

Annexe F

International comparisons of pharmaceutical prices

February 2007

OFT885f

© **Crown copyright 2007**

This publication (excluding the OFT logo) may be reproduced free of charge in any format or medium provided that it is reproduced accurately and not used in a misleading context. The material must be acknowledged as crown copyright and the title of the publication specified.

CONTENTS

| <i>Chapter</i> | <i>Page</i> |
|--|-------------|
| Executive Summary | 4 |
| 1 Introduction | 7 |
| 2 Outline of methodological issues | 8 |
| 3 DH price comparisons | 16 |
| 4 Case studies illustrating methodological issues | 22 |
| 5 International price comparisons from different countries | 34 |
| 6 Conclusions | 41 |
| 7 Attachment 1: Subgroup comparisons | 43 |
| 8 Attachment 2: Exchange rates data | 51 |
| 9 Attachment 3: Obtaining ex-manufacturer prices | 53 |
| 10 Attachment 4: Pack size variation and discounts | 55 |
| 11 Attachment 5: Inconsistent pricing across presentations and dose levels | 60 |
| 12 Attachment 6: Data sources | 64 |

EXECUTIVE SUMMARY

This annexe reviews the available evidence on how UK drug prices compare to those of other countries.

The process of making international price comparisons is conceptually straightforward but involves addressing a range of issues, regarding, for example, the types of drugs and the countries covered. Other issues are:

- **decisions about which prices should be compared** – these include choosing which countries should be used as comparators and at what point in time comparisons should be made
- **the price data used to make the comparison** - issues include how big a sample from the relevant population of drugs should be used, how this sample should be selected and what adjustment for discounts and rebates should be undertaken
- **the methodology used to make the comparison** – this includes identifying matching criteria and choosing between bilateral or multilateral comparisons, and
- **the parameters used in constructing overall price indices** – this includes deciding which countries' volumes are used as weights and what kind of exchange rate adjustment is used.

As a starting point to our analysis, we examine results from international price comparisons undertaken on an annual basis by the Department of Health (DH). These comparisons show that, historically, prices in the UK have been higher than those in most European countries. DH assessment of results for 2004, published in its ninth report to parliament, showed the weighted index of prices in the UK to be, 'significantly lower than those in the USA', and, 'higher than those in the other European comparator countries except Germany and Ireland, where prices are broadly comparable'.

DH has provided us with results from the analysis of 2005 data, which are not yet published, for use in this Annexe. The 2005 results show evidence of some realignment with European prices resulting from the seven per cent price cut that came into effect on 1 January 2005. In 2005 the UK was the fourth highest among the ten European countries, behind Germany, Finland and Ireland.

However, it is important to note that these results do not take account of rebates paid by manufacturers in some countries as part of cost containment policies, which mean that the prices used in the comparison may not always correspond closely to what is actually paid in practice. We found evidence that rebate systems exist in the USA, Germany, Ireland, and France. Our research was not exhaustive and there may be other countries where these also operate. These rebates amount to between two and seven per cent of total expenditure on drugs in Germany, three and a half per cent in Ireland, about three per cent in France and up to 30 per cent off list prices (and an estimated eight per cent off IMS data) for the United States.

Taking into account rebates, prices paid at ex-manufacturer level in the UK are likely to be broadly comparable with those in Ireland and closer to those in Germany than is apparent from the DH price comparisons.

Supplementary analyses provided by DH suggest that there are variations in the relative prices of different groups of drugs. These price differentials may be driven by various factors. We hypothesise, for example, that they are influenced by the prevailing exchange rate at the time the products were introduced to the market. When introduction coincided with periods of high or low exchange rates relative to current rates, subsequent movements in exchange rates may have left relative differentials observable as an historic effect.

It should be noted that there is a number of practical problems associated with international price comparisons. The OFT has undertaken a small number of case studies with the intention of better understanding the implications these practical problems may have. We looked at five key issues:

- discounts and rebates, as discussed above
- obtaining consistent ex-manufacturer prices
- pack sizes and discounts
- sensitivity to weightings, and
- inconsistent price differences between different presentations and dose levels.

These illustrative 'case studies' are used to probe the index calculation process to see if there is evidence that it may not deliver representative results. Even a limited look at examples of real data identifies cases where results seem very sensitive to volume weightings, and price differences show a disturbing degree of inconsistency across different presentations and dose levels. Comparison results may also be influenced by both the basket of products chosen, which may be specific to particular countries, and by methodological choices in their calculation.

The sensitivity of results to methodological assumptions is also illustrated through evidence from comparison studies conducted by other countries. Comparing results from six relevant studies to those undertaken by DH, we identified broad similarities in the rankings produced in the studies, but found divergences in price indices of up to 15 percentage points.

This annexe concludes that international price comparisons are subject to a variety of methodological difficulties and therefore need to be interpreted with caution. Given the widespread interest in the comparisons they cannot be ignored, however. Conducted properly they can provide some useful information provided that results are interpreted with caution and account is taken of the influence of the range of factors discussed in this annexe, such as rebate schemes and exchange rate movements. This is particularly relevant for countries that use the results of price comparisons to set the domestic price of pharmaceuticals, through international reference pricing mechanisms.

We therefore suggest that price comparisons should only be used as one factor among many others to inform government policies towards the pharmaceutical sector, and that the limits of

these studies should be clearly recognised. The studies can give answers to a very narrow set of questions but cannot alone give answers to questions such as, 'does the UK pay the right price?' or 'are UK prices too high?'. Nor are we convinced that changes in overall levels of expenditure provide any useful way of addressing internal efficiencies within the PPRS.

1 INTRODUCTION

- 1.1 This annexe reviews the available evidence on whether drug prices in the UK are higher or lower than in other countries. The process of making international comparisons of drug prices is conceptually straightforward but subject to a range of practical difficulties. This annexe therefore includes in Chapter 2 a discussion of various methodological issues, such as selecting which countries and prices are used for comparisons, how to select and match like products under the assumption of different drug availability in different countries, and what exchange rates to use when comparing prices in different currencies.
- 1.2 Many of the methodological issues leave open the possibility of alternative approaches to making the comparisons. Where appropriate, the implications of these alternatives are discussed.
- 1.3 International drug price comparisons are published routinely by the Department of Health (DH). Chapter 3 presents an overview of these comparisons since 1999 and some recent DH analysis of unpublished 2005 data.
- 1.4 During the course of the PPRS study, the OFT assembled evidence on drug pricing systems from a number of other countries and was able to obtain data relating to reimbursable drug prices from four countries: Australia, Sweden, Germany and Finland. These price data sets are not sufficiently comprehensive to support systematic price comparison analysis, but they are able to support a number of illustrations of the practical difficulties of making international price comparisons. The discussion in Chapter 4 demonstrates some of the particular complexities associated with rebate systems in different countries, exchange rates and the way in which prices depend on different pack sizes, presentations, and dosage levels.
- 1.5 In Chapter 5 we look at international price comparison studies conducted by governments or industry bodies in different countries. The studies vary in approach, in the products covered and were undertaken in different years. They therefore illustrate the variety of choices available in undertaking international price comparisons and demonstrate the divergent results they can generate.
- 1.6 Chapter 6 presents some conclusions and policy implications.

2 OUTLINE OF METHODOLOGICAL ISSUES

Fundamentals

- 2.1 The process of making international price comparisons is conceptually simple. Data is assembled on the price of comparable products in different countries, and overall comparisons are made by using weighted average prices, with weights chosen to reflect a suitable basket of products.
- 2.2 When such a procedure is followed using weights that reflect UK purchases, the process answers the question: 'if the basket of products currently purchased in the UK were purchased in another country what would we expect to pay for that basket of goods?'
- 2.3 We would emphasise that it is an entirely distinct question to ask 'if the basket of products currently purchased in another country were purchased in the UK what would that basket of goods cost?' and that there may be significant differences in the answer to these two questions.
- 2.4 Practical difficulties in conducting price comparisons are numerous. Mostly these involve, in one form or another, difficulties in ensuring comparisons are made on a comparable basis, but some arise because of limitations in the available data and some for statistical reasons. The focus of this chapter is to highlight the methodological choices and problems related to those choices that have to be made when undertaking international price comparisons

Comparator countries

- 2.5 Any overall assessment of UK prices relative to other countries has the potential to be affected by whether high price or low price countries are included among the comparators. Ideally, comparisons would be made against as wide a field of countries as possible.
- 2.6 However, as will be explained in more detail below, finding comparable products can be difficult, and this may be exacerbated by attempts to increase the number of countries included.
- 2.7 Results published by DH confine themselves to the USA and major European countries, while those found in the academic literature generally provide similar coverage though sometimes also include countries such as Canada and Japan.

Prices at different points in the supply chain

- 2.8 Ensuring that prices are comparable raises a number of important issues of further detail. Different prices will apply at different stages of the supply chain. This raises the possibility of making comparisons in different ways, such as at the ex-manufacturer price, at a wholesale level, or in terms of the cost to the public purse.

2.9 It is also important that comparisons are consistent in their treatment of co-payments or any personal contributions that the consumer makes towards the prescription charge, and in terms of taxation.

2.10 While this appears to constitute a very wide range of options in relation to properly comparable prices, in practice we are interested in the comparisons most relevant to the PPRS and that implies the ex-manufacturer price is the key focus.

When the comparisons are made

2.11 As pricing regimes and exchange rates change over time, the point in time at which comparisons are made can affect results. These effects are sometimes highly visible. Under the PPRS, periodic price cuts are made to UK drug prices. For example, comparisons of UK prices before and after the seven per cent price cut agreed under the 2005 PPRS and effective from 1 January 2005 shows a marked realignment of the UK with respect to other countries.

2.12 Price comparisons are also influenced by exchange rates. Results are generally presented on the basis of the prevailing exchange rates at the time the comparison was made, or averaged over a suitably matched period (such as multi-year averages of market rates).

2.13 However, market exchange rates are erratic and can move substantially over the short, medium or long term. Hence pharmaceutical price comparisons that rely on them are not guaranteed to offer an accurate guide to effective price differences in the future.

2.14 Although currency movements are erratic, many economists believe that over the medium to long term certain 'economic fundamentals' can push a country's exchange rate towards an equilibrium level.¹ If this is so, the UK's equilibrium exchange rate (EER) with major trading partners bears investigating because future differences in effective drug prices are likely to be more important to most stakeholders than past ones. The main difficulty with this concept is that the EER is not directly observable since it may incorporate, depending on the model, predicted trend movements of many macroeconomic variables. It is therefore possible to derive several different but plausible EERs for the same current rate.

2.15 In light of this, our approach in conducting analysis later on in this annexe is to use market exchange rates, usually averaged over the year being considered, but sometimes more short term depending on the context.

¹ More accurately, varying fundamentals may affect each of a country's bilateral exchange rates with other currencies, such as GBP/Euro, GBP/US Dollar, etc. Discussions in the literature often refer to as 'the' exchange rate of a country some multilateral rate, for example a trade-weighted average of major bilateral rates.

Box 2.1 Equilibrium exchange rate (EER)

There are many models of EERs in the macroeconomic literature, motivated by competing theoretical insights and various pragmatic concerns of empirical estimation. In each case the EER can be thought of as a 'weak but steady attractor'² for the observed current rate, gradually pulling the observed rate towards it.

The main difficulty with this concept is that the EER may be unobservable since it may incorporate, depending on the model, predicted trend movements of many macroeconomic variables. It is therefore possible to derive several different but plausible EERs for the same current rate.

Because it can be difficult to choose between EER models, it is tempting instead to take as a best-guess medium-term exchange rate today's level plus or minus some margin of error. Such an approach is not as flippant as it may seem, since many academic observers have commented on the resiliency of the 'random walk hypothesis' according to which the best predictor of tomorrow's exchange rate is indeed today's.³

One explanation could be that the overwhelming bulk of demand for currency exchange relates to transactions in financial assets that can be driven by many unpredictable factors that do not feature in models of EERs, including speculation, irrational exuberance among investors and the opaque activities of significant players such as off-shore hedge funds.

Motivated by the euro debate, Government has given some consideration to EERs in the Treasury paper *Estimates of equilibrium exchange rates for sterling against the euro* (2003). The paper provides a lucid summary of the issues that could affect the choice of an EER for many purposes. The paper categorises available EER models into four main types. All are models of real exchange rates, which are currency exchange rates adjusted for the differences in price levels between countries. Real exchange rates therefore measure the comparative cost of the same basket of real goods between countries.

The HMT paper reviews three leading methods of calculating EERs that consider the real exchange rate as part of a complete macroeconomic system. Since the three methods are essentially variant empirical approaches to the same underlying ideas we consider only their common principles here.

The theoretical proposition behind each approach is that the EER between two countries should be determined by the equilibrium supply and demand for their currencies in the long run. Long-run equilibrium in foreign exchange would be characterised by an absence of shorter-term movements driven by transient factors (such as portfolio shifts to take advantage of changes in relative interest rates). Rather, equilibrium would reflect long-run capital flows driven by fundamental characteristics of the two economies. Such fundamentals could include the propensity of private agents and governments in each country to save and invest (and the availability of investment opportunities in each country, as well as elsewhere in the world). Other fundamentals might be the competitiveness of the two economies, driving long-term

² The term is due to Wren-Lewis (2003), *Estimates of equilibrium exchange rates for sterling against the euro*, HM Treasury – referred to later in this discussion.

³ See for example Rogoff (1997), 'The Purchasing Power Parity Puzzle', *Journal of Economic Literature*, (34). Similar issues are reported in: Kilian and Taylor (2003), 'Why is it so difficult to beat the random walk forecast of exchange rates?', *Journal of International Economics*, (60). Small victories can be of a technical nature, for example in: Clark and West (2005), 'Using out-of-sample Mean Squared Prediction Errors to Test the Martingale Difference Hypothesis', *Journal of Econometrics*, (135).

foreign direct investment projects, or the countries' comparative advantages in producing goods and services with significant world demand.⁴⁵

A clear difficulty with these 'system' EER models is that the fundamentals they rely on are open to interpretation – and may not turn out as expected. As a result an estimated EER may not provide a useful guide to future spot exchange rates. Another way of expressing the same problem is that any EER model using a realistic range of outturns for future fundamentals might produce a range of EERs including the present exchange rate often enough that it would never be practicable to determine whether a market rate was over or undervalued.

To take a concrete example of this, the Treasury paper estimates a model suggesting that as of 2002-2003 sterling was overvalued against the euro⁶ and that an EER based on a macroeconomic model would be around 1.37 euros per pound, compared to a spot rate of around 1.45 euros per pound in early 2003. The model's base case assumes an equilibrium current account deficit for the UK of zero. However, the UK has run a current account deficit of between 0.5 per cent and three per cent of GDP since before 2000. Assuming that the UK might run a current account deficit in equilibrium – that is, a position of net borrowing from the world⁷ – and taking into account the implication for supply and demand of sterling, the model outputs an EER of between 1.41 and 1.47 euros to the pound. The annual average exchange rate in each of the last three years (2004 to 2006) has been €1.46 or €1.47 to the pound.

The choice of price data to use in the comparison

Random sampling

- 2.16 In circumstances where conclusions on a complete population have to be based on incomplete data, that data would ideally be obtained by random sampling. The important advantages of data that is randomly selected are that any estimates will be free of bias, and that it should also be possible to derive sampling errors about the estimates.
- 2.17 The methods used here make use of data that do not arise through a random selection process. The methods therefore do not provide any protection against the risk of bias in the results. There is a possibility that data used in any comparison may not be suitably representative.

⁴ For a longer list of fundamentals often used in EER models, see for example: Clark and MacDonald (1999), *Exchange Rates and Economic Fundamentals: A Methodological Comparison of BEERs and FEERs* in MacDonald and Stein (eds), *Equilibrium Exchange Rates*, Kluwer.

⁵ The fundamentals given above clearly also relate to the wider international scene beyond the two countries for which a bilateral EER might be calculated. The fact that foreign exchange is global means that it is difficult to avoid calculating EERs as a global system – which is challenging.

⁶ Over 2002 to 2003 sterling traded in the range 1.40 to 1.60 euros per pound, somewhat stronger than today. Since 2003 the pound has remained in the range 1.40 to 1.45 euros.

⁷ This would not be unusual for a leading industrialised country like the UK whose currency is often held in reserve by foreign central banks in the form of government debt (long-dated bonds).

- 2.18 While there is nothing that can be done to change this basic situation, the risk of bias will be proportionately less when the comparison is based on a greater number of matches and when it covers an increased fraction of the total UK basket.
- 2.19 Nevertheless it is important to consider any supplementary analyses that can help to demonstrate that there is nothing obviously unusual about the data being used. Such analyses might, for example, check that the comparison included examples of all major therapeutic categories, and that the drugs included were not biased towards being generally older or newer than the overall basket of prescribed drugs.

Types of drugs to be covered

- 2.20 The overall basket of drugs prescribed within the UK (or elsewhere) contains both branded and generic drugs, and drugs have other observable characteristics such as availability as parallel imports, and being on or off-patent. In general, to be feasible within time and data constraints, price comparison exercises are required to make many choices over which types of drugs to cover.
- 2.21 Academic papers that have no direct UK focus, tend to be based on drugs that are major sellers in a variety of countries. DH results are directly concerned with branded drugs available in the UK and derive from data on the prices of all preparations for the top 150 branded medicines in the UK, though the actual comparisons are dependent on the availability of matching preparations in other countries.

Discounts and rebates

- 2.22 In some countries there may exist discount or rebate schemes that result in differences between list prices and actual prices. These may arise simply from commercial agreements between buyers and sellers, but may also arise through countries' regulation of sales volumes that lead to institutional buyers paying lower than published list prices.
- 2.23 These differences are difficult to research and for those rebates that arise by commercial agreement between businesses, may not be foreseeable or may be of a confidential nature.
- 2.24 Our wide ranging consultations, especially with overseas experts, identified the existence of ex-post rebate schemes in several.. As a result of those rebates, existing price estimates for some countries may be biased upward and give an imprecise picture about actual price levels. The interpretation of any international price comparison results should take into account such evidence as is known about rebate schemes.

Health care sector coverage

- 2.25 Data used in international price comparisons must avoid any distortions that might arise because of price differences in different parts of the care sector.. The drug prices in the

secondary care sector may differ from those available under the primary care system, for example.

- 2.26 DH comparisons only consider prices in primary care. When researching data on other countries these differences in prices between primary and secondary care should be taken into account.

Methodology used to make the comparison

Multilateral and bilateral comparisons

- 2.27 It is possible to make comparisons of prices between countries that are either bilateral, that is comparisons that are made for pairs of countries at a time and based on drugs available in both countries, or multilateral, that is comparisons involving a number of countries simultaneously and based on drugs which are available in all comparator countries.
- 2.28 Bilateral comparisons lead to conclusions that are less general. For example, a series of bilateral comparisons between the UK and other countries does not provide the most efficient basis for comparisons between those other countries. Better results could be obtained by making direct comparisons.
- 2.29 But while multilateral comparisons have wider applicability, they have weaknesses of their own. Since drugs must be available in all the countries being compared in order to apply this approach, the frequency of matches is much reduced and the comparisons based on a correspondingly smaller part of the drugs basket.
- 2.30 The choice between the bilateral and multilateral approach essentially involves a trade-off between breadth of conclusions and the size of basket used to generate the comparisons. For research of this sort, which has a UK focus, it is normally advantageous to use bilateral comparisons on the basis that the larger basket of prescribed medicines will provide a more reliable picture of the UK in relation to other countries. Any attempt to relate prices to other national statistics would arguably be better based on multilateral comparisons, subject to there being sufficient available data.

Selecting matching products

- 2.31 Matches between products in different countries may be made either on the basis of exact presentations or on the basis of the same active molecule. Comparisons that are based on exact presentational matches ('like for like') will rely on a more limited data set than comparisons where matches are made on the basis of the same active molecule.
- 2.32 However, in order to make active molecule comparisons and take advantage of the potentially larger data set, some common unit of comparison is needed. The process of arriving at a common unit can be complicated. It may involve producing a weighted

average price across doses but as drugs available in different countries may employ different pack sizes, doses, and other presentational differences such as enteric coating or delivery as a suppository rather than a tablet, this can be difficult⁸.

- 2.33 The choice between the two approaches is partly a trade-off between the ideal or perfect 'like for like' comparisons and the size of the basket of drugs. Comparisons that are based on active molecule matching require substantially more accompanying information about the amount of each presentation sold in order to weight together different prices. In the absence of such weighting information, simple averages are potentially a source of major bias.
- 2.34 It appears that published research has used exact presentation matches more frequently than molecule matching, though this may be for convenience rather than for any objective scientific reason.
- 2.35 Our view is that comparisons based on exact 'like for like' matches, whilst potentially having fewer matches and involving a smaller basket of drugs are nevertheless much more robust than those based on active molecule matches. The following paragraphs further explain why matching according to the same active molecule is potentially problematic and may even result in misleading or biased results.
- 2.36 Drugs are sold in a wide variety of different presentations. These may involve the form, packaging, the way the drug is delivered, dosages and pack sizes. If price differences between countries for particular drugs were consistent across different presentations and dose levels, then any matches would be representative of that difference. If, however, the differences are inconsistent across different presentations and dose levels, the relative prices will reflect the price differences for the sporadic matches that occur, and will be subject to increased levels of random error. Since the matches do not arise through any random sampling process we cannot guarantee these errors will not lead to bias in the final results.
- 2.37 In cases where matches can be found for all presentations and dose levels, a weighted average of the differences will reflect the true underlying situation. However, this is certainly not guaranteed and will be of little benefit if matches are sparse.
- 2.38 For example, consider a price comparison for a single drug between a home country (A) and another country (B), where country B has presentations that do not exist in country A. This could arise either because of different controls and policy in relation to the presentations available under the primary care system, or at a more prosaic level simply through gaps in coverage from available data sets.

⁸ Other factors that add to the difficulty of arriving at a common unit of comparison are that some drugs are marketed in ways that may fix the price for a standard adult daily dose even where the amount of active ingredient may differ between patients.

2.39 Such a situation constrains the applicability of the results. Matched price comparison data can simply never occur for the presentation in question. The worked example below illustrates the problem.

Box 2.2: Example analysis

We assume that the example drug is available:

- at a common drug dosage level
- in a common pack size
- prices are compared after adjustment to a common currency

| Country A | | Country B | |
|------------------|----------------|------------------|----------------|
| Presentation | Price per dose | Presentation | Price per dose |
| Tablet | 100 | Tablet | 100 |
| Coated table | Not available | Coated table | 110 |

Case 1: A comparison based on strict like-for-matches would conclude that the price of the drug in the two countries was equal. This is correct, although it is a conclusion whose applicability is constrained by the absence of the presentation not available in country A.

Case 2: In contrast, a comparison based on active molecule matches will be problematic. Regardless of how prices are averaged, the price in country B will be higher than that in country A.

This resulting conclusion that the drug price was not equal but was more expensive in country B is valid, but with different applicability.

It is a type of comparison where the observed differences are driven both by price differences and also partly by differences between the presentations available. Our study into the PPRS is concerned with drug prices and in this context the outside influences are misleading. This reinforces our view that appropriate price comparison analysis for PPRS purposes should be limited to exact matches.

Weighting issues

2.40 Most price comparisons involve the use of a weighted averaging process. The use of weights in itself is not controversial, and allows those drugs that are more heavily prescribed to exert a greater influence on the results than those that are less heavily prescribed.

2.41 However, there is empirical evidence to show that each country will appear to have lower prices when using its own volumes as weights, reflecting higher use within that country of lower priced drugs⁹. This is not in any way paradoxical, but does emphasise that statements about comparative prices should be accompanied by a statement about the choice of weights on which the comparison is based.

⁹ Danzon, P., Chao, L. (2000), "Cross-national price differences for pharmaceuticals: how large and why?", *Journal of Health Economics*, 19, 159-195.

3 DH PRICE COMPARISONS

- 3.1 The Department of Health undertakes its own international price comparisons on an annual basis and results are regularly presented in its reports to parliament. The most recently published is the Pharmaceutical Price Regulation Scheme: Ninth Report to Parliament: July 2006. International price comparisons are reported in Section 5 of the DH report. Results for 2005 are not yet published by DH, but have been provided directly to OFT by DH and remain provisional at this time.
- 3.2 In addition to the overall results presented in this chapter, DH has undertaken some further analyses in relation to 2005 data, and has provided these directly to OFT. In these analyses, drugs were considered in a number of common therapeutic groups, and the same comparison analysis was undertaken separately for each of the groups. We present this analysis in Attachment 1.
- 3.3 DH's international price comparison compares branded medicines in the UK with a range of European countries and the USA. As the PPRS is applicable to the prices of branded drugs (regardless of whether they are in or off patent), as set by manufacturers, the most relevant evidence for making price comparisons should be branded drugs at ex-manufacturer prices. However, in making the comparisons, many of the theoretical options set out above are constrained by the availability of suitable data. To quote the DH report:
- 'It [the DH price comparison exercise] compares the prices of all preparations for the top 150 branded medicines in the UK with other countries, depending on the availability of matching preparations elsewhere'.*
- And continues in footnotes to record that:
- 'More specifically, the data relates to all the branded products covered by the chemical name to which the top selling brands relate where there is a match for the form and strength. Rather than just taking the best selling brand for comparison, the analysis uses all matches found. The number of brands covered therefore exceeds the number of chemical entities covered.*
- For 2003, there were 117 molecules for which data were available and at least one other country match for form and strength was found. This covered 157 brands'.*
- 3.4 The market coverage for the 2003 (bilateral) analysis is reported to range between 29 per cent and 39 per cent of expenditure in England on branded medicines, with a median coverage of 34 per cent.
- 3.5 As the comparisons are based strictly on branded medicines, the comparisons are clearly free of any distortions that might arise from generic prices. That said, the coverage is necessarily limited and the results therefore are not exact. The report comments:

'the prices used [in the comparison] do not, in the main, take account of rebates paid by manufacturers in some countries as part of cost containment policies. This means that prices in some countries may be overstated relative to the true position.'

- 3.6 Direct discussions with DH have clarified the basis on which comparisons are made:
- a. the data are obtained from commercial suppliers
 - b. the data are ex-manufacturer prices
 - c. the data are exclusive of co-payments, and relate to the primary care sectors in each country and not the hospital sector, and
 - d. analysis is based on exact matches within the base data set.

For items b, c and d we fully endorse these choices as those most appropriate for examination of issues relating to the PPRS or on the grounds of providing reliable analysis.

- 3.7 The report presents the bilateral comparisons of ex-manufacturer prices, which are reproduced in the table below.¹⁰ Results for 2005 are not yet published by DH, but have been provided directly to OFT by DH and remain provisional at this time.

Table 3.1: Bilateral comparisons of ex-manufacturer prices

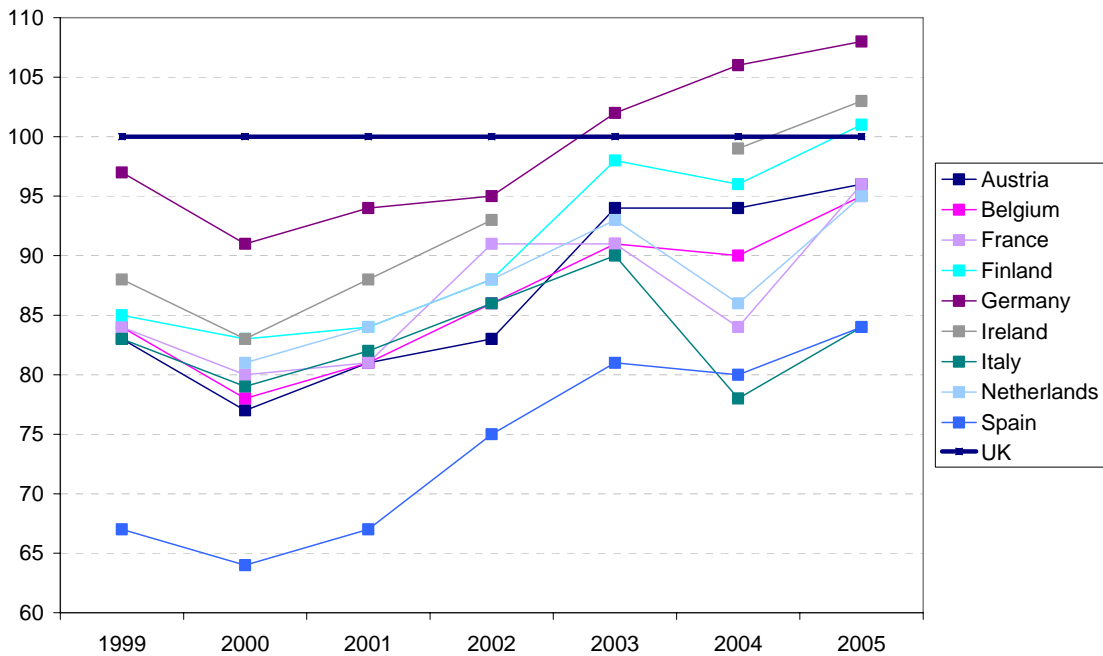
| Country | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 5 year '00 to '04 |
|-------------|------|------|------|------|------|------|------|----------------------|
| France | 84 | 80 | 81 | 81 | 91 | 84 | 96 | 78 |
| Germany | 97 | 91 | 94 | 95 | 102 | 106 | 108 | 98 |
| Italy | 83 | 79 | 82 | 86 | 90 | 78 | 84 | 72 |
| Netherlands | n/a | 81 | 84 | 88 | 93 | 92 | 95 | 86 |
| Spain | 67 | 64 | 67 | 75 | 81 | 80 | 84 | 74 |
| USA | 184 | 209 | 217 | 201 | 190 | 176 | 198 | 192 |
| Austria | 83 | 77 | 81 | 83 | 94 | 94 | 96 | 87 |
| Belgium | 84 | 78 | 81 | 86 | 91 | 90 | 95 | 84 |
| Finland | 85 | 83 | 84 | 88 | 98 | 96 | 101 | 89 |
| Ireland | 88 | 83 | 88 | 93 | n/a | 99 | 103 | n/a |
| UK | 100 | 100 | 100 | 100 | 100 | 100 | 100 | |

Source: DH 9th Report to Parliament and unpublished data from DH

- 3.8 The position of the EU countries alone is shown in the graph below.

¹⁰ The ninth DH report also provides the same comparisons averaged over the five year period from 2000 to 2004.

Figure 3.1: Bilateral comparisons of ex-manufacturer prices in EU countries



Source: DH, Ninth Report to Parliament and unpublished data from DH

3.9 The results produced by DH for 2005 indicate the UK prices have historically been higher than those in the rest of Europe but that after the 1 January 2005 price reductions, prices fell, to rank fourth out of ten in comparisons with other European countries.

3.10 DH reports its conclusions as follows.

'The bilateral comparisons, based on 2003 market exchange rates showed the weighted index of prices in the UK to be:

- *significantly lower than those in the USA*
- *higher than those in the other European comparator countries except Germany and Finland, where prices are broadly comparable.*

However, if the longer-term five-year average exchange rate is used UK prices remain significantly lower than those in the USA but are higher than all other European countries.'

3.11 The data also suggest that the price reductions in 1999 and 2005 have resulted in a considerable realignment of UK prices in relation to other European countries. In 1999 every European comparator country had prices lower than the UK with an average index of 84 compared with the UK's index of 100. However, in the 2005 results, three European comparator countries (Germany, Ireland and Finland) had higher prices and six countries lower prices with an average index of 96 compared, again, with the UK's index of 100.

- 3.12 DH also presents results in its report for indices averaged over a five year period. This is a lagged result and is influenced by historic results, and for the ninth report covering results between 2000 and 2004 is effectively centred on 2002. Assuming a consistent approach for the tenth report, averages covering 2000 to 2005 will be centred on 2003. While the averaging process helps to smooth out some of the effects of exchange rate variation, this lagging effect is a drawback, as results do not reflect the latest available picture.
- 3.13 If results are considered year by year in conjunction with the exchange rates prevailing at the time, evidence for 2005 (and on the basis of 2005 exchange rates) points to UK prices being above the European average.¹¹ However, it is important to remember that, as explained in more detail below, the results being discussed here do not take account of rebates paid by manufacturers in some countries as part of cost containment policies. This means that prices in some countries (especially Germany, Ireland and the US) may be overstated.
- 3.14 Note that the effects of 1999 PPRS price reduction of 4.5 per cent¹² are not highly visible in the price comparison results presented in Table 3.1. Indeed from 1999 to 2000, relative to prices for other European countries, UK prices actually increased variously between two and seven per cent, with a typical increase of five per cent.
- 3.15 However, during the period from the start of 1999 until the end of 2000, the pound rose steadily against the euro, and overall the average rate for 2000 was about eight per cent higher than for 1999. This was enough to mask the price reduction effect.
- 3.16 The 2005 scheme also included a price reduction. The reduction was operational from 1 January 2005 and was deliverable either by an across the board reduction of seven per cent or by a modulated reduction having the same aggregate effect.
- 3.17 In the absence of other changes, a small change in the observed price indices between 2004 and 2005 would have been expected as a result of the small depreciation (about one per cent) in the average exchange rate between these two years.
- 3.18 Figure 3.2 below shows the data in Table 3.2 plotted in conjunction with the average exchange rate for the pound against the euro. The price indices are plotted against the left hand axis ranging from 60 to 100 and the exchange rate is plotted against the right hand axis ranging from 1.2 to 1.8. The chart also includes a simple average index of the European comparator country prices.

¹¹ See Table 3.2 below

¹² The price reduction specified in the 1999 scheme was 4.5 per cent and became operational from the 1st October 1999, and deliverable either by an across the board reduction of 4.5 per cent in all NHS list prices covered by the scheme, or a modulated reduction having the same aggregate effect. Companies with NHS home sales of drugs of less than £1 million in the previous financial year were not required to reduce prices.

3.19 The individual lines have been depicted in grey so that the general picture can be appreciated without too much reference to detail. There are many other factors that influence the comparison results, and the shape of the graph is controlled by more than just price reductions and exchange rates. Nevertheless, the influence of the exchange rate is clear in the chart below, where the average comparison shown in the chart as a strong black line closely mirrors the changes in the exchange rate, and is clearly an important controlling influence on the annual comparisons.

Figure 3.2: Bilateral comparisons of ex-manufacturer prices, plotted with exchange rate £ against the Euro

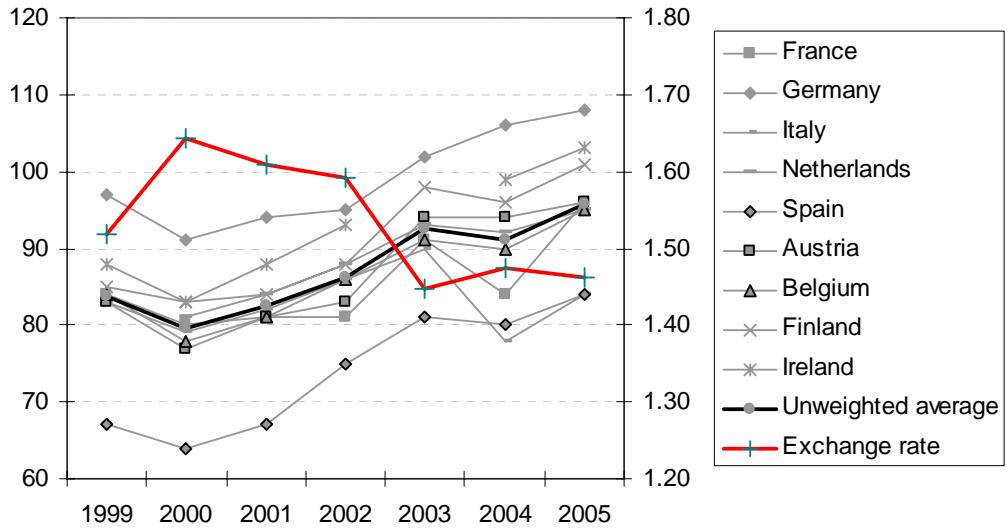


Table 3.2: Bilateral comparisons of ex-manufacturer prices: evaluation of 1999 and 2005 prices, adjusted for exchange rate movements

| Country | Indices | | Exchange rate (Euros/GBP) | | Fall in relative UK prices | |
|----------------|---------|------|------------------------------|------|----------------------------|--|
| | 1999 | 2005 | 1999 | 2005 | Unadjusted | Adjusted for exchange rate differences |
| France | 84 | 96 | 1.52 | 1.46 | 14% | 10% |
| Germany | 97 | 108 | 1.52 | 1.46 | 11% | 7% |
| Italy | 83 | 84 | 1.52 | 1.46 | 1% | -3% |
| Netherlands | n/a | 95 | 1.52 | 1.46 | n/a | n/a |
| Spain | 67 | 84 | 1.52 | 1.46 | 25% | 20% |
| Austria | 83 | 96 | 1.52 | 1.46 | 16% | 11% |
| Belgium | 84 | 95 | 1.52 | 1.46 | 13% | 9% |
| Finland | 85 | 101 | 1.52 | 1.46 | 19% | 14% |
| Ireland | 88 | 103 | 1.52 | 1.46 | 17% | 13% |
| Average | 84 | 96 | 1.52 | 1.46 | 14% | 10% |
| | | | (US\$/GBP) | | | |
| USA | 184 | 198 | 1.62 | 1.82 | 7% | 21% |

- 3.20 The same calculation can be applied to individual comparator countries and the results of such analyses are shown in Table 3.2. For completeness the table includes similar calculations for USA comparisons and the exchange rates for the US dollar against the pound. Understandably there is some variation from country to country, but among European countries, two in particular show observable departures from the general trend.
- 3.21 Compared with Italy, UK prices have actually risen by roughly three per cent, clearly indicating that important factors outside the scope of this analysis have influenced Italian prices over this period. In contrast, the result for Spain shows that Spanish prices have risen by considerably more relative to the UK than might have been expected purely as a result of exchange rate movements and UK price reductions under the PPRS.

Conclusion

- 3.22 In broad terms, we believe the DH methodology for comparing prices is a sensible and pragmatic one. It focuses on ex-manufacturer prices – clearly most relevant for considering the PPRS – and generally avoids reliance on more speculative and hence potentially contentious methodologies. For example, it relies on historical exchange rates rather than projected equilibrium exchange rates and only on exact presentation matches rather than on some weighted average per molecule. This can be at the expense of generalisability, so, as always, care should be taken not to draw broader conclusions than the results warrant. One area that future that future comparisons might, in our view, usefully explore would be the use of rebate systems in a number of countries.
- 3.23 In further analyses, drugs were considered in a number of common therapeutic groups, and the same comparison analysis was undertaken separately for each of the groups. These results are peripheral to the main results and so are presented in Attachment 1 below.

4 CASE STUDIES ILLUSTRATING METHODOLOGICAL ISSUES

4.1 The OFT has not undertaken any primary research to replicate the analyses produced by DH. Instead we have concentrated on a small number of case studies looking at drug price data using information available in the public domain from a number of countries, with the intention of better understanding the practical problems associated with this work. We looked at five key issues, as listed below, each of potential importance to the validity of international price comparisons:

- obtaining consistent ex-manufacturer prices
- discounts and rebates
- pack sizes and discounts
- sensitivity to weightings
- inconsistent price differences between different presentations and dose levels.

4.2 The first two of these issues are external to the detailed calculation of comparisons, but the latter three have a direct influence on the calculations themselves, and to some degree are inter-related.

4.3 Each of these issues is discussed in greater detail in the series of attachments to this annexe. This section summarises the main findings and the implications for the robustness of the comparison process.

Obtaining consistent ex-manufacturer prices

4.4 Even our limited look at other data highlighted complexities in establishing comparable ex-manufacturer prices from the available data. Our experience was that price data seemed more readily available at the retail and wholesale levels (that is the price paid by the pharmacy) than at the ex-manufacturer level.

4.5 In the countries we studied we encountered varying degrees of difficulty in adjusting the publicly available price data back to wholesale and ex-manufacturer prices. In some cases it was possible to derive ex-manufacturer prices from prices later in the supply chain exactly, relying on prescriptive arrangements that allow for wholesale and pharmacy mark-ups. Such detailed and prescriptive arrangements existed for both Germany and Australia and are presented in the attachments below.

4.6 In other cases, including the UK, the adjustments could be done on an overall basis, under the assumption of a uniform wholesale margin. In the UK an allowance of 12.5 per cent of the list price is assumed for the wholesale margin on branded drugs. This assumption is considered robust by DH experts, though it unclear whether the margin is exactly 12.5 per cent in every case.

- 4.7 However, we were unable to establish such clear understanding in all cases, and believe that for some countries the adjustment of prices later in the supply chain may deliver less robust estimates of ex-manufacturer prices.
- 4.8 In the case of Finland we were advised that an appropriate overall mark-up was four per cent, but this was advice given orally by experts we consulted and we were unable to identify authoritative published sources of the same information.
- 4.9 In Sweden wholesale operations are conducted by two independent commercial companies. Though we made contact with both companies, we were not able to find the wholesale margin in time for the publication of this report. Orally we were told that margins were about three per cent.
- 4.10 This leads us to hypothesise that in countries where wholesaling is conducted by competing companies, information about wholesale mark-ups is likely to be commercially sensitive and not available to researchers or commercial suppliers of pharmaceutical data.
- 4.11 In summary, we did not find it easy to assemble data sets of ex-manufacturer drug prices for other countries. Publicly available data sets of prices at other points in the supply chain were more commonly available, but mechanisms to adjust these to ex-manufacturer level were variable.
- 4.12 In some countries the mechanisms for calculating wholesale mark-ups are exact and prescriptive, but in others they required assumptions about the level of mark-up. While this is the case in the UK, the assumptions in this case are understood to be robust. In some countries such adjustments might not be possible due to commercial confidentiality and data would need to be assembled by other means. For more detailed information we have prepared some examples in Attachment 2 that outline how public retail data was adjusted to ex-manufacturer prices.

Discounts and rebates

- 4.13 A fundamental problem when making international comparisons of ex-manufacturer prices is the existence of ex-post rebates in certain health care systems. These rebates are generally paid to the public body/insurer administering the health budget, and effectively reduce the price of drugs in ways that are not captured in most comparison analysis.
- 4.14 As a result of contact with overseas experts (see also Annexe K) we found evidence that several countries apply ex-post rebates. Some countries impose rebates for different drug categories paid by public bodies, while others enter into price-volume agreements with manufacturers that are effectively ex-post rebates for the public payer. Those rebates lead to institutional buyers paying less than published list prices. In the UK, under the PPRS, companies may make cash payments in lieu of price reductions and/or if they earn excess profits, but the amount of such cash payments is negligible. During the years 2000 to 2004, cash payments in lieu of price reductions

were less than £10 million, or 0.4 per cent of sales value at ex-manufacturer prices (see Table 3.1 in Annexe J) and repayments of excess profits were less than 0.01 per cent of sales value (see Annexe H).¹³

- 4.15 We found that rebates are between two and seven per cent of total expenditure on drugs in Germany, three and a half per cent in Ireland, about three per cent in France and up to 30 per cent off list prices (and an estimated eight per cent off IMS data) for the United States. Other countries known to use rebate schemes are Austria and Australia. The existence of further arrangements in other countries cannot be discounted. Rebates in other countries where information is in the public domain and that have come to our attention thus vary between 3 to 16 per cent of retail price.

Box 4.1 Rebate systems

Germany

Ex-post rebates from manufacturers to the Social Insurance System are a common measure of the German government to contain costs. In 2004 there was a temporary increase in manufacturers' rebates from 6 to 16 per cent as a result of other changes in the health care system. The temporary change of policy led to an increase in wholesalers' rebates to €1.6 billion in 2004 – 7.3 per cent of total expenditure on pharmaceuticals in the public insurance system.

In 2005, a three tier rebate structure was introduced such that manufacturers' rebates amount to:

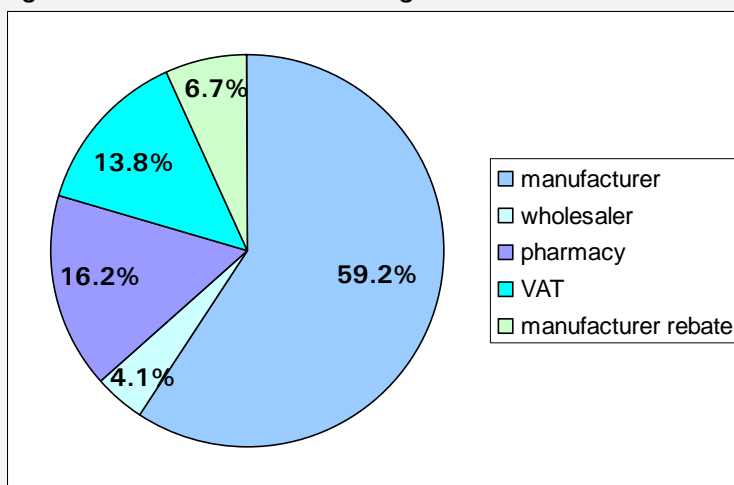
- six per cent of retail price for on-patent drugs that are not included into the reference price system
- six per cent of retail price for generic products not included into the reference price system
- ten per cent of retail price for all generic drugs and off-patent brands where a generic copy is available¹⁴.

After this policy change, rebates from wholesalers amounted to €545 million in 2005; 2.1 per cent of the total expenditure on drugs from public insurance (€25.4 billion in 2005) and on average 6.7 per cent of the retail price of any product sold in pharmacies (see below).

¹³ These figures cover companies making annual financial returns to DH (those with sales of more than £25 million per year). We have no information on UK cash payments by smaller companies.

¹⁴ Drugs exempted from rebates are on-patent drugs that underlie the reference price system. Generic drugs that are not included in a reference price group pay a (cumulative) rebate of 16 per cent. To find out more about the reference price system in Germany please refer to Annexe K.

Figure 11.1: Distribution of drug revenue in the value chain, Germany



Source: Arzneiverordnungs-Report 2006

Pharmacies' rebates in the same period amounted to circa €1.1 billion.¹⁵ In total, pharmacies' and wholesalers' rebates amounted to €1.6 billion in 2005 and are estimated to have increased to €2 billion in 2006 (circa £1.3 billion¹⁶).

Although wholesalers' rebates amount to between two and seven per cent of total expenditure on drugs (in 2004-2006), those rebates are generally not taken into account when German prices are benchmarked to other countries. As a result, international price comparisons may be biased and overestimate German price levels. For comparisons with UK prices, such as that of DH, the six per cent rebate for patented drugs that are not included in the reference price system may be especially important.

France

Ex-post annual rebates (based on price-volume agreements) are regulated by the French 'framework agreement' and are agreed during the initial listing process of a drug. The framework sets out manufacturers' obligations to give an aggregate rebate to the government if a class of drugs¹⁷ (as a whole) exceeds its agreed budget, average growth rates or volume thresholds. Rebates are distributed among the companies selling drugs in a specific class such that the individual rebates given by each company are based on the sales growth of a company's drug and overall sales volumes of the company in this class¹⁸. As well as standard price-volume agreements, the French government also negotiates special rebates for certain drugs where prescribing volumes in France are high, and/or for some of those products that are eligible for 'free' pricing. These rebates are often confidential. In 2004 total (known) rebates were made up of:

¹⁵ Pharmacy rebate: two euros per prescription-only drug dispensed (and 5 per cent for OTCs).

¹⁶ All currency exchanges from Euro to British Pounds were based on exchange rates from February 2007. The numbers only give an indication of values in pounds and were not period or purchasing power parity adjusted.

¹⁷ Classes of drugs are defined here as 'markets with sufficient (economic) substitutability between products where drug companies are in direct competition'.

¹⁸ 65 per cent of the aggregate rebates are shared according to sales within a product class and 35 per cent are shared among only those companies whose sales exceeded the agreed threshold agreed with government.

- €250 million from agreements on a specific products;
- €420 million of rebates by drug group from aggregate rebates.

Thus rebates (special and aggregate rebates) amounted to €670 million (circa £450 million); roughly three per cent of the French drug's bill at ex-manufacturer prices.

This shows that rebates are an intrinsic part of the French pricing system often not accounted for in international price comparisons. This is because rebates cannot be factored into price level data, as detailed volume data would need to be available as well as detailed data on the exact rebates by each company in a certain product/class. For the DH price comparison French rebates are very relevant as it may be likely that high volume drugs in France (and thus drugs that pay rebates) might be also drugs with high volumes (and thus heavy weights) in Britain. Thus, price comparisons with France can be distorted (if ex-post rebates are not taken into account) and results may overestimate the French price level.

Ireland

Ex-post annual rebates on pharmaceuticals are an intrinsic part of the agreement between the Irish pharmaceutical healthcare association ltd and the Irish health services executive since at least 1997.¹⁹ The agreement from 2006 states in Chapter 8 that '*each manufacturer/importer will rebate to the HSE an amount equal to 3.53% of the value (at price to wholesaler) of all medicines dispensed in the GMS²⁰ Scheme*'.

Thus, the Irish scheme sets out an obligatory rebate, agreed with manufacturers, that is payable on all patented drug volumes supplied to the government's medical services. As the drugs covered are likely to be similar to those covered by the PPRS system in the UK, the effect of this 3.5 per cent rebate is likely to be that Irish ex-manufacturer prices lie in effect, much closer (if not below) UK prices (compare Table 4.1).

United States

In international price comparisons the United States is consistently shown to have higher prices than all European (and most other) countries. It is difficult to identify rebates in the United States because the general system of pharmaceutical pricing and reimbursement system is highly disaggregated compared to that of the UK and other European systems, with a large number of players involved. Rebates are given from manufacturers to wholesalers, to pharmacies and to PBMs (Pharmaceutical Benefit Managers). Good estimates of these rebates are very hard to gather and rebates may differ significantly over the range of pharmaceutical

¹⁹ http://www.dohc.ie/publications/ipha_agreement.html

²⁰ HSE: The Irish Health Service Executive, GMS Scheme: General Medical Services

²¹ Panos Kanavos, Joan Cost-Font and Bengt Jönsson, '*Explaining Cross-County Drug Price Differences: What is the value of innovation*', forthcoming;

²² 'AWP is a published list price for a drug sold by wholesalers to retail pharmacies and nonretail providers. It is often used as a basis for payment to retail pharmacies' (CBO 2007).

²³ Please refer to the Annexe K for further information

²⁴ CBO, '*Prescription Drug Pricing in the Private Sector*', January 2007;

²⁵ The study was based on IMS Health data for the fourth quarter 2003 and a sample of 40 per cent of US sales prescription drugs in 2003.

²⁶ IMS is one of the biggest commercial suppliers of pharmaceutical price data and widely used as data source for international price comparisons.

²⁷ Patricia Danzon, Michael Furukava, '*Prices and availability of pharmaceuticals: Evidence from nine countries*', Health Affairs, 2004;

products.

A very recent and (unpublished) study by Panos Kanavos et al.²¹ investigates pharmaceutical rebates in the United States and comes to the conclusion that *'US public prices are comparable to and in many cases, lower than, prices in a number of European countries'*.

The study's results are based on Federal Supply Schedule (FSS) prices, as publicly available data contains mainly average wholesale prices²² (AWPs), that is 'list prices' that are subject to further negotiations and discounting. FSS prices are prices charged to the federal government and are obligatorily based on manufacturers' 'best deals'; that is, the lowest price that any private buyer receives.²³ As the extent of rebates on publicly available AWP is unknown and subject to confidential agreements, this technique is the best available estimate of rebates received by market players from manufacturers.

The results of the study show that there is a large discrepancy in the United States between list prices and the prices that are actually reimbursed by health insurance organisations. Rebates seem to vary with drug classes and seem to be highest for Statins, PPIs, ACE inhibitors and Opioids. In those classes rebates seem to range between 32 per cent and 47 per cent. In other drug classes such as Alzheimer drugs and anti-depressants, rebates range between 13 and 23 per cent (of list price). Across all therapeutic categories the study finds an average discount of 32 per cent, reaching 39 per cent if weighted by volumes.

The study also shows that reimbursement prices in the USA (public prices) may be in the same range as Germany and the UK. A price index comparison using FSS prices even finds that prices in the USA are lower than in Germany and just higher than that of the UK.

Another study of the USA congressional budget office (CBO)²⁴ on prescription drug pricing in the private sector finds that prices for single-source branded drugs for conventional retail pharmacies amount to circa 83 per cent of AWP and no more than 78 per cent for mail-order pharmacies²⁵. This study uses IMS prices and states that IMS prices²⁶ for mail-order pharmacies and non retail providers (hospitals, nursing homes etc) may not reflect all discounts as mail-order pharmacies may *'receive further rebates from manufacturers on the basis of their ability to affect a drug's market share'*. Mail-order pharmacies constitute 21 per cent of supplies through retail pharmacies to consumers.

Finally, a study of Danzon and Furukawa (2004)²⁷ states that *'IMS data for the United States do not reflect off-invoice manufacturer discounts given to managed care and government buyers'*. The authors thus use an estimate for off-invoice discounts of on average eight per cent to adjust prices (discounts differ across buyers and a product's buyer mix).

The conclusion for international price comparisons, including that of DH, is therefore that rebates and discounts not accounted for in publicly (and privately) available data may bias the results of any comparisons with US prices (and other countries' prices) significantly.

- 4.16 Where such rebate arrangements as described in Box 5.1 are known they can be taken into account when interpreting price comparison results. Yet, we are concerned that some arrangements between governments and drug companies might be subject to commercial confidentiality and therefore relevant information on the arrangements might not be in the public domain.
- 4.17 Several governments may for example have no interest in providing detailed information about the value of rebates given that their stance in negotiations with manufacturers

may depend on the secrecy of those arrangements. This is because due to international reference pricing, parallel trade and ongoing negotiations in other neighbouring countries, companies have an interest / preference in preserving high public list prices and paying 'hidden' ex-post rebates. This is the case in France and the United States.

- 4.18 Establishing a reliable and comprehensive understanding of such rebates is a resource-intensive undertaking. Even when known, information on rebates may be difficult to incorporate into comparisons based on raw data, as rebates may not be applicable to specific drugs, but could operate at company level or in other ways. Alternatively, if rebate data is known on an aggregate level, detailed volume data would be needed to calculate drug level rebates.
- 4.19 However, it is of considerable importance that some of the most well known price comparisons do not take into account rebates when calculating prices at ex-manufacturer level. Failure to do so will result in overestimates of the effective prices paid by public bodies for drugs. Most of the data would thus need to be re-adjusted to account for rebates in certain countries.
- 4.20 In its reports to parliament on the PPRS, DH registers the considerable importance of rebates and specifically emphasises that the price relativities do not take account of refunds paid by manufacturers in Germany as part of cost containment policies.
- 4.21 However, the DH report does not provide any comprehensive examination of such discounts. In view of the potential to arrive at an incorrect interpretation of results in cases where such discounts and rebates exist but are not taken into consideration, wider research into this topic is warranted. We think future comparisons should attempt to take greater account of the effect of such rebates.

Issues that affect price comparison calculations

- 4.22 As discussed above in Chapter 3, we think the approach used by DH to calculate international price comparisons is a pragmatic and sensible one.
- 4.23 Nevertheless, operationally, the approach remains something of a 'black box', not providing any clear insights into why the overall results emerge as they do. Such large scale analyses are often quite opaque. The publicly available sets of data on prices that we obtained were mostly very large, one containing 28,000 lines of data, another 11,000 and even the smallest more than 4,000. Our advice from DH is that the commercial dataset on which their own calculations are based is similarly large, at some 15,000 data entries.
- 4.24 The processes of matching and comparing prices must necessarily be computer automated and the size of the task does not allow scope for much direct human understanding of how the final results are influenced by the data.
- 4.25 We therefore took the opportunity to look in greater detail at one or two specific groups of drugs to better understand how the processes work in practice. The data

were almost exactly contemporaneous, and all related to either the late summer or early autumn period of 2006. Foreign currencies were converted to pound sterling using exchange rates relevant at the time.

- 4.26 Before looking at the issues individually it is worth reiterating why we are concerned about the detailed processes used to compute the price comparisons. This has its roots in the observation that the calculation process is mechanical rather than statistical. This is a result of the available data and is unavoidable, but as a consequence, the process does not rely on random sample data. The results therefore may contain some bias.

Sensitivity to weightings

- 4.27 Our first illustrative example concerns the sensitivity of results to weightings. The theoretical difficulties that arise because different countries purchase different baskets of drugs were explained in Chapter 2, where it was pointed out that the question **'if the basket of products currently purchased in the UK were purchased in another country what would we expect to pay for that basket of goods?'** and **'if the basket of products currently purchased in another country were purchased in the UK what would that basket of goods cost?'** are distinctly different questions. There are a priori reasons for believing that prices in a particular country will appear less expensive if its own volume weights are used (as opposed to the volume weights of the other country).
- 4.28 Our ability to research the extent to which results to these complementary questions differ was severely limited by the lack of available volume data. Even where we had price data, complementary information on the baskets of goods being purchased in other countries was difficult to find.
- 4.29 Consequently, our illustration is limited to an example using German drug prices, since some information on drug purchases in Germany was found in a report entitled *Arzneiverordnungs - Report 2006*. The case we have chosen, presented in detail in Box 4.2, provides an excellent illustration of the degree to which the two different questions can generate dissimilar results about drug prices in other countries.
- 4.30 We examined the prices of lipid lowering drugs (statins) and concluded that the UK basket of statins if purchased in Germany would cost one per cent less than the price in the UK. In contrast if the German basket of statins was purchased in the UK it would cost 26 per cent more than in Germany.
- 4.31 Working with this degree of detail we observed that these results arise due to a particular set of circumstances, namely some differences in availability, and major differences in the level of use of some drugs.
- 4.32 The results provide an important reminder that vague and unqualified statements about drug prices may be misleading. General statements such as **'UK drug prices are higher than the prices enjoyed by our European neighbours'** need qualification if they are to be properly interpreted. It is only correct to draw conclusions in relation to the basket of goods currently being used in the UK.

Box. 4.2: Weighting

The tables below show a very limited set of data in relation to lipid lowering drugs (statins) concerning price information for the UK and Germany. This would constitute one small part of the price comparison between the two countries, and, in practice, the process would be replicated across a much larger group of countries.

Nevertheless the data illustrates well how an ideal approach can not always be achieved in practice and how substantial compromises have to be made in order to produce results.

At a detailed level, it should be noted that there is one drug (Rosuvastatin) available for the UK market that does not appear in the German price or volume data, and additionally there is one drug (Lovastatin) available for the German market that does not appear in the UK price or volume data. The comparisons are immediately constrained by this asymmetry.

Table 4.1: Lipid lowering drugs (statins): availability in UK versus Germany

| In patent drugs | UK | Germany |
|-------------------------|-----------|----------------|
| Atorvastatin | Yes | Yes |
| Fluvastatin | Yes | Yes |
| Rosuvastatin | Yes | No |
| Off patent drugs | UK | Germany |
| Lovastatin | No | Yes |
| Pravastatin | Yes | Yes |
| Simvastatin | Yes | Yes |

It is also necessary to equate pack sizes of 28 in the UK with 30 in Germany. This does not appear to be an unreasonable compromise, but it is strictly not in accordance with the more desirable exact like for like matching.

The comparisons necessarily have to omit the German price data for larger pack sizes, further constraining the applicability of the results. However, in accordance with previous arguments, this reduction in applicability is preferable to utilising the larger pack size data which does show in cases some slight discount in the per tablet price.

In some cases, these equate to two or three per cent reductions, and depending on the weightings applied in any calculation could easily trigger a one or two per cent shift in the overall comparisons.

Once all these factors have been taken into consideration, the data on which actual comparisons can be based is a fairly restricted subset of the data as a whole.

We also observe other interesting features about the price of some drugs. Generally, prices increase with dose, but the price increases are not in direct proportion to the dosage increases. At lower doses a doubling of the active ingredient usually results in an increased price though certainly not a doubling. At higher dosage levels, however, a doubling of the active ingredient sometimes has no effect on the price at all.

Table 4.2 : Drug prices per tablet at ex-manufacturer level in GBP

| Drug | Dosage | UK | Germany | Germany | Germany | Germany |
|---------------------|---------------|------------------|------------------|------------------|------------------|------------------|
| | | Pack size | Pack size | Pack size | Pack size | Pack size |
| | | 28 | 30 | 50 | 90 | 100 |
| Atorvastatin | 10 | 0.57 | 0.50 | 0.48 | 0.50 | - |

| | | | | | | |
|---------------------|----|------|------|------|------|------|
| | 40 | 0.88 | 0.95 | 0.92 | 0.92 | - |
| | 80 | 0.88 | 0.95 | 0.92 | 0.93 | - |
| Fluvastatin | 20 | 0.44 | 0.14 | 0.15 | - | 0.15 |
| | 40 | 0.44 | 0.22 | 0.23 | - | 0.23 |
| | 80 | 0.55 | 0.34 | 0.34 | - | 0.35 |
| Rosuvastatin | 10 | 0.56 | - | - | - | - |
| | 20 | 0.93 | - | - | - | - |
| | 40 | 0.93 | - | - | - | - |

Moreover, for pack sizes 28/30, comparing the two countries at different doses, we observe that in the case of atorvastatin at low dosages, UK prices are higher than Germany, but at intermediate and high dosages, UK prices are lower than German prices.

In this situation, the correct course of action that can combine these data to be properly reflective of comparative prices is a weighted average dealing with each dosage level separately.

This adds an important extra dimension to the comparisons. In order to obtain valid comparisons, it is necessary to have accompanying weighting data available at a level of detail matching the dosage, pack size and presentational form. In the event, data from DH prescription cost analyses are available at different dosages to undertake such weighting. Tables of suitable weights derived from DH prescription cost analyses are shown below.

Table 4.3: Weightings based on DH prescription cost analyses

| | Dosage (mg) | UK Net ingredient £ million 2005 | Germany Turnover € million |
|-------------------------------|-------------|--|----------------------------------|
| Atorvastatin | 10 | 164.1 | |
| | 20 | 136.3 | |
| | 40 | 80.0 | |
| | 80 | 16.3 | |
| All | | 396.8 | 54.3 |
| Fluvastatin | 20 | 2.8 | |
| | 40 | 4.3 | |
| | 80 | 2.2 | |
| All | | 9.3 | 93.8 |
| Rosuvastatin | 10 | 25.3 | |
| | 20 | 7.4 | |
| | 40 | 1.4 | |
| All | | 34.2 | 0 |
| Lovastatin | | 0.0 | 11.3 |
| Pravastatin | | 29.5 | 70.3 |
| Simvastatin | | 108.5 | 375.6 |
| | | 578.3 | 605.3 |
| Using UK weights | | | |
| Overall relative price | | 100.0 | 99.3 |
| Using German weights | | | |
| Overall relative price | | 100.0 | 79.3 |

Finally we compute a weighted price comparison based on these data indicating that if the UK basket of drugs was purchased at German prices it would be approaching one per cent cheaper than in the UK.

In this very restricted case, the accompanying raw data on prices and weights make it possible to understand how this result arises. Generally there are cases where UK prices for atorvastatin, depending on dosage, are both higher and lower than their exact counterparts in Germany. For atorvastatin the UK drug price is dearer at one dose level and cheaper at three, but the single case where it is dearer carries a substantial weighting, producing nearly a very rough balance overall for this drug. For fluvastatin where UK prices are a lot higher than German data, the data carry very low weights as this drug is not much prescribed in the UK, so although the difference is large it has no strong influence on the overall results.

The result depends critically on the availability of the weighting data, and is quite sensitive to changes in the weights. Weighted, atorvastatin would be assessed as costing 99 per cent of the UK price when purchased in Germany, whereas unweighted and in the absence of weights based on a simple average of the four dosage levels, atorvastatin would be assessed as costing 103 per cent of the UK price when purchased in Germany.

Finally, we observe that from the German perspective the same data provide a very different set of final results. There are two very important factors to note. Firstly our best searches were unable to establish German data that would allow separate weights for different dosage levels. For the purpose of the analysis below we made use of the Arzneiverordnungs Report 2006 by U Schwabe, and D Paffrath which presents some statistics on drug usage levels in Germany, though not to the same degree of detail available from DH prescribing data.

Any analysis based on German weights of this type will necessarily fall short of the preferred approach. Moreover, even if such weights were available, the outcome from a German perspective would look very different. This is because fluvastatin would carry a much heavier weight, approximately double that carried by atorvastatin prices. For a UK centred analysis, fluvastatin carries only about two per cent of the overall weight and has a correspondingly muted impact on the results.

While accepting that we cannot use our preferred method of weighting for the German analysis, we can fall back on weightings that apply for each drug rather than each drug/dosage combination. The result of this analysis would be that if the German basket of drugs was purchased at UK prices it would be approaching 26 per cent more expensive than in Germany.

Pack size variation and discounts

- 4.33 One specific feature for which differences in drug availability between countries can be observed is pack sizes. From the data we gathered it was possible to see that some countries, for example UK and Australia, provided reimbursable drugs in generally smaller and less variable pack sizes than others.
- 4.34 Complimentary to this there was also evidence that, in some countries, average prices per tablet for larger pack sizes carried varying degrees of discount. This is exactly the issue discussed above from 2.37 onwards.
- 4.35 As a result, when comparing UK prices with those of other countries on the basis of exact matches, the comparison is constrained to only the smaller pack sizes generally

available in the UK. The results have no wider applicability. A further detailed discussion can be found in Attachment 3.

Inconsistent price differences between presentations and dose levels

- 4.36 In making comparison calculations, it would clearly be advantageous if price differences between countries for particular drugs were consistent across different presentations and dose levels.
- 4.37 In these circumstances, the same relative prices would be observed regardless of which presentational and dose level matches were found in the data. The observed data would always be representative of this uniform difference and results would not be sensitive to the matches that occurred.
- 4.38 So an examination of price differences across presentations and dosages will help determine if such consistent differences are either present and therefore reinforce confidence that results are representative, or absent and therefore sensitive to chance matches.
- 4.39 In the event, even within a sample dataset of modest size we observed very little consistency in price differences, and regular examples of highly inconsistent differences.
- 4.40 Various examples of this type are presented in greater detail in Attachment 4. Overall, we view these observations with caution. The picture that emerges is one where the matches that arise, far from being consistently representative of a uniform picture, are drawn from data where price difference between countries for the same drug can vary considerably according to dose and presentation.

Conclusion

- 4.41 The evidence we have accumulated suggests that at a technical level the process of measuring price differences has inherent weaknesses. As a result of exchange rate movements and the existence of known and unknown rebates, final interpretation of the results may be complicated further. Taken together this raises concerns about the robustness of the results.

5 INTERNATIONAL PRICE COMPARISONS FROM DIFFERENT COUNTRIES

- 5.1 In the following section, we look at international price comparison studies conducted by governments or industry bodies in different countries. We have identified recent studies undertaken in Spain, Sweden, Finland, Norway, Mexico, Canada and the Netherlands. The studies vary in approach, in the products covered and were undertaken in different years. They therefore illustrate the variety of choices available in undertaking international price comparisons and demonstrate the divergent results they can generate.
- 5.2 The table below summarises the different approaches that have been taken in the studies. The table is accompanied by a short explanatory text that provides additional detailed information on each study.

Table 5.1: Summary of international price comparison studies undertaken by other governments and industry bodies

| | Source of data | Selection of drugs used | Number of matches | Price used for comparison | Level used for comparison | Weights |
|----------------|--|---|---------------------|--|---|--|
| Norway | Company survey (11 companies) | 300 highest revenue drugs/ packages in Norway in 2005 | 104 -267 | Pharmacy purchasing prices | Price per package | Own country weights |
| Canada | IMS data | All drugs on the Canadian market with more than 1 Million of sales in 2005 | 204- 336 | Pharmacy purchasing prices | Price per unit (tablet, capsule or millilitre of same strength) | Own country weights |
| Sweden | Company survey (45 companies) | 180 most selling drugs in the Swedish market in first half of 2004 | 73-147 | Pharmacy purchasing prices (sometimes estimated) | Price per unit (tablet, capsule or millilitre of same strength) | Own country weights |
| Sweden | Company survey (45 companies) | Newly approved medicines between October 2002 and November 2005 | (55 ²⁸) | Pharmacy purchasing prices | Price per unit (tablet capsule or millilitre of same strength) | Own country weights |
| Spain | IMS data | Newly launched innovative drugs between 2002-2004 | 35-56 | Ex-manufacturer price at launch | Price per unit (tablet, capsule or millilitre of same strength) | Own country weights |
| Finland | Survey data from 9 governmental health institutions | 8 drugs in 17 presentations that received marketing authorisation in 2000 | 7-13 | Retail price without VAT and dispensing fee | Price per package per strength | No weights – average of product by product indexes |
| Mexico | Information on drug prices (sold in different countries) reported by manufacturers in Mexico ²⁹ | Basket of molecules (based on active ingredients) from 317 presentations of branded drugs (2004-2005) | 17-23 | Producer prices/ ex-manufacturer price; estimated for Mexico | Price per mg ³⁰ of equal molecule | US weights (the US was used as reference country) |

²⁸ 'When the answers [from manufacturers] for products marketed in three countries or less [apart from Sweden] had been excluded 55 observations remained'.

²⁹ Drug companies in Mexico are under the new price regulatory scheme supposed to report this information.

³⁰ Methodology based on Danzon and Furukawa (2003).

Spain

- 5.3 'Indice de precios de productos nuevos 2002-2004 (Bilateral Espana vs cada pais individualmente)', Source: Farmaindustria based on IMS data. This study is a bilateral price comparison of 35-56 new products commercialised between January 2002 and October 2004 in Spain. In total 63 products were analysed. Data was taken from IMS and reflects ex-manufacturer prices at launch (called PVL). Each bilateral comparison comprised between 35 - 56 products. Prices were compared on the basis of unit prices (in euros) of products of identical composition and form. Volume weights based on Spanish volumes were used.

Netherlands

- 5.4 The study is based on a 'European price indices 2004/ Q3'. It was commissioned by the Dutch Ministry of Health, Wellbeing and Sport and undertaken by the 'Stichting Farmaceutische Kengetallen'. No further explanation on the price comparison was provided by the Ministry but information may be found under www.sfk.nl.

Canada

- 5.5 The PMPRB undertook an extensive study in generic and non-patented drug prices called 'Non patented prescription drug prices reporting – Canadian and Foreign Price Trends, June 2006'. The data shown here is taken from Table 3.1e, 'Average foreign to Canadian Price ration at market exchange rates, patented drugs, by bilateral comparator, 2005'. IMS data was used as the source of the price comparison. The study looked at 204 - 336 pharmacy buying prices of patented drugs, accounting for between 4,534 - 6,357 million dollars of sales and representing 94 per cent of total sales to pharmacies in 2005. Only drugs with at least CAN \$1 million of sales in 2005 were covered. Prices in foreign countries were compared to prices in Canada using annual average (spot-market) foreign to Canadian exchange rates. Volume weights were based on Canadian sales data from 2005

Norway

- 5.6 Study of the price level in September 2005 called 'Prisnivaet pa legemidler I Norge I forhold til andre land I Europa' sponsored by Legemiddelindustriforeningen.³¹ The analysis is based on the 300 highest revenue drugs/packages in Norway, representing 42.4 per cent of total turnover in Norway. Drugs from 11 companies were included in the study. For each country between 104 (Portugal) and 267 (Sweden) drugs were used for the comparison. Indices are based on the pharmacy buying prices (excluding VAT and other public taxes) per package (per strength – as we understand this)). For those countries where pharmacy buying prices were not available, wholesale prices were used and average wholesale margins (based on EFPIA data) were deducted. For matching products a ten per cent difference in package size was tolerated (we

³¹ http://www.lmi.no/Prisrapport%202006_h9tQk.pdf.file

understand this means that matches between 28 and 30 tablets per packages were seen as equivalent). Packages were chosen based on Norwegian usage. Six monthly average exchange rates were used to compare foreign prices with Norwegian Kroner (average taken based on March 2005 – August 2005 exchange rates).

Finland

- 5.7 'European price of newly launched reimbursable pharmaceuticals – a pilot study' taken from Jaana Martikainen and Ismo Kivi, Ismo Linnosmaa, *Health Policy*, 74 (2005), 235-246. The study is based on the retail price excluding VAT of eight newly launched products for which marketing authorisation had been granted by the EC during the year 2000. A questionnaire was used including the eight products with a total of 43 different strengths and package sizes. The index we are presenting is the mean index of all the individual indexes calculated on each of the 17 presentations of the eight different products.

Sweden

- 5.8 The sample was based on sales statistics for the first six months of 2004 from Apoteket AB. The 180 most selling products in Sweden were selected, which together represent about 80 per cent of total sales on the Swedish market. International price data was requested from 45 companies. The prices used in this study are those paid by the pharmacy to the wholesaler. The number of products reported per country was on average 114 and varied between 73 and 147. Only products which sell in at least four countries were included in the analysis. This was the case for 143 pharmaceuticals. In the comparison, the price per tablet, capsule or millilitre was used adjusted with the average exchange rate for 2004. The data is not weighted based on sales volume in the respective countries but, as we understand, weighted according to Swedish data.

Sweden II

- 5.9 The products studied in this report were all new pharmaceuticals (original substances not generics) which the LFN has approved for reimbursement between October 2002 and November 2005. Products marketed in three countries or less had been excluded; 55 observations remained.

Mexico

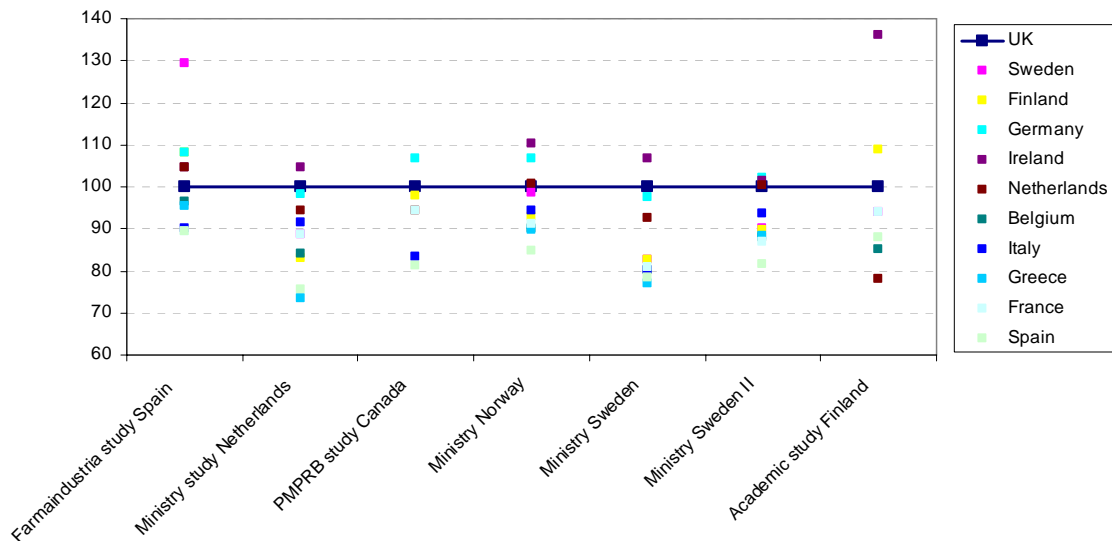
- 5.10 The study of the Mexican Ministry of Health is based on a methodology used by Danzon and Furukava (2003) and the Department of Commerce, International Trade Administration (2004). Information on patented products prices at ex-factory level in Mexico and abroad was reported by the manufacturers in Mexico under the new price regulatory scheme. Based on 317 presentations of 81 substances, 37 molecules (active ingredient also considering compound formulations) were selected and six baskets of different combinations of countries and molecules compared. Each basket included between 17 and 23 molecules. As quantities sold in Mexico were unavailable, the

United States were taken as a reference country (using US volumes). Countries compared were Mexico, Japan, US, Germany, Spain, France, Italy, Canada and the UK. Quantity weights from Spain and Canada and reduced baskets to include countries such as Greece, Brazil, the Philippines, Saudi Arabia and Venezuela were used to test the sensitivity of the analysis.

Comparison

- 5.11 Below, a graph outlines the different results of the above mentioned studies.³² All results have been based such as the UK equals 100. The results are shown along the x-axis (so the graph has to be read vertically).
- 5.12 If all studies agreed about the relative price level of different countries compared with the UK, all coloured points would have been horizontally aligned. This is certainly theoretical as all the studies have looked at different products, but it can be taken as a reference.
- 5.13 We can see from the graph that most studies seem consistently to find certain countries to be higher priced than the UK; this is for example the case for Ireland. All studies also see Spain, Greece and France at the lower end of the spectrum. However, looking closer at the relativities there is a wide range of differences. (the raw data of Figure 5.1 is presented in Table 5.2)

Figure 5.1: Comparison of international pharmaceutical price comparison studies



³² The results of the Mexican study are not in the public domain yet and can thus not be presented here.

Table 5.2: Comparison of international pharmaceutical price comparison studies

| | (1) | (2) | (3) | (4) | (5) | (6) | (7) | (8) | (9) |
|--------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| UK | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Sweden | 129 | 89 | | 99 | 83 | 90 | 94 | | |
| Finland | 108 | 83 | 98 | 93 | 83 | 90 | 109 | 96 | 101 |
| Germany | 108 | 98 | 107 | 107 | 98 | 102 | | 106 | 108 |
| Ireland | 104 | 105 | | 110 | 107 | 101 | 136 | 99 | 103 |
| Netherlands | 104 | 94 | 94 | 101 | 93 | 100 | 78 | 92 | 95 |
| Belgium | 96 | 84 | | 90 | 80 | 88 | 85 | 90 | 95 |
| Italy | 90 | 92 | 83 | 94 | 80 | 94 | | 78 | 84 |
| Greece | 96 | 74 | | 90 | 77 | 88 | | | |
| France | 89 | 89 | 94 | 91 | 81 | 87 | 94 | 84 | 96 |
| Spain | 89 | 75 | 81 | 85 | 79 | 82 | 88 | 84 | 80 |

(1) Farmaindustria study: Spain 2002 to 2004: New products

(2) Ministry study: Netherlands 2004

(3) PMPRB study: Canada 2005

(4) Ministry Norway: Sep 2005

(5) Ministry Sweden: 2004

(6) Ministry Sweden II: New pharmaceuticals Oct '02 to Nov '05

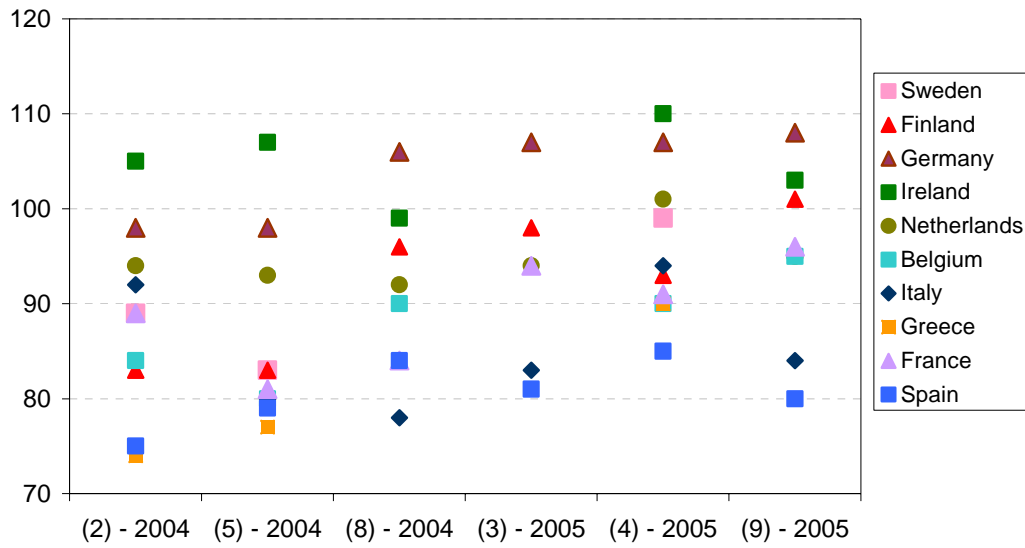
(7) Academic study Finland: Newly authorized pharmaceuticals 2000

(8) UK DH 2004

(9) UK DH 2005

5.14 Some of the above studies concerned newly launched or newly authorised pharmaceuticals and are therefore not directly comparable to the DH results. In Figure 5.2 below, we exclude some studies and consider only those that look at a wider range of pharmaceuticals - that is (2), (3), (4) and (5) in the notes above. We then look at the consistency between these studies and the 2004 and 2005 DH results taken from Table 5.2. To improve clarity, UK prices have been fixed at 100, but are not shown using any symbol.

Figure 5.2: Comparative drug prices: Various studies 2004 and 2005: UK = 100



- 5.15 Allowing for changes between 2004 and 2005 perfect consistency would produce a graph in which results for any country in any year remained parallel to the x-axis. This is certainly not the case, although the charts do exhibit some general consistency for some countries.
- 5.16 For example, a degree of consistent behaviour can be observed for Spain with indices considerably below 100 and often close to an index of 80, for Germany with several results in the range from 105 to 110, and for the Netherlands in 2004, in the low 90s. Despite this there are also examples of substantial movements, and the range between the highest and lowest index results for many countries is typically around 15 index points, and even at the lowest as much as 10 index points (at the highest 46 index points).

6 CONCLUSIONS

- 6.1 In broad terms, we believe the DH methodology for comparing prices is a sensible and pragmatic one. It focuses on ex-manufacturer prices – clearly most relevant for considering the PPRS – and generally avoids reliance on more speculative and hence potentially contentious methodologies. For example, it relies on historical exchange rates rather than projected equilibrium exchange rates and only on exact presentation matches rather than on some weighted average per molecule. This can be at the expense of generalisability, so, as always, care should be taken not to draw broader conclusions than the results warrant.
- 6.2 The results produced by DH for 2005 indicate the UK prices have historically been higher than those in the rest of Europe but that after the 1 January 2005 price reductions, prices fell, to rank fourth out of ten in comparisons with other European countries. These results, however, do not take into consideration discounts and other related schemes that involve repayments between manufacturers and governments. Taking rebates into consideration suggests that UK prices are understated with respect to other countries where these schemes exist. We have examples where the degree of understatement is known, but discount arrangements in some countries may not always be public knowledge.
- 6.3 The comparison analysis involves large volumes of data so it is difficult to gain any detailed appreciation of what contributes to the overall result. Our examination of limited amounts of detailed data convinces us that the difficulties are numerous. Data sources do not always provide prices at ex-manufacturer level and where they do not, reliable ways of working back from prices at different points in the supply chain sometimes exist but in some cases may not always be easy to determine.
- 6.4 Even for single drugs, we observed there are difficult issues relating to pricing of different pack sizes, dosages, and presentations that would make comparisons sensitive in an unpredictable way to the matches that occur and to the weightings used to combine the results. To briefly review the situation, we have found fundamental complexities in each of the four separate areas listed below:
- establishing reliable ex-manufacturer prices
 - technical complexities with the comparison calculations
 - rebates that are known and unknown
 - choice of suitable exchange rates
- 6.5 Without more comprehensive data there is no way of knowing with any degree of exactness the extent to which these various effects might combine to produce distortions.
- 6.6 Taken together these complications weaken our confidence in the price comparison analysis method. They certainly convince us that the DH results need to be strictly interpreted, and it should always be born in mind that the results relate to very specific

circumstances. The analysis provides an answer to the question 'if the basket of products currently purchased in the UK were purchased in another country what would we expect to pay for that basket of goods?' but the evidence suggests that when viewed from the perspective of other countries, results could look considerably different.

- 6.7 A review of various comparison exercises undertaken by other government and research organisations seems to confirm that results can be strongly influenced by the factors mentioned above.
- 6.8 We conclude that price comparison analysis results should be viewed with a degree of circumspection. Despite the obvious political interest in price comparisons, the best available estimates may not be sufficiently robust to be afforded the highest weight as a policy driver. Methodological concerns are particularly relevant for countries that use the results of price comparisons to set the domestic price of pharmaceuticals, through international reference pricing mechanisms
- 6.9 We therefore suggest that price comparisons should only be used as one factor among many others to inform government policies towards the pharmaceutical sector, and that the limits of these studies should be clearly recognised. The studies can give answers to a very narrow set of questions but cannot alone give answers to questions such as, 'does the UK pay the right price?' or 'are UK prices too high?'. Nor are we convinced that changes in overall levels of expenditure provide any useful way of addressing internal efficiencies within the PPRS.

7 ATTACHMENT 1: SUBGROUP COMPARISONS

7.1 This attachment presents the results of two sets of analyses that have been conducted using subgroups of drugs. The first, conducted by DH, disaggregates products into common therapeutic groups. The second, conducted by ABPI, looks at recently launched products.

DH comparisons for common therapeutic groups

7.2 In addition to the overall results presented in Chapter 3, DH has undertaken some further analyses in relation to 2005 data, and has provided these directly to OFT. In these analyses, drugs were considered in a number of common therapeutic groups, and the same comparison analysis was undertaken separately for each of the groups.

7.3 Given the available data there were occasions where the comparisons only identified limited numbers of drugs, and where the size of the basket involved was also limited. In these instances, the comparisons might be potentially unreliable and are not presented here. The final groups for which these additional analyses were completed are shown in Table 7.1 below, showing in each case the price relative to the UK's index of 100.

Table 7.1: Bilateral comparisons of ex-manufacturer prices: results for 2005 divided into selected therapeutic groups

| | France | Germany | Italy | Netherlands | Spain | Austria | Belgium | Finland | Ireland |
|-----------------------------------|--------|---------|-------|-------------|-------|---------|---------|---------|---------|
| Overall | 96 | 108 | 84 | 95 | 84 | 96 | 95 | 101 | 103 |
| Proton pump inhibitors | 100 | 121 | 91 | 106 | 97 | 101 | 116 | 102 | 115 |
| Non-steroidal anti- | 85 | 109 | 74 | 91 | 86 | 85 | 92 | 82 | 96 |
| Statins | 90 | 97 | 79 | 95 | 87 | 98 | 108 | 107 | 112 |
| Angiotensin-ii receptor | 106 | 98 | 79 | 87 | 84 | 93 | 94 | 101 | 98 |
| Calcium-channel blockers | 101 | 88 | 91 | 87 | 116 | 46 | 94 | 122 | 111 |
| Antiplatelet drugs | 101 | 120 | 88 | 100 | 83 | 101 | 97 | 106 | 101 |
| Selective beta2 agonists | 68 | 75 | 68 | 69 | 74 | 78 | 65 | 89 | 90 |
| SSRIs | 77 | 116 | 66 | 97 | 87 | 83 | 93 | 68 | 132 |
| Other antidepressant drugs | 61 | 125 | 73 | 73 | 78 | 95 | 84 | 88 | 98 |
| All other | 96 | 110 | 89 | 99 | 83 | 96 | 91 | 102 | 99 |

7.4 This presentation does not make it entirely obvious what patterns can be found in the results. However, a variety of accompanying charts are presented below that suggest that two groups have prices that are systematically higher in Europe, three systematically lower, and four have a pattern that is mixed with some European countries being relatively more expensive and some less.

7.5 Each chart is drawn so that the overall prices relative to the UK are shown in the grouping to the left hand side, and relative prices for the group are shown on the right hand side. Where drugs are systematically cheaper or dearer in other European countries the points on the left hand side will tend to be higher or lower respectively than the overall results. All charts relate to 2005 and are bilateral comparisons.

Figure 7.1: Bilateral comparisons of ex-manufacturer prices 2005: proton pump inhibitors

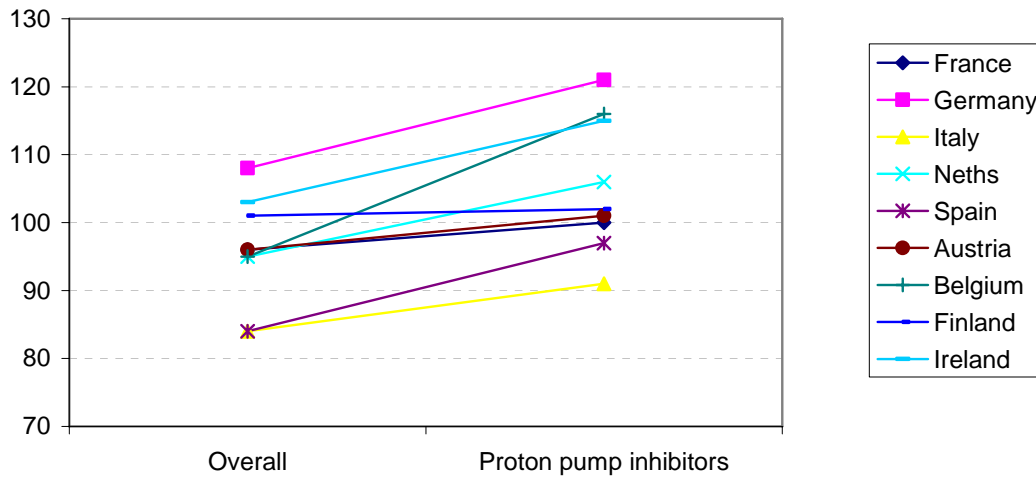
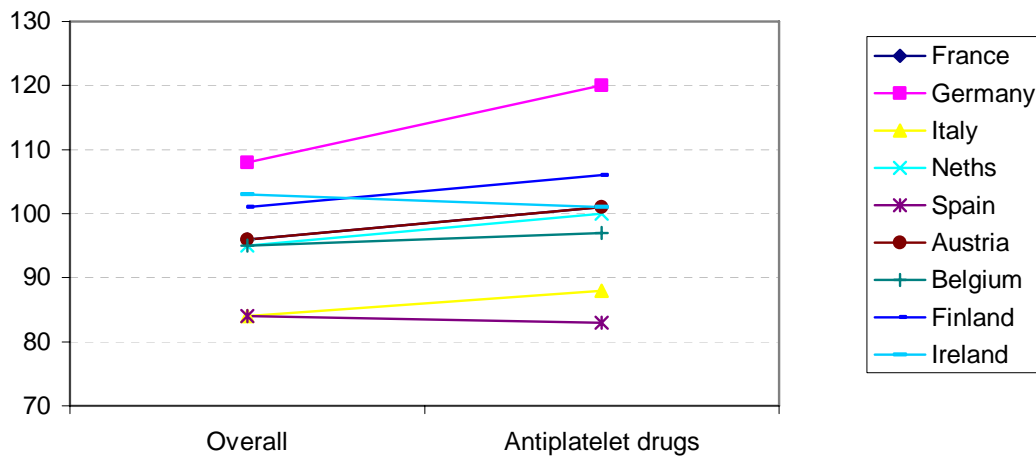


Figure 7.2: Bilateral comparisons of ex-manufacturer prices 2005: anti-platelet drugs



- 7.6 For the two groups of drugs shown above in Figures 7.1 and 7.2, that is proton pump inhibitors and anti-platelet drugs, it seems clear that relative prices in 2005 were generally higher among European neighbours than in the UK.
- 7.7 The groups of drugs shown below in Figures 7.3 to 7.5 are, with a high degree of consistency, relatively cheaper in Europe than their comparative overall result. There is clear and strong consistency in Figure 7.3, though minor degrees of inconsistency occur in the other charts.

Figure 7.3: Bilateral comparisons of ex-manufacturer prices 2005: selective beta2 agonists

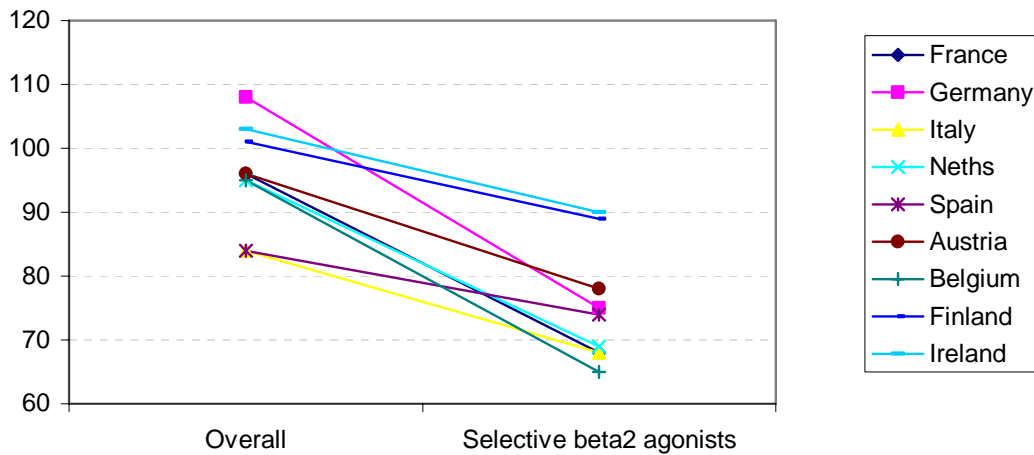


Figure 7.4: Bilateral comparisons of ex-manufacturer prices 2005: non steroidal anti-inflammatory drugs

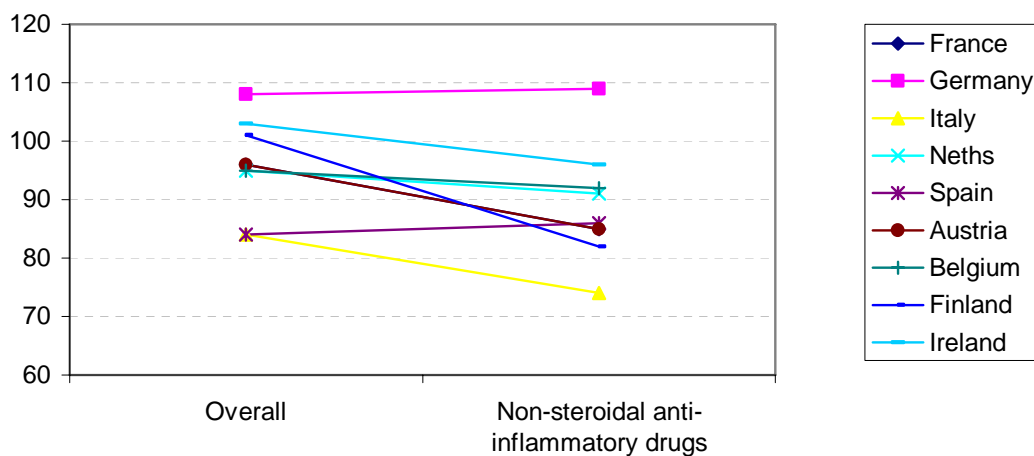
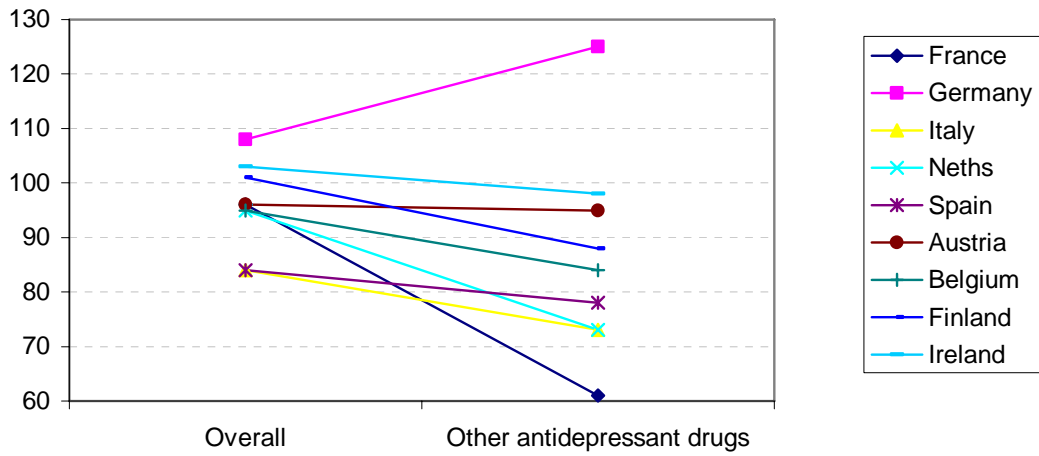
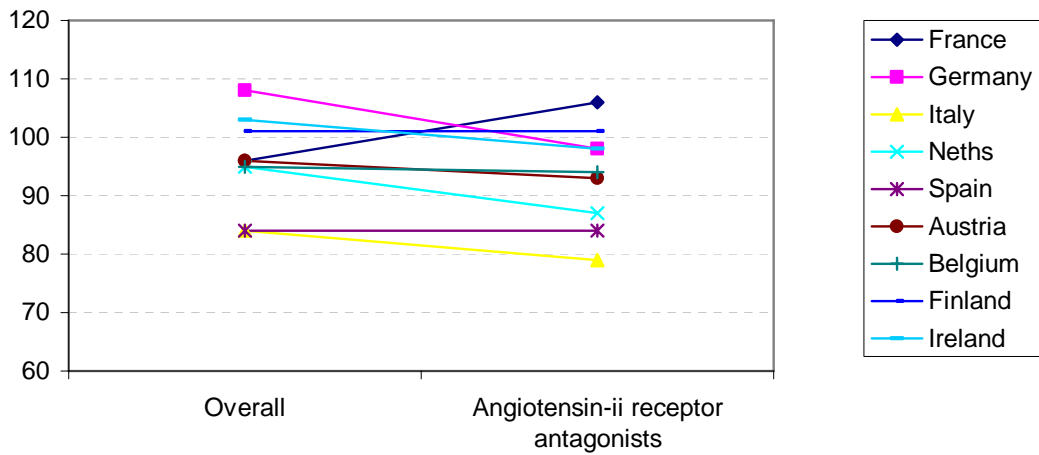


Figure 7.5: Bilateral comparisons of ex-manufacturer prices 2005: other anti-depressant drugs



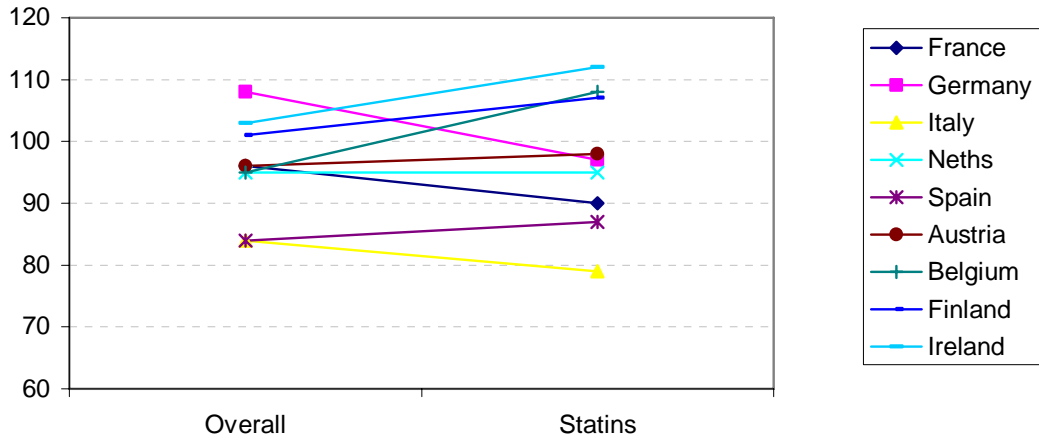
7.8 The results shown in Figure 7.6, for angiotensin II receptor antagonists, show a broadly similar pattern of being cheaper in Europe with some increase in the number of exceptions.

Figure 7.6: Bilateral comparisons of ex-manufacturer prices 2005: angiotensin II receptor antagonists:



7.9 Finally the three remaining charts, Figures 7.7 to 7.9, demonstrate patterns that are mixed with a selection of European countries having cheaper prices and others dearer prices without any obvious pattern or order.

**Figure 7.7: Bilateral comparisons of ex-manufacturer prices 2005:
Statins**



**Figure 7.8: Bilateral comparisons of ex-manufacturer prices 2005:
Calcium channel blockers**

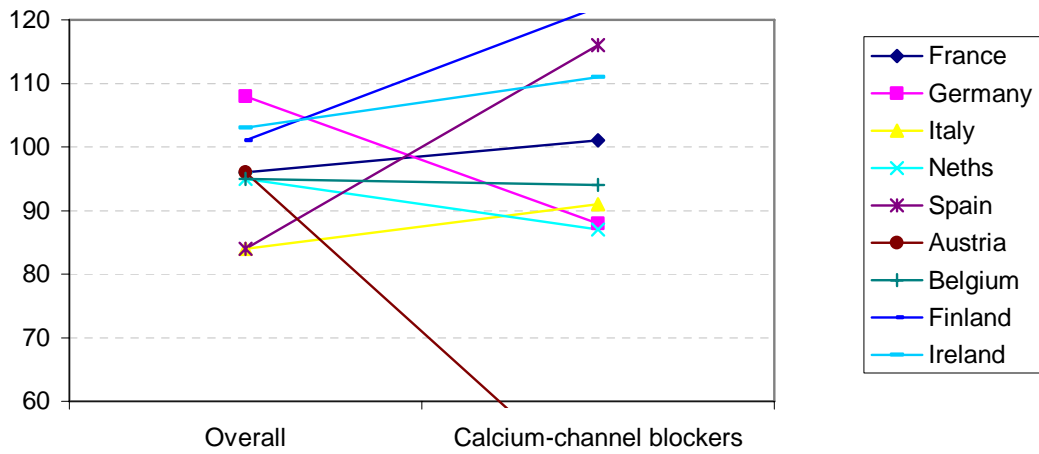
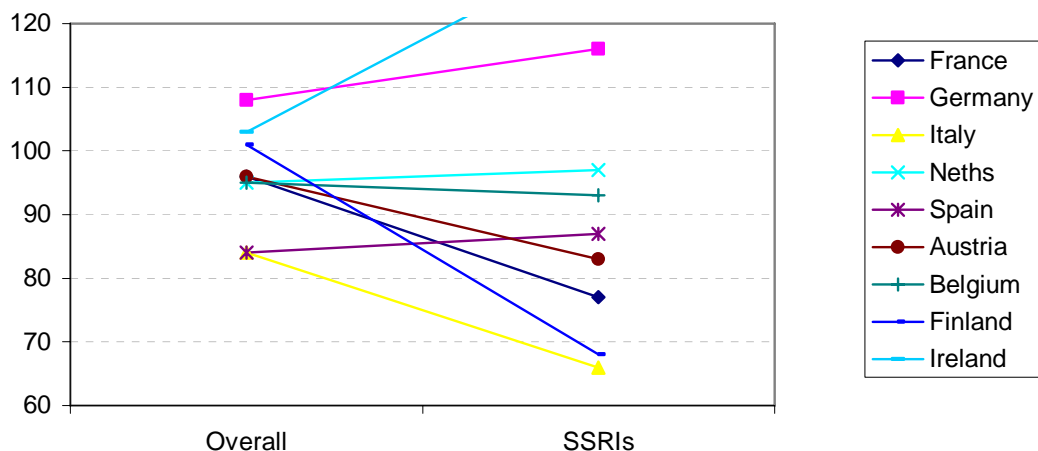


Figure 7.9: Bilateral comparisons of ex-manufacturer prices 2005: selective serotonin re-uptake inhibitors



7.10 Given the degree of consistency visible in some groups, we are persuaded that these results are not chance effects. We hypothesise that the similarities in relative prices are the combined result of price setting by manufacturers that in part take into account existing drugs on the market providing similar therapeutic benefits, and that the drugs in some of these therapeutic groups may have been launched roughly at the same time.

7.11 When the period during which drugs are launched coincides with periods of consistently high or low exchange rates (relative to current rates) between the pound and the euro, subsequent movements in exchange rate may leave these large relative differentials as an historic effect.

7.12 We do not attempt any more detailed examination of these results. We simply observe that it cannot be expected that the prices will relate efficiently to health outcomes. There does not appear to be a clear correlation between the extent that the UK has certain types of health problems relative to the rest of Europe, and the relative prices of drugs used to treat these problems.

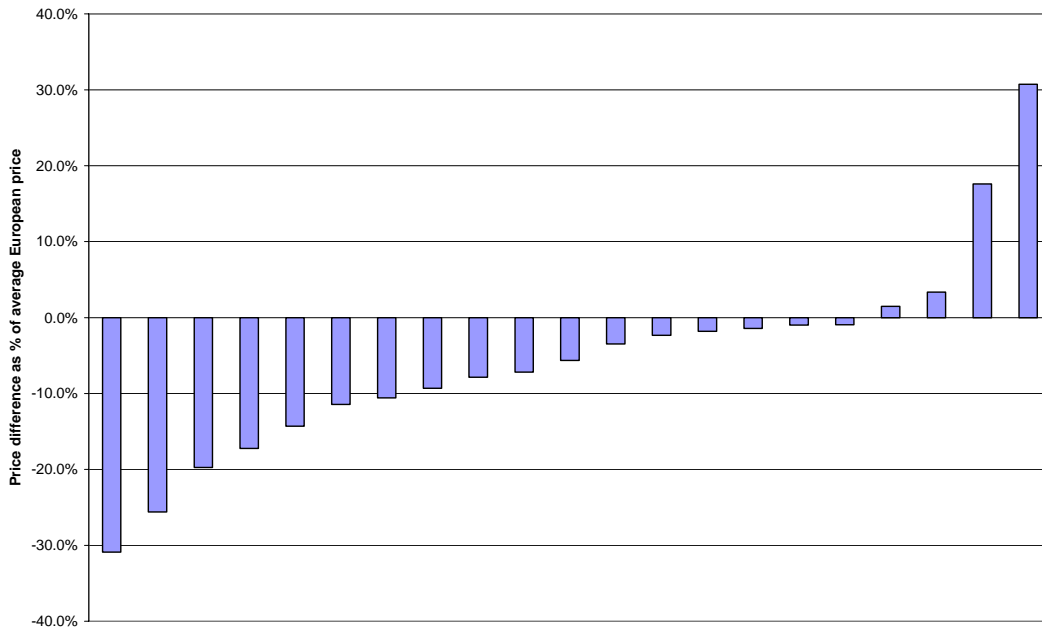
ABPI comparison of prices of recently launched drugs

7.13 The ABPI provided us with an international comparison of the prices of drugs launched in 2004 and 2005, also using IMS data. In comparison to the larger European markets (France, Germany, Italy, Netherlands and Spain), the UK price was generally lower than average in September 2005 (see Figure 7.10 below).³³

³³ Source: IMS data on sterling ex-manufacturer prices per standard unit. The figure shows the UK price as a percentage of a simple average of available prices for other larger European markets. IMS data were available on prices of at least one other country for 21 out of 25 drugs introduced in 2004 and 2005.

7.14 The ABPI subsequently extended the comparison to 76 products launched in the UK since 2000. This similarly showed that UK prices in June 2006 tended to be below the average of the other five larger European markets—on average, UK prices of 15 products reviewed by NICE were around 15 per cent lower, and UK prices of 57 products not reviewed by NICE were around three per cent lower. Of these, prices of 17 'first in class' products were about nine per cent lower than the average and prices of the remaining 40 products were at a similar level.

Figure 7.10: Prices of new drugs in UK versus other European countries (September 2005)



Source: ABPI analysis of IMS data

7.15 Not all drugs shown in the figure above were available in all of the larger European markets, thus the coverage of the comparison varies. However, a country by country comparison suggests UK prices were lower than France (by seven per cent), Germany (eight per cent) and the Netherlands (nine per cent) but higher than Italy (by 13 per cent) and Spain (by 10 per cent).³⁴

7.16 In contrast, the DH comparison (see Table 3.1), which covers both newer and older branded drugs, suggests UK prices in 2005 were higher than in France and the Netherlands and higher by a greater margin than prices in Italy and Spain—the result for Germany was similar. The implication appears to be that UK prices are relatively lower on recently launched drugs and relatively higher on brands that have been on the

³⁴ Unweighted average of ratios of UK price per standard unit to price in other country, for all drugs where prices were available in both countries. Source: OFT analysis of IMS data supplied by ABPI. A comparison of available prices for specific strengths showed similar results.

market longer. The analysis also suggests that the price of first in class products are relatively lower in the UK, compared with products for which there are available substitutes.

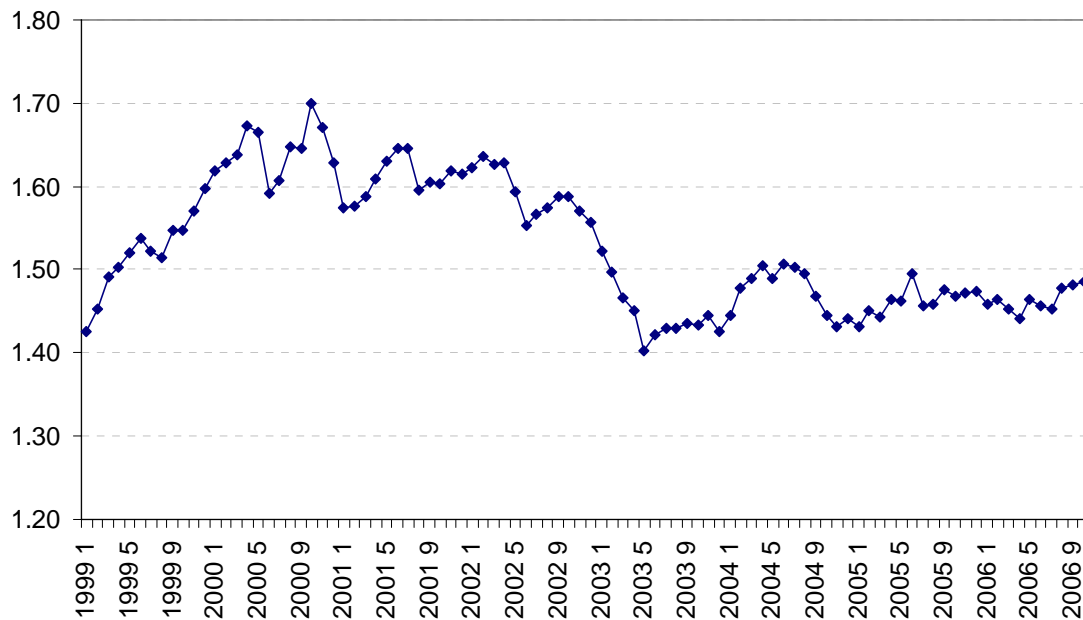
- 7.17 Again, it should be stressed that a number of factors could be driving these results and, as with all price comparisons, interpretations should be heavily caveated. However, we note that they are at least consistent with our view, expressed in Annexe B, that under current pricing arrangements in the UK, existing products are not always subject to the same level of controls as new products coming onto the market.

8 ATTACHMENT 2: EXCHANGE RATES DATA

8.1 These data are provided for reference purposes and to support the discussion of DH results presented above in Chapter 4. The chart below shows the average monthly inter-bank exchange rate between the pound and the euro from January 1999 to September 2006.

8.2 From the start of 1999 onwards the pound went through a period of appreciation against the Euro so that by the beginning of 2000 it was trading at or about €1.60. Then, whilst exhibiting some short term variations continued to trade in a range roughly between €1.60 and €1.70 until the middle of 2002, after which it entered a period of steady decline to reach an exchange rate of about €1.40 to around the middle of 2003.

Figure 8.1: GBP and Euro

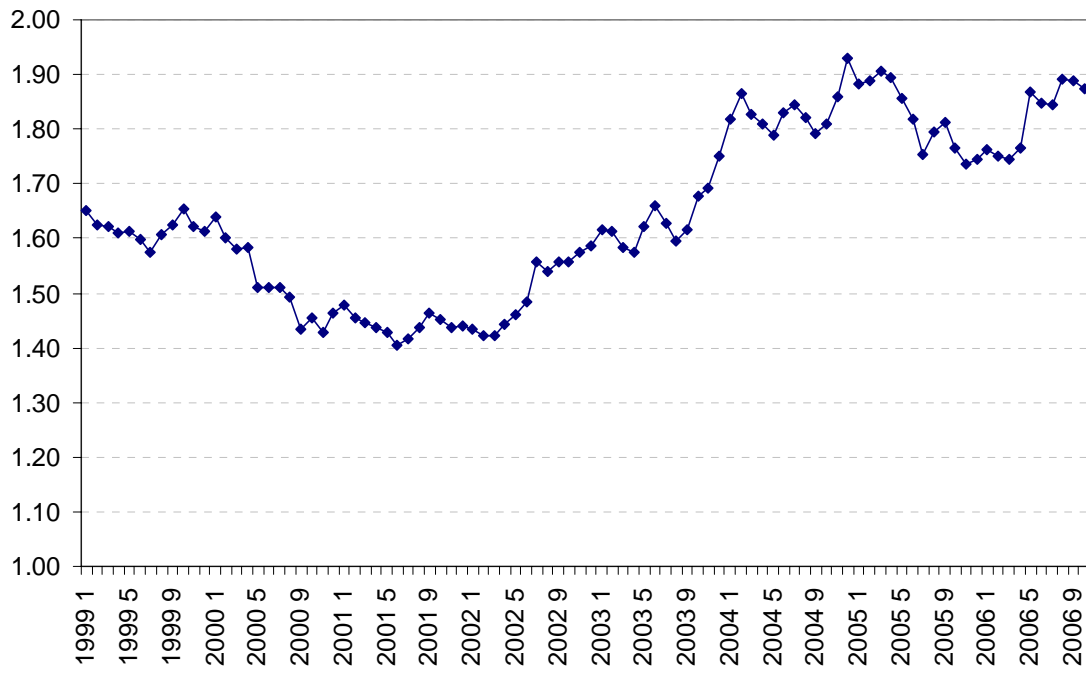


8.3 From early to mid 2003 until the present, the exchange rate has shown greater stability, rarely if ever trading outside the range between €1.4 and €1.5 to the pound.

8.4 Comparable data on the exchange rate between the pound and the American dollar show a rather different picture, the period between the beginning of 1999 and the end of 2000 shows a fall in the pound against the US dollar, followed by a period of during 2001 and part of 2002, before rising steadily until the end of 2004.

8.5 Since then there appear to have been fluctuations that have seen the pound trade against the dollar from US \$1.90 to US \$1.75 without establishing any strong trend.

Figure 8.2: GBP and US dollar



Pharmacy mark-up is calculated as follows: -

Approved price to pharmacist

| From | To | Mark-up |
|----------|-------|---------|
| \$0.01 | \$180 | 10.0% |
| \$180.01 | \$450 | \$18.00 |
| \$450.01 | | 4.0% |
| £1000.01 | | \$40.00 |

Dispensing fee \$5.15 from 1st July 2006

Notes: Prices are in Australian dollars

There are various exceptions to the above that include dangerous drugs of various forms and extemporaneously prepared items. These do not affect the specific comparisons presented below.

- 9.2 Contrary to Germany and Australia where we were able to calculate the exact margins of each product, in the case of two other example countries (Finland and UK), the estimation of ex-manufacturer prices relies on the assumption of fixed wholesale margins. Adjusting for a fixed margin is a simple process, but the results are then dependent on the validity of the assumption. If the data contain unknown exceptions and departures from the assumptions the results could be misleading.
- 9.3 In the UK an allowance of 12.5 per cent of the list price is assumed for the wholesale margin on branded drugs. The 12.5 per cent wholesale margin on branded drugs is considered a robust assumption by DH experts, though it is unclear whether the margin is actually 12.5 per cent in every case.
- 9.4 In circumstances where a wholesaler is able to secure drugs from a supplier at a price that is lower than the list price minus the 12.5 per cent margin, the wholesaler is in a position either to retain this difference or to pass some of the difference on to the pharmacist.
- 9.5 In order to monitor and measure this behaviour in the UK DH carries out a study known as the 'discount enquiry'. However, the primary purpose of the 'discount enquiry' is to monitor activity in relation to parallel trade and discounts available on generic drugs, and this would not include branded drugs covered by the PPRS.
- 9.6 Sweden has two commercial wholesalers, and we were not able to establish wholesale margins from these sources, though we do not exclude the possibility that more research might have established more detailed and clearer information. For the case study analysis (below) the Swedish data remain unadjusted wholesale prices. We are therefore careful about the use of these data in our illustrations.

10 ATTACHMENT 4: PACK SIZE VARIATION AND DISCOUNTS

- 10.1 In Chapter 2 we expressed our view that comparisons based on strict like-for-like matches were potentially more robust and less problematic than comparisons based on active molecule matches. In this section, we identify an instance of systematic price differences between presentations that parallel the examples given previously.
- 10.2 In this case, the differences relate to pack sizes, and the presence in some countries of larger pack sizes offering lower prices per tablet, that do not exist in other countries. We believe this is a concrete example of the potential for comparisons based on molecule matches to mislead, and reinforces our view that comparisons should if at all possible be based on strict like-for-like matches.
- 10.3 It is a simple and observable feature of the data sets we examined that some sets contained a wider range of pack sizes than others. There is clear evidence that Australia and the UK both tend to have lower average and maximum pack sizes within their lists of reimbursable drugs. Table 10.1 below is illustrative of these features for a selection of drugs.
- 10.4 It appears that this approach may reflect policy on cost control and the limitation of waste in some countries. It is an unavoidable eventuality that some patients may not complete courses of treatment. Some may experience changes in their condition that requires a change of drug, a change of dosage or to cease taking the prescribed medicine, and sadly a few may die. All these would lead to unused drugs going to waste.
- 10.5 While the changes in circumstances are unavoidable, the consequent waste can be more tightly limited if drugs are prescribed in, say, 30 day packs rather than say 90 day packs

Table 10.1: Examples of variability in available pack sizes: case study countries

| Examples | Country | Pack sizes (tablets, capsules, etc) |
|--------------------|-----------|-------------------------------------|
| Esomeprazole: 20mg | Australia | 30 |
| | Finland | 14,28,56,98 |
| | Germany | 15,30,60,90 |
| | Sweden | 14,15,28,30,56,60,90,98,105 |
| | UK | 28 |
| Irbesartan: 150mg | Australia | 30 |
| | Finland | 28 |
| | Germany | 28,56,98 |
| | Sweden | 28,98 |
| | UK | 28 |
| Sumatriptan: 50mg | Australia | 2,4 |
| | Finland | 2,6,12 |
| | Germany | 6,12 |
| | Sweden | 6,18 |
| | UK | 6,12 |
| Citalopram: 20mg | Australia | 28 |
| | Finland | 28,30,56,100 |
| | Germany | - |
| | Sweden | 28,98,250 |
| | UK | 28 |

10.6 These differences raise potential difficulties for international price comparisons of the type discussed in Chapter 2. Where prices per tablet are not uniform across different pack sizes, any comparison based on active molecule matches would to some degree reflect not price differences, but the variation in pack sizes and prices available.

10.7 The most important potential problem is that per tablet prices for larger pack sizes might be systematically different to smaller packs, as for example if there was a degree of discount compared to smaller pack sizes. We examined the three data sets for evidence of this discounting behaviour.

Pack sizes and discounts: analysis methodology

10.8 Moving from theoretical arguments to empirical examination of data, we looked at those countries for which pack size variation was most apparent. This meant that data for the UK and Australia were not included, as in many circumstances pack sizes were fixed and available only in a single size.

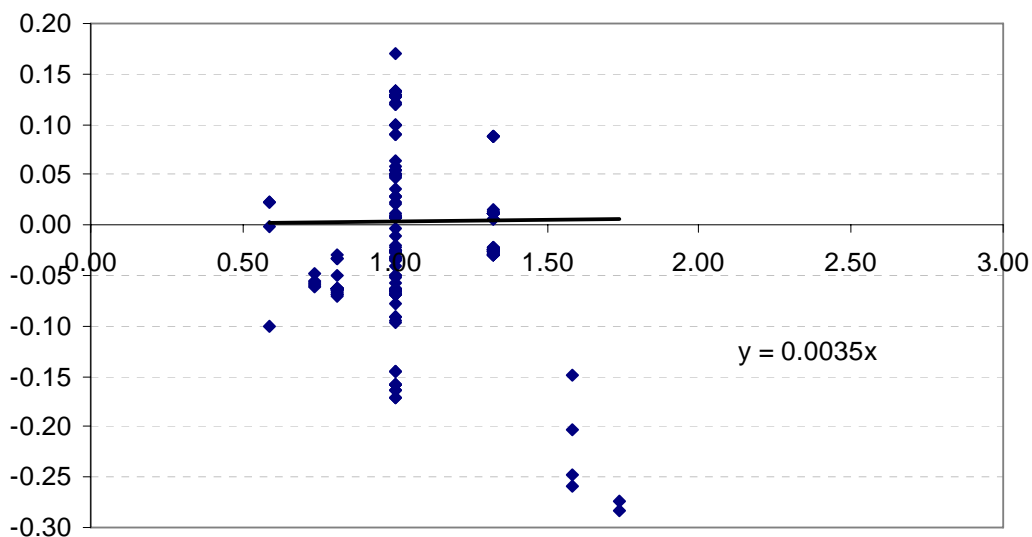
10.9 The data were arranged to provide comparisons that matched on all available criteria except pack size. It was observed that pack sizes come in a variety of commonly occurring presentations. These commonly include 28, 56 and 98 dose packs, 30, 60 and 90 dose packs and 50, 100 and 200 dose packs. Less commonly we also observed packs with 6, 7, 10, 12, 14, 20, 84, 102 and 500 doses, and very infrequently a variety of others.

- 10.10 In the above form, the numerous different combinations of sizes are difficult to analyse. The analysis therefore proceeded by taking logarithms to base 2 of both pack sizes and prices. This approach produces a consistent difference in the logarithm of one unit whenever pack sizes are doubled. For example, \log_2 of 28 and 56 are 4.8074 and 5.8074 respectively and \log_2 of 30 and 60 are 4.9069 and 5.9069, and in each case the larger pack size is one logarithmic unit bigger than the smaller.
- 10.11 This allowed the relative pack sizes to be analysed on a consistent basis using log-log plots. From this plot we computed the regression of log price on log pack size, and by taking the antilog of various results to compute the expected discount for various relative increases in pack size.

Pack sizes and discounts: empirical results

- 10.12 The results for each of the three countries we examined are presented below in Figures 10.1, 10.2 and 10.3 respectively. They are drawn to common scales to allow comparisons across the charts and also include trend-lines fitted to pass through the origin.
- 10.13 The results from the German data illustrate a rather complex and inconclusive picture. The trend line is very flat and has a slope that is not statistically significant from zero. These results do not support the hypothesis that there is any systematic discounting of larger pack sizes.

Figure 10.1: Plot of log (base 2) price per tablet on log (base 2) pack size: German data

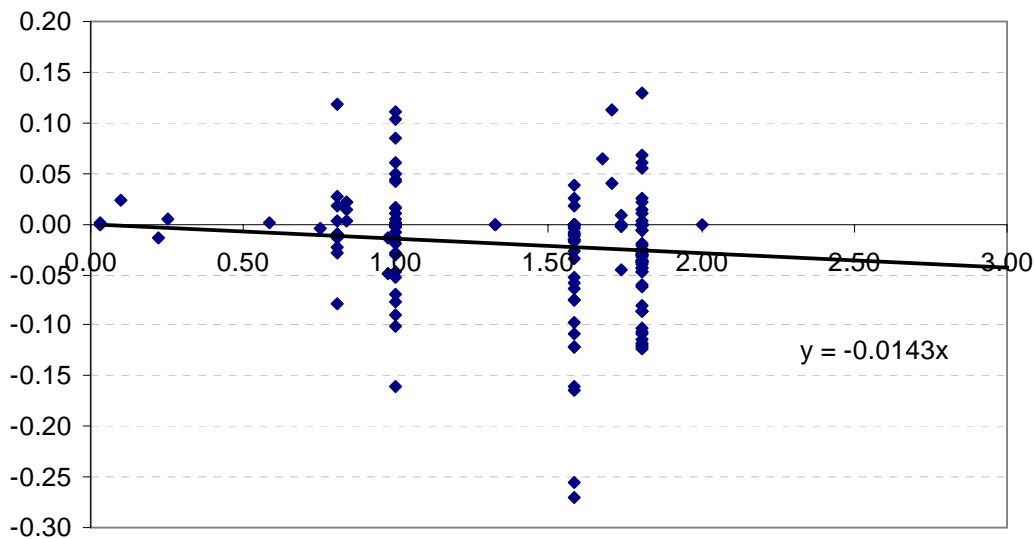


- 10.14 However, both of the data sets available to us from Sweden and from Finland carried a lot of specific detail about the drug, the source, the presentation, and the form. For these data, it proved possible to restrict the comparison of pack sizes to comparisons

that were alike in every way that we could specify except the pack size. In these cases a simpler and clearer picture emerged from the analysis.

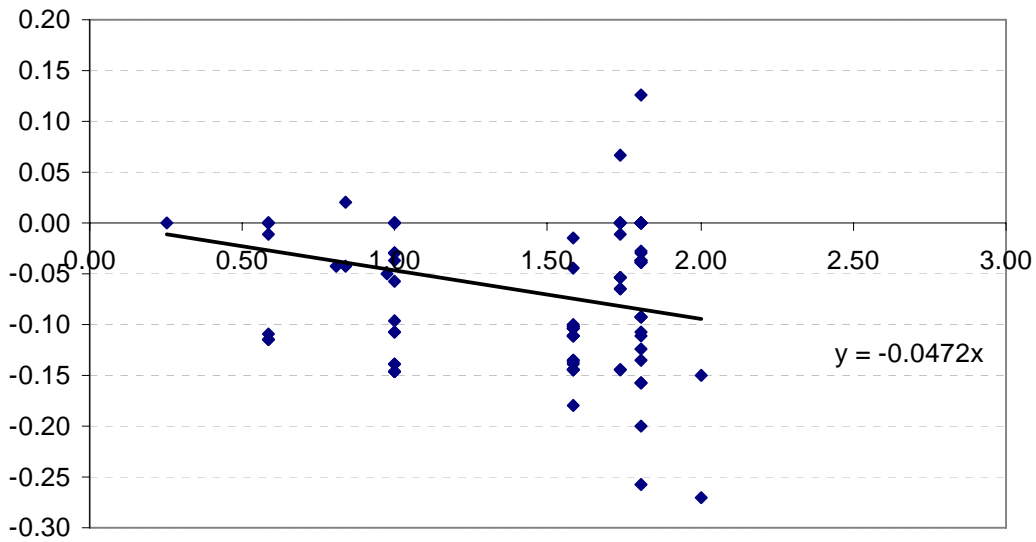
- 10.15 Both countries showed some evidence that prices were set so that some degree of discount in the price per tablet was apparent. It was not present for all the data and the results carried a number of outliers that we cannot explain. Overall there appears to be real evidence for this pricing behaviour.
- 10.16 The relative discounts in Finland appeared considerably larger overall than for Sweden where though present, they amounted to no more on average than roughly one per cent discount for a doubling of the pack size. Lacking the same degree of extra detail in the data available to us on German prices, we were unable to detect any clear evidence of discounts.
- 10.17 We do not argue that this feature is always present, nor that its effect will always be large but it appears real in some circumstances, and to be present to varying degrees in the sort of data commonly used for price comparison calculations.
- 10.18 Note that per tablet prices for larger pack sizes can be higher than for smaller packs, to some degree, without retail prices showing the same behaviour. This is because most systems include some element of fixed mark-up - commonly a pharmacy dispensing fee – that add much less per tablet for larger packs.

Figure 10.2: Plot of log (base 2) price per tablet on log (base 2) pack size: Swedish data



- 10.19 Table 10.2 below summarises the results of these analyses in a simpler form, showing the estimated average discount per tablet that results for a doubling and trebling of pack sizes.

Figure 10.3: Plot of log (base 2) price per tablet on log (base 2) pack size: Finnish data



Pack sizes and discounts: discussion

Table 10.2: Price discounts per tablet for larger pack sizes: case study estimates

| <u>Country</u> | <u>Average price reductions per tablet</u> | |
|----------------|--|--------------------------|
| | <u>Pack size doubled</u> | <u>Pack size trebled</u> |
| Germany | 0.0% | 0.0% |
| Sweden | 1.0% | 1.6% |
| Finland | 3.2% | 5.1% |

10.20 Overall this evidence provides a clear example of the type of difficulties that were discussed in theoretical terms in section two. The items for which prices can be compared between the UK and other countries are, on a strict like-for-like basis, limited to smaller pack sizes.

11 ATTACHMENT 5: INCONSISTENT PRICING ACROSS PRESENTATIONS AND DOSE LEVELS

- 11.1 In a similar way, we examined prices for four proton pump inhibitor drugs. The drugs we looked at were Pantoprazole, Lansoprazole, Rabeprazole and Esomeprazole. In this particular analysis we illustrate a wide variability between countries in the relative prices of drugs at different dose levels, and compounded with this effect some similar variability in relative pricing of different presentations.
- 11.2 Though we do not attempt to take the analysis to any final conclusions, we discuss how this makes relative price comparisons sensitive to the availability of matched data, and to the weightings used to compute the comparisons.
- 11.3 Again, this analysis provides examples where exact matches are absent but there is scope to use close substitutes. The tables presented below show some of the basic results for price per tablet, capsule or other delivery unit, calculated (as far as we were able) to provide ex-manufacturer prices, and using current exchange rates.
- 11.4 While the issue of presentation does not cause much complication for three of the four drugs, one of the drugs is available in several different forms. Differences between prices for different forms show little or no consistency across countries. For example, the price of orol-dispersible tablets in the UK is between double and treble the price of gastro-resistant capsules. In Sweden (though at wholesaler level) the price appears no greater than for capsules.
- 11.5 Below, we provide an additional table that focuses on pack sizes of either 28 or 30 tablets, and, wherever data are available, compute relative prices for a doubling of the dosage.
- 11.6 In these tables a number of matches between data from different countries are highlighted. This is to draw attention to examples where the comparison may be considered to be sensitive to the weightings.

Drug prices per tablet, capsule or other delivery unit in GBP at ex-manufacturer level, using current exchange rates

Table 11.1: Esomeprazole: gastro-resistant tablets

| Dosage (mg) | Pack size | Country | | | | |
|-------------|-----------|-----------|---------|---------|--------|------|
| | | Australia | Finland | Germany | Sweden | UK |
| 20 | 14 | | 0.44 | | 0.73 | |
| 20 | 15 | | | 0.38 | | |
| 20 | 28 | | 0.44 | | 0.69 | 0.58 |
| 20 | 30 | 0.39 | | 0.39 | | |
| 20 | 56 | | 0.41 | | 0.67 | |
| 20 | 60 | | | 0.41 | | |
| 20 | 90 | | | 0.42 | | |
| 20 | 98 | | 0.40 | | 0.67 | |
| 20 | 100 | | 0.40 | | 0.76 | |
| 40 | 14 | | 0.80 | | 0.86 | |
| 40 | 15 | | | 0.58 | 0.86 | |
| 40 | 28 | | 0.80 | | 0.93 | 0.79 |
| 40 | 30 | 0.66 | | 0.60 | 0.93 | |
| 40 | 56 | | 0.74 | | 0.92 | |
| 40 | 60 | | | 0.61 | 0.93 | |
| 40 | 90 | | | 0.62 | 0.93 | |
| 40 | 98 | | | | 0.92 | |
| 40 | 100 | | 0.72 | | 0.95 | |

Table 11.2: Rabeprazole: gastro-resistant tablets

| Dosage (mg) | Pack size | Country | | | | |
|-------------|-----------|-----------|---------|---------|--------|------|
| | | Australia | Finland | Germany | Sweden | UK |
| 9.42 | 7 | | | 0.34 | | |
| 9.42 | 14 | | | 0.35 | | |
| 9.42 | 28 | | | 0.37 | | |
| 9.42 | 56 | | | 0.39 | | |
| 9.42 | 98 | | | 0.39 | | |
| 10 | 28 | 0.24 | | | | 0.36 |
| 18.85 | 7 | | | 0.51 | | |
| 18.85 | 14 | | | 0.54 | | |
| 18.85 | 28 | | | 0.56 | | |
| 18.85 | 56 | | | 0.58 | | |
| 18.85 | 98 | | | 0.59 | | |
| 20 | 28 | | | | | 0.66 |
| 20 | 30 | 0.41 | | | | |

Table 11.3: Lansoprazole: various forms: pack sizes 28 or 30 tablets

| Dosage | Form | Country | | | | |
|--------|-----------------------------------|-----------|---------|---------|--------|------|
| | | Australia | Finland | Germany | Sweden | UK |
| 15 mg | Capsule | 0.23 | | 0.34 | | |
| 15 mg | Gastro-resistant capsule | | 0.09 | 0.34 | 0.45 | 0.13 |
| 15 mg | Gastro-resistant capsule, hard | | 0.09 | | 0.34 | |
| 15 mg | Orodispersible tablets | | | | 0.34 | 0.34 |
| 30 mg | Capsule | 0.39 | | 0.47 | | |
| 30 mg | Gastro-resistant capsule | | 0.09 | 0.41 | 0.83 | 0.20 |
| 30 mg | Gastro-resistant capsule, hard | | 0.15 | | 0.67 | |
| 30 mg | Gastro-resistant granules sachets | | | | | 1.06 |
| 30 mg | Granules for oral suspension | | | | 0.67 | |
| 30 mg | Oral suspension | 0.39 | | | | |
| 30 mg | Orodispersible tablet | | | | 0.65 | 0.62 |

Table 11.4: Pantoprazole: gastro-resistant tablets

| Dosage | Pack size | Country | | | | |
|--------|-----------|-----------|---------|---------|--------|------|
| | | Australia | Finland | Germany | Sweden | UK |
| 20 mg | 28 | | 0.26 | 0.39 | 0.36 | 0.38 |
| 20 mg | 30 | 0.21 | | 0.39 | | |
| 40 mg | 28 | | 0.47 | 0.64 | 0.67 | 0.68 |
| 40 mg | 30 | 0.39 | | 0.60 | | |

- 11.7 The highlighted examples are not the only cases of inconsistent relative prices. They have been chosen because they tend to represent the most obvious cases and are easily visible because prices at one dose level are similar but at another dissimilar. However, less obvious inconsistencies are common within the data, where comparative prices at different dose levels are found to be dissimilar.
- 11.8 Referring to Table 11.1 above, we highlight the prices of Esomeprazole at 20mg and 40mg doses in UK compared with Finland. At the higher dose level the prices are more or less the same, with the UK price fractionally higher of the two, but at the lower dose level the UK price is some 31 per cent higher. This is an example of raw data where any computed comparison would be sensitive to the weighting between the two dose levels.
- 11.9 Prescription cost analysis data for 2005 indicates that around 57 per cent of prescribing by value is for the lower dose form. At this level, the combined effect would estimate a price index for Finland as 89 where UK prices equal 100. Even a small shift in prescribing patterns say to 50 per cent or 60 per cent at the lower level would move the Finland index to 91 and 88 respectively.
- 11.10 Table 11.2 shows a number of prices for Rabeprazole, and we highlight the comparison of UK prices with those of Germany. The match is not exact as the drug in Germany

appears to be a dose of 9.42 mg compared with 10mg in UK. For 28 tablet packs the price per tablet are similar at this dose level, with UK at 36 pence per tablet just a little less expensive than the German price at 37 pence per tablet. However, at the upper dose level of 18.85mg / 20mg the situation is quite different, with the UK price more expensive by some way at 66 pence per tablet compared with 56 pence per tablet, or some 18 per cent higher.

- 11.11 In Table 11.3 we consider price information for Lansoprazole. This drug is available in a variety of presentations and in the UK it is noticeable that orodispersible tablets are much more expensive than the equivalent dose in gastro-resistant capsules, by a factor almost three times for 15mg doses, and by more than three times at 30mg doses. In Sweden, however, the orodispersible form is actually less expensive than the capsule form.
- 11.12 The UK patents on Lansoprazole in capsule form expired towards the end of 2005, but additional patents on the form as FastTabs, that is the orodispersible form, remain in place. The branded form of Lansoprazole (Zoton) is therefore now in competition with generic alternatives and the UK price for capsules may be influenced by the presence of these alternatives.
- 11.13 Any comparison of UK and Swedish prices will be sensitive to the relative weightings between the capsule and orodispersible form. In the event, in 2005 data from DH, prescription cost analysis results suggest that the Orodispersible form accounted for roughly 17 per cent about of all Lansoprazole prescribing.
- 11.14 In the same table, we again observe how a doubling of the dose has a wide variety of effects on price. In Finland, capsule prices are similar for the 15mg and 30mg capsules both cost around nine pence per tablet. The price of the higher dose is actually some four per cent higher though this is not apparent in data shown to the nearest penny. But compared to the smaller dose the larger dose costs 70 per cent more in Australia, some 50 per cent more in the UK but 87 per cent more in Sweden.
- 11.15 Features of the type we identify and describe above are important not because individually they have any special consequence but because there are no guarantees that such effects will average out and have no net influence on the results. As previously observed, the data included in comparison analyses arise by chance as and when exact presentational matches are observed, but are not randomly sampled. This provides no guarantee that final results will be free from bias.

12 ATTACHMENT 6: DATA SOURCES

Germany

Drug prices

DIMDI

German Institute of Medical Documentation and Information

Reference pricing For Medicinal Products

List of all medicinal

<http://www.dimdi.de/static/en/amg/fbag/index.htm>

Explanatory quote from DIMDI website

The DIMDI is authorised to publish the reference pricing lists and the medicinal products involved (issued by the leading associations of the Health Insurance Companies) so that they are accessible via the internet.

Legal foundation is section 35a sub-section 5 of the Fifth Book Code of Social Law - Compulsory Health Insurance - (article 1 of the ruling from December 20, 1988 BGBl. I S.2477, 2482) supplemented by article 1 no. 3 of the Bill for the Adjustment of the Regulations concerning the Setting of Fixed Amounts for Medicinal Products in the Compulsory Health Insurance from July 27, 2001 (BGBl. I S. 1948).

Moreover, due to the Compulsory Health Insurance Modernisation Act (GKV-Modernisierungsgesetz) publicised by the leading associations of the Compulsory Health Insurance in the Federal Law Gazette (Bundesgesetzblatt) on 11/19/2003, Part I, S. 2190, the DIMDI released - in accordance with section 35 sub-section 8 SGB V in combination with section 35a sub-section 5 SGB V - the "Official Notification of the leading associations of the Health Insurance Companies concerning the Adaptation of Fixed Amounts for Prescription Drugs in the new Medicinal Product Price Directive pursuant to section 35 sub-section 8 SGB V".

Weightings data

Arzneiverordnungs-Report 2006

U. Schwabe D Paffrath

Australia

Drug prices

Australian Government

Department of Health and Aging

Schedule of pharmaceutical benefits for approved pharmacists and medical practitioners

Sweden

Drug prices

Pharmaceutical Benefits Board

Läkemedelsförmånsnämnden