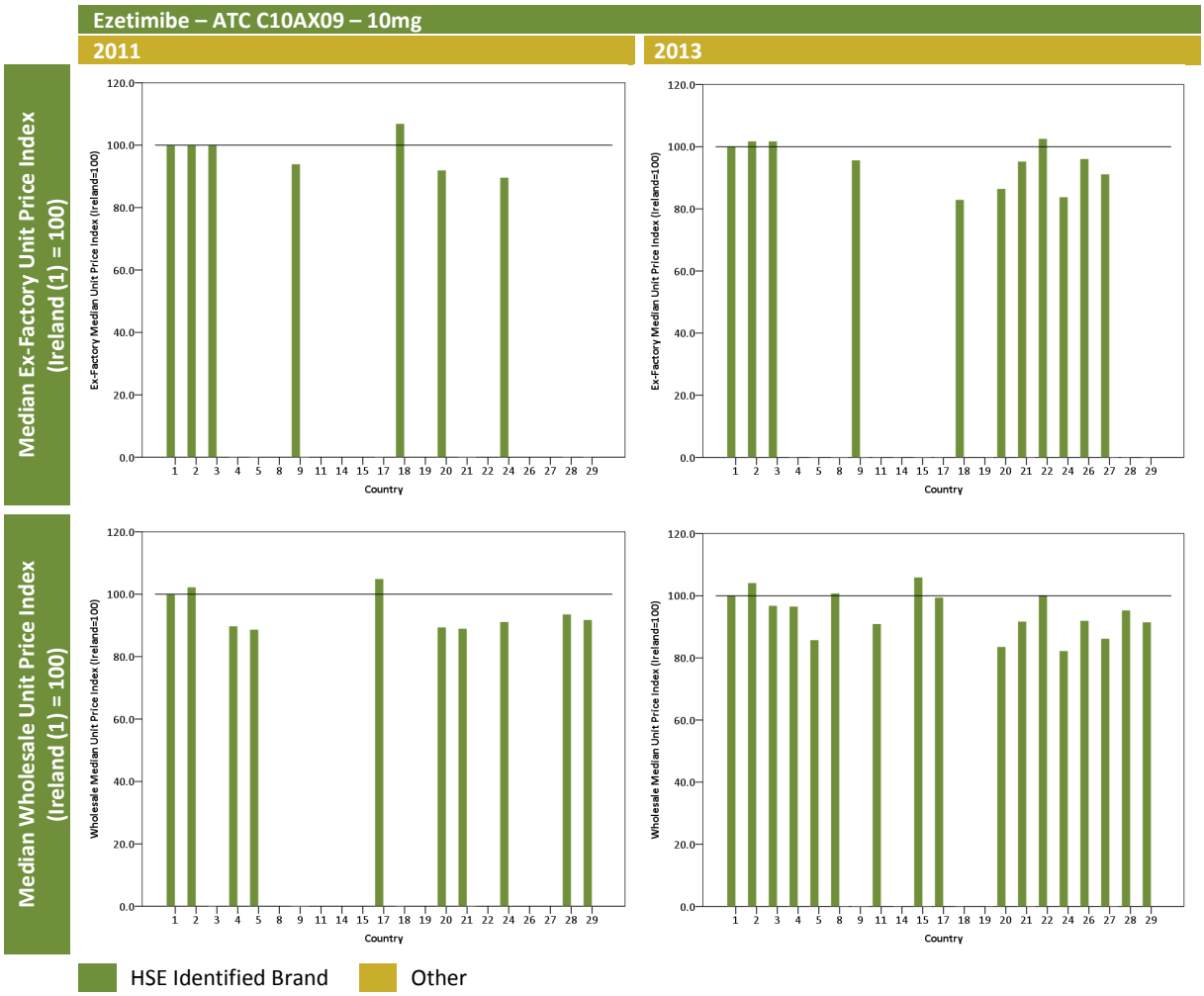
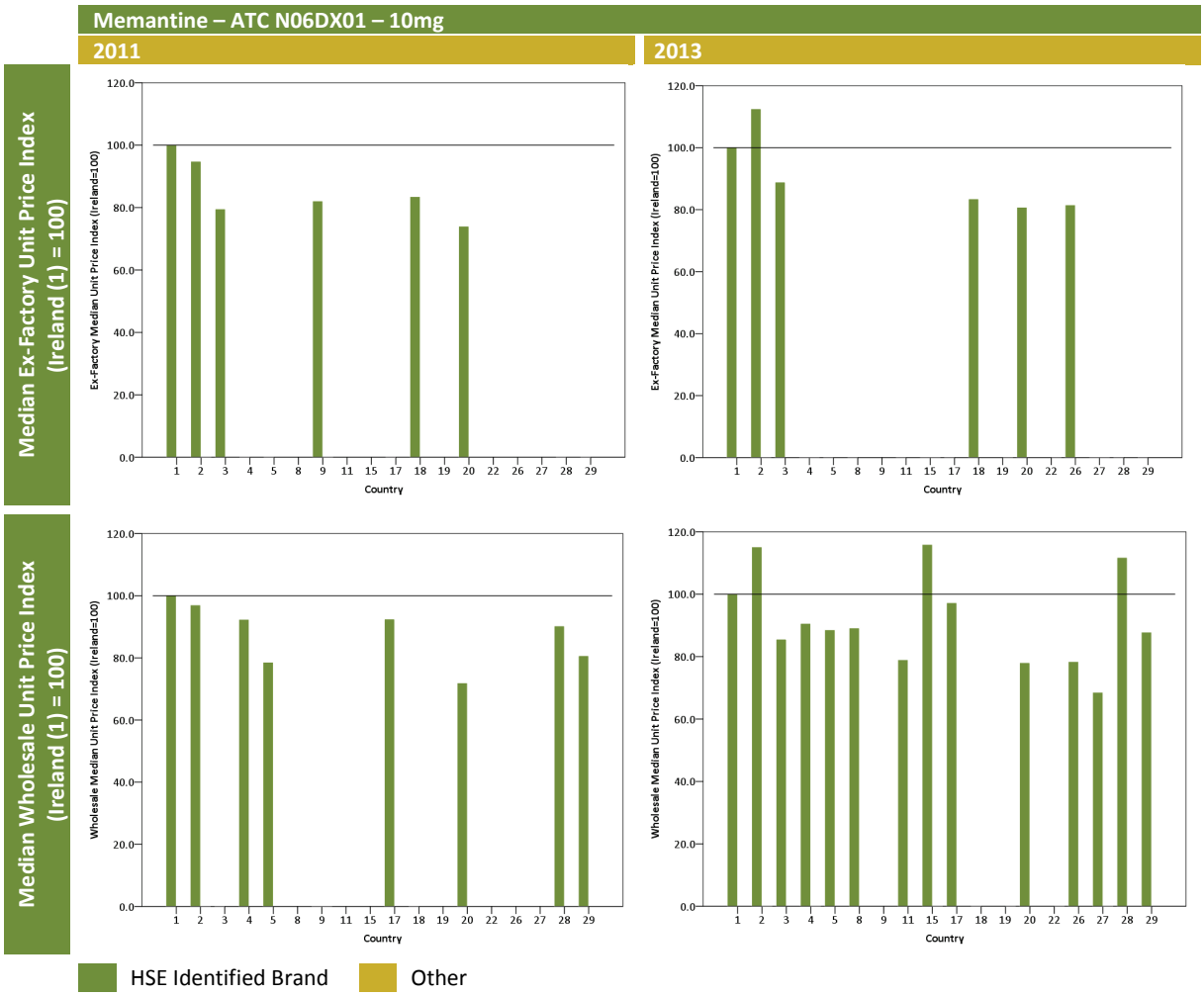
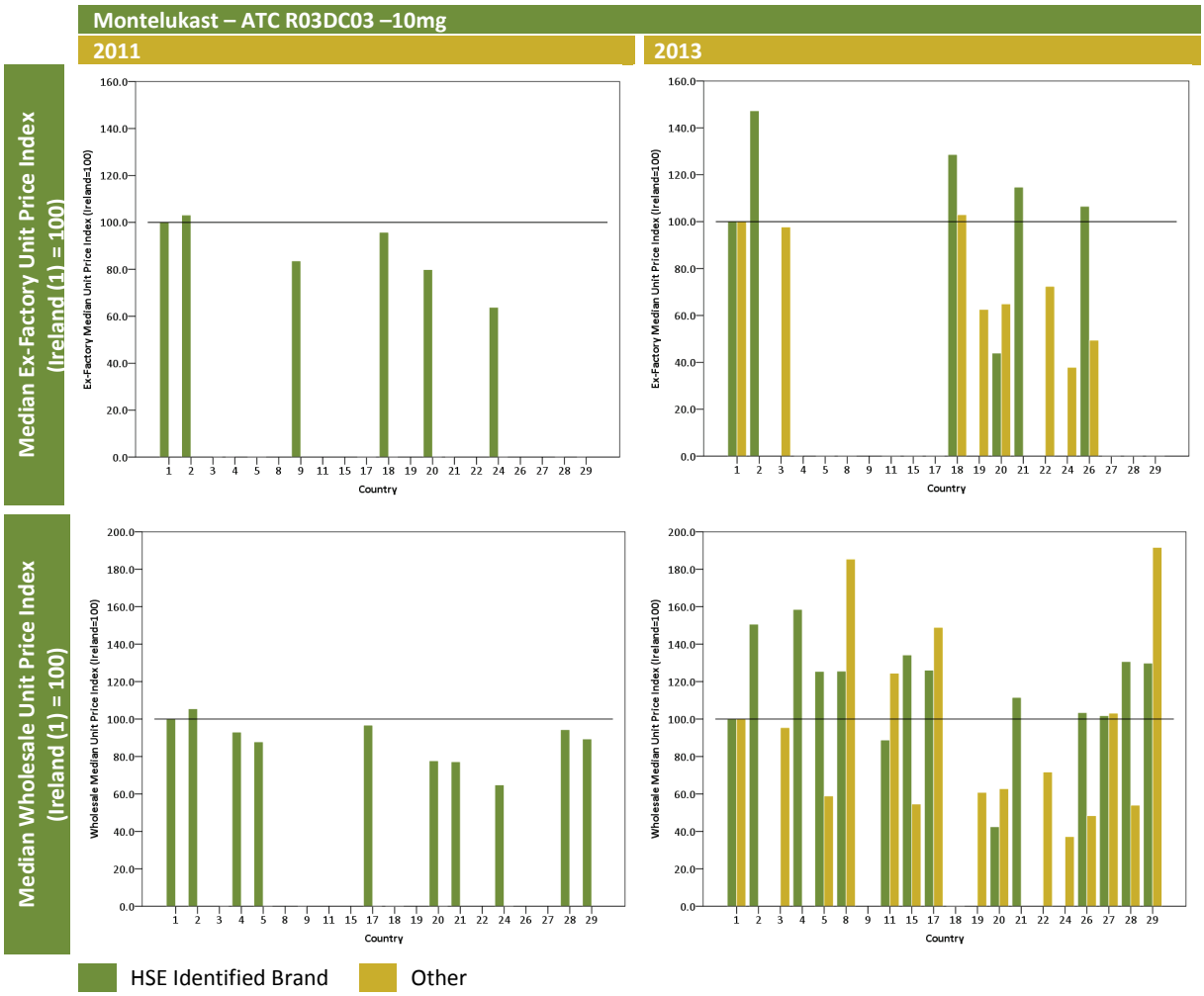


Figure C.1 Median Unit Price Indices for Single Source In-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)



Note: Excludes oral solution and oral drops.

Figure C.1 Median Unit Price Indices for Single Source In-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)



Note: Excludes chewable tablets.
Montelukast went off-patent in Ireland in March 2013.

Figure C.1 Median Unit Price Indices for Single Source In-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)

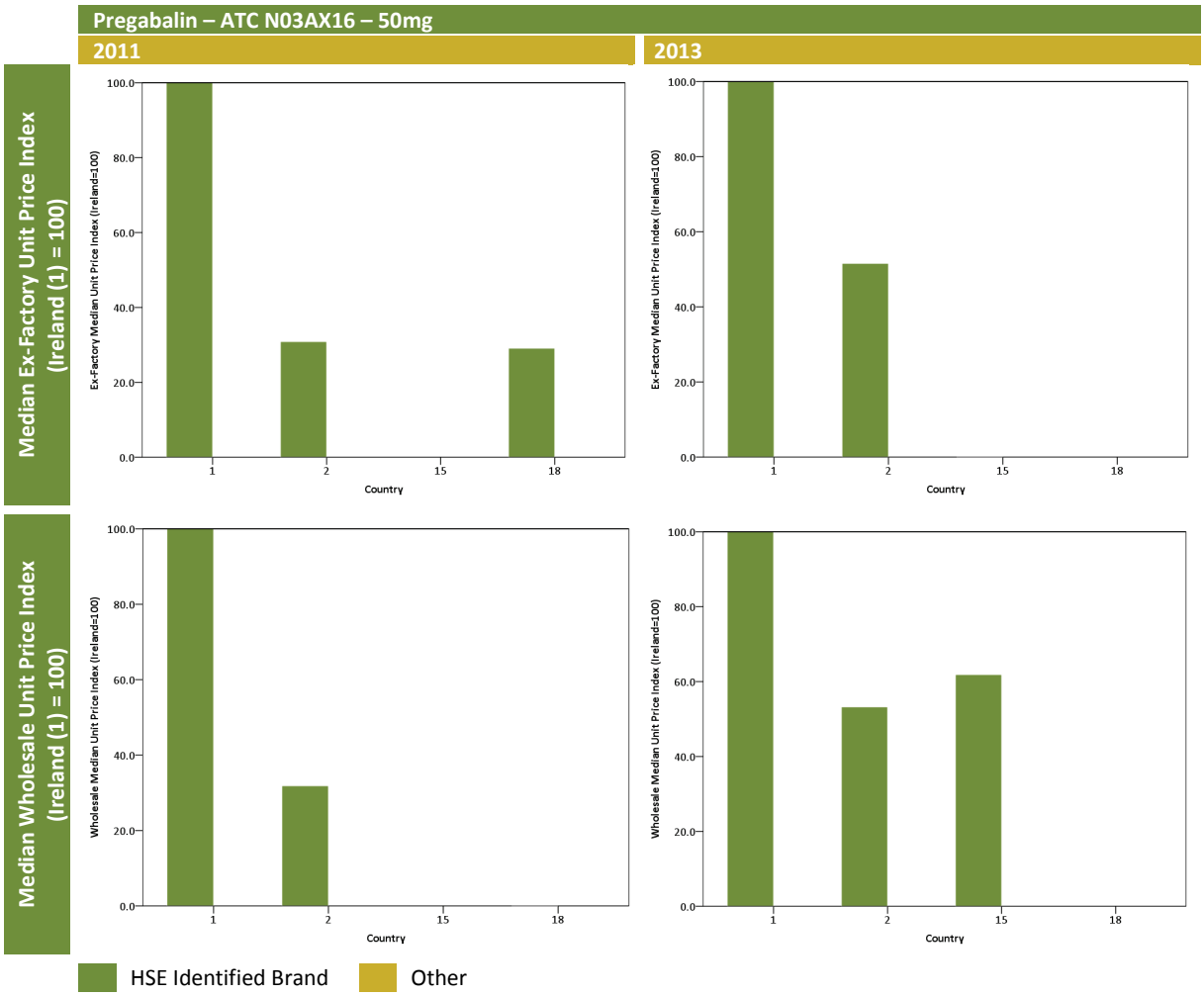


Figure C.1 Median Unit Price Indices for Single Source In-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)

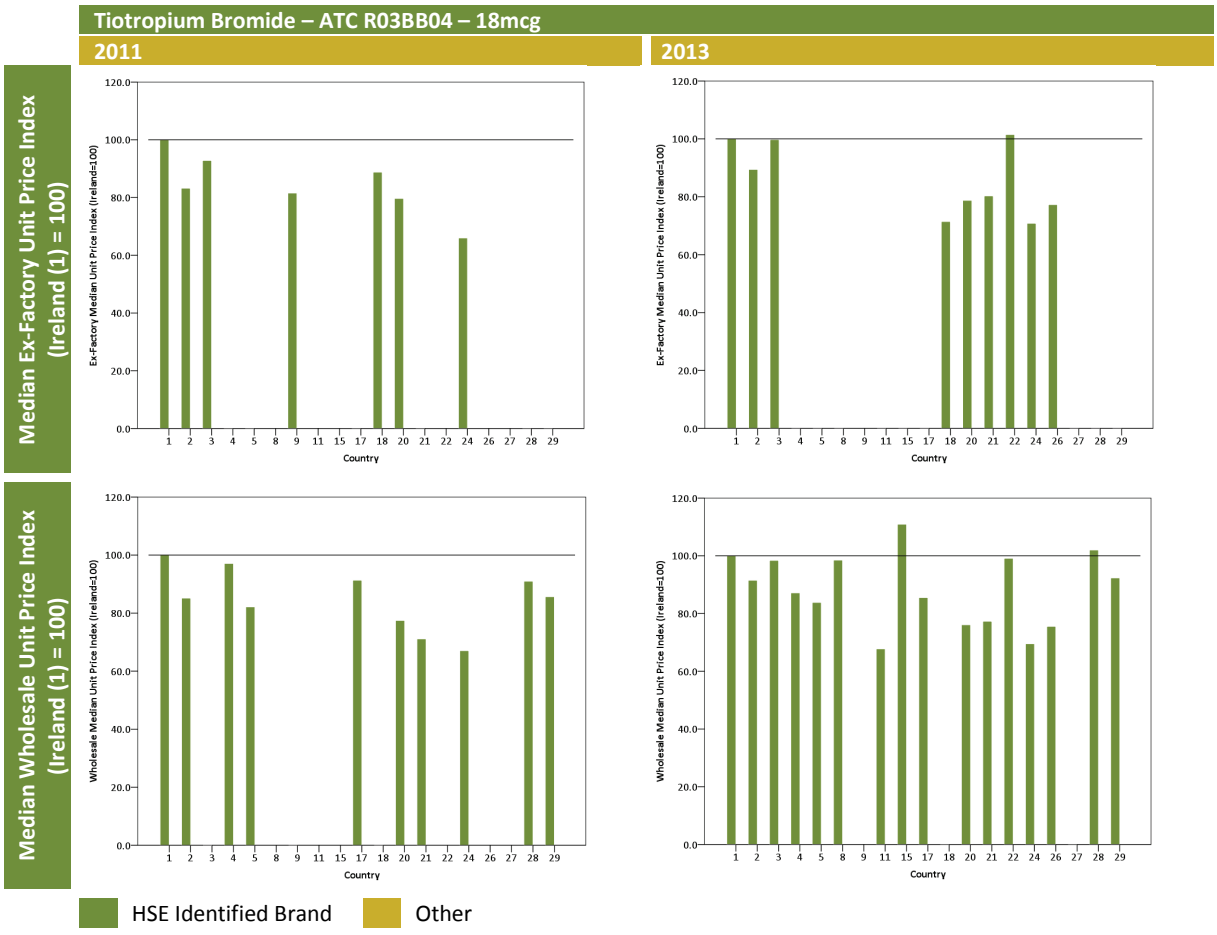


Figure C.1 Median Unit Price Indices for Single Source In-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)

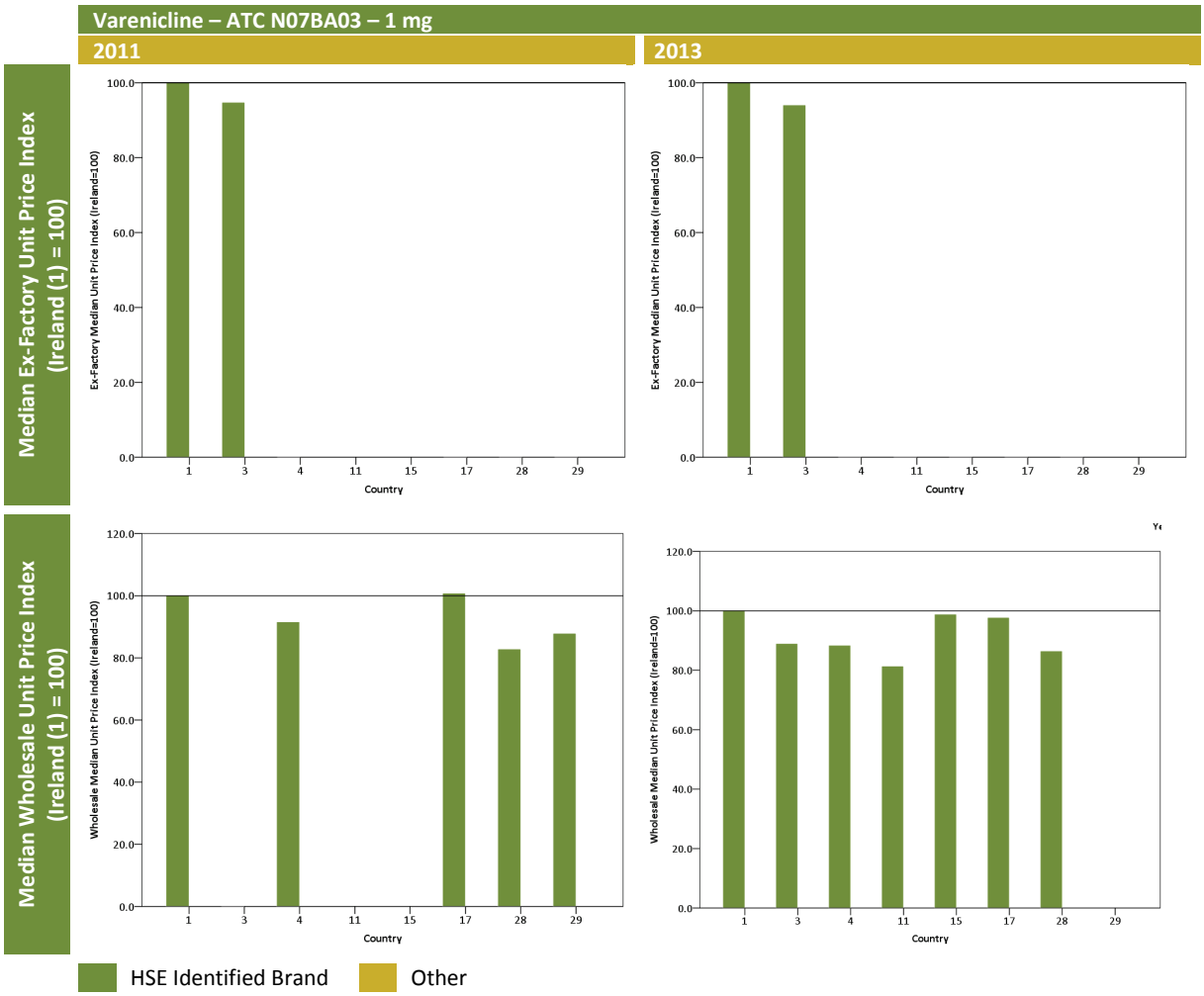
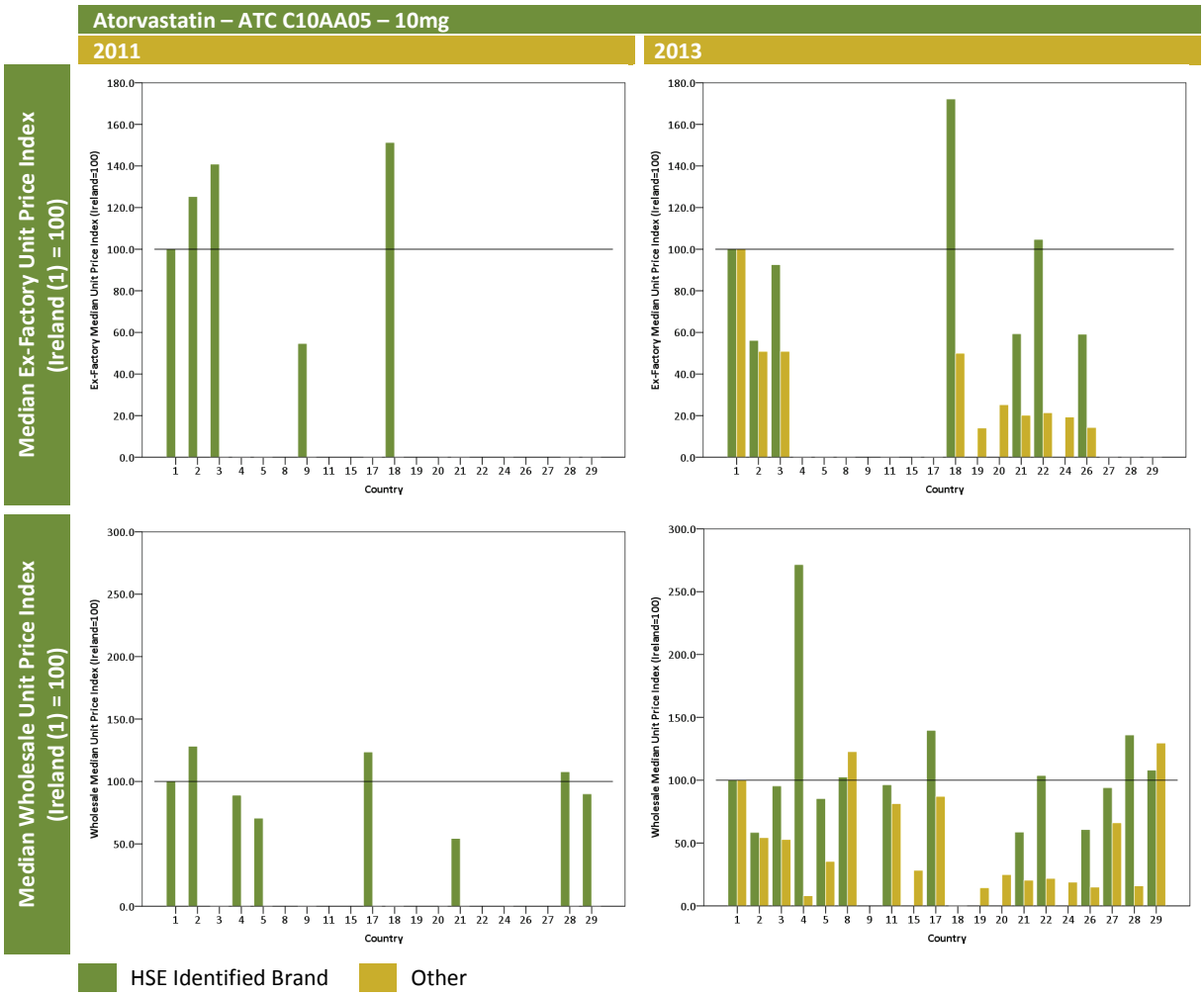


FIGURE C.2 Median Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100)

Note: Excludes orodispersible tablets.

Figure C.2 Median Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)



Notes: Transitioned from single source to multiple source in Ireland over the period.
Excludes chewable tablets.

Figure C.2 Median Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)

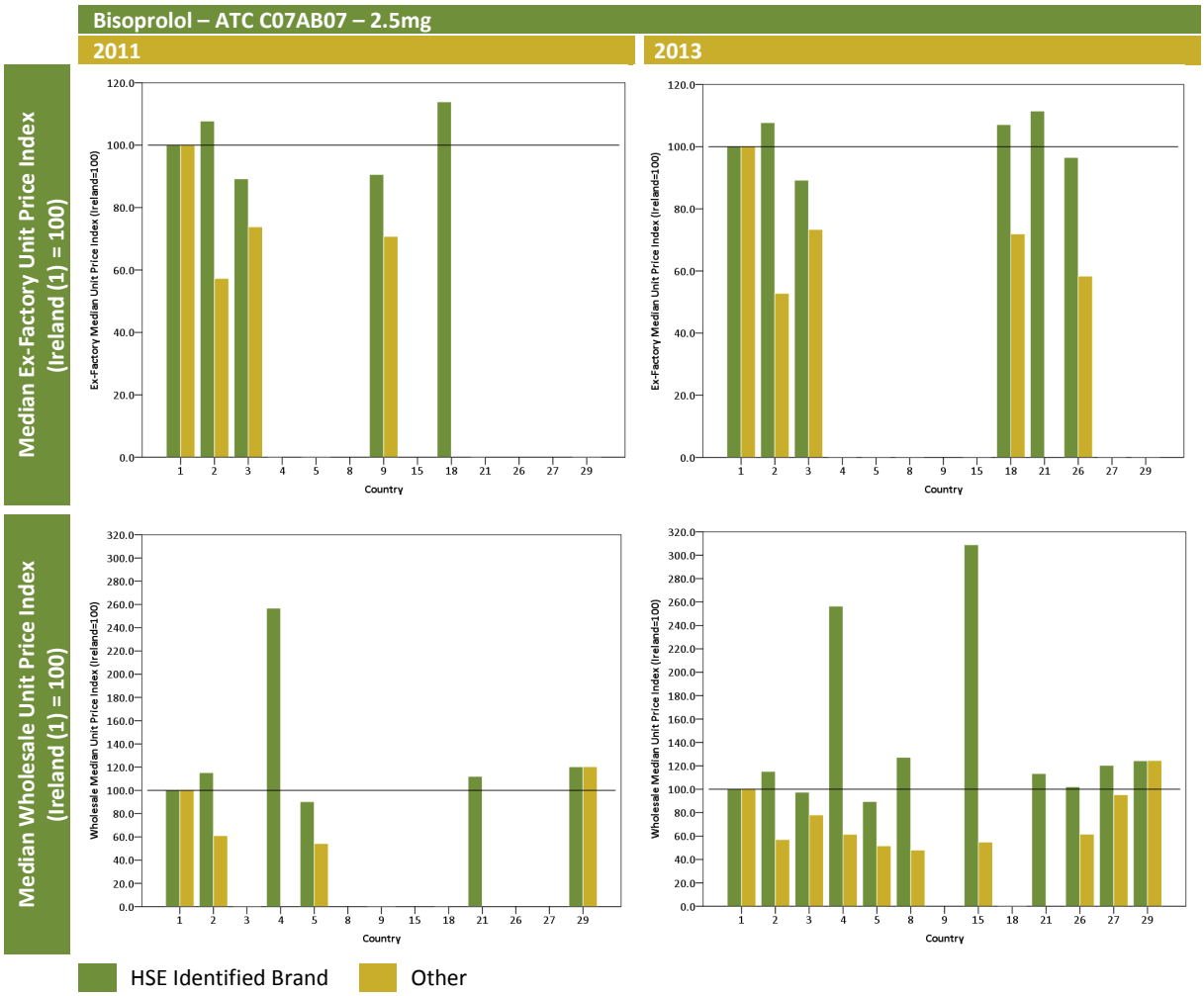
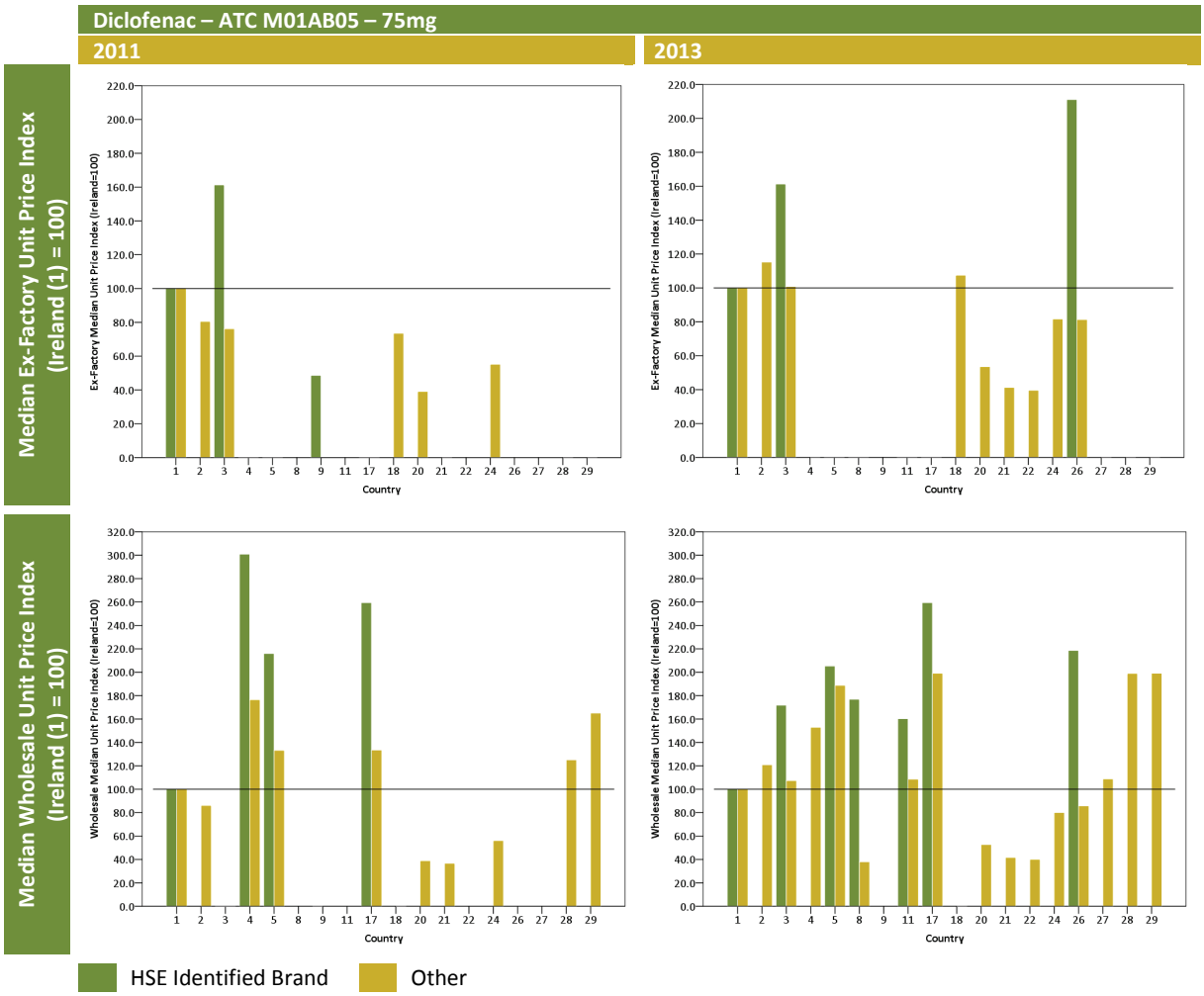
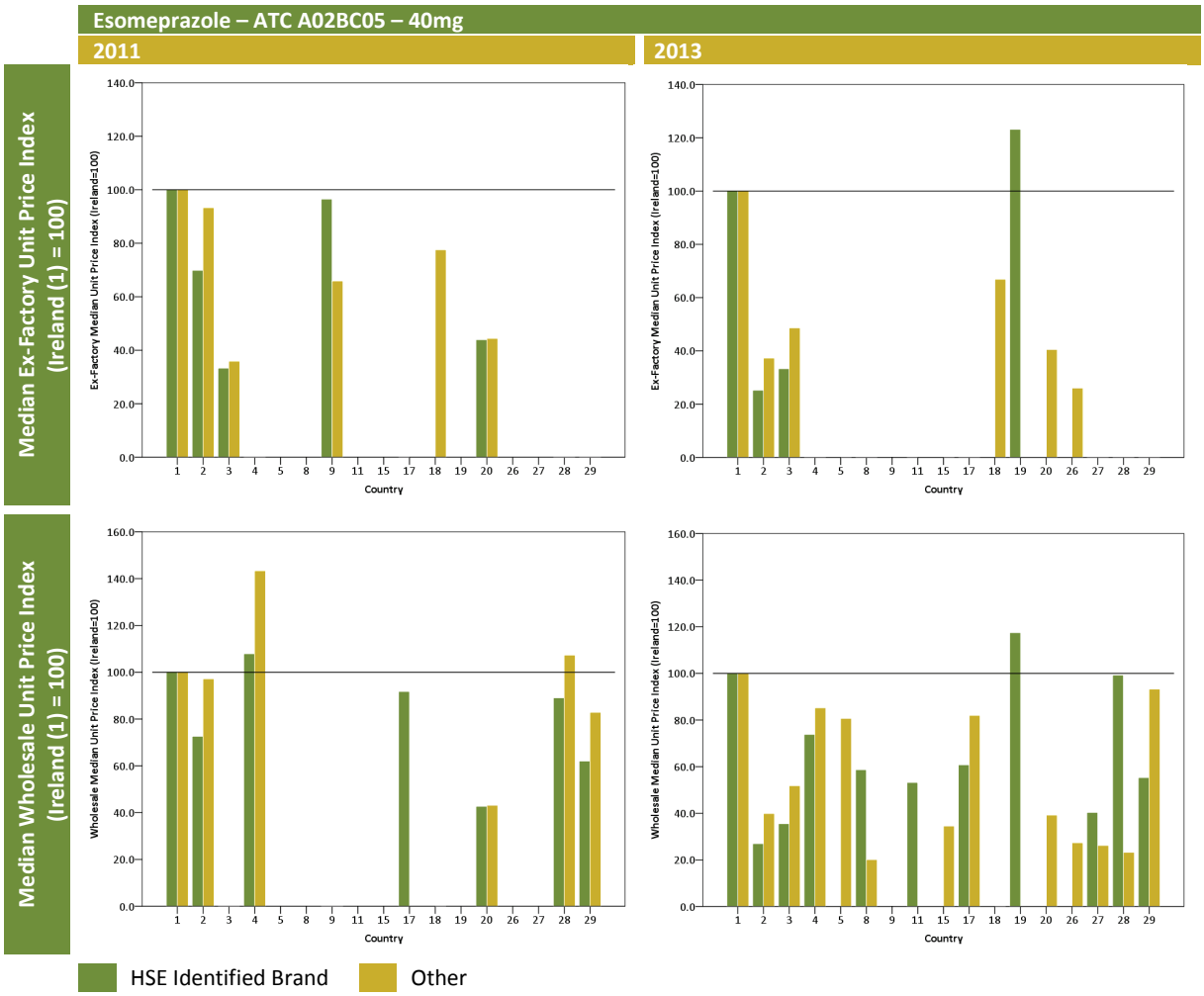


Figure C.2 Median Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)



Note: Excludes solution for injection/infusion.

Figure C.2 Median Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)



Note: Excludes powder for injection/infusion.

Figure C.2 Median Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)

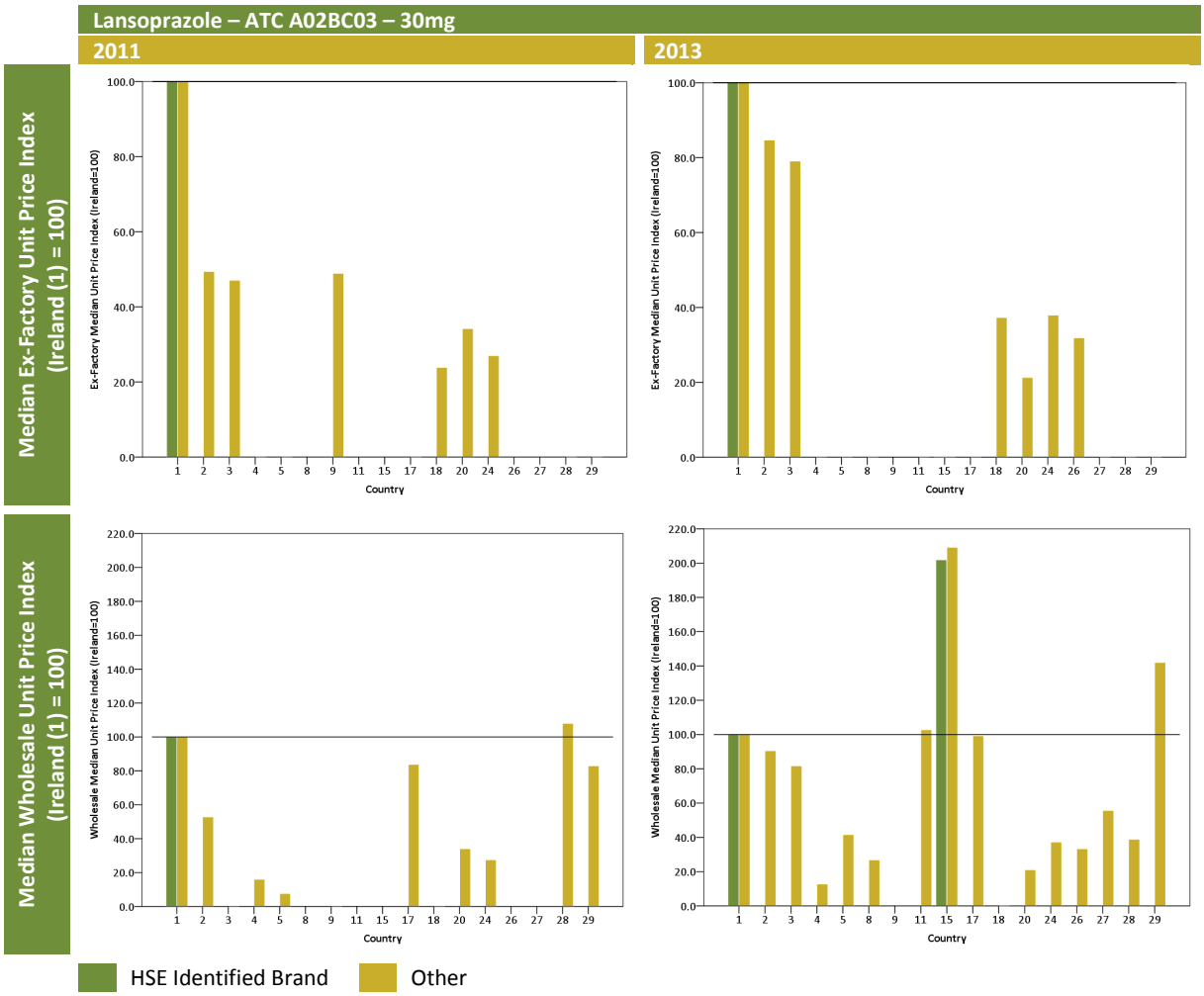
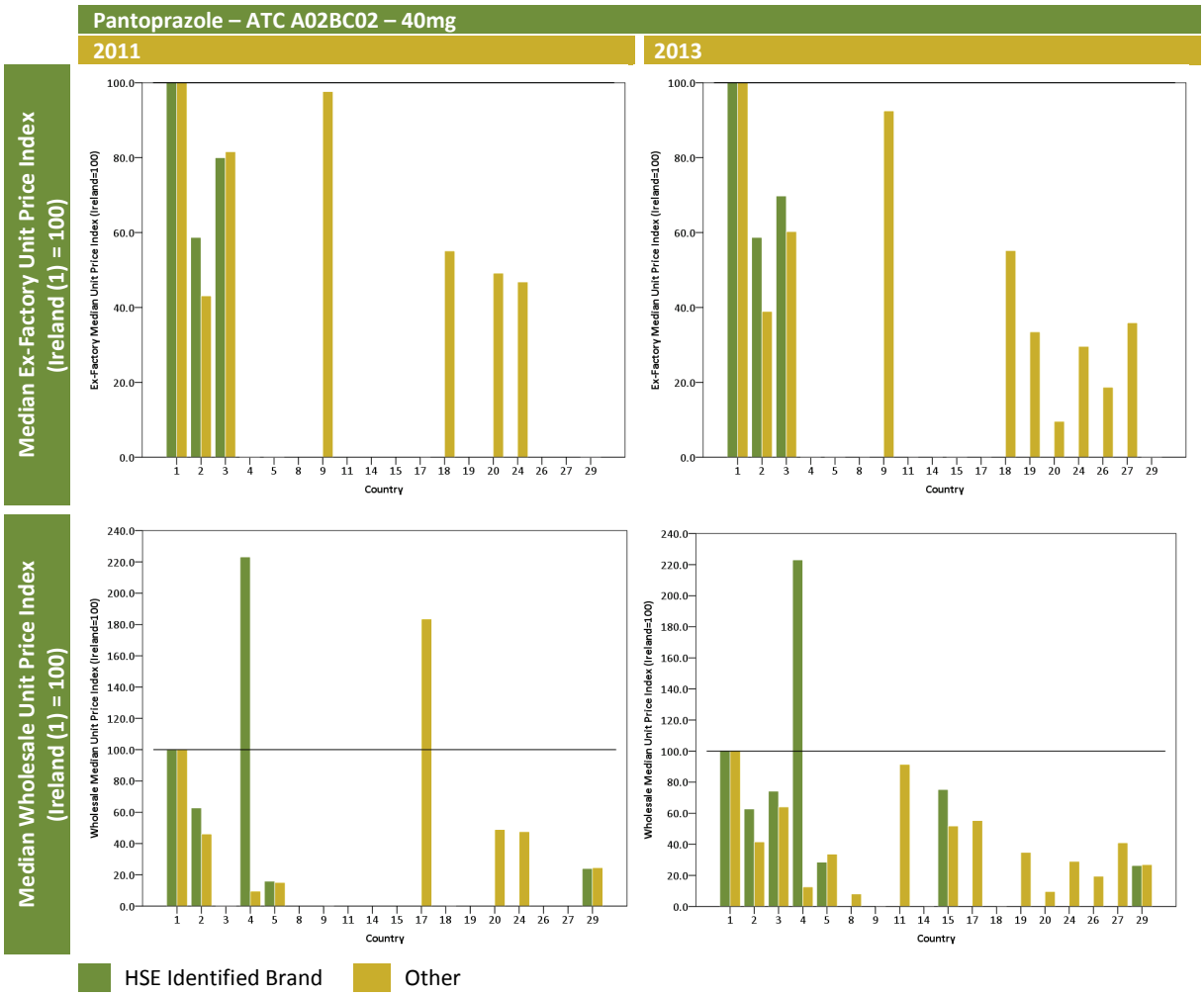


Figure C.2 Median Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)

Notes: Transitioned from single source to multiple source in Ireland over the period.
Excludes oral lyophilisate and orodispersible tablets.

Figure C.2 Median Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)

Figure C.2 Median Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)



Note: Excludes powder for injection/infusion.

Figure C.2 Median Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)

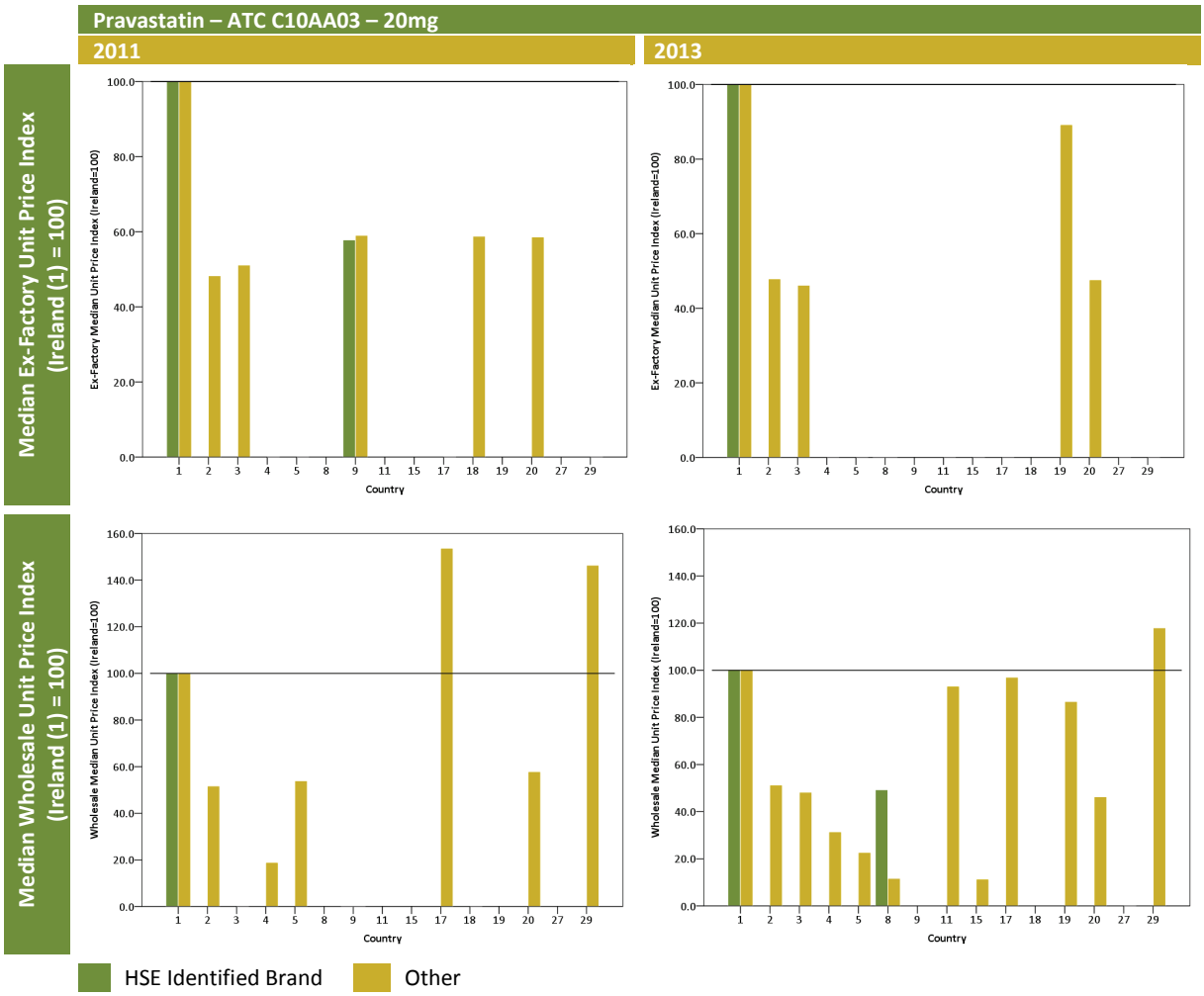
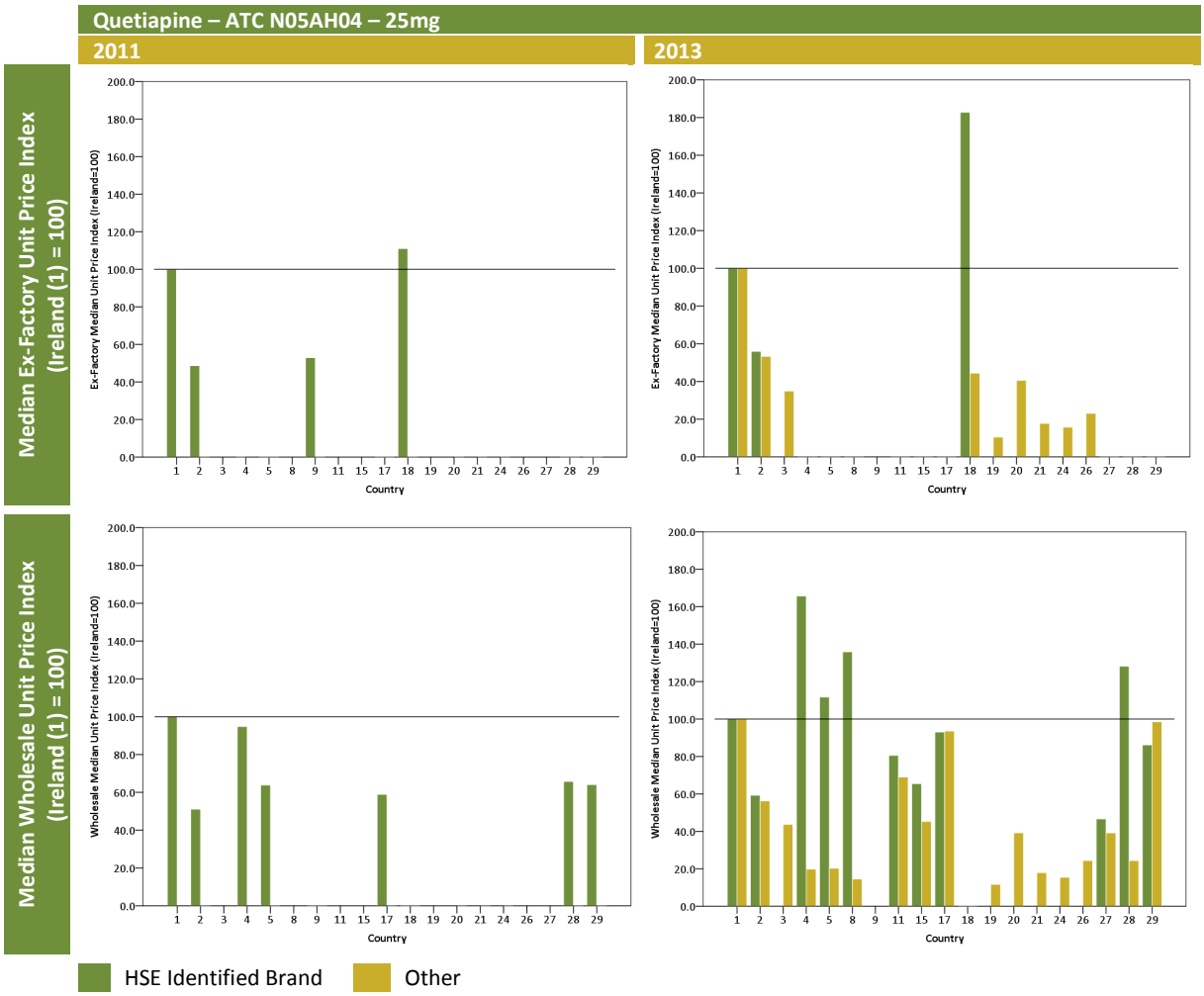


Figure C.2 Median Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)



Notes: Transitioned from single source to multiple source in Ireland over the period.

Figure C.2 Median Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)

Figure C.2 Median Unit Price Indices for Multiple Source Off-Patent Pharmaceuticals, 2011 and 2013 (Ireland (1) = 100) (contd.)

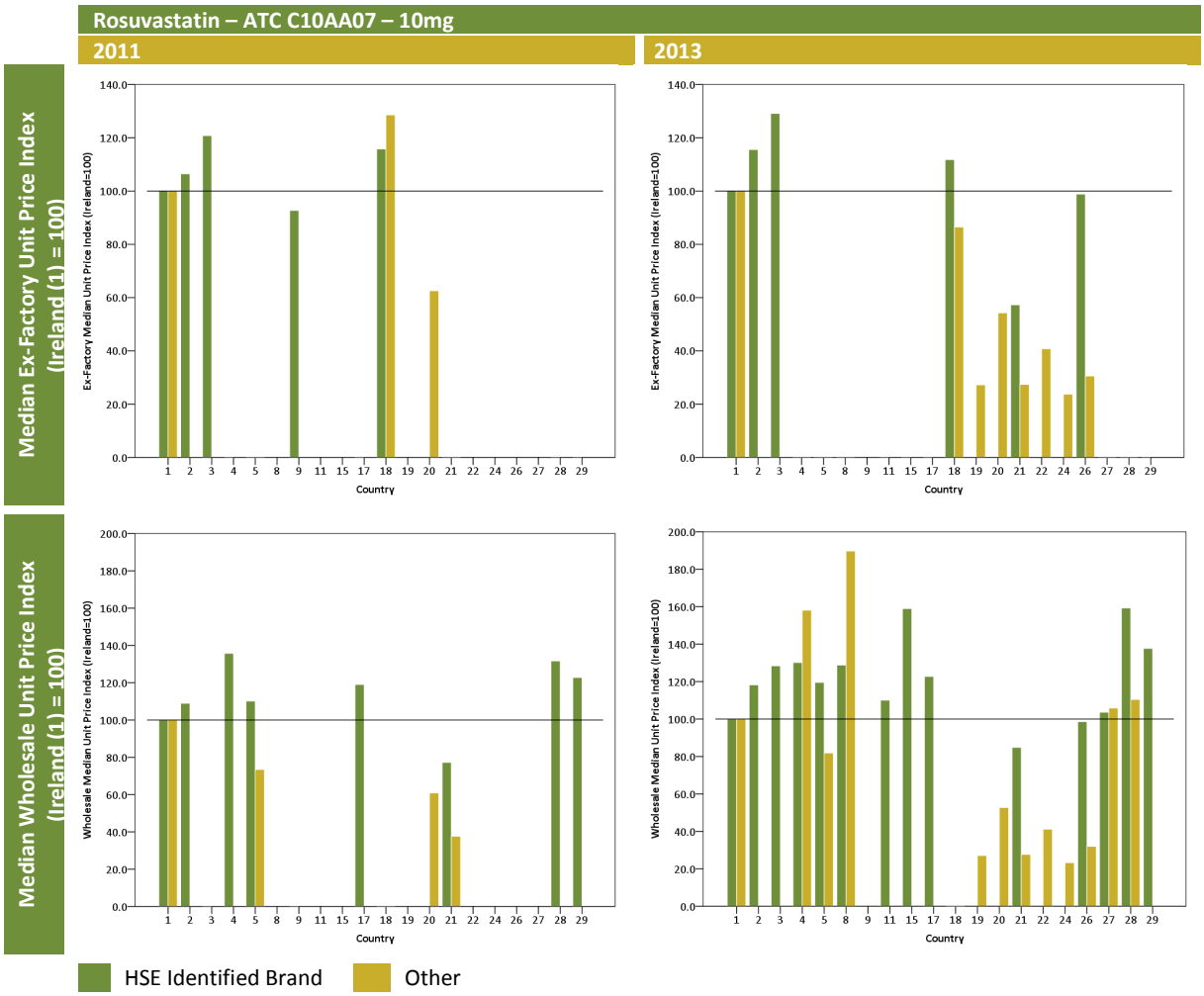
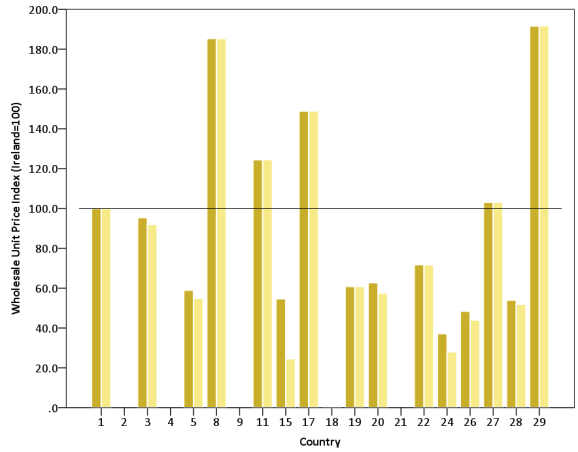


FIGURE C.3 Wholesale Unit Price Indices for Non-Patent Holder Single Source[a] In-Patent Pharmaceuticals, 2013 (Ireland (1) = 100)

Montelukast – ATC R03DC03 – 10mg[b]



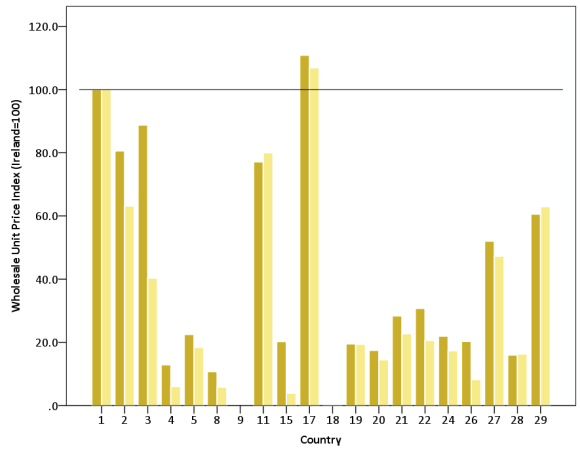
Other – Median Other – Minimum

Note: a Montelukast went off-patent in Ireland in March 2013.
b Excludes chewable tablets.

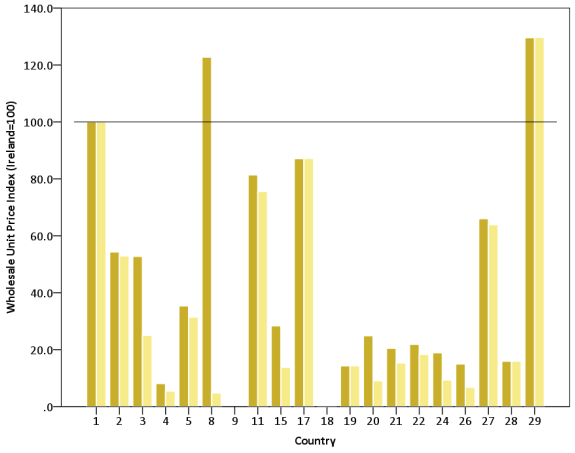
Source: ESRI Calculations. Based on Euripid information supplied by the HSE, personal communications, April 2013

FIGURE C.4 Wholesale Unit Price Indices for Non-Patent Holder Multiple Source Off-Patent Pharmaceuticals, 2013 (Ireland (1) = 100)

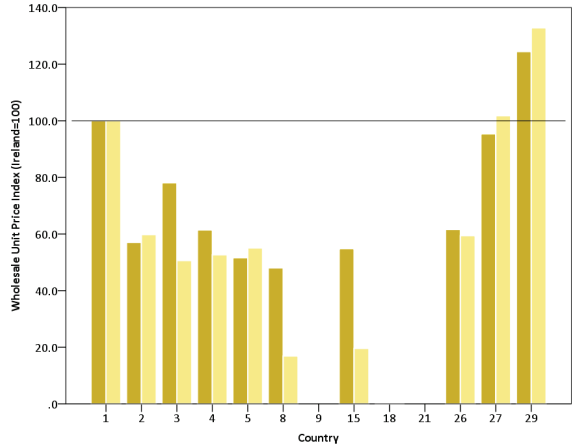
Amlodipine – ATC C08CA01 – 5mg[b]



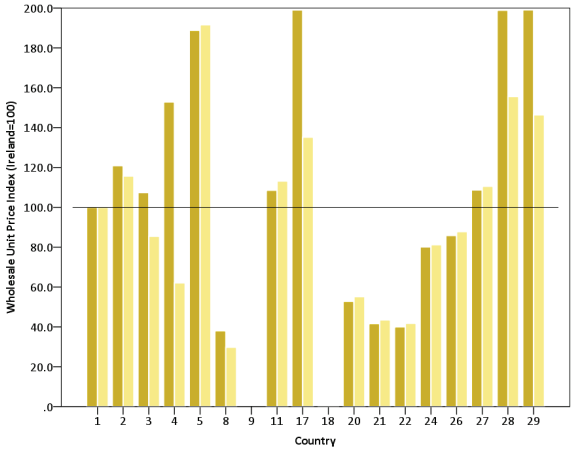
Atorvastatin – ATC C10AA05 – 10mg[a]



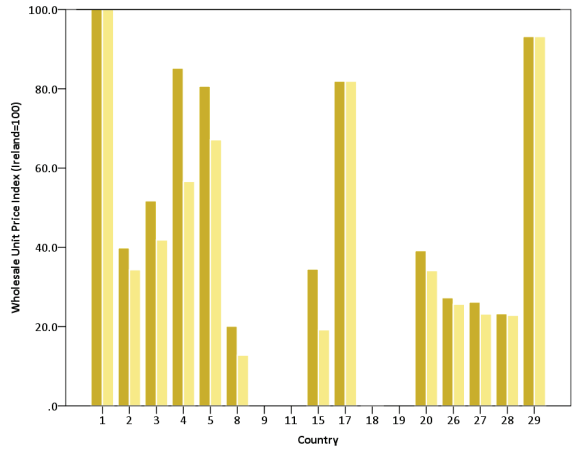
Bisoprolol – ATC C07AB07 – 2.5mg



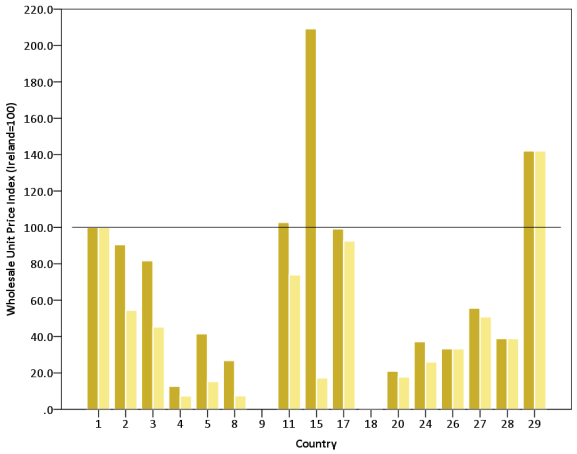
Diclofenac – ATC M01AB05 – 75mg[c]



Esomeprazole – ATC A02BC05 – 40mg[d]



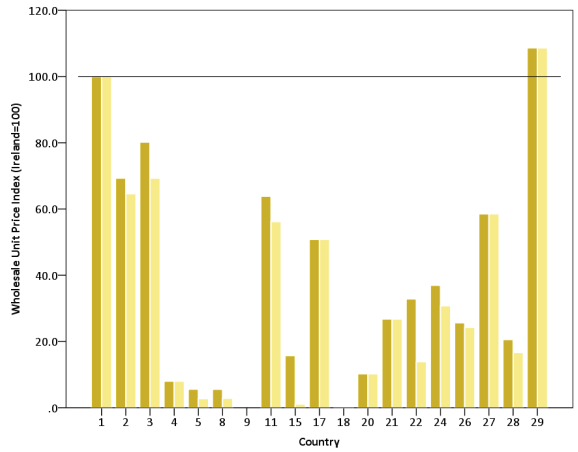
Lansoprazole – ATC A02BC03 – 30mg



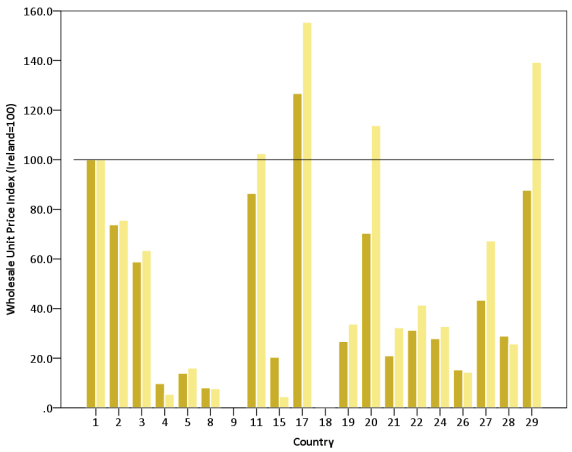
Other – Median Other – Minimum

Figure C.4 Wholesale Unit Price Indices for Non-Patent Holder Multiple Source Off-Patent Pharmaceuticals, 2013 (Ireland (1) = 100) (contd.)

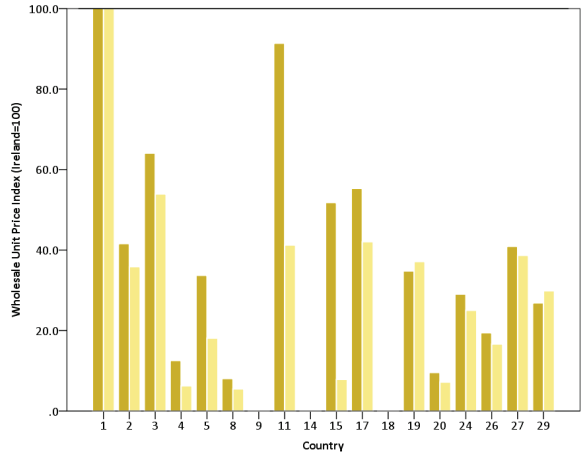
Olanzapine – ATC N05AH03 – 5mg[e]



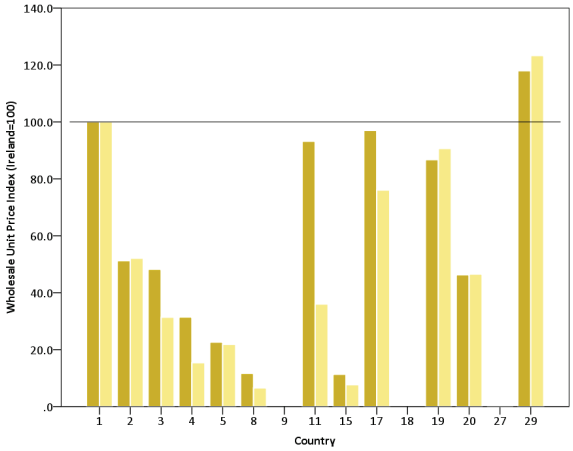
Omeprazole –ATC A02BC01 – 20mg



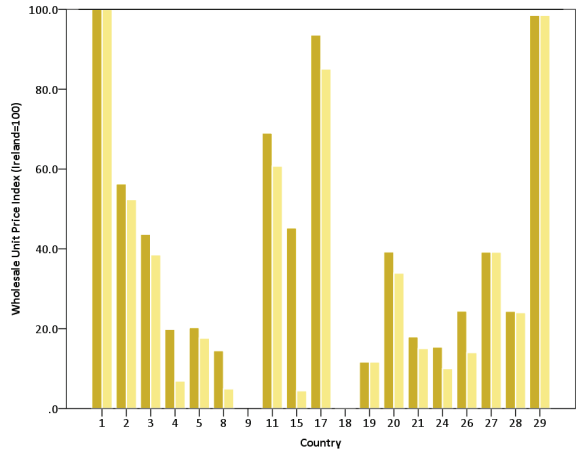
Pantoprazole – ATC A02BC02 – 40mg[e]



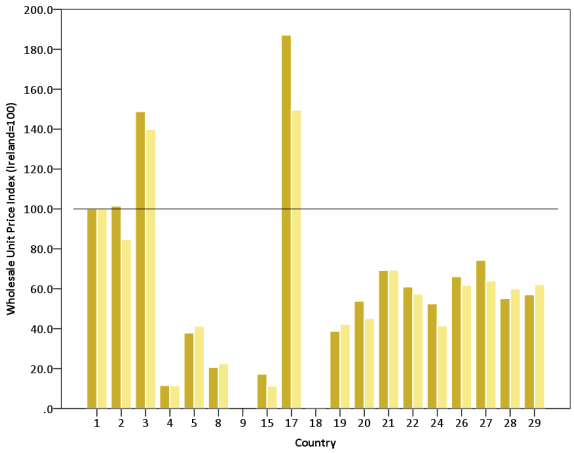
Pravastatin –ATC C10AA03 – 20mg



Quetiapine – ATC N05AH04 – 25mg



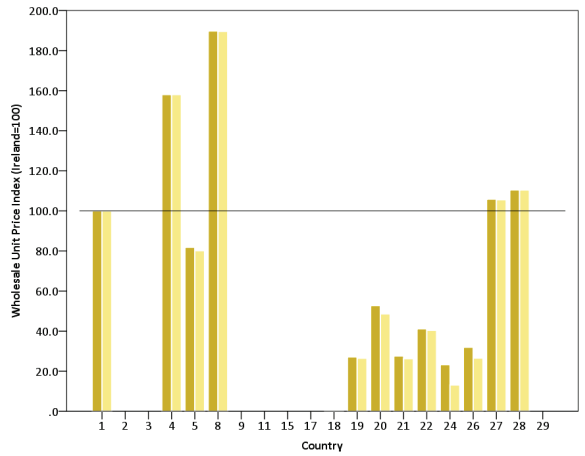
Ramipril – ATC C09AA05 – 10mg



Other – Median Other – Minimum

Figure C.4 Wholesale Unit Price Indices for Non-Patent Holder Multiple Source Off-Patent Pharmaceuticals, 2013 (Ireland (1) = 100) (contd.)

Rosuvastatin – ATC C10AA07 – 10mg



Other – Median Other – Minimum

Notes:
a Excludes chewable tablets.
b Excludes orodispersible tablets.
c Excludes solution for injection/infusion.
d Excludes oral lyophilisate and orodispersible tablets.
e Excludes powder for injection/infusion.

Source: ESRI Calculations. Based on Euripid information supplied by the HSE, personal communications, April 2013

TABLE C.1 Ireland, Ranking of Wholesale Unit Price Indices, Groups of Selected Leading Pharmaceuticals, 2013[a]

ATC Description	ATC	Basket of Nine and Ireland	EU-27 and EEA
Single Source In-Patent			
Aripipriazole	N05AX12	2/5	4/11
Duloxetine	N06AX21	3/6	4/17
Escitalopram	N06AB10	2/6	3/16
Etoricoxib	M01AH05	2/6	4/15
Ezetimibe	C10AX09	3/6	5/17
Memantine	N06DX01	2/6	4/14
Montelukast[b]	R03DC03	5/5	12/14
Pregabalin	N03AX16	1/2	1/3
Tiotropium Bromide	R03BB04	1/6	3/16
Varenicline	N07BA03	1/3	1/7
Multiple-Source Off-Patent			
HSE Identified Patent-Holder			
Atorvastatin	C10AA05	3/6	7/14
Amlodipine	C08CA01	3/6	6/14
Bisoprolol	C07AB07	4/6	9/11
Diclofenac	M01AB05	4/4	7/7
Esomeprazole	A02BC05	1/5	2/11
Lansoprazole	A02BC03	1/1	2/2
Olanzapine	N05AH03	3/6	4/13
Omeprazole	A02BC01	4/6	6/11
Pantoprazole	A02BC02	2/5	2/7
Pravastatin	C10AA03	1/2	1/2
Quetiapine	N05AH04	4/5	5/11
Ramipril	C09AA05	4/6	5/13
Rosuvastatin	C10AA07	6/6	12/14
Other			
Atorvastatin[c]	C10AA05	2/6	3/18
Amlodipine	C08CA01	1/6	2/18
Bisoprolol	C07AB07	1/6	2/10
Diclofenac	M01AB05	5/6	10/16
Esomeprazole	A02BC05	1/6	1/13
Lansoprazole	A02BC03	1/6	4/15
Olanzapine[c]	N05AH03	1/6	2/17
Omeprazole	A02BC01	1/6	2/18
Pantoprazole	A02BC02	1/6	1/15
Pravastatin	C10AA03	1/6	2/12
Quetiapine[c]	N05AH04	1/6	1/17
Ramipril	C09AA05	3/6	4/17
Rosuvastatin	C10AA07	3/4	5/12

Notes:
a For instance, a ranking of 1/6 indicates that Ireland recorded the highest median wholesale price in 2013 out of six countries for that pharmaceutical.
b Montelukast went off-patent in Ireland in March 2013.
c While atorvastatin, olanzapine and quetiapine are recorded as 'single to multiple source' pharmaceuticals for the analysis of price changes in Ireland over the period 2011–2013 (see Table 4.3). As all three pharmaceuticals were off-patent in 2013, they are regarded as multiple source for the analysis of prices across Member States using the Euripid data (see Figure 4.2).

Source: ESRI Calculations. Based on Euripid information supplied by the HSE, personal communications, April 2013

APPENDIX D

Progress on Implementation of Recommendations in *Delivery of Pharmaceuticals in Ireland*

Recommendation Number[a]	Recommendation[a]	Implementation[b]
Recommendation 2.1	We recommend that the HSE should be responsible for the collection, preparation and publication of a comprehensive time series of all components of pharmaceutical expenditure (public, private, community and hospital) on an annual basis.	This recommendation is being progressed and significant data and trends are published. To provide all information in the outpatient sector the sub-threshold pharmacy expenditure is required. The current report reinforces this recommendation for the cash paying patient.
Recommendation 2.2	We recommend that pharmacists should be required to inform the PCRS of the out-of-pocket expenditure, i.e., sub-threshold expenditure, by those who do not exceed the DP threshold.	As above.
Recommendation 3.1	We recommend that the two objectives of the pharmaceutical delivery system from the perspective of the HSE should be obtaining value for money and ensuring security of supply.	Accepted, and an integral part of the ongoing strategic thrust of Department of Health Policy.
Recommendation 4.1	We recommend that, initially at least, the basket of Member States used for the purposes of determining the maximum ex-factory price of in-patent pharmaceuticals should be confined to the nine Member States in the 2006 IPHA/HSE agreement.	Accepted and in place.
Recommendation 4.2	We recommend that the maximum ex-factory price of in-patent pharmaceuticals should be the lowest price of the basket of nine Member States in the 2006 IPHA/HSE agreement.	While this was the Department of Health/HSE objective during the negotiations of the new IPHA framework agreement, within the current framework of voluntary engagement was not conceded by the Industry.
Recommendation 4.3	We recommend that the maximum ex-factory price for in-patent pharmaceuticals should be updated every six months, i.e., on 1 January and 1 July.	Realignment was completed in January 2013. Mid Term Review can afford an opportunity to revisit. Section 18 of the Health (Pricing and Supply of Medical Goods) Act can be invoked on a regular basis by the HSE.

Recommendation Number[a]	Recommendation[a]	Implementation[b]
Recommendation 4.4	We recommend that the HSE monitor parallel imports in order to assist it to (i) validate the pricing information provided to set the maximum ex-factory price for the current basket of nine Member States (ii) determine whether additional Member States should be added to the basket of Member States.	Industry information is harnessed where possible in this regard.
Recommendation 4.5	We recommend that the HSE negotiates risk sharing agreements with firms seeking eligibility for reimbursement under the GMS and Community Drug Schemes for new pharmaceuticals on introduction in terms of expected sales and market penetration.	Accepted and in place.
Recommendation 4.6	We recommend that the HSE set an ex-factory price for parallel imports that shares the difference between the imported price of the parallel import and the brand name ex-factory price of the in-patent pharmaceutical between the parallel importer and the HSE.	The HSE has endeavoured to progress this recommendation but continues to experience significant resistance in this regard.
Recommendation 4.7	We recommend that the reference price for high volume off-patent interchangeable pharmaceutical products should be set through competitive tendering.	The Health (Pricing and Supply of Medical Goods) Act provides for competitive tendering as appropriate.
Recommendation 4.8	We recommend that for the HSE to reimburse an interchangeable pharmaceutical product at a price higher than the reference price, the medical practitioner must complete an IMB Adverse Reaction Report Form and write, in his/her own handwriting, 'no substitution' across the prescription form.	The Health (Pricing and Supply of Medical Goods) Act provides that where the medical practitioner wishes to invoke a clinical exemption, s/he will be required to write in his/her own handwriting 'no substitution' across the prescription form. The legislation also allows the Minister to make regulations on the circumstances for clinical exemption.
Recommendation 4.9	We recommend that if a prescription is written using the international non-proprietary name then the pharmacist is reimbursed at the reference price.	Accepted. Will be in place when the Health (Pricing and Supply of Medical Goods) Act is implemented.
Recommendation 4.10	We recommend that the definition of interchangeability should be broad enough to accommodate minor changes in formulation (e.g., use of different salts) and presentation (e.g., different shaped solid dose forms).	Accepted. Subject to the IMB designation of Interchangeable Groups, this will be in place when the Health (Pricing and Supply of Medical Goods) Act is implemented.

Recommendation Number[a]	Recommendation[a]	Implementation[b]
Recommendation 5.1	We recommend that the HSE actively monitor the importance and service levels offered by DTP brand name manufacturers. If the service levels fall below levels considered acceptable to the HSE, then it should negotiate minimum quality standards with brand name manufacturers using the DTP model.	Accepted and in place.
Recommendation 6.1	We recommend that pharmacists are compensated for dispensing a prescription on the basis of a professional dispensing fee only. This should apply to both prescriptions dispensed under the GMS and Community Drug Schemes as well as for the cash paying patient.	The question of any change in rates of payment would be a matter for consideration in accordance with the provisions of the Financial Emergency Measures in the Public Interest Act 2009.
Recommendation 6.2	We recommend that all pharmacies be required to post, in a manner clearly accessible to patients, a notice setting out their usual and customary dispensing fee and mark-up together with what services are included for the dispensing fee. A standard template should be used.	Department of Health has been in contact with the Pharmaceutical Society of Ireland regarding price transparency.
Recommendation 6.3	We recommend that PSI permit pharmacists to advertise dispensing fees, services provided, and price discounts and rebates with respect to prescription pharmaceuticals.	As above.
Recommendation 6.4	We recommend that pharmacists are able to offer and to advertise that they will pay, in part or whole, any patient co-payment that is part of the GMS and Community Drug Schemes.	Primary legislation governing the GMS and DP schemes does not permit pharmacists to pay, in part or whole, any patient co-payment. Issues also arise in relation to offering discounts or 'consideration' in relation to Clause 4(4) of the HSE Contractor Agreement.
Recommendation 6.5	We recommend that the HSE should carefully monitor the pharmacy market, conducting regular surveys of dispensing fees and offers made by pharmacies.	Noted. National Consumer Agency Survey reported in recent weeks.
Recommendation 7.1	We recommend that, taking into account forthcoming legislation on reference pricing and generic substitution, including interchangeability and no substitution prescriptions, mandatory prescription by INN should be introduced for all medical practitioners to encourage safe and cost-effective prescribing.	This is under active consideration as outlined in recent Department of Health report to the Troika.

Recommendation Number[a]	Recommendation[a]	Implementation[b]
Recommendation 7.2	We recommend that, on the basis of existing evidence, financial incentives to reduce pharmaceutical expenditure should not be introduced for medical practitioners in Ireland.	Noted.
Recommendation 7.3	We recommend (i) the PCRS should coordinate the provision of periodic benchmarking information to GPs (ii) the HSE should undertake a similar exercise for hospital consultants practising in public hospitals. Both the PCRS and the HSE should be pro-active in following up with individual medical practitioners who demonstrate prescribing behaviour that is at variance with clinical guidelines. Protocols should be developed with the Medical Council that specify the procedures to be followed for cases referred to the Medical Council for inappropriate prescribing.	This work is on-going. A significant body of information is routinely available to GPs and this is being enhanced to provide prescribing guidance. The HSE has established a Medicines Management Programme under Clinical Leadership to work in collaboration with the PCRS in this regard.
Recommendation 7.4	We recommend that consideration should be given to centralising and standardising the provision of prescription guidelines to both GPs and hospital medical practitioners	This work has commenced. Initial Guidelines on 'Programme Preferred' Medicines for PPIs and Statins have been circulated to both GPs and Hospital Medical Practitioners.

Notes: a The recommendations are taken from Gorecki *et al.* (2012).
b The progress in implementation of the recommendations is provided by the Department of Health.

Sources: Gorecki *et al.*, 2012, and DoH, personal communication, 24 May 2013

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