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LÄKEMEDELSFÖRMÅNSVERKET

International price comparison of pharmaceuticals 2016

– a volume based analysis of Swedish pharmaceutical prices relative to 19 other European countries.

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Preface

The Dental and Pharmaceutical Benefits Agency's (TLV's) mandate includes monitoring and analysing the price development of pharmaceuticals from an international perspective.

In this report, TLV presents the results of the analysis of price and volume data for the first quarter of 2014, the first quarter 2015 and the first quarter of 2016 in Sweden compared with 19 other European countries. Segments analysed are pharmaceuticals not exposed to competition as well as pharmaceuticals exposed to competition, which includes all pharmaceuticals available as substitutable medicines in the product-of-the-month system as per March 2016.

The report should be viewed as a basis for further analysis of the dynamics of Swedish prices and price changes compared to that seen internationally.

Sofia Wallström
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Summary

This report is part of TLV's mandate to monitor developments in the Swedish pharmaceutical market from an international perspective and is the third annual report of its kind. The analysis is based on prescription pharmaceuticals in outpatient care. TLV has used price and sales data from IMS Health for the first quarters of 2014, 2015 and 2016. Price levels in Sweden are compared with 19 other European countries. The report is based on national list prices at an AIP (pharmacy purchase price) level. The pharmaceuticals have been divided into segments based on the premise of competition in Sweden.

The segment '*pharmaceuticals not exposed to competition*' includes products where competition between different substitutable pharmaceuticals in Sweden has not arisen. In total, this segment has sales in Sweden of approximately 16.6 billion SEK (AIP moving annual total March 2016). The segment pharmaceuticals not exposed to competition represents 81 percent of total sales, and approximately half of the volume. Since 2014, Swedish prices have declined relative to other countries. Between 2014 and 2015, Swedish relative prices fell due to several extensive reassessments for pharmaceuticals already included in the benefits scheme. Changes between 2015 and 2016 are, however, minor. Swedish prices have been marginally lower compared to other countries. Of the 20 countries compared, Swedish prices for 2016 and 2015 can be found among the eight countries with the highest prices. On average, Swedish prices are thus in line with prices in other countries and the cross-section index was 99,6 Q1 2016 for the segment pharmaceuticals not exposed to competition.

The segment '*pharmaceuticals exposed to competition*' includes all pharmaceutical groups in the sample found in the product-of-the-month system in March 2016. In total, segment sales in Sweden were around 3.8 billion SEK (AIP moving annual total March 2016). The segment pharmaceuticals exposed to competition represents 19 percent of total sales, and approximately half of the volume. Sweden is found among the three countries with the lowest prices in the sample. Between 2014 and 2015, differences in price between the countries fell somewhat. Between 2015 and 2016, however, the differences increased again and in most countries they are greater than they were in 2014. The analysis also shows that the Swedish 'product-of-the-month' system quickly lowers prices relative to other countries. The price falls quickly after the competition is strengthened.

It is pharmaceuticals in the ATC-1 groups cardiovascular diseases and nervous system that mostly explains why the segment pharmaceuticals exposed to competition exhibit lower prices than in most other countries. For the area of cardiovascular diseases, the index values are higher in all other countries than in Sweden and for the area nervous system it is only Denmark, the Netherlands and Slovakia that demonstrate lower index values than Sweden. There may nevertheless, be pharmaceuticals within these ATC-1 groups that are more expensive in Sweden.

Price information is based on official list prices for the outpatient care. This is due to the fact that it is only these prices that may be collected in a simple and standardized way. Pricing for procured pharmaceuticals not handled by prescription is not taken into account. Some countries also have discounts of various kinds that are not reflected in list prices. Sweden also has managed entry agreements that reduce the cost or uncertainty for certain expensive pharmaceuticals. In some countries and for some specific pharmaceuticals, it can therefore be difficult to make direct comparisons.

How the index relative to other countries develops over time is probably quite a good yardstick of how dynamic and adaptable the Swedish system is. A major focus in this report is therefore given to analysing differences over time.

Terms and concepts

ATC – *Anatomical Therapeutic Chemical Classification (ATC)* is a system for classifying pharmaceuticals. The ATC system consists of 14 main groups where the pharmaceutical is positioned on the basis of its main indication.

- A Alimentary tract and metabolism
- B Blood and blood-forming organs
- C Cardiovascular system
- D Skin
- G Genitourinary organs and sex hormones
- H Endocrinology
- J Infectious Diseases
- L Tumours and immune system disorders
- M Musculoskeletal
- N Nervous system
- P Anti-parasitic products, insecticides and repellents
- R Respiratory
- S Eyes and ears
- V Various

Active substance – the substance in a pharmaceutical product that gives it its medical effect.

Ceiling prices in substitutable groups – the maximum accepted price (AIP / unit) of a pharmaceutical in a package size group.

Dosage form – different forms of how a pharmaceutical can be delivered to the body, for example, via tablet, injection or patch.

Ex factory – selling price from the market holder. Costs of transport from the factory plus taxes and surcharges may be added.

Generic pharmaceutical – medicines containing the same active substance in the same dosage form and with the same strength and which give the same medical effect.

Generic name (INN) – describes the chemical name of a substance. INN stands for *International Non-proprietary Name*. The purpose of the generic name is to enable brand name-independent communication of pharmaceutical substances. Generic names are established by various countries and by the WHO.

International reference prices (IRP, EPR, ERP) – pricing method where the price(s) of a pharmaceutical in one or more countries is taken into account in the national pricing of medicines. Common synonyms are *international reference pricing* (IRP), *external price reference* (EPR) or *external reference pricing* (ERP). The pricing method can be formal or informal, in combination with another method (e.g. assess-

ment of the benefit or value). Certain countries employ the concept of internal reference pricing, which is why in some literature, the acronym IRP is used differently than in this report.

Pharmaceutical benefit – a pharmaceutical included in the pharmaceutical benefit system is subsidized and included in the high-cost protection threshold scheme.

Pharmacy purchase price (AIP) – pharmacy operator's purchase price in SEK.

Pharmacy sales price (AUP) – pharmacy operator's sales price in SEK.

Price index bilateral – the same product needs to be available in Sweden and in one of the compared countries to be included in the price index against that country.

Price index cross-sectional – the same product needs to be available in several countries to be included in any of the countries' price indexes. The threshold, referred to as matching degree, has been set at 40 percent in those cases where cross-sectional indices are used. This means that a pharmaceutical (substance, dosage form and strength) needs to be available in at least eight other countries in addition to Sweden.

Product – a pharmaceutical with the same ingredient, dosage form and strength.

Product-of-the-month – Products-of-the-month are the generic substitutable pharmaceuticals that have the lowest price and that the pharmacies must offer their customers when they replace pharmaceuticals. Every month, the product in each package size group with the lowest unit sales price, and that the pharmaceutical company has confirmed can be provided to the entire market with a sufficient durability for the entire pricing period price, becomes the product-of-the-month.

Original pharmaceutical – the first pharmaceutical on the market that contains a particular active substance. These pharmaceuticals are under patent protection and are thus not exposed to competition from generic equivalents for a number of years.

The segment pharmaceuticals not exposed to competition – includes products where competition between two different substitutable pharmaceuticals in Sweden has not arisen. Competitive conditions may nevertheless differ between the various countries in this price comparison.

The segment pharmaceuticals exposed to competition (in the product-of-the-month system) – includes all pharmaceuticals available as substitutable medicines for the product-of-the-month as per March 2016.

Subsidy – that part of the cost of a pharmaceutical, a dental procedure or a consumable item paid by the state.

Substitutable pharmaceuticals – pharmaceuticals that the Swedish Medical Products Agency (MPA) has determined are exchangeable with one another because they contain the same active ingredient in the same formulation and with the same strength and that they give the same medical effect.

1 Introduction

1.1 Assignment

The Dental and Pharmaceutical Benefits Agency, hereafter TLV, has a mandate to monitor and analyse the developments in the pharmaceutical, pharmacy and dental care markets in Sweden. One of TLV's aim is to develop the value-based pricing in order to ensure that pharmaceuticals are cost effective throughout their entire lifecycle. The instruction to TLV states among other matters that the agency has a mandate to monitor and analyse developments in other countries and take advantage of experiences, compare the price level in Sweden with prices in other countries for relevant products and also monitor price developments in an international perspective.¹ This report is one part in the monitoring of the Swedish price developments of pharmaceuticals from an international perspective and this is the third annual report of this kind.

The report describes how the prices of prescription pharmaceuticals in Sweden relate to 19 other European countries: Belgium, Denmark, Finland, France, Greece, Ireland, Italy, Netherlands, Norway, Poland, Portugal, Switzerland, Slovakia, Spain, United Kingdom, Czech Republic, Germany, Hungary and Austria. The comparison includes pharmaceuticals exposed to competition², as well as pharmaceuticals not exposed to competition.³

The purpose is to analyse the Swedish prices compared to an international perspective. The dynamics in terms of prices, volumes, exchange rates and product range changes that affected Swedish prices between 2014, 2015 and 2016 relative to other countries are also examined.

Determining whether Swedish pharmaceutical prices are at the desired level, or how possible changes to possibly reach such a level should be designed, are not included in the task.

1.2 Previous studies

In Sweden, TLV has conducted extensive studies both in 2014 and 2015. This, the third report of its kind, follows a similar methodology.

In Norway, there have been a number of price comparison studies including those of Kurt Brekke at the Norwegian School of Economics. Particularly relevant in this

¹ Förordning (2007:1206), 2§.

² The segment drugs not exposed to competition - includes products where competition between two different interchangeable drugs in Sweden has not arisen.

³ The segment drugs exposed to competition (in the product-of-the-month system) - includes all drugs available as substitutable medicines for the product-of-the-month system as per March 2016.

regard are: Brekke et al. 2008, Brekke et al. 2011 and Brekke and Holmås 2012. The reports often answer somewhat different issues. Additionally, the surveyed segments, sub-populations of pharmaceuticals, time periods and comparison countries vary, making comparisons of one report's results with another's difficult. A comparison can, perhaps, indicate overall context and relationships. To evaluate the dynamics of Swedish prices compared with international equivalents requires repeated studies done on the same population of pharmaceuticals in the same sample of countries. More importantly is whether the analysis in an international comparison is based on price and sales data or only on price data without any relation to the actual pharmaceutical use within a country.

1.2.1 Price and volume analyses

Brekke and Holmås 2012⁴ studied how different countries' volume weighting affects the price comparison. They examined the extent to which Swedish pharmaceutical consumption / Swedish volume weights affect the price index from a Norwegian perspective. The prices of 73 substances without generic competition in all countries and their sales data from Sweden and Norway constituted the data set. Brekke and Holmås showed that changing the base for weight from Norwegian to Swedish consumption influenced the index level. Countries with a relatively high index had this increased, i.e. became relatively more expensive compared to Sweden, and countries with a relatively low index had this lowered (closer to zero), i.e. became even less expensive in relative terms to Sweden. Appendix 1 in this present study compared the replacement of base country from Swedish to Finnish and Austrian volume weights, which was also done in TLV's international comparison of 2015. Finland and Austria have been chosen for the change of base weight because the two countries demonstrated a high overall matching to Sweden, regardless segmentation. Finland and Austria are similar to Sweden in several aspects, e.g. concerning the financing of pharmaceuticals. The countries' list-prices also closely reflect the actual prices.

TLV's international price comparison 2014

TLV's study from 2014⁵ compared the price level in Sweden with 15 other European countries divided into three segments. The analysis was based on price and sales data from IMS Health. The result of the analysis of the segment pharmaceuticals not exposed to competition showed that Swedish pharmaceutical prices were slightly higher than in several of the comparison countries. Of the 15 comparison countries, Swedish prices were among the five highest. The analysis showed that a relatively small number of substances explained a large part of this price difference. It also showed that older pharmaceuticals introduced up to and including 1998 had prices that were in line with other countries. Prices were slightly higher in Sweden in relative terms for pharmaceuticals introduced after 1998. Previous reports, which are, however, not entirely comparable, have indicated that prices of older pharma-

⁴ Brekke, K. R., och Holmås, T. H., (2012).

⁵ TLV (2014a).

ceuticals not exposed to competition had been higher in Sweden than in other countries.

In addition, in 2014 TLV studied two other segments; pharmaceuticals exposed to competition not included in the product-of-the-month system and substitutable pharmaceuticals available in the product-of-the-month system. This analysis showed that by international standards, Sweden exhibited a low price level of pharmaceuticals exposed to competition, i.e. that part of the segment included in the product-of-the-month system. Sweden, along with Denmark and the Netherlands, constituted the group of countries that exhibited a significantly lower price in this segment compared to the other 13 countries.

TLV's international price comparison 2015

TLV's study from 2015⁶ compared price levels in Sweden with 19 other European countries based on price and sales data from IMS Health. The report was based on national list prices at AIP-level and pharmaceuticals were grouped based on the conditions for competition. The study found that reassessments of pharmaceuticals already within the benefits scheme are important for pharmaceuticals without competition. Changes in prices for pharmaceuticals that had been exposed to an authority intervention (either revision or the 15-year rule) had contributed most to lowering Swedish relative prices. For the exposed to competition segment pharmaceuticals, which included all groups of medicines in the sample included in product-of-the-month list in March 2015, the study showed that Sweden, along with Denmark and the Netherlands, was among the three countries with the lowest prices in the sample. Between 2014 and 2015, the difference in prices between the countries declined slightly, but major differences still existed. Above all, it was in countries that in 2014 were considerably more expensive than Sweden where prices had fallen the most. Large price differences should be smoothed out over time when several countries utilize some degree of international reference pricing and thus in the longer term be affected by other countries' prices. At the same time, we can also see that several countries have begun to work more actively to reduce the prices of pharmaceuticals with generic competition. An in-depth analysis of the product-of-the-month system also showed that the Swedish system works best relative to other countries when sales volumes are high.

1.2.2 Price comparisons lack volume data

During 2015-2016, two studies were published in *Lancet Oncology* in which price differences of cancer pharmaceuticals in European countries were analysed.

A study by van Harten et al. 2016⁷ analysing prices in 15 European countries found that the list prices of cancer pharmaceuticals could vary widely and be up to 92 percent lower than the highest reported price, and that actual prices could be up to 58 percent lower.

⁶ TLV (2015).

⁷ van Harten WH, Wind A, de Paoli P, Saghatchian M, Oberst S. (2016).

A study by Vogler et al. 2015⁸ analysing prices of 30 cancer pharmaceuticals in 16 European countries, as well as Australia and New Zealand, and found that the price differences of 31 cancer medicines measured as the highest to lowest list price could vary between 28 percent and 388 percent. Among other things, the study found that Greek prices were low and that the price levels in Sweden, Switzerland and Germany were high.

Vogler et al. discussed the limitations of using list prices as compared to actual prices. The authors write that they are aware that discount agreements and specially arranged adoption processes have increased in number and have been signed for cancer pharmaceuticals, but because of the lack of transparency, an analysis on this level is not possible. However, one aspect that the authors do not mention is how the actual use of the 30 cancer pharmaceuticals appears.

In order for a price comparison analysis to be as fair as possible, it is vital that the price data is supplemented by volume data for the actual use as well as whether or not the use is prescription-based. With such a slightly more complex analysis, it is possible to better evaluate how costly use is in Sweden and also what the actual use looks like.

By all accounts, Sweden has relatively high prices for many of the cancer pharmaceuticals listed in Vogler et al. The study addresses only the magnitude of the differences in list price and not factors such as actual use or whether the pharmaceuticals are used primarily in outpatient or inpatient care. It generally pervades that the medicines where Sweden has the highest prices are used mainly in inpatient care. Inpatient care prices differ from outpatient prescriptions, where TLV is able to influence prices. Due to procurement processes, inpatient care prices are generally lower than those of prescriptions. For these pharmaceuticals, the official list prices play a minor role. Since prices also vary between Swedish County Councils, it is difficult to provide an overall view.

In TLV's price comparisons of 2012, 2014, 2015, and in this report, price differences are weighted according to the actual use in Sweden. The analyses for 2015 and 2016 also included a sensitivity analysis on the effect of replacing the base country of the volume-weighting. With this method, the impact of differences in prices, based on Swedish consumption, can be evaluated. But even this comparison is limited to only looking at pharmaceuticals used via prescriptions and where there are list prices and use in other countries. In cases where hidden discounts or different variations of refund agreements occur, or when procurement takes place via hospitals, prices are likely to be lower than the list price.

⁸ Vogler, S. Vitry, A. och Zaheer-Ud-Din, B (2015).

1.3 Outline

This report has the following outline. Section 2 describes the underlying data and methodology. Then follows a section on the pharmaceutical markets for the countries in the sample. Appendices 2, 3 and 4 contain detailed descriptions of the countries' pharmaceutical pricing and reimbursement systems.

Results are broken down by segment. Results for the segment pharmaceuticals without competition follow in section 4. Results for the segment pharmaceuticals with competition follow in section 5.

The analysis used the average exchange rate for the first quarter of 2016. The exception is, however, section 6, in which a sensitivity analysis of foreign exchange effects is found.

Finally, the discussion is found in section 7. As in previous studies (Brekke and Holmås 2012 and TLV 2015) of how various countries' volume weights affect the price comparison is found in Appendix 1.

2 Data and methodology

2.1 Different segments depending on the conditions for competition

Pharmaceuticals are divided into segments based on the premise of competition in Sweden. The present report applies segmentation according to the same method used in TLV's 2015 report on international price comparison.

These segments are:

- Pharmaceuticals not exposed to competition
- Pharmaceuticals exposed to competition (within the product-of-the-month system)

The segment *pharmaceuticals not exposed to competition* includes products where competition between two different substitutable pharmaceuticals in Sweden has not arisen. The segment includes both products that are patented and products whose patent protection has expired, but where competition between two substitutable pharmaceuticals has not emerged. Biosimilars are also included in this segment as they are not directly substitutable to a reference product. The reason these pharmaceuticals are included in the same segment is that TLV's possibility to influence the price is the same. Competitive conditions may differ between countries in the price comparison.

The segment *pharmaceuticals exposed to competition (within in the product-of-the-month system)* includes all pharmaceuticals included in generic substitution within the product-of-the-month system in March 2016. The pharmaceuticals to be included in this system are determined by TLV's regulation 2009: 4.⁹

2.2 Data set and selection of pharmaceuticals

The starting point of the analysis is the most selling prescription pharmaceuticals in Sweden within the pharmaceutical benefits scheme. Prior to the 2015 report, IMS Health was given the task of delivering data for 200 products in the segment protected pharmaceuticals, 180 products in the segment unprotected original pharmaceuticals without competition, and 200 substances in the segment unprotected pharmaceuticals with competition with the most sales. For this analysis, data has been updated with new pharmaceuticals that have demonstrated high sales during the period from March 2015 to March 2016.

The 2016 segmentation is similar to the 2015 analysis but differs from the 2014 analysis. Therefore, comparable data for the first quarter's 2014, 2015 and 2016 are analysed and presented. In other words, all the analyses that compare with 2015 or

⁹ See TLV's regulations <http://www.tlv.se/ty/regelverk/foreskrifter> for regulation 2009: 4 TLVFS 2009: 4 on the pricing of generic substitution and replacement of medicines, etc. as well as amendments to the regulation.

2014 refer to the new analysed data and not to TLV 2015 or TLV 2014 if not explicitly stated otherwise.

Only products with sales in outpatient settings are included in this analysis. How one chooses to treat one disease may differ between countries. This may partly be due to different handling in the context of outpatient or inpatient care. In addition, treatment therapies also vary and may involve treating an ailment with pharmaceuticals other than what is the case in Sweden. Furthermore, not all pharmaceuticals are approved or introduced in all countries.

This means that pharmaceuticals selected from a Swedish perspective are not found to the same extent in comparison countries. The calculation of a weighted price index that includes all countries is affected by the mix of pharmaceuticals that is available in the different countries.

If sales channels differ between countries, this may also affect the analysis. Products sold by prescription in Sweden may not necessarily be sold in the same way in other countries. These products will then not be assigned a price in the comparison country. This is particularly common for different cancer pharmaceuticals and pharmaceuticals against autoimmune diseases (e.g. TNF-alpha inhibitors). A number of countries have chosen to manage this type of medicine in inpatient care instead of, as in Sweden, in an outpatient setting. Outpatient and inpatient care follow different laws and in Sweden there is a distinction in their financing.

The reason why the selection is limited to prescription pharmaceuticals in outpatient care is that it is these pharmaceuticals that TLV prices and is able to influence. Products in inpatient care also have less transparent prices, which complicates such an analysis.

Price indices reported in this study are based on list prices and on the pharmacy purchase price (AIP) or equivalent.¹⁰ The reason why AIP is used as a price measure is that it does not contain pharmacy trade margins, which can vary between countries depending on how compensation to pharmacies is handled in each country.

2.3 Method of matching of pharmaceuticals

This price comparison analyses weighted prices for different 'baskets' of medicines. What is defined as a product can be interpreted differently. Matching of pharmaceuticals can occur in different ways with different consequences on precision and on how many countries include the pharmaceuticals in the comparison.

In this analysis, a product is defined as a pharmaceutical with the same substance, dosage form and strength. The definition does not include package size, since the choice of packaging size used differs depending on the country.

¹⁰ IMS Health describes price data as *ex-wholesaler price or price to chemist per pack*.

In Sweden, medicines are normally provided for a three-month period, while in southern Europe, one month is generally the norm. This means that normally, bigger packages are sold in Sweden compared with countries where medicines are collected more frequently. If the pack sizes that are sold often have a lower price than those with less frequent sales, this would mean that large packs would be given a greater weight and would thus benefit Sweden. To correct for this, the price has been calculated as the cost per dose of a particular substance, dosage form and strength. This allows different pack sizes to be compared against each other and makes the price indices more accurate. This practice increases the degree of matching with other countries, although the precision of the comparison is somewhat worse than for matching at packaging level.

An alternative would be matching at the packaging level, which means that exactly the same package in terms of substance, formulation, strength and size needs to be available in both Sweden and the comparison country in order to be included. This method has a high degree of precision, as the pharmaceuticals are consistent from a packaging point of view. At the same time, the risk is greater that one specific package is not available in very many countries. Size of packaging can often be related to dispensing frequency. The longer the duration between dispensing times, the greater the probability is that larger packages are used more frequently, and vice versa.

A further option would be to measure the costs that each country has for a specific therapy group, regardless of the pharmaceutical used, and then weigh together these expenses to see what the country pays to treat various diseases. The problems with such a price comparison are difficulties in qualifying which pharmaceuticals belong to a specific therapy group, and that treatment traditions can differ between countries.

2.3.1 Pharmaceuticals with very low volumes in a country are excluded

Some countries that have a matching with a product in Sweden may exhibit sales that are considerably lower than in Sweden. If the volume per capita is less than 0.5 percent of the Swedish, the pharmaceutical is excluded from the calculation of the bilateral Index. The reason for this is to avoid attributing a product that has very little use in the comparison country a disproportionate weighting in the comparison and thereby potentially overestimate the relative price level. When calculating information about volumes during the current 12 months up to and including March 2016 and the total number of inhabitants in each country in 2016 is used.

2.3.2 Descriptive statistics

The overall Swedish sales value of the pharmaceuticals included in the selection is described in the following table. In total, Swedish sales amount to 20.4 billion SEK, which is approximately 93 percent of total sales of subsidised pharmaceuticals in Sweden. The selection is based on the main products in each segment and is thus not random. It is therefore not possible to generalize the price indices for the selection to the total market. Products not included in the sample have on average a lower price per package. The pricing mechanism of these pharmaceuticals may be dif-

ferent to the pharmaceuticals in the selection and therefore it is difficult to draw too far-reaching conclusions about the level of prices.

Table 1. Sales of pharmaceuticals on an AIP level in the selection for different segments, MSEK, Moving annual total March 2014, 2015 and 2016.

Segment	Sales March 2016, MAT (AIP MSEK)	Sales March 2015, MAT (AIP MSEK)	Sales March 2014, MAT (AIP MSEK)
Without competition	16 585	15 053	13 317
With competition	3 803	4 067	4 164
Sum (in the data set)	20 388	19 121	17 481
Total sales of pharmaceuticals in the benefits scheme in Sweden	21 984	20 141	16 168
Share of sales in data set to total sales in Sweden	93%	95%	91%

Source: TLV analyses.

Total sales of pharmaceuticals in the benefits scheme has increased in recent years. The increase was nine percent during the period from March 2016 to March 2015 and five percent the year before. The increase is partly due to new products for the treatment of various types of cancer has been introduced and in part by the increased use of older products, mainly NOAK.¹¹

The substances for which the cost as a result of price cuts has declined the most is aripiprazole, quetiapine, and duloxetine. All of these substances have been subjected to generic competition since 2015 and are included in product of the month-system.

In 2016, approximately every two package sold in the outpatient sector in Sweden was a pharmaceutical included in the product of the month-system, but accounted only for around one fifth of the total cost.

2.4 Sales volumes and volume weighting

It is common practice to weight the volume of various product prices in a price index. Price differences for products that have high sales are assigned a greater importance than products with low sales and vice versa.

A price index is a weighted average of a number of products usually calculated over time. If we have two periods (period 0 and period t) and n products, a price index is generally written as:

$$I_P = \frac{p_1^t w_1 + p_2^t w_2 + \dots + p_n^t w_n}{p_1^0 w_1 + p_2^0 w_2 + \dots + p_n^0 w_n} * 100$$

¹¹ TLV (2016b) p. 9.

To calculate the relative importance of a product's price, it is normal to use sales volume q as a product weight. In this analysis, the index is calculated for a time period at a time, which means that period 0 and period t are the same. Time is replaced by the country; foreign U and Sweden S .

The weight can be either sales volume in a foreign country or sales volume in Sweden. This choice affects whether the price index should be interpreted from a Swedish perspective or not. The convention for price analyses in the pharmaceutical field is to calculate the Laspeyres price index, that is, with the country as a base from whose perspective the price differences should be seen, in this case Sweden's:

$$L_p = \frac{p_1^U q_1^S + p_2^U q_2^S + \dots + p_n^U q_n^S}{p_1^S q_1^S + p_2^S q_2^S + \dots + p_n^S q_n^S} * 100$$

Where p^U refers to the price abroad and q^S to the quantity in Sweden. If the price is the same in Sweden and abroad, the index has value of 100. If the index is <100 (or > 100) it means the product has a lower (or higher) price in a foreign country than in Sweden.

A price index lower (or higher) than 100 means a theoretical increase in costs (cost savings) can be achieved if the Swedish prices change in relation to the foreign, given that Swedish consumption is assumed to be unchanged. This is a strong and improbable assumption that requires perfectly inelastic demand. If demand is not inelastic, then the change in demand either strengthens or weakens a theoretical increase in costs or cost savings. The range of pharmaceuticals, i.e. the entry of competing products and improvements to existing ones, is also important.

The price index gives a good view of how the price level in comparable countries is related to the price level in Sweden during the current period. However, the absolute price index should be interpreted with caution, since it is influenced by both volume and currency effects. In this study, however, the average exchange rate for the first quarter of 2016 is consistently applied. This also applies to the index data reported for 2014 and 2015. The only exception is in section 6, with a sensitivity analysis to illustrate the effect of if the exchange rate is not constantly keep. See section 2.5 for further information.

If another country's volume weight is used as a base instead of its own, the absolute level of the price index is adjusted, but not necessarily the relative order between the countries. See Section 9.1, where the effect of using other countries (Finland and Austria) as the base is analysed.

2.4.1 Definition of 'price basket'

To calculate a price index, whether it is bilateral or cross-sectional, 'a basket' needs to be defined.

A bilateral price index requires that the product is available in Sweden and in one of the comparison countries for it to be included in the price comparison against that country.

A cross-sectional index, however, requires that the product be available in several countries for it to be included in any of the countries' price index. The threshold limit, referred to as matching degree, has been set at 40 percent in cases where cross-sectional indices are used. This means that a pharmaceutical (substance, dosage form and strength) is required to be available in at least eight other countries in addition to Sweden. To create a single basket for all countries, values are filled out with Swedish rates for countries where sales for a particular product are lacking.

The set limit for how many countries must have sales in order for a pharmaceutical to be included in the comparison affects both the number of values filled out and the number of pharmaceuticals that are eligible for comparison. The higher matching requirements set, the less data has to be filled out but fewer pharmaceuticals are eligible for comparison. A lower matching requirement increases the number of pharmaceuticals in the comparison, but requires that more data be filled out with Swedish data, which tends to smooth out differences between countries. With this method, it is possible to calculate the average since the mix of pharmaceuticals is the same in all countries (the degree of filling out nevertheless varies).

Another option is to compare with the pharmaceuticals that match bilaterally in each country. This maximizes the number of pharmaceuticals included in the comparison and filling out with Swedish values when a pharmaceutical is not available in another country is not required. The dilemma is that the mix of pharmaceuticals varies between countries. It is therefore not possible to compare price levels between countries, but only the relationship with Sweden.

In this report, we work mainly from bilateral indices, which captures all pharmaceuticals that match with each individual country. The value that these pharmaceuticals represent, compared to the total Swedish sales in the sample, therefore varies between countries. Countries' positions relative to each other are nevertheless the same regardless of which index method is used. Selection of price index (bilateral or cross-sectional) marginally affects the level of indices relative to Swedish prices, which was illustrated in TLV's international price comparison 2014.

2.5 Exchange rates

One factor that influences prices over time is the exchange rate. Exchange rate fluctuations affect relative prices compared to other countries. If the currency of a country is strengthened, prices in other countries appear to have been cut, even if they are nominally unchanged in each country's currency. All things being equal, a stronger Swedish crown means that Swedish prices appear to be higher compared with if the crown has been weak.

This report consistently uses the average exchange rate for the first quarter of 2016 in its analyses. This also applies to index data reported for 2014 and 2015. The only

exception is in section 6, which shows the results of the sensitivity analysis to illustrate the effect of not keeping exchange rates constant.

Average exchange rates for the Swiss franc (CHF), Danish crown (DKK), euro (EUR), British pound (GBP), Norwegian crown (NOK), Czech korunas (CZK), Hungarian forint (HUF), Polish zloty (PLN) and US dollar (US \$) relative to the Swedish crown (SEK) 2013-2016 are illustrated in the following table.

Table 2. Average exchange rates and relative change against SEK.

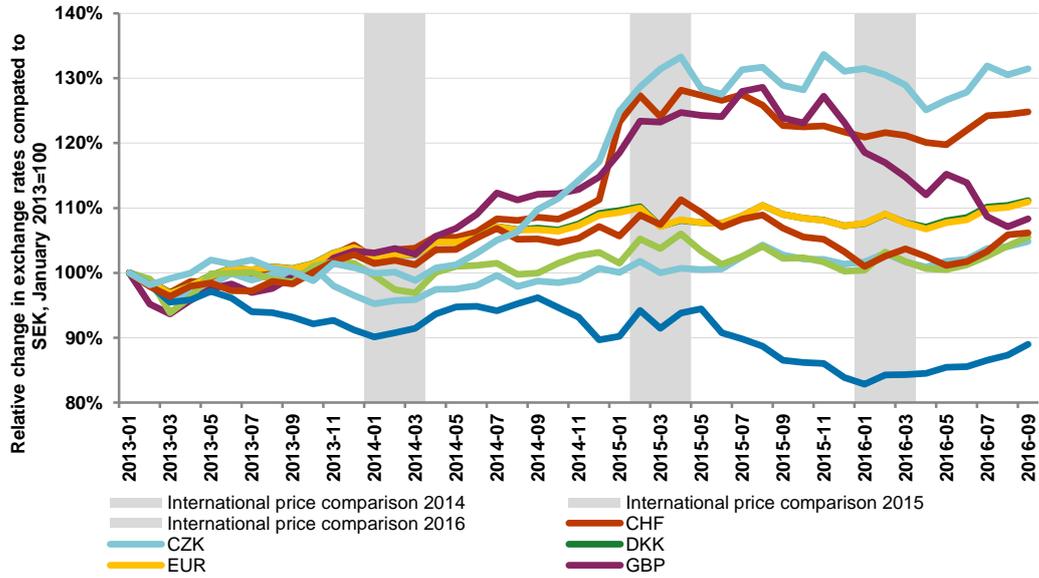
	Average exchange rate Q 1 2014	Average exchange rate Q 1 2015	Average exchange rate Q 1 2016	Relative change, Q 1 2015 – Q 1 2014	Relative change, Q 2016 – Q 2015
SEK	1	1	1	0%	0%
EUR	8.86	9.39	9.33	6%	-1%
CZK	0.32	0.34	0.35	5%	2%
DKK	1.19	1.26	1.25	6%	-1%
GBP	10.70	12.63	12.11	18%	-4%
HUF	0.03	0.03	0.03	6%	-2%
NOK	1.06	1.08	0.98	1%	-9%
PLN	2.12	2.24	2.14	6%	-5%
CHF	7.24	8.76	8.52	21%	-3%

Note: Higher numbers and a positive change mean that the Swedish currency has weakened more against local currencies.

Source: Swedish Central Bank, NASDAQ OMX Stockholm AB and TLV analyses.

The relative changes in exchange rates against the Swedish crown for the period 2013-2016 is illustrated in the following figure. The period has at times been characterized by large fluctuations in the foreign exchange market. The Swiss franc, British pound and US dollar rose sharply against the Swedish crown at the end of 2014. At the same time as the British pound fell back in 2016, the US dollar and Swiss franc remained at a high level against the Swedish crown. The Euro and currencies pegged against the Euro (e.g. DKK) show relatively little change. The Norwegian crown has tended to weaken against the Swedish crown during the period 2013-2016, but shows a slight recovery during in 2016.

Figure 1. Relative change in exchange rates against the Swedish crown during the period January 2013 - September 2016 per month. 100 = January 2013



Note: Broken axis. The shaded areas illustrate the time periods examined in the previous international price comparisons (TLV 2014 and TLV 2015) and the period that is the subject of this study. Since quarterly data are the subject of the analyses, the average exchange rate for the period January-March is used for the relevant currencies.

Source: Swedish Central Bank, NASDAQ OMX Stockholm AB and TLV analyses.

3 The pharmaceuticals market

3.1 Market overview

The purpose of the sections on market overview, pricing models and facts about the countries in the study (Appendices 2, 3 and 4) is to provide a background to the context in which the results of the international comparison of prices for medicines should be seen. Some of the countries in the study have major similarities in their healthcare systems and systems for pricing of pharmaceuticals, while others are more diverse. This may relate to transparency regarding list prices and whether or not rebate systems are institutionalized and included in pharmacy purchase prices, or whether other agreements mean that certain official list prices do not fully reflect the actual price of a pharmaceutical.

Comparisons using data solely for outpatient care should be made with caution. For example, Denmark and Norway handle some pharmaceuticals for autoimmune diseases (e.g. TNF-alpha inhibitors) largely in inpatient care, whereas in Sweden they are largely managed in outpatient care. Just how one chooses to handle pharmaceuticals – by prescription in outpatient settings or in hospital via inpatient care – means that it is difficult to draw far-reaching conclusions from this type of comparison without knowledge of the specific national circumstances for how pharmaceuticals are handled.

Pharmaceuticals have annual global sales of around 6701 billion SEK calculated as the price from the factory.¹² North America dominates and represents about 49 percent of the world market. Europe in its broadest sense constitutes about 22 percent.¹³ Africa, Asia and Australia make up just under 17 percent, Japan represents about eight percent of the world market and Latin America just over four percent.

Overall, for the 20 countries in the study, the total sales amount to 1047 billion SEK at AIP level according to IMS Health (996 billion SEK for 2015). Together, the countries make up an estimated 66 percent of the European market in a broad sense¹⁴ and just under 15 percent of the world market, as measured at AIP level.¹⁵

Sales of pharmaceuticals included in the analysis amount to 659 billion SEK, which represents 63 percent of the total sales in outpatient settings for the countries in the sample. The corresponding figure for 2015 is 638 billion (64 percent). According to IMS Health, the explanation for the difference compared to total sales is the limitation that in order to be included in the analysis, the product needs to demonstrate registered sales in the Swedish market, not just in another country.

¹² This means that transport costs from the factory, and other taxes and surcharges may be added. EFPIA states \$ 794,393 billion for 2015. Calculation to SEK at average exchange rate (8,435) according to Sweden's central bank.

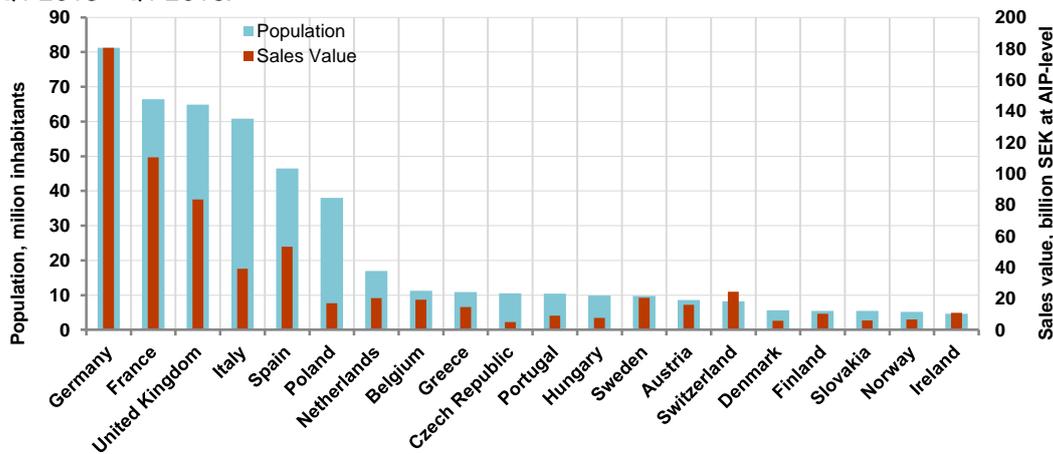
¹³ EFPIA (2016).

¹⁴ Europe in a wider sense also includes Turkey, Russia and Ukraine, as defined on p. 15 of EFPIA (2016).

¹⁵ For the calculation, a distribution margin of 7 percent has been adopted as a flat rate between ex factory and AIP. In other words, the total market is estimated at 7170 billion SEK.

The combined population of the 20 countries in the study amounts to approximately 480 million inhabitants. The five largest countries in terms of population (Germany, France, United Kingdom, Italy and Spain) together account for nearly 67 percent of the population base. At the same time, these five countries account for about 70 percent of the 20 countries' total sales in the analysis at AIP level. Sweden's share of the population is two percent and its share of total sales is just over three percent.

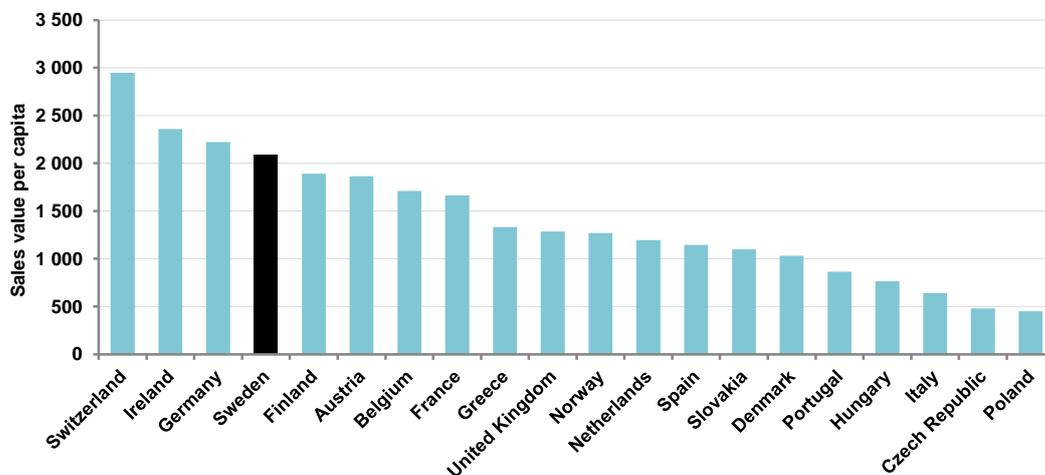
Figure 2. Population by country and sales value within outpatient care, AIP, for the period Q1 2015 - Q1 2016.



Source: IMS Health and TLV analyses.

The following figure illustrates sales value per person in Europe. The average sales per capita is approximately 1 400 SEK. Sweden has the fourth highest sales value in outpatient care per resident. Norway has the eleventh and Denmark, the fifteenth. The fact that Denmark is so far down is explained by the fact that in Denmark, a larger portion of expensive pharmaceuticals is handled within the framework of inpatient care compared with other countries.

Figure 3. Sales value in outpatient care per resident, AIP, for the period Q1 2015 - Q1 2016.



Source: IMS Health and TLV analyses.

4 Results: pharmaceuticals without competition

This section describes Swedish prices for the segment pharmaceuticals not exposed to competition and not included in the product-of-the-month system. Since 2014, Swedish prices declined relative to other countries. Between 2014 and 2015, Swedish relative prices were lowered through reassessments. The change between 2015 and 2016 is small; Swedish prices have been marginally lower compared with other countries. In 2015 and 2016, Sweden is found to be among the eight countries with the highest prices of the 20 countries compared. Calculated as a cross-sectional index, the 2016 price index is just under 100. On average, therefore, Swedish prices are in line with prices in other countries. The exchange rate is held constant to the average first quarter in 2016 in all of the analyses.

4.1 Description of pharmaceuticals without competition

This section describes pharmaceuticals not exposed to competition and not included in the product-of-the-month system. It includes both patented pharmaceuticals as well as pharmaceuticals that are not patented but where competition has not emerged. This segment includes recently launched and often the most costly pharmaceuticals. The cost of the pharmaceuticals in this segment included in the price comparison amounts to approximately 16.6 MSEK at an annual rate, up to and including Q1, 2016.

4.1.1 Top ten substances without competition

This section describes how the products available in Sweden are used in the other countries in the survey. All analyses are based on products available in Sweden. Products used in another country but not used in Sweden within a certain field are not included in the analysis.

The table below shows the top ten substances in this segment as used abroad (i.e. in the countries that are not Sweden). The substances represent about 25 percent of total sales both abroad and in Sweden. The list consists largely of TNF-alpha inhibitors (L04A) and agents for treating respiratory diseases (R03).

Table 3. The top ten substances for pharmaceuticals without competition with the highest volume of sales abroad. Moving annual total March 2016.

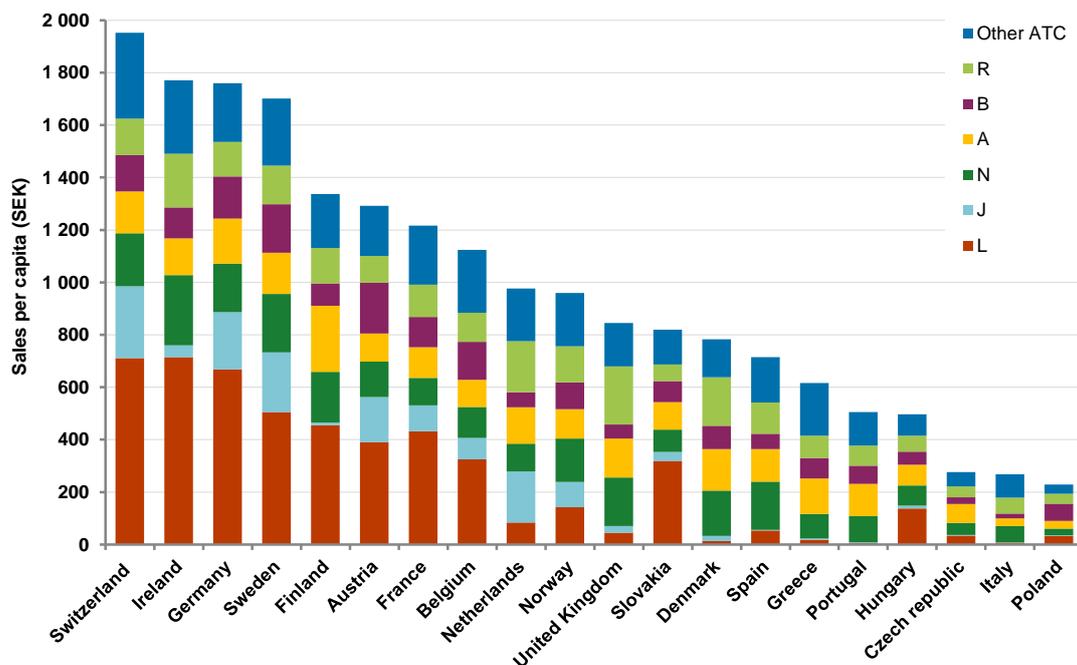
ATC4	Substance	Share of sales value abroad	Share of sales volume abroad	Share of sales value Sweden	Share of sales volume Sweden
L04A	Adalimumab	3.8%	0.0%	6.2%	0.0%
R03A	Salmeterol, flutikason	3.3%	4.5%	0.7%	1.2%
B01A	Rivaroxaban	3.1%	0.6%	1.1%	0.3%
N03A	Pregabalin	2.7%	2.3%	1.5%	1.6%
R03B	Tiotropium	2.4%	1.6%	1.7%	1.4%
R03A	Budesonid, formoterol	2.3%	3.6%	2.8%	5.6%
L04A	Etanercept	2.0%	0.0%	4.7%	0.0%
A10A	Insulin, glargin	2.1%	0.4%	1.3%	0.3%
J05A	Sofosbuvir, ledipasvir	1.8%	0.0%	3.8%	0.0%
C10A	Rosuvastatin	1.3%	1.2%	0.7%	0.6%
Total		24.9%	14.1%	24.6%	11.0%

Source: IMS Health and TLV analyses.

4.1.2 Differences in how pharmaceuticals are handled

The handling of new and or costly pharmaceuticals varies between countries. Swedish management is mainly characterized in that medicines suitable to be handled by the individual are prescribed by prescription in outpatient care – no matter how expensive the medicine is. In other countries, this varies. Several have chosen to deal with costly pharmaceuticals in inpatient care associated with a hospital. Reasons for this may be that they gain better management and control of the pharmaceutical's use. It may also be easier and less costly to procure the pharmaceuticals through hospitals.

Figure 4. Sales per capita for pharmaceuticals without competition grouped on ATC1 level and country for pharmaceuticals sold in Sweden. Moving annual total March 2016.



Note: See Terms and concepts for an analysis of the ATC system's 14 main groups.

Source: IMS Health and TLV analyses.

ATC L covers costly cancer pharmaceuticals and TNF-alpha inhibitors, especially against rheumatism. The low sales in countries like the UK, Norway, Denmark and the Netherlands suggest a more comprehensive inpatient management of this type of medicine.

Differences in sales may indicate variations in how pharmaceuticals are used in outpatient care. Four countries (Switzerland, Ireland, Germany and Sweden) distinguish themselves from other countries with relatively high sales. Costs in these countries are between 1700 and 2000 SEK per inhabitant. In these countries, the handling of the more expensive pharmaceuticals, just as in Sweden, tends to take place in an outpatient setting. Finland is the Nordic neighbour where sales of the analysed pharmaceuticals are most in line with Sweden. Sales in Finland are approximately 1300 SEK per inhabitant, compared with 1700 SEK in Sweden. In Norway, sales are nearly 1000 SEK per inhabitant and in Denmark just under 800 SEK.

It is the mix of the sold pharmaceuticals available in each respective country and that matches those found in Sweden that is used in the bilateral price comparison. In the comparison with Danish prices, the inclusion of medicines in ATC groups J (Infectious Diseases) and L (Tumours and immune system disorders) is thus very limited.

4.1.3 Degree of matching

The degree of matching shows the proportion of Swedish products that have sales in another country. Sweden has a total of 1437 products from the sample for this segment. In the table below, the degree of matching is divided on ATC-1 level. A blue shade in the table indicates a high degree of matching while red shows a low degree. On average, 47 percent of Swedish products are found in other countries. The degree of matching remained at this level also in 2014 and 2015.

The degree of matching ranges from 69 percent of the products in Germany to 32 percent of the products in Portugal. A low degree of matching may indicate that the pharmaceutical is more widely handled in inpatient care than in outpatient care, which is what this analysis measures. Differences may also be due to other countries using substances or forms that do not match Swedish products. In some countries, certain substances are not used at all.

ATC group J is the group where the degree of matching is lowest. On average, 36 percent of products in Sweden are found in other countries. Within ATC groups R (Respiratory) and A (Alimentary tract and metabolism), the degree of matching is at the most 56 percent and 55 percent respectively.

Table 4. The degree of matching for pharmaceuticals without competition, Q1 2016 (the higher the degree of matching, the more blue; the lower the degree of matching, the more red)

	A	B	J	L	N	R	Other. ATC	Mean
Sweden	100	100	100	100	100	100	100	100
Germany	73	68	66	89	65	64	65	69
UK	77	46	62	35	63	63	61	58
Austria	66	60	60	77	58	52	47	58
Finland	65	61	26	57	61	67	53	56
Netherlands	76	58	64	37	60	67	49	55
Switzerland	57	48	54	69	54	55	50	55
Ireland	58	47	32	61	52	59	53	52
Norway	65	49	37	15	58	73	59	51
Denmark	62	28	25	30	65	69	51	50
France	38	47	50	69	46	53	43	49
Belgium	52	22	50	36	41	46	43	42
Slovakia	53	36	31	57	38	55	33	41
Spain	47	18	17	25	52	57	41	39
Italy	43	44	14	22	45	53	43	39
Czech Rep.	50	31	17	38	41	52	33	37
Hungary	39	29	25	46	31	46	35	35
Greece	52	30	18	21	38	44	36	34
Poland	37	24	18	24	38	51	37	34
Portugal	42	16	11	12	43	47	38	32
Mean	55	40	36	43	50	56	46	47

Note: See Terms and concepts for an analysis of the ATC system's 14 main groups.
Source: IMS Health and TLV analyses.

Germany is the country where the degree of matching is highest, just under 70 per cent. This is followed by five countries with degrees of matching of approximately 55 percent (UK, Austria, Finland, the Netherlands and Switzerland). Our other Nordic neighbours (Norway and Denmark) have degrees of matching of around 50 percent. The lowest degrees of matching are against countries such as Greece, Poland and Portugal. This pattern has been stable since 2014.

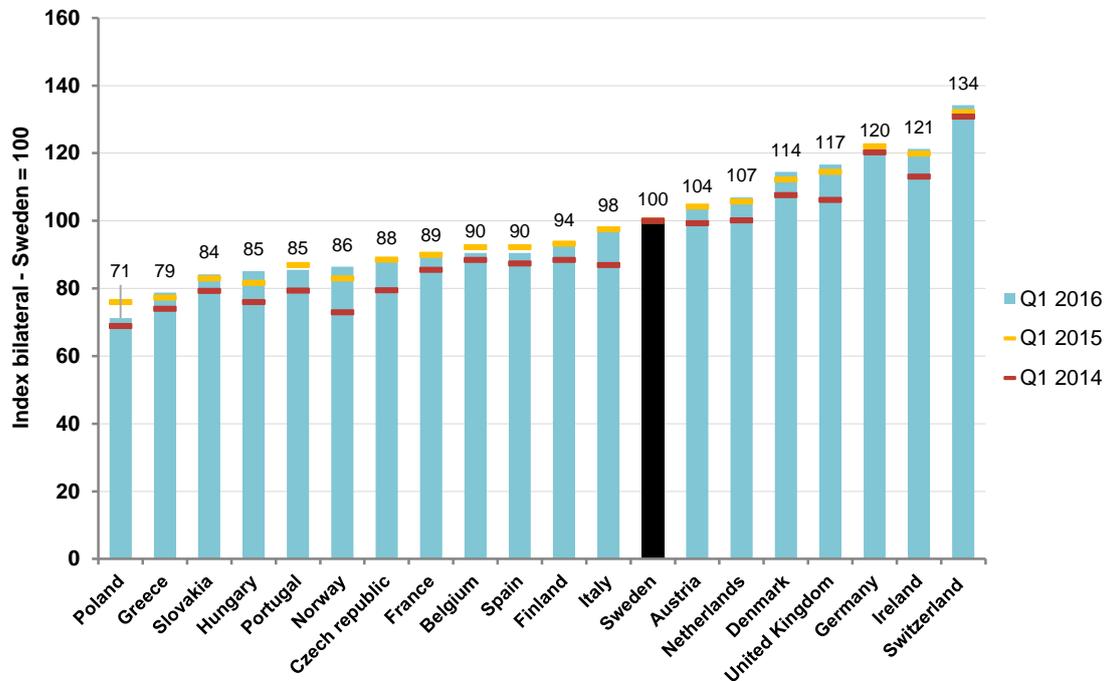
4.2 Small price changes during 2016

Compared to 2015, 2016 saw relatively small changes in list prices. Figure 5 shows that in 2016, as in 2015, the bilateral price index is almost the same compared with other countries. Sweden is among the eight countries with the highest rates in the pharmaceuticals without competition segment. As usual, prices are highest in Switzerland followed by Ireland and Germany.¹⁶ List prices in Denmark are around 14 index points higher than in Sweden for comparable pharmaceuticals. Swedish prices are roughly on par with Austria and Italy.

¹⁶ In Germany there are regular discounts of seven percent, KBV (2016) Verordnungssteuerung, Rabatte und Rabattverträge.

Twelve countries have prices lower than Sweden. Of our other Nordic countries, prices in Finland are the equivalent of six index points lower and Norway they are 14 index points lower.

Figure 5. Bilateral price index for pharmaceuticals without competition, Sweden = 100.



Source: IMS Health and TLV analyses.

Between 2014 and 2015, Swedish prices relative to other countries were reduced, largely due to reassessments of blockbuster products. In 2016, no similar comprehensive reassessments were undertaken. Despite this, the price index against other countries remains stable; the variation is generally +/- 2 index points between 2015 and 2016. In terms of the cross-sectional index, the average price index is just under 100 for Q1 2016. This means that the Swedish prices are in line with the average for the other countries in this analysis.

4.2.1 Substances affecting the index the most

Table 5 lists the ten substances that lower the cross-sectional index the most, namely those that have relatively low prices in other countries compared with Sweden. They are ranked by how much these pharmaceuticals cost in Sweden compared with if other countries' average prices would have been used. These do not necessarily have a very low index; it is the index combined with the magnitude of sales in Sweden that leads to the effect. All comparisons are at list price level and does not take any deviations (e.g. discounts or any manage entry agreements) from list price into account for any country.

Four substances in ATC group N (Nervous system) are found in this list, of which three are near the top. The pharmaceuticals with the highest cost difference are from the fields of analgesics (NO3AX) and psychoanaleptics (NO6BA). The index of the substances on this list is relatively stable in 2016 compared to 2015. However,

the newcomer Pregabalin (Lyrica) occupies the top position. The patent on Lyrica expired in early 2016 and as a result, prices declined in several other countries more than in Sweden and the index fell from 100 for Q1 2015 to 83 for Q1 2016.

Adalimumab (Humira) has previously had the biggest impact on the index, but has now fallen to a middle position following a reassessment in early 2016. Humira and golimumab (Simponi) are two TNF-alpha inhibitors on the list. Etanercept (Enbrel) has also previously occupied a top position but dropped down due to a price cut following reassessment in early in 2016.

Table 5. The ten substances for pharmaceuticals without competition that increased the cross-sectional index the most ranked by highest average highest cost difference in Sweden compared with abroad, Q1 2016.

Substance	ATC5	Cross-sectional index 2016 (2015 prices)	Average cost difference Sweden - abroad, MSEK	No. countries with lower price	No. countries with sales
Pregabalin (Lyrica)	N03AX	83 (100)	42	16	20
Metylfenidat (Ritalin)	N06BA	81 (81)	38	14	17
Levetiracetam (Keppra)	N03AX	67 (69)	33	16	20
Golimumab (Simponi)	L04AB	90 (89)	32	12	14
Takrolimus (Prograf)	L04AD	84 (85)	29	15	20
Adalimumab (Humira)	L04AB	98 (95)	21	10	14
Tiotropium (Spiriva)	R03BB	93 (94)	20	12	19
Liraglutid (Victoza)	A10BX	92 (94)	14	15	19
Insulin, Glargin (Lantus)	A10AE	95 (97)	12	13	20
Risperidon (Risperdal)	N05AX	80 (79)	11	15	19
Total		91 (92)	252	14	18

**Higher cost in Sweden compared with abroad, annual rate Q1, 2016.*

Note. The international names with the most sales are given in parentheses after the ingredient names.

Source: IMS Health and TLV analyses.

Altogether, these pharmaceuticals cost on average about 252 MSEK more in Sweden than in other countries.

Table 6 lists the ten substances where the costs are on average lowest in Sweden compared with other countries. This list is rather more heterogeneous than the list of pharmaceuticals with the highest prices in Sweden. Overall, these ten substances are approximately 230 SEK cheaper with Swedish prices compared to foreign prices.

Table 6. The ten substances for pharmaceuticals without competition that increased the cross-sectional index the most ranked by lowest average cost in Sweden compared with abroad, Q1 2016.

Substance	ATC5	Cross-sectional index 2016 (2015 prices)	Average cost difference Sweden - abroad, MSEK	No. countries with higher price	No. countries with sales
Budesonid (Pulmicort)	R03BA	124 (97)	-40	13	19
Gabapentin (Gabapentin Aler)	N03AX	139 (120)	-30	7	20
Darbepoetin Alfa (Aranesp)	B03XA	139 (147)	-26	1	17
Interferon Beta-1A (Avonex)	L03AB	125 (132)	-24	1	16
Insulin, Aspart (Novorapid)	A10AB	113 (113)	-22	6	20
Sofosbuvir (Sovaldi)	J05AX	104 (105)	-19	1	8
Insulin, Human, Isofan	A10AC	117 (118)	-19	5	20
Mykofenolat (Cellcept)	L04AA	138 (136)	-19	6	19
Dalteparin (Fragmin)	B01AB	111 (108)	-16	5	13
Enzalutamid (Xtandi)	L02BB	111 (82)	-16	1	14
Total		115 (111)	-231	14	41

*Higher cost in Sweden compared with abroad, annual rate Q1, 2016.

Note. The international names with the most sales are given in parentheses after the ingredient names.

Source: IMS Health and TLV analyses.

The substance with the lowest cost compared to if prices in other countries were used is budesonide (Pulmicort). The cost is about 40 million SEK lower with Swedish prices from Q1 2016 compared with the average in other countries. Budesonide is new to the list and has index 124 measured in 2016 prices (Q1) compared with index 97 calculated with 2015 prices (Q1).

The list price on Sofosbuvir (Sovaldi), which is a very costly pharmaceutical against hepatitis C, is relatively low in Sweden and only one of eight countries that use Sovaldi in outpatient care has a lower price than Sweden. The same applies for enzalutamid (Xtandi), which is a costly prostate cancer pharmaceutical. In other countries, this type of expensive pharmaceutical has a tendency to be purchased in inpatient care, or via different types of rebate agreement that mean lower actual prices compared to list prices. Sweden has an agreement on risk sharing as well as rebates between county councils and companies for these pharmaceuticals.

4.3 Changes between periods

The average cross-sectional index in 2016 is just under 100, i.e. prices of pharmaceuticals without competition are on average about as high abroad as in Sweden. The difference from 2015 is marginal. The price effect when maintaining a constant volume shows slightly lower relative prices in Sweden, i.e. foreign prices have been slightly higher between 2015 and 2016 (0.4 index points).

Table 7. Cross-sectional indices 2014-2016 for pharmaceuticals without competition and changes in constant prices and volumes.

	Q1 2014	Q1 2015	Q1 2016	Difference 2014 / 2015	Difference 2014 / 2015
Cross-sectional index	95.0	99.3	99.6	4.3	0.3
With constant volumes *	95.1	99.4	99.8	4.3	0.4
With constant prices *	99.9	99.9	99.8	0.0	-0.1
Effect of changes in assortment *				0.0	0.0

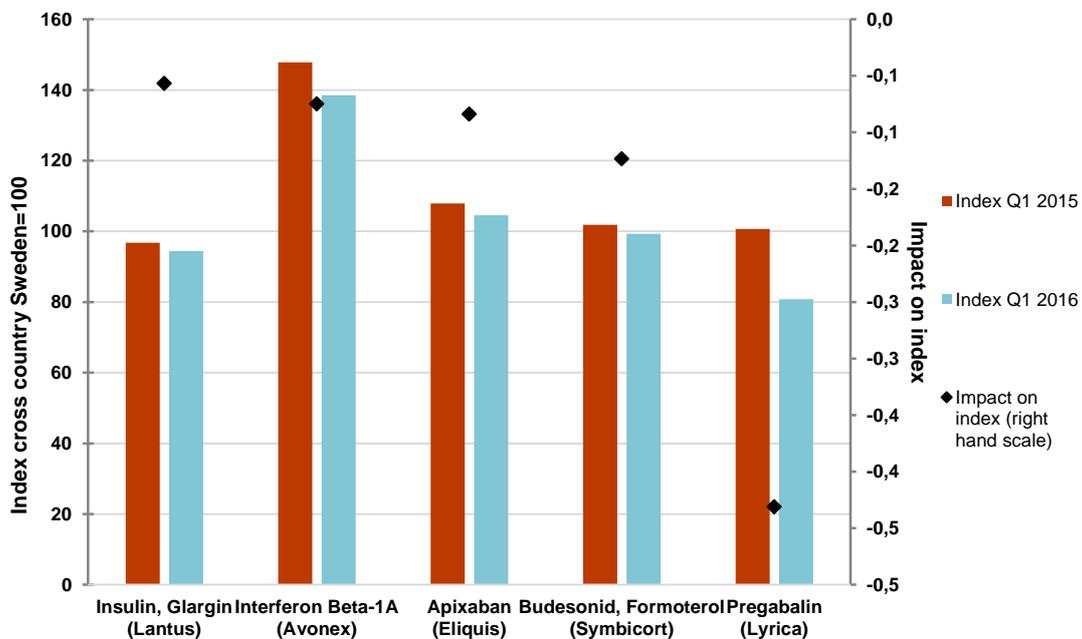
*These calculations include only products found in all periods

Source: IMS Health and TLV analyses.

The relatively large change between 2014 and 2015, where foreign prices increased by about four index points, was due to reassessments that lowered the prices of Swedish blockbuster pharmaceuticals. The pharmaceutical that most contributed to this change was budesonide, formoterol (Symbicort).

Figure 6 shows the five substances where foreign prices have fallen most compared to Swedish between the first quarters of 2015 and 2016. The impact on the index is quite small but the price of pregabalin (Lyrica), used against anxiety, has fallen from about 100 to just over 80 between the first quarters of 2015 and 2016. This change lowers the overall index by 0.5 index points. The patent on pregabalin expired at the beginning of the year. In Sweden, pregabalin is not substitutable and its price has not fallen to the same extent as in other countries. Otherwise, the changes are small.

Figure 6. The five substances for pharmaceuticals without competition where foreign prices declined the most relative to Swedish prices.

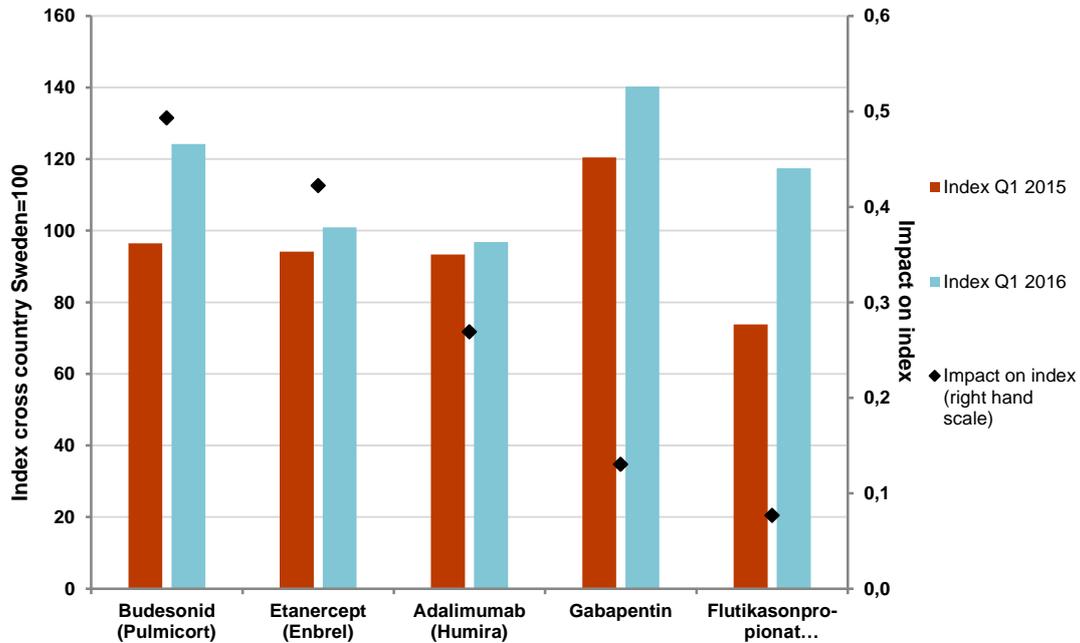


Source: IMS Health and TLV analyses.

Figure 7 shows the five substances where Swedish prices declined the most relative to those abroad. Respiratory disease is the area in which the Swedish relative prices

fell. This area was reassessed partly in late 2014 regarding Symbicort (budesonide, formoterol) and in April regarding budesonide (Pulmicort) and fluticasone propionate (Flixotide). Due to this reassessment, the index increased by 0.6 index points in Q1 2016 compared with Q1 2015.

Figure 7. The five substances for pharmaceuticals without competition where Swedish prices decreased the most relative to foreign prices.

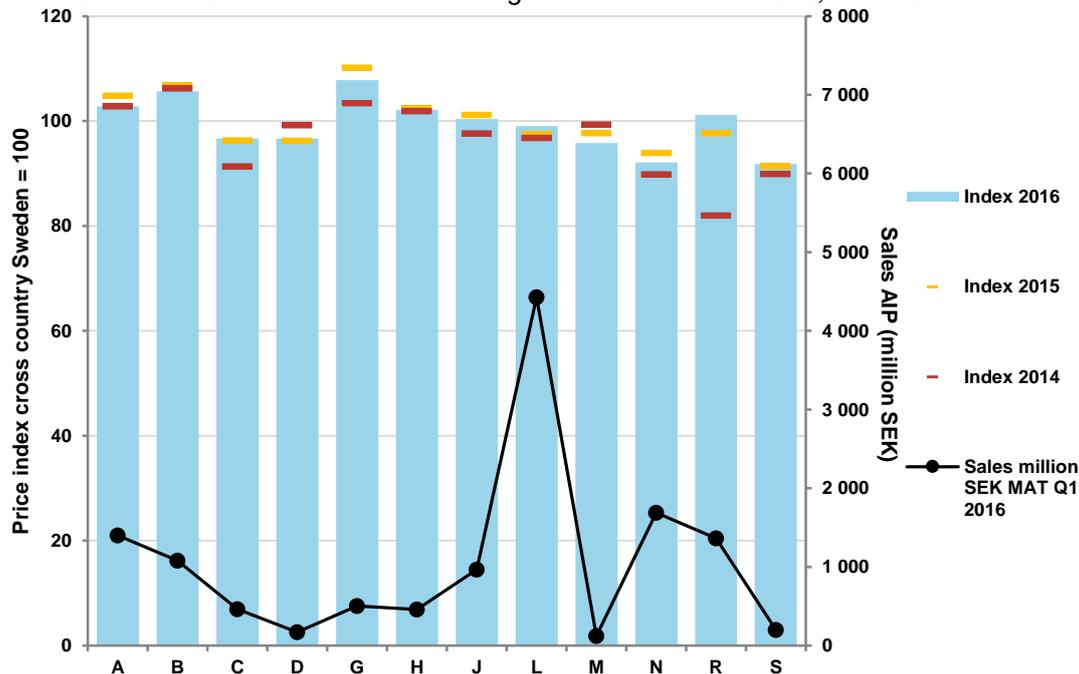


Source: IMS Health and TLV analyses.

4.3.1 Price indices in different ATC-1 groups

Over the ATC group at level one, the index varies between 92 and 108. In many of the groups, the index is around 100, i.e. in line with prices in other countries. In ATC group N (the nervous system), where sales are high in Sweden, prices are lower in other countries. The index of ATC group N is 92, i.e. eight index points lower than prices in Sweden. One reason for this is that four of the ten substances with the highest prices are found in ATC group N (see Table 5).

Figure 8. Cross-sectional index for pharmaceuticals without competition for the ATC-1 group from 2014 to 2016 and annual sales moving annual total March 2016, AIP MSEK.



Note: See Terms and concepts for an analysis of the ATC system's 14 main groups.
Source: IMS Health and TLV analyses.

The biggest sales are in ATC group L (Tumours and immune system disorders), where the index of 99 is just below the average in other countries. The index has changed from 97 in 2014 to 99 in 2016. This increase is due to reassessments, mainly in the field of TNF-alpha inhibitors in early 2016, which lowered relative prices in Sweden.

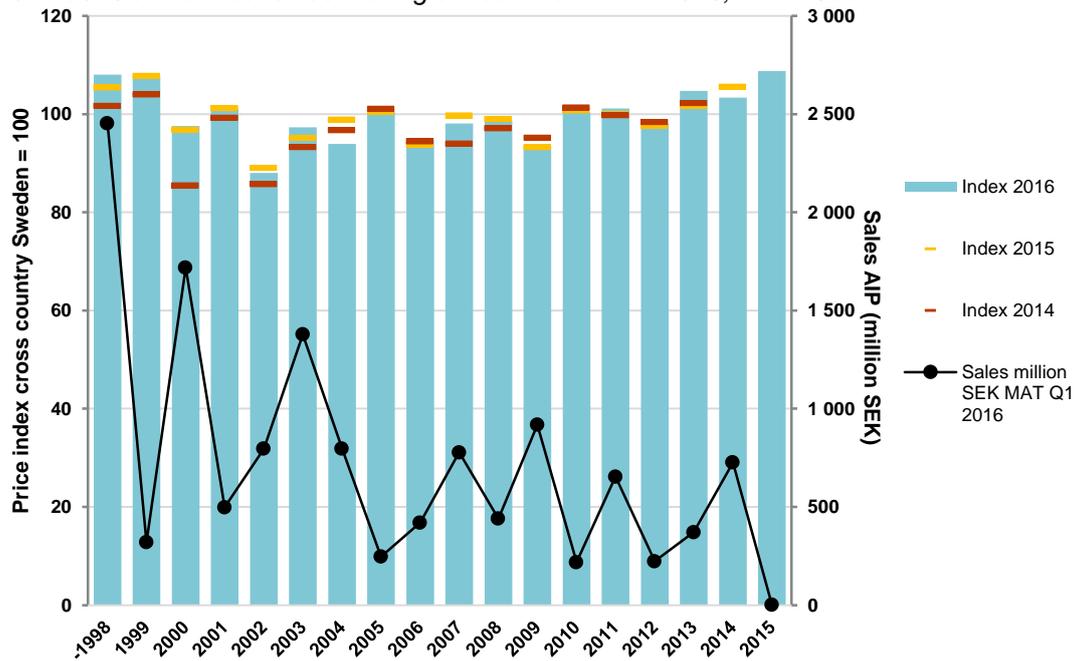
4.4 Price differences according to launch year

The average cross-sectional indices per year of launch in the benefits scheme calculated as a cross-sectional index are shown below. The prices for pharmaceuticals introduced up to and including 1999 are relatively low in Sweden, with an index of about 110. Interventions such as the 15-year rule¹⁷ and reassessments have lowered Swedish prices relative to other countries over time. Prior to 2014, the prices of older pharmaceuticals were relatively high in Sweden.

The largest increase in the index can be found for pharmaceuticals launched in 2000. Pharmaceuticals launched in 2000 have large sales (about 1.7 billion SEK), which means that this year has a great impact on the overall index. The index is about 98 in Q1 2016 compared with 85 in Q1 2014. The reassessment and price reduction of the big seller Symbicort primarily explains this change.

¹⁷ The 15-year rule means that drugs that become 15-years old routinely have their price lowered by 7.5 percent.

Figure 9. Cross-sectional index for pharmaceuticals without competition by launch year* 2014-2016 and annual sales moving annual total March 2016, AIP MSEK



* Launch year is defined as the earliest year for the substance and dosage form.
Source: IMS Health and TLV analyses.

The prices for pharmaceuticals introduced during 2002 are low in other countries compared to Sweden; the index is around 12 points below Swedish prices. The main reason is methylphenidate (Ritalin), which occupies second place among the substances that have the highest prices in Sweden compared with other countries (Table 5). Even the asthma pharmaceutical tiotropium (Spiriva), also a big seller, has a relatively high price in Sweden and thus affects the index for the launch year 2002.

The index of products launched during 2004 has fallen from 96 during 2015 to 94 in 2016. The main reason is that pregabalin (Lyrica) has, as previously mentioned, become relatively cheaper in other countries following its patent expiry compared to Sweden.

Products launched during 2009 that also have high sales have relatively lower prices in other countries. It is mainly the TNF-alfa inhibitors Simponi and Cimzia that weigh heavily for this particular year.

The price index of recently launched pharmaceuticals is in most cases over 100, i.e. prices in Sweden are lower than the average in other countries. Sales values are relatively low, despite expensive blockbuster pharmaceuticals against hepatitis C being introduced during this period. Few countries employ these pharmaceuticals in outpatient care and only Sovaldi (launched 2014) has been captured in the cross-sectional index.

5 Results: pharmaceuticals exposed to competition (within the product-of-the month-system)

The pharmaceutical segment 'exposed to competition' (with competition) includes all pharmaceutical groups in the selection included in the product-of-the-month list in March 2016. In total, this segment accounts for sales in Sweden of around 3.8 billion SEK (AIP moving annual total March 2016). This represents 19 percent of sales in the selection. In this segment, Sweden is one of three countries with the lowest prices in the selection. Between 2014 and 2015, the difference in price between the countries fell somewhat. Between 2015 and 2016, however, it increased again and in most countries the price differences are greater than they were in 2014. The analysis also shows that the Swedish product-of-the-month system quickly lowers prices relative to other countries. In all the analyses in this chapter, the exchange rate is held constant at the average for Q1 2016.

5.1 Description of pharmaceuticals with competition in the product-of-the-month system

This section describes how the products available in Sweden are used in the other countries included in the survey. All analyses are based on products available in Sweden. If product that is not available in Sweden is used in a certain area in another country, it will not be included in the analysis. The table below shows the top ten substances in this segment found abroad (countries that are not Sweden). The substances account for 41 percent of sales overseas. In Sweden, the proportion of sales volume for these substances is 33 percent. Sales differ somewhat between Sweden and other countries. The biggest difference is seen in the use of pantoprazole (a selective proton pump inhibitor), which is used to a greater extent outside Sweden.

Table 8. The ten substances in the product-of-the-month segment with the highest sales volume in foreign countries, AIP MSEK moving annual total March 2016.

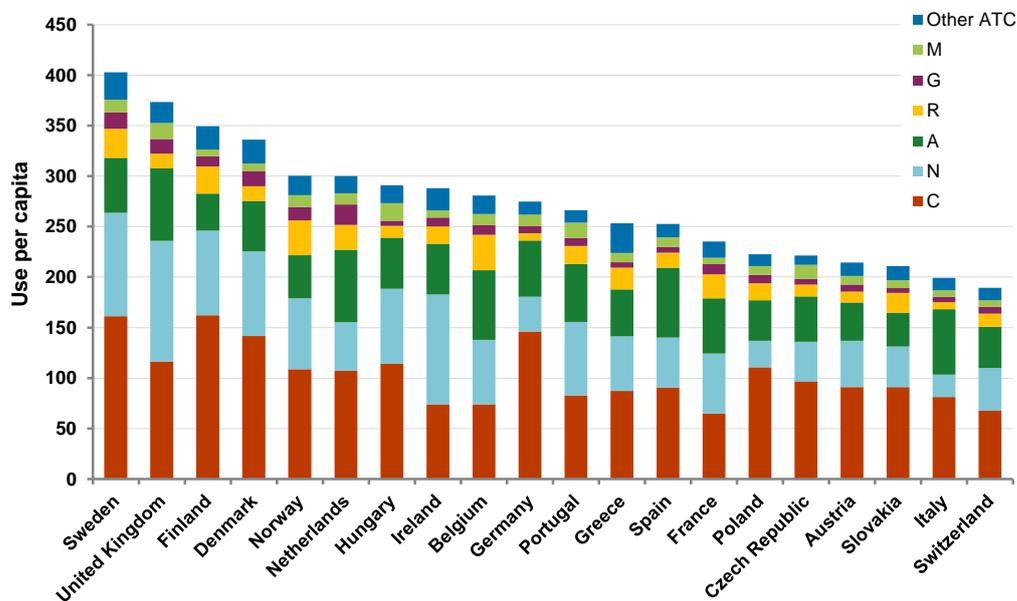
ATC4	Substance	Share of sales volume abroad	Share of sales value abroad	Share of sales volume Sweden	Share of sales value Sweden
A10B	metformin	7.4%	1.9%	6.4%	1.5%
C10A	simvastatin	4.7%	2.3%	4.7%	0.9%
A02B	omeprazol	4.7%	3.1%	3.7%	1.3%
C07A	bisoprolol	4.4%	1.8%	1.8%	0.8%
C10A	atorvastatin	4.1%	5.7%	2.0%	1.8%
A02B	pantoprazol	3.9%	4.1%	0.3%	0.1%
C08C	amlodipin	3.6%	1.2%	3.3%	0.6%
C09A	ramipril	3.4%	1.5%	1.4%	0.4%
R01A	mometasonfuroat	2.4%	0.9%	3.6%	1.7%
C07A	metoprolol	2.2%	0.8%	5.4%	3.8%
Total		40.8%	23.2%	32.6%	12.9%

Source: IMS Health and TLV analyses.

The five treatment areas (ATC-1 codes)¹⁸ that account for the largest sales in the product-of-the-month system are cardiovascular system (C), nervous system (N), alimentary tract and metabolism (A), respiratory (R), genitourinary organs and sex hormones (G) and the musculoskeletal system (M). These areas together constitute more than 90 percent of the use in almost all countries (in Greece they constitute 88 per cent).

The groups of pharmaceuticals where the Swedish usage is greatest will have the heaviest weighting when calculating the price index. The country whose consumption per capita differs most from Sweden in this segment is Switzerland, whose use is less than half of Sweden's. The countries where usage is most similar to Sweden are the UK and Finland.

Figure 10. Use per capita grouped on ATC-1 level and country for pharmaceuticals sold in Sweden, within the pv-system, moving annual total March 2016.



Note: See Terms and concepts for an analysis of the ATC system's 14 main groups.
Source: IMS Health and TLV analyses.

A large difference in use may be due to the choice of pharmaceutical for a treatment differing greatly between countries, or that a certain treatment is carried out in in-patient care in one of the countries. For those countries whose use is quite different from that in Sweden, interpreting the results of the price comparison becomes more difficult.

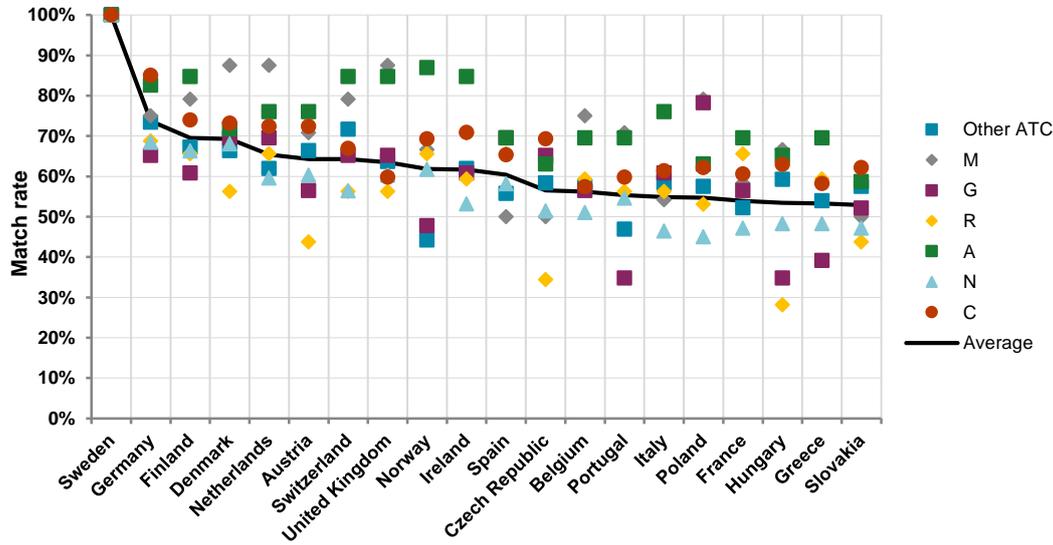
5.1.1 Degree of matching

The degree of matching shows the proportion of Swedish products that have sales in another country. In Sweden, a total of 647 products are available in the selection for this segment. In the figure below, the degree of matching is divided on ATC-1 level. The ATC group where the average degree of matching between countries is the highest is A and where it is lowest is N. The country in which the degree of matching

¹⁸ See Terms and concepts for an analysis of the ATC system's 14 main groups.

is highest is Germany, where 74 percent of Swedish products are available. Generally, the degree of matching is good for all groups. The only groups found below 40 percent are R and G, and then only in a few countries.

Figure 11. Degree of matching for pharmaceuticals with competition (within the pv-system) in percent by country, Q1 2016.



Note: See Terms and concepts for an analysis of the ATC system's 14 main groups.
Source: IMS Health and TLV analyses.

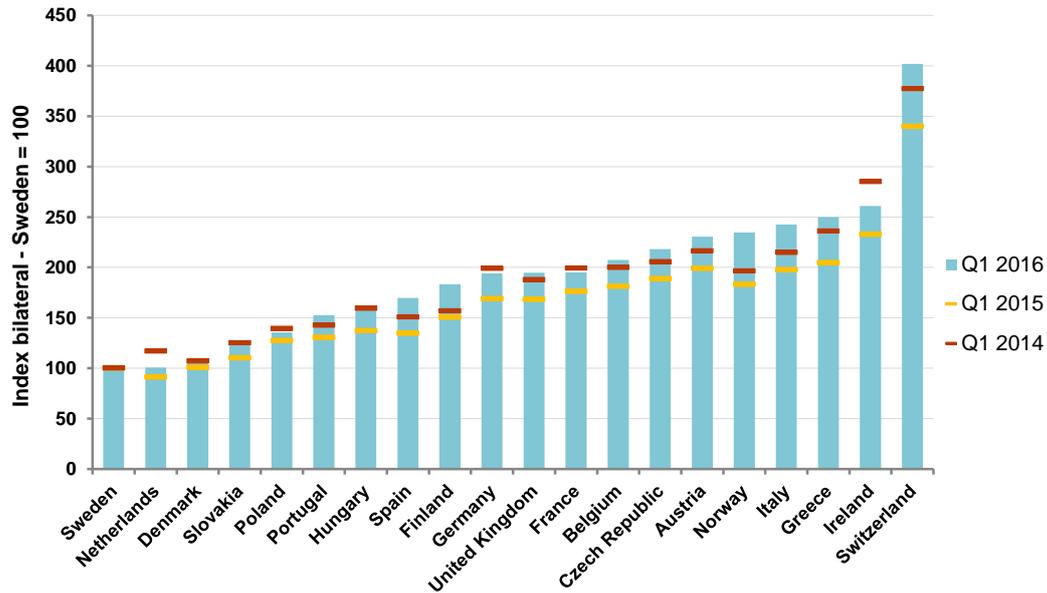
A high degree of matching and similar use of pharmaceuticals to that found in Sweden makes the price comparison more robust.

5.2 Low prices for pharmaceuticals within the product-of-the-month system

In the segment within the product-of-the-month system, Swedish prices are found to be among the three lowest. Netherlands, Sweden and Denmark form a group of countries whose prices differ from those in other countries. It is these countries that have developed a substitution system that in a clear manner steers sales to the cheapest product when opportunities for substitution exist. The differences between countries are much larger than for pharmaceuticals without competition. In Switzerland, which is the most expensive, the price for these products 302 percent higher than in Sweden.

Between the Q1 2014 and Q1 2015, the price levels of other countries was lowered in relation to Sweden. Between Q1 2015 and Q1 2016, however, Sweden's price level was lowered compared to other countries, and in over half of the countries, the level is higher than it was in Q1 2014.

Figure 12. Bilateral price index for pharmaceuticals exposed to competition available in the Swedish product-of-the-month system, Sweden = 100.



Source: IMS Health and TLV analyses.

To see which groups of pharmaceuticals explain the difference in index between the countries, the different ATC-1 level's impact on the bilateral index has been analysed. The analysis describes how the various groups contribute to a difference compared to Sweden, which has index 100. For example, in Belgium, where the index is 108 units greater than the Swedish, this depends to a large extent on C (Cardiovascular system) and N (Nervous system), which affect the Belgian index by 39 and 35 index points upwards respectively.

Table 9. Different ATC-1 groups' impact on bilateral price index in the product-of-the-month system, Q1 2016.

Country	Total difference against Sweden	A	C	G	M	N	R	Other ATC
Belgium	108	11	39	8	2	35	2	10
Denmark	9	0	7	0	1	-2	0	3
Finland	83	8	47	7	3	13	2	4
France	95	15	38	7	4	18	3	9
Greece	150	21	79	5	3	31	3	7
Ireland	161	9	63	9	2	60	5	14
Italy	143	16	47	12	3	42	10	12
Netherlands	1	-1	1	1	0	-2	1	1
Norway	135	19	61	4	3	39	4	4
Poland	36	4	19	5	1	6	1	0
Portugal	52	5	27	2	2	4	4	7
Switzerland	302	37	103	16	6	96	9	35
Slovakia	26	2	17	6	0	-1	1	-1
Spain	70	5	27	6	1	18	5	8
UK	95	6	36	3	1	40	1	7
Czech Republic	118	6	45	6	2	37	5	18
Germany	94	8	16	5	3	38	6	19
Hungary	58	14	20	5	1	13	1	3
Austria	131	19	43	4	4	40	4	17

Note: See Terms and concepts for an analysis of the ATC system's 14 main groups.

Source: IMS Health and TLV analyses.

The ATC-1 groups that best explain why pharmaceuticals with competition are cheaper in Sweden than in the other countries are C and N. For C, the index is higher in all other countries and for N, only Denmark, the Netherlands and Slovakia are cheaper. Within the groups, there may nevertheless be substances that are more expensive in Sweden.

5.3 Changes during the periods

Between Q1 2014 and Q1 2015, price differences decreased between countries for products with competition. Between 2015 and 2016, however, the differences increased again, and the average index is higher in Q1 2016 compared with Q1 2014. The table below describes how price, volume and assortment changes between periods affect the change in the index. *Constant volumes* shows the effect of a price change, *constant prices* shows the effect of a change in volume, and a *change in the assortment* shows the effect of newly-added and discontinued products.

Table 10. Cross-sectional index of the product-of-the-month Q1 2014 and Q1 2015 with constant volumes. Moving annual total March 2016 as well as fixed prices Q1, 2016.

	Q 2014	Q1 2015	Q1 2016	Difference 2014 and 2015	Difference 2015 and 2016
Cross-sectional index	174	157	181	-16	24
With constant volumes *	186	168	193	-18	25
With constant prices *	190	190	193	0	3
Effect of mix change				2	-4

* These calculations include only products found in all periods

Source: IMS Health and TLV analyses.

The effect that has the greatest impact on the index change between periods is the price effect (*with constant volumes*). This price effect will be investigated in further analyses in this chapter. This means that volumes will remain constant at the 2016 level and that only products found during all three periods are included.

Table 11 shows the price effect on the total cross-sectional index broken down by country. Between Q1 2014 and Q1 2015, Ireland, Germany and Switzerland influenced the index the most and caused the Swedish level to deteriorate relative to other countries. Between Q1 2015 and Q1 2016, it was primarily changes relative to Switzerland, Norway and Greece that strengthened Sweden against the other countries.

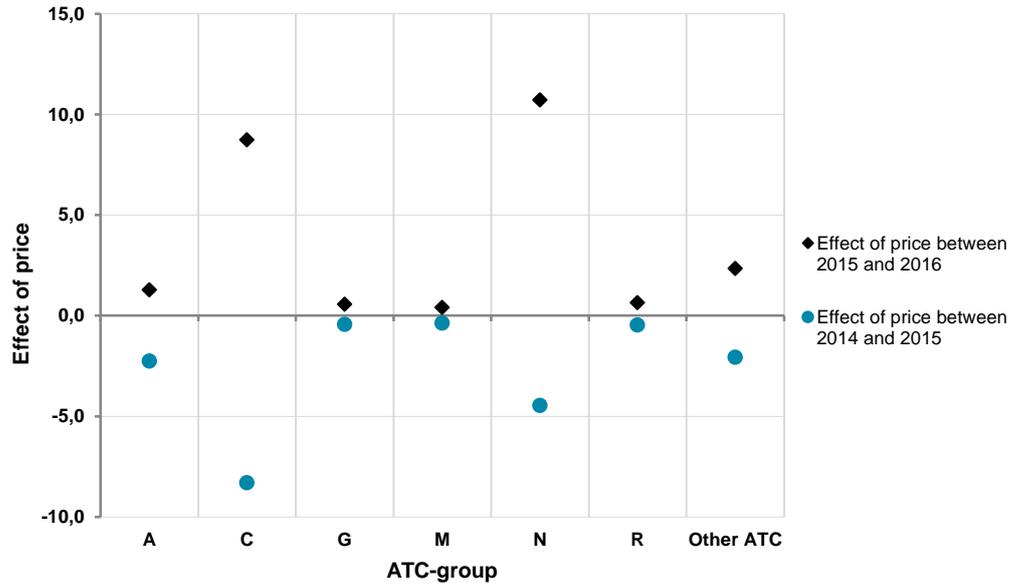
Table 11. The effect of price on the cross-sectional index in the product-of-the-month system by country between Q1 2014 and Q1 2015 and between Q1 2015 and Q1 2016.

Country	Price effect between 2014 and 2015	Price effect between 2015 and 2016
Belgium	-0.8	1.1
Denmark	-0.1	0.6
Finland	-0.3	1.8
France	-1.1	1.0
Greece	-1.3	1.8
Ireland	-2.8	1.1
Italy	-0.6	1.7
Netherlands	-1.4	0.5
Norway	-0.6	2.3
Poland	-0.5	0.4
Portugal	-0.4	0.9
Switzerland	-1.8	3.4
Slovakia	-0.7	0.6
Spain	-0.8	1.4
UK	-0.9	1.0
Czech Republic	-0.8	1.2
Germany	-1.8	1.4
Hungary	-0.6	0.8
Austria	-0.7	1.7
Total	-18.3	24.8

Source: IMS Health and TLV analyses.

When broken down by ATC-1 level, the analysis shows that the best-selling groups C (Cardiovascular system) and N (Nervous system) have the greatest impact, both upwards and downwards, between the periods. The general trend that the relative levels decreased between Q1 2014 and Q1 2015 and then increased between Q1 2015 and Q1 2016 applies to all ATC-1 groups.

Figure 13. The effect of price on the cross-sectional index in the product-of-the-month system per ATC-1 level between Q1 2014 and Q1 2015 and between Q1 2015 and Q1 2016.



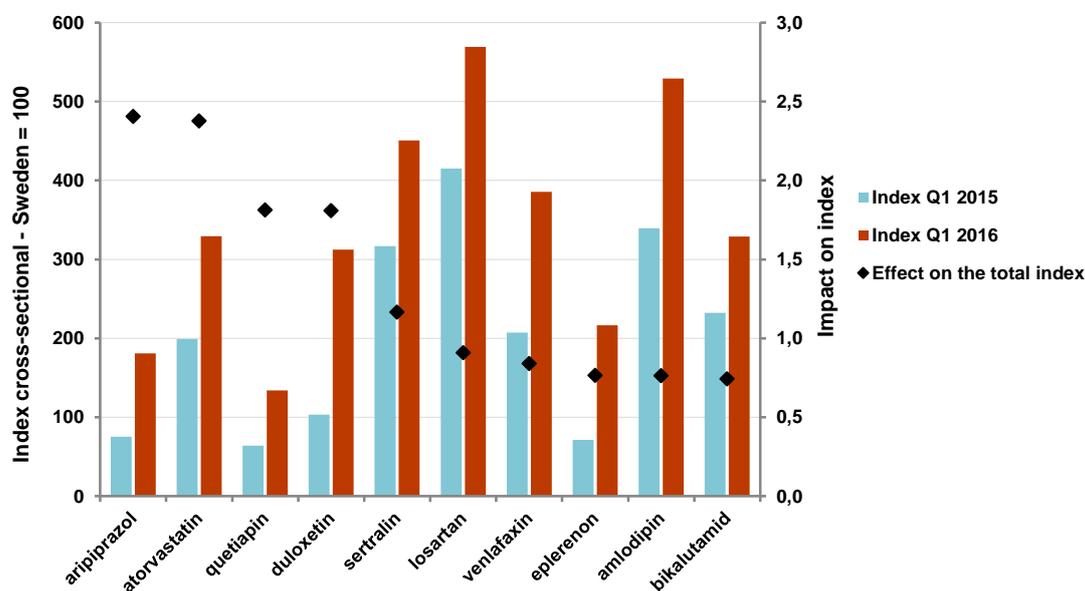
Note: See Terms and concepts for an analysis of the ATC system's 14 main groups.
Source: IMS Health and TLV analyses.

That it is the ATC groups with high sales volumes that also impacted the price effect is not surprising. For pharmaceuticals exposed to competition, the absolute difference in price between different pharmaceuticals is significantly lower than for pharmaceuticals not exposed to competition. This means that the volume of sold pharmaceuticals has a greater impact on the index.

5.3.1 The product-of-the-month system creates rapid price reductions

As shown in the paragraph above, Sweden was strengthened relative to other countries between Q1 2015 and Q1 2016. When broken down by substance, as shown in the following figure, the ten substances where the price effect is the greatest account for 13.3 index points of the total price effect of 24.8 units. The greatest effect is due to aripiprazol (anti-psychotic) followed by atorvastatin (lowers blood fat levels).

Figure 14. Cross-sectional index for the 10 substances for pharmaceuticals with competition (within the pv-system), that have had the greatest impact on the price index between Q1 2015 and Q1 2016 as well as the impact on the total index.



Source: IMS Health and TLV analyses.

For the substances aripiprazol (anti-psychotic), quetiapine (anti-psychotic), duloxetine (for depression) and eplerenone (for heart failure), Sweden has gone from being much more expensive or on par with other countries to being considerably cheaper. Common to these substances is that they have been exposed to competition in 2015. Table 12 shows that the price at the AIP level in Sweden has dropped between 64 percent and 80 percent for these four substances between Q1 2015 and Q1 2016.

Table 12. Price effect for the ten substances that have had the greatest impact on the cross-sectional index in the product-of-the-month system between Q1 2015 and Q1 2016

Substance	Price development between Q1 2015 and Q1 2016 in Sweden	Price development between Q1 2015 and Q1 2016 abroad	Effect on index	Exposed to competition in Sweden year
aripiprazol	-77%	-42%	2.4	2015
atorvastatin	-42%	1%	2.4	2012
quetiapin	-64%	-20%	1.8	2015
duloxetine	-80%	-36%	1.8	2015
sertraline	-31%	-2%	1.2	2005
losartan	-28%	-6%	0.9	2010
venlafaxin	-25%	-6%	0.8	2008
eplerenon	-73%	-18%	0.8	2015
amlodipin	-40%	-7%	0.8	2005
bikalutamid	-28%	-4%	0.7	2008
Total	-59%	-14%	13.6	

*The patent was first challenged in 2012, but following a legal dispute, generic companies were forced to withdraw their products. In 2015, the product became exposed to competition again.

Source: IMS Health and TLV analyses.

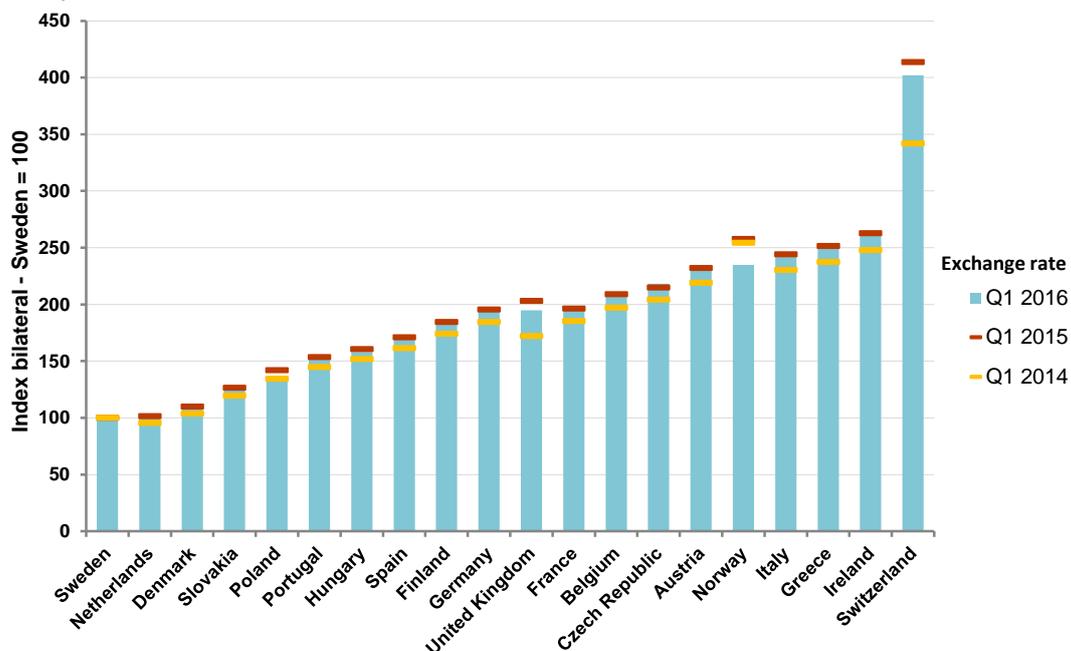
For nine substances, the price effect shown is due to the fact that the price in Sweden has fallen more relative to other countries between the periods and not that prices have increased abroad. For atorvastatin, however, the price increased abroad by one percent, while in Sweden it decreased by 42 percent.

6 Exchange rate effects

One factor that affects the relative prices over time is change in exchange rates. If the currency of a country is strengthened, prices in other countries will appear to have been reduced relative to that country, even if they are nominally unchanged in each country's currency.

The premise used in this report is the exchange rate as an average for Q1 2016 (as described in Section 2.5). To exemplify the effect that changes in exchange rates may have between the different periods, the figure below shows the bilateral index in the product-of-the-month system for Q1 2016 broken down according to the average exchange rates prevailing for Q1 2014, 2015 and 2016.

Figure 15. Bilateral index in the product-of-the-month system broken down by exchange rate, price Q1 2016



Source: IMS Health and TLV analyses.

The change in the exchange rate between the first quarter of 2015 and first quarter of 2016 has been small in most countries. The country that stands out is Norway, where its currency has fallen against the Swedish between these periods. This means that relative to Sweden, Norway appears cheaper than it would with the second period's exchange rate.

The greatest effect of exchange rates between 2014 and 2015 is seen for Switzerland and the UK. Between the periods, these countries' respective currency appreciated against the Swedish crown, which means that the relative price level increases.

7 Discussion

This report shows that prices for pharmaceuticals without competition have only changed marginally between 2015 and 2016. For pharmaceuticals with competition, however, Swedish prices have declined relative to other countries.

Only official list prices are included in this comparison because it is only these that can be collected in a simple and standardized way. Prices for procured pharmaceuticals that are not handled by prescription are not captured. Some countries also have discounts of various kinds that are not reflected in list prices. In Sweden, there are also managed entry agreements that reduce the costs of certain expensive pharmaceuticals. In some countries, and for some particular pharmaceuticals, it can therefore be difficult to make direct comparisons. A greater degree of transparency where it is at least revealed if any form of rebate agreement exists would facilitate the interpretation of price comparisons.

As mentioned above, official list prices are applied in this report, and even pharmaceutical use is taken into consideration. In essence, it is the Swedish volumes that constitute the starting point, since it is these that are relevant from a Swedish perspective. It thus follows that it is the price differences for pharmaceuticals that also have large sales that most affect the price comparison. It is important to take into account volume when price comparisons are made, otherwise large price differences for pharmaceuticals with only insignificant sales would have a disproportionate impact on the index. It should be kept in mind that only those pharmaceuticals that are available bilaterally in Sweden and in the respective comparison country that are included.

Pharmaceuticals available in a different country but handled entirely by hospitals are not included in the comparison. Comparisons can only be made against a mix of pharmaceuticals that matches bilaterally. Neither can the impact of different kinds of discount or refund agreements be captured in a price comparison. There is no transparent compilation of the occurrence of such discounts or how extensive they are. In Sweden, different types of agreements relating to risk sharing or refunds between county councils and companies do exist. It is not possible to evaluate the effect of this type of hidden pricing, but for the vast majority of pharmaceuticals, such an occurrence is probably not very extensive.

How the index develops over time relative to other countries is probably a pretty good yardstick of how dynamic and adaptable the Swedish system is. The major focus of this report is therefore to analyse differences over time.

For pharmaceuticals without competition, Swedish prices have generally fallen since 2014. To a large extent, this is due to the reassessments conducted during 2015. Between 2015 and 2016, prices for the segment without competition have been relatively stable, but they have fallen marginally in Sweden. It is noteworthy that some changes have occurred 'below the surface'. In some cases, prices in Swe-

den have not fallen to the same extent as in other countries when patents have expired, at the same time as generic competition has not arisen (pregabalin or Lyrica). In other cases, reassessments in Sweden have lowered prices more than has been the case in other countries (budesonide or Pulmicort). It is important to follow the dynamics of the system to ensure that prices in Sweden are not systematically becoming ever higher as compared to other countries.

The product-of-the-month system shows greater dynamism and it appears that the Swedish substitution system is very effective when patents expire and when competition also arises. In this context, the goal is to monitor progress over time so that this momentum can be maintained and low prices and strong competition be ensured.

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Appendix 1: Effects of changing the base country for volume weighting

Throughout this report (as described in Section 2.4), Swedish volumes are used for weighting the price baskets. The country whose volumes are used for weighting tends to strengthen its position in relation to other countries. For more discussion, see among others, Brekke and Holmås 2012.¹⁹

The fact that the country whose sales volumes are used as the base weight can appear to have a better outcome depends on the connection between use and price. If a pharmaceutical is cheaper, the use of the product often tends to be high.

This section compares the replacement of the base country for Sweden, Finland and Austria. This type of analysis with the replacement of native country to the Finnish and Austrian weights was also made in TLV's international price comparison of 2015.²⁰

Finland and Austria have been chosen for the change of base weight because the two countries demonstrated a high overall matching to Sweden, regardless segmentation. The only country that exhibited a higher overall matching was Germany. Nevertheless, Finland and Austria were chosen instead for this comparison since the list-prices in the countries more closely reflect actual prices.

Earlier in the report, the pharmaceuticals have been divided into segments based on the prerequisite for competition in Sweden.

1. Pharmaceuticals without competition
2. Pharmaceuticals with competition (in the product-of-the-month system)

Pharmaceuticals within the product-of-the-month system include all pharmaceuticals available for substitution for the period in March 2016. For the volume weight analysis, IMS Health's definition of competition is used instead. The exposed to competition segment partly includes in pharmaceuticals without competition and partly in pharmaceuticals in the product-of-the-month system (as described in section 2.1). This difference depends on how the substitutability of medicines is defined.

IMS's definition of the prerequisite for competition is in several aspects broader than that determined by the Sweden Medical Products Agency, which means that pharmaceuticals in the product-of-the-month system include fewer products than IMS's definition of exposed to competition pharmaceuticals. For this reason, IMS's broader definition of the exposed to competition segment is used in the sensitivity analysis with the replacement of the native country. The narrower Swedish perspective –

¹⁹ Brekke, K. R., och Holmås, T. H., (2012).

²⁰ TLV (2015).

pharmaceuticals in the product-of-the-month system or not – has a volume that is too small when changing to Finnish and Austrian sales volumes respectively compared to the Swedish volume that is used in the rest of the analysis.

Index and index differences presented in Appendix 1 should be viewed separately and are not directly comparable to any other indices presented in this report, because several substances change category.

Changing the base country for pharmaceuticals without competition

The following table shows the order into which countries' price indexes fall when changing base weighting from Swedish to Finnish and Austrian sales volumes.

Table 13. Rank 1-20, lowest to highest, bilateral price index with Swedish, Finnish and Austrian sales volumes and volume weightings Q1 2016 for the segment pharmaceuticals without competition.

Country	Swedish weight	Finnish weight	Austrian weight
Poland	1	1	1
Greece	2	2	2
Norway	3	3	6
Czech Republic	4	4	3
Slovakia	5	5	7
France	6	7	8
Hungary	7	6	4
Portugal	8	9	5
Spain	9	10	9
Finland	10	8	10
Belgium	11	11	11
Sweden	12	12	13
Italy	13	13	12
Austria	14	14	14
Netherlands	15	17	15
UK	16	15	16
Denmark	17	16	17
Ireland	18	19	18
Germany	19	18	19
Switzerland	20	20	20

Note: IMS's broader definition of the exposed to competition or not exposed to competition segments is used in the sensitivity analysis with change of native country.

Source: IMS Health and TLV analyses.

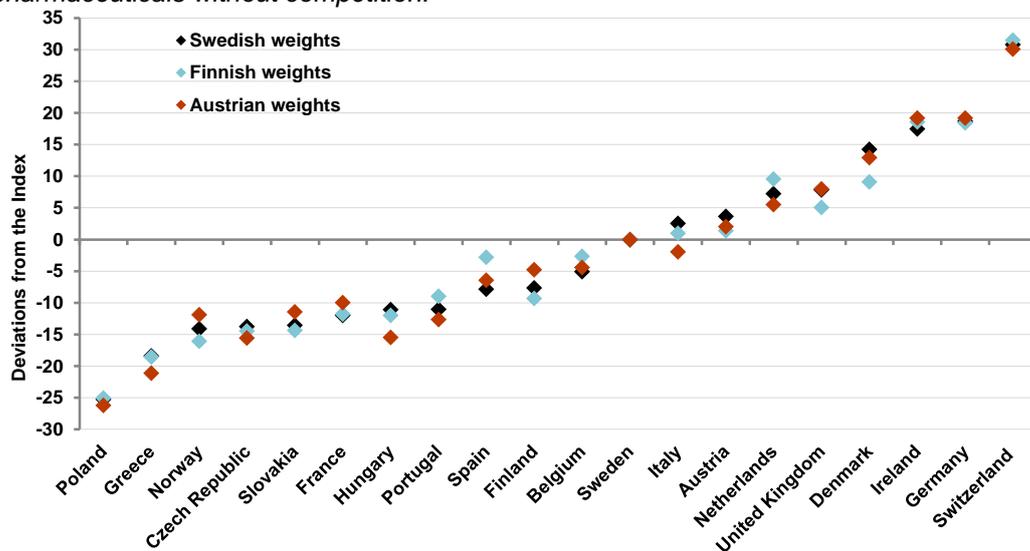
Five of the 20 countries retain their position, ranking 1-20, regardless of which country's sales volumes are used as the base weight. These are Poland, Greece, Belgium, Austria and Switzerland. Twelve countries retain their position with either Finnish or Austrian weightings compared to Swedish. Three of the countries have completely different rankings when changing base weighting. These are France, Hungary and Portugal.

Overall, the difference between the Swedish and Finnish base weightings is less than between the Swedish and Austrian. This is because Sweden and Finland generally have a more uniform pharmaceutical consumption for pharmaceuticals without competition. Sweden's position is stable; it is either ranked 12 or 13 of the 20 coun-

tries. Austria's position is 14 regardless of which country's volume weighting used. Finland's position is eight or ten.

The following figure illustrates deviations from the Swedish index in percentage points (index points).

Figure 16. Bilateral price index with the Swedish, Finnish and Austrian sales volumes and volume weightings and relative deviations from the Swedish Index Q1 2016 for the segment pharmaceuticals without competition.



Note: The index of other countries base weights has been normalized so that Sweden is always 0, irrespective of whether it is Swedish, Finnish or Austrian volume.

Note: IMS's broader definition of the exposed to competition or not exposed to competition drug segments is used in the sensitivity analysis with change of native country.

Source: IMS Health and TLV analyses.

The difference in index between Sweden and Finland is -7.6 with Swedish volume weightings. After the change, all else being equal, the difference increases to -9.3 with Finnish volume weighting. In other words, the Finnish index for the segment without competition will be 1.7 percentage points lower relative to Sweden when changing the base volume.

For Austria, the result is similar. The difference in index between Sweden and Austria is 3.6 with Swedish volume weightings. After the change, all else being equal, the difference falls to 2.1 with Austrian volume weighting. That is to say, the Austrian index for the segment without competition will be 1.6 percentage points lower relative to Sweden when changing the base volume.

This is consistent with the theory that the country whose sales volumes are used benefits in relative terms compared with if another country's volumes would be used.

Table 14. Relative impact on the index after changing the base weighting, price index bilaterally with the Swedish, Finnish and Austrian sales volumes and volume weightings Q1 2016 for the segment pharmaceuticals without competition.

	Swedish weight	Sweden with Finnish weight	Sweden with Austrian weight	Difference Swedish weight	Difference other weight	Cumulative change (percentage points)
Finland	0.92	1.10		-7.6%	-9.3%	-1.7%
Austria	1.04		0.98	3.6%	2.1%	-1.6%

Note: IMS's broader definition of the exposed to competition or not exposed to competition drug segments is used in the sensitivity analysis with change of native country.
Source: IMS Health and TLV analyses.

Changing the base country for pharmaceuticals with competition

For the market segment, pharmaceuticals with competition according to IMS Health's definition (which is broader than the previously analysed product-of-the-month definition), it can be seen that the ranking among the 20 countries changes slightly more than for the previous segment, without competition. Only four countries retain the same position in the ranking regardless of which country's base weighting is used. These are Switzerland, Ireland, Portugal and the United Kingdom.

Sweden's position is the second lowest with Swedish weighting and third lowest with Finnish, but with Austria, the position adjusts to sixth. Finland's position is eighth and tenth respectively while Austria's position is 14 or 18, depending on which country's volume weighting is used.

Table 15. Rank 1-20, lowest to highest, bilateral price index with Swedish, Finnish and Austrian sales volumes and volume weightings Q1 2016 the segment pharmaceuticals with competition.

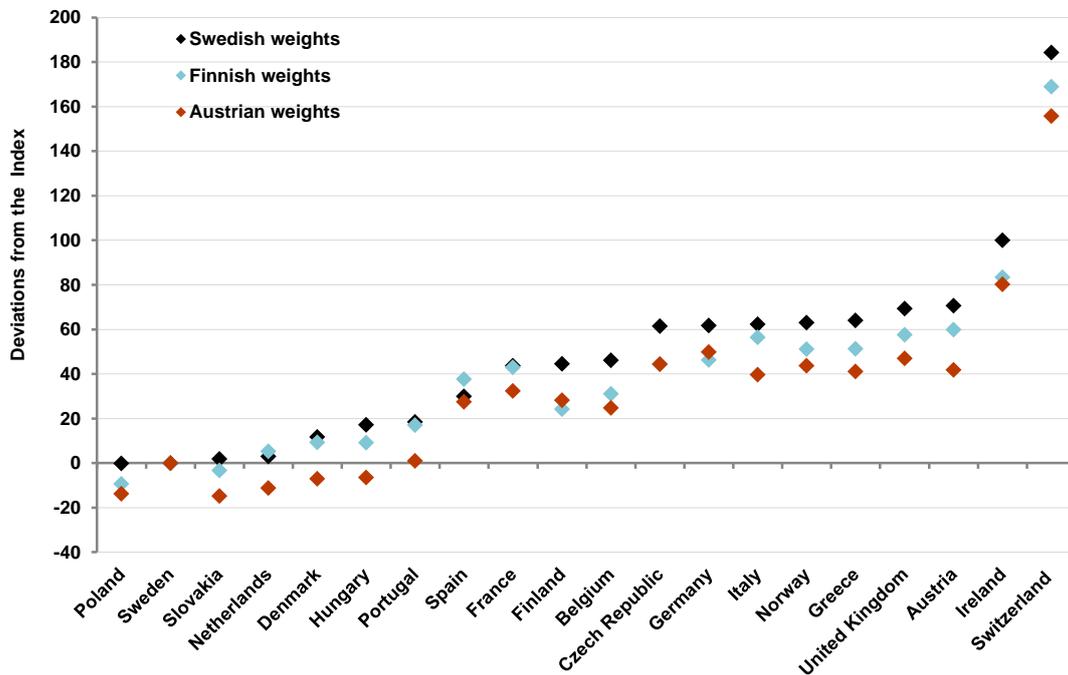
Country	Swedish weight	Finnish weight	Austrian weight
Poland	1	1	2
Sweden	2	3	6
Slovakia	3	2	1
Netherlands	4	4	3
Denmark	5	6	4
Hungary	6	5	5
Portugal	7	7	7
Spain	8	10	9
France	9	11	11
Finland	10	8	10
Belgium	11	9	8
Czech Republic	12	12	16
Germany	13	13	18
Italy	14	16	12
Norway	15	14	15
Greece	16	15	13
UK	17	17	17
Austria	18	18	14
Ireland	19	19	19
Switzerland	20	20	20

Note: IMS's broader definition of the with competition or without competition segments is used in the sensitivity analysis with change of native country.

Source: IMS Health and TLV analyses.

The following figure illustrates deviations from the Swedish index in percentage points (index points).

Figure 17. Bilateral price index with the Swedish, Finnish and Austrian sales volumes and volume weightings and relative deviations from the Swedish Index Q1 2016 for the segment pharmaceuticals with competition.



Note: The index of other countries' base weights has been normalized so that Sweden is always 0, irrespective of whether it is Swedish, Finnish or Austrian volume.

Note: IMS's broader definition of the exposed to competition or not exposed to competition drug segments is used in the sensitivity analysis with change of native country.

Source: IMS Health and TLV analyses.

Table 16. Bilateral price index with Swedish, Finnish and Austrian sales volumes and volume weightings and relative deviations from the Swedish Index Q1 2016 for the segment pharmaceuticals with competition.

	Swedish weight	Sweden with Finnish weight	Sweden with Austrian weight	Difference Swedish weight	Difference other weight	Cumulative change (percentage points)
Finland	1.45	0.80		44.6%	24.2%	-20.4%
Austria	1.71		0.70	70.7%	41.9%	-28.8%

Note: IMS's broader definition of the exposed to competition or not exposed to competition segments is used in the sensitivity analysis with change of native country.

Source: IMS Health and TLV analyses.

The difference in index between Sweden and Finland is 44.6 with Swedish volume weightings. After the change, all else being equal, the difference falls to 24.2 with the Finnish volume weighting. In other words, the Finnish index for the without competition segment becomes -20.4 percentage points lower relative to Sweden when changing the base volume.

The difference in index between Sweden and Austria is 70.7 with Swedish volume weighting. After the change, all else being equal, the difference falls to 41.9 with Austrian volume weighting.

In other words, the Austrian index for the without competition segment becomes 28.8 points lower relative to Sweden when changing the base volume.

Appendix 2: Pricing models

Prices of pharmaceuticals can either be set freely by the market or by direct or indirect regulation. A frequently used method is to consider the price situation in a number of reference countries²¹ or to base pricing on appraised values or profitability.

Table 17. How are pharmaceuticals priced?

1	Alternative method to international reference pricing	a) Value-based pricing	b) indirect price control by assessing value and profitability	c) Free pricing
2	International reference pricing	a) <u>Formal</u>	b) <u>Informal</u> , in combination with another method (e.g. assessment of the benefit or value)	

Source: TLV analyses.

Reference pricing can be formal or informal. This means that on average, the median or the maximum price calculated either directly govern the set price, or constitute a level that is taken into account for negotiation, during procurement or that forms part of a wider additional health economic evaluation.

Methods for how reference countries are designated vary. In some cases, the method is described, for example, that countries should be similar in terms of certain characteristics, e.g. economy or geographical proximity. In most cases, however, the motivation for why some countries constitute reference countries is not given.

The number of countries in the price basket varies greatly within Europe, from 3 to 31 countries. This may thus have great importance on the extent to which an individual country's price or price change affects the price basket in another country. For average value pricing, a single country's weighting may vary from 33.3 percent (1 of 3 countries) to 3.2 percent (1 of 31 countries). The direct or indirect force of the price impact also varies depending on whether the country applies a form of additional assessment in addition to international reference pricing.

Exchange rate fluctuations affect pricing in countries that use reference pricing. The rules vary regarding whether one only lowers prices or whether prices can also be increased due to exchange rate fluctuations. These changes thus affect the dynamics of other countries' prices. The Netherlands and Norway use international reference pricing and currency-adjust fixed ceiling prices following, among other things, exchange rate fluctuations in the reference countries, but at predetermined time intervals. Even Ireland currency-adjusts set reference prices. Other countries with reference pricing have not specifically stated whether price is adjusted for changes in exchange rates in the reference countries following the initial price decision. The following table shows how often the price in countries with reference pricing is au-

²¹ This is referred to as IRP = international reference pricing. Sometimes the abbreviation EPR = external reference pricing is seen. International and external reference pricing are the same thing. Certain countries employ the concept of internal reference pricing, which is why some literature uses IRP differently than this report.

tomatically adjusted. Price is readjusted between three to sixty months after a price decision.

Table 18. Pricing models for the 20 countries included in the survey.

	Country	Pricing model (pharmaceuticals without competition)	# countries	Reference countries	Method	Time to new readjustment (months)
1	Denmark	No IRP	-	.	-	-
	UK	Indirect price control	-	-	-	-
	Sweden	VBP	-	-	-	-
2a	Greece	IRP, formal	27	Other EU	Average of the lowest 3	3
	Ireland	IRP, formal	9	Austria, Belgium, Germany, Denmark, Spain, Finland, France, Netherlands, UK	Average	36
	Netherlands	IRP, formal	4	Belgium, Germany, France, UK	Average	6
	Norway	IRP, formal	9	Belgium, Denmark, Finland, Ireland, Netherlands, UK, Sweden, Germany and Austria	Average of the lowest 3	12
	Portugal	IRP, formal	3	Spain, France, Slovenia	Average	12
	Switzerland	IRP, formal	9	Belgium, Austria, Germany, Denmark, Finland, France, the Netherlands, Sweden and the UK	Average	36
	Slovakia	IRP, formal	27	Other EU	Average of the lowest 3	6
	Czech Republic	IRP, formal	*28/19	Other EU subsidy decision. For pricing decisions: Belgium, Germany, Spain, Finland, France, the Netherlands, Croatia, Ireland, Italy, Lithuania, Latvia, Hungary, Poland, Portugal, Greece, Slovakia, Slovenia, Sweden, United Kingdom	Average of the lowest 3	36
	Hungary	IRP, formal	31	EU and EEA	Lowest price	-
	Austria	IRP, formal		Other EU	Average	-
2b	Belgium	IRP, informal	27	Other EU	Average	-
	Finland	IRP, informal	29	EEA (Other EU + Norway and Iceland)	Average	60
	France	IRP, informal	4	Britain, Italy, Spain and Germany	Moderate / price 'close'	60
	Italy	IRP, informal	24	Other countries in EURIPID database	Lowest price	24
	Poland	IRP, informal	31	EU and EFTA	Average	24
	Spain	IRP, informal	*18/3	Euro-countries, but more emphasis is given to the 3 countries; France, Italy and Portugal	Lowest price	12
	Germany	IRP, informal	15	Austria, Belgium, Cyprus, Denmark, Greece, Spain, Finland, France, Ireland, Italy, Netherlands, Portugal, Sweden, Slovakia, United Kingdom	Average	-

Source: TLV analyses.

Denmark, Sweden and the UK apply pricing methods that are different to the reference price-setting. Until 2011, Germany also applied another method, but then switched to take into account reference prices as part of the assessment of certain new pharmaceuticals.

Pharmaceuticals prescribed in Sweden within the outpatient setting can, for example, be used in inpatient care in Denmark, Norway and the Netherlands. One reason for this is that some countries offer a greater potential for rebates in inpatient care via use of a procurement procedure. In the Netherlands, pharmaceuticals for autoimmune diseases (e.g. TNF-alpha inhibitors), have in recent years been transferred from outpatient to inpatient care settings in order to achieve price reductions.

Only a few countries in Europe apply a form of pricing other than international reference prices. Sweden applies value-based pricing. Denmark has free pricing on the AIP level while AUP (the pharmacy retail price) is nationally regulated, which means that the same prices are found in pharmacies across the country. In the UK, price is regulated through a voluntary PPRS (Pharmaceutical Price Regulation Scheme) agreement with the pharmaceutical industry. There is freedom in pricing at the launch of new substances, but price is subsequently regulated by limiting the permitted profitability. The UK also assesses the pharmaceutical's value-based benefit.

The system for generic substitution coupled with the lowest price for a particular product during a certain time period is found in; Denmark, which has a two-week period; in Sweden with the product-of-the-month for a one-month period; in the Netherlands, where a product can be the one preferred for sale for three, six or twelve months; in Finland, with a system where the 'product-of-the-month' period is three months. In Finland, the price can vary during this period. The systems for generic substitution in these countries differ, but the basic idea is the same; the product with the lowest price within a defined substitution group is the pharmaceutical that is primarily sold in pharmacies during a set period. Norway applies a step-wise pricing model for a generic pharmaceutical. This model involves linking the price to the time after a different number of competitors have entered the market and to sales volume. Other examples are Austria, France and Ireland that connect price reduction of the original and generic pharmaceuticals to certain periods of time after that competing pharmaceuticals entered the market.

Portugal, Germany²² and Spain are examples of countries with a general rebate system that is probably not seen in list prices.²³ The lack of complete information about any discounts is a weakness in all price surveys. Nevertheless, an analysis of changes over time and, as specifically in this report, a comparison of the exact same products' development between 2014, 2015 and 2016, offers a clear advantage. Assuming that any discounts relate to a similar level from one year to another, such a

²² KBV (2016). Institutionalised rebate system in Germany: Generally, 7 percent on the ex-factory price and 6 percent for drugs exposed to competition outside the reference price system. Generics and parallel imports are discounted an additional ten percent unless the price is at least 30 per cent below the reference price.

²³ European Commission (2015) p. 39 and 46.

relative comparison provides a relatively good picture of the relative price movements between different countries.

The aim of the following appendices is to improve the understanding of the pricing and reimbursement systems in the 20 countries analysed in TLV's international price comparison.

Appendix 3: Dependencies between countries' price baskets

Table 19. Overview of dependencies in pricing (direct and indirect dependencies)..

Countries included in the study	Countries used as reference countries	Belgium	Bulgaria	Cyprus	Denmark	Estonia	Finland	France	Greece	Ireland	Island	Italy	Croatia	Latvia	Lithuania	Luxembourg	Malta	Netherlands	Norway	Poland	Portugal	Romania	Switzerland	Slovakia	Slovenia	Spain	UK	Sweden	Czech Republic	Turkey	Germany	Hungary	Austria	TOTAL
		BE	BG	CY	DK	EE	FI	FR	EL	IE	IS	IT	HR	LV	LT	LU	MT	NL	NO	PL	PT	RO	CH	SK	SI	ES	UK	SE	CZ	TR	DE	HU	AT	
Belgium	BE	X																																27
Denmark	DK				X																													0
Finland	FI						X																											29
France	FR							X																										4
Greece	EL								X																									27
Ireland	IE									X																								9
Italy	IT											X																						24
Netherlands	NL																	X																4
Norway	NO																		X															9
Poland	PL																			X														30
Portugal	PT																				X													3
Switzerland	CH																						X											9
Slovakia	SK																							X										27
Spain	ES																									X								18
UK	UK																										X							0
Sweden	SE																												X					0
Czech Republic	CZ																													X				27
Germany	DE																														X			15
Hungary	HU																														X			30
Austria	AT																															X		27

Note: Denmark, Britain and Sweden are the countries in the study that apply a pricing method different from international reference pricing.

Appendix 4: Description of the different countries' pricing systems

This chapter aims to improve the understanding of the pricing and reimbursement systems in the 20 countries analysed in TLV's annual international price comparison. The chapter begins with a Nordic perspective. This is followed by information on other countries.

Nordic countries

Sweden

TLV determines which pharmaceuticals should be included in the pharmaceutical benefits scheme. In 2015, the cost of medicines in the benefit scheme amounted to approximately 24.7 billion SEK including patient own payments.

For pharmaceuticals with no generic competition, value-based pricing is applied.²⁴

TLV takes into account three basic principles:

- human value principle - healthcare should respect that all people are equal,
- needs and solidarity principle - those with the greatest medical needs should be entitled to more healthcare resources,
- cost-effectiveness principle - the cost should be reasonable from a medical, humanitarian and socioeconomic perspective.

For a pharmaceutical to be subsidized, a pharmaceutical company must first submit an application for a subsidy to TLV. Thereafter, TLV assesses, among other things, how cost effective the pharmaceutical is and whether the pharmaceutical should be included in the pharmaceutical benefits scheme. It is the Board for Pharmaceutical Benefits that makes the decision.

Managed entry agreements

A managed entry agreement is a contract between the County Councils and a pharmaceutical company and may be one of several grounds in TLV deciding on price and reimbursement status. New pharmaceuticals are introduced earlier, and some pharmaceuticals are sometimes associated with uncertainties regarding their use and effect in everyday clinical practice. Risk-sharing via managed entry agreements is an increasingly important tool for TLV and the County Councils to manage uncertainties. Such agreements may ensure cost effectiveness and also dampen the increasing costs for new pharmaceuticals. Tripartite discussions between County Councils, pharmaceutical companies and TLV can thus enable the use of such

²⁴ See for example TLV (2016c), TLV (2016d), and TLV (2016e).

pharmaceuticals, even when there is significant uncertainty about their medical effect and its cost-effectiveness.²⁵

Managed entry agreements between County Councils and pharmaceutical companies also have potential as powerful tools to create competition and drive down prices within established pharmaceutical areas where, for various reasons, competition and price pressure has not arisen. One example is biologic pharmaceuticals, where price competition rarely arises, despite the presence of biosimilars. In 2016, thanks to managed entry agreements, competition emerged in the area of TNF-alpha inhibitors as a result of the introduction of a biosimilar.

So far, managed entry agreements are found in six therapeutic groups and in total encompass 16 products.²⁶ This primarily applies to new pharmaceuticals in the benefits scheme where different types of risk following their introduction are handled within the framework of the lateral agreements.

The first case where a managed entry agreement was one part of the grounds for TLV deciding on price and reimbursement status was for a pharmaceutical against hepatitis C at the end of 2014. This was followed by pharmaceuticals for prostate cancer during the summer of 2015 (Xtandi and Zytiga). Several pharmaceuticals have subsequently been added. Zykadia (against lung cancer) was added at the end of 2015 and Entresto (to treat heart failure) came into the benefits scheme in April 2016. In these cases, managed entry agreements have concerned refunds at high patient volumes.

June 2016 saw the inclusion of an additional anti-cancer pharmaceutical Mekinist (against malignant melanoma) where the risk of long duration of treatment is handled through the agreement. In the same month, Repatha (for high LDL cholesterol) was added. Here, the managed entry agreement dealt with the risk for a high number of patients and the uncertainty surrounding the effect. The case concerning the orphan pharmaceutical Raxone (against eye disease) from October 2016, has a managed entry agreement that deals with risk for the number of patients who will be treated and the uncertainty about the effect. Raxone is the first case where an orphan pharmaceutical product was covered by a managed entry agreement. The reason why Raxone already has sales figures in September, even though the benefits scheme decision was not taken until October, is due to sales having taken place previously via a special permission license.²⁷ Pharmaceuticals granted a special permission license are automatically covered by the benefits, even before a decision on the possible benefit has been taken.

In October 2016, lateral agreements for Enbrel and Benepali were renewed while agreements for Cimzia and Humira were added.

²⁵ TLV (2016a).

²⁶ TLV (2016b).

²⁷ Pharmaceuticals granted market authorisation in a different country, that are not authorised to be marketed in Sweden, may receive a special permission license to be dispensed to specific patients. The cost will be covered by the benefits scheme and the patients' co-payment within the high-cost threshold scheme.

Table 20. Pharmaceuticals with lateral agreements, entry into benefits scheme, and date of lateral agreement.

Area	Pharmaceuticals	In the benefit scheme as from (month / year)	Lateral agreement as from (month / year)
1 Hepatitis C	Sovaldi	Oct 14	Jul 15
	Harvoni	Feb 15	Feb 15
	Daklinza	Dec 14	Dec 14
	Viekirax/ Exviera	March 14	Apr 15
2 Heart failure	Entresto	Apr 16	Apr 16
3 Cancer	Xtandi	Jul 15	Jul 15
	Zytiga	Jun 15	Jun 15
	Zykadia	Dec 15	Dec 15
	Mekinist	Jun 16	Jun 16
4 TNF, etanercept	Enbrel	Jun 02	Apr 16, Oct. 16
	Benepali	Mar 16	Apr 16, Oct 16
	Cimzia	Mar 10	October16
	Humira	Sep 03	October 16
5 PCSK9 inhibitors	Repatha	Jun 16	Jul 16
6 Eye disease	Raxone	Oct 16	Oct 16

Source: TLV (2016b) p. 24.

Co-payment within the high-cost protection threshold

The cost of pharmaceuticals in the pharmaceutical benefits scheme is included in the patients' co-payment within the high-cost protection. The maximum amount a patient pays for pharmaceuticals in the benefit scheme is 2 200 SEK in own contributions per 12-month period. The county council pays the remainder. The state provides annual government grants to the county councils for pharmaceutical benefits scheme costs.

Since January 1, 2016, pharmaceuticals in the pharmaceutical benefits scheme are free for children under 18 years.

Generic substitution

Generic substitution leads to lower prices, and afterwards significant price differences between generic substitutes can arise. TLV then lowers the maximum accepted selling price within the benefits scheme by setting a lower ceiling price for substitutable pharmaceuticals. Each month, TLV analyses prices and sales volumes in order to find groups where the criteria for setting a ceiling price are met. When the prices of a group of substitutable pharmaceuticals have dropped by at least 70 percent of the price that the pharmaceuticals had before generic competition arose, and when generic competition has been ongoing for at least six months, TLV sets a ceiling price.

The new fixed ceiling price is 65 percent of the price that the pharmaceuticals had before generic competition arose.²⁸ Setting the ceiling price in this way thus reduces the differences in price between substitutable pharmaceuticals within the benefits scheme, but it also has the effect of further lowering costs in addition to the cost-lowering effect of generic substitution itself.

The purpose of the substitution system of pharmaceuticals in pharmacies is to keep down society's cost for pharmaceuticals. Products-of-the-month are substitutable medicines that have the lowest price and that pharmacies offer their customers when they replace pharmaceuticals. Each month, TLV designates the product in each package size group with the lowest unit sales price and that the pharmaceutical company has confirmed can be provided to the entire market during the pricing period. Which substitutable pharmaceuticals have the lowest prices can vary, which means that pharmacies can offer different pharmaceuticals at different times. TLV also designates two back-up products that pharmacies can switch to if it is not possible to obtain the cheapest.

Some older pharmaceuticals have no or only weak generic competition. This may, for example, be due to a generic pharmaceutical not being substitutable with the original medicine, or that the pharmaceutical is a so-called biological pharmaceutical. In January 2014, a price reduction of pharmaceuticals that are older than 15 years, included the pharmaceutical benefits scheme, and that have no or only weak generic competition was introduced. The price reduction is equivalent to 7.5 percent of the price applying at October 2012.²⁹

For prescription pharmaceuticals not eligible for the benefits scheme, free pricing applies. Patients either pay the entire cost themselves or, in some cases, the county council takes the costs.

There is no VAT on prescription pharmaceuticals (prescription and non-prescription medicines on prescription). 25 percent sales tax on non-prescription pharmaceuticals.

Finland

Finland has applied informal reference pricing since 2009. In 2014, Finland increased the number of reference countries from 15 to 29 (EU 27, Norway and Iceland.) In addition to reference prices, the efficacy and price of similar products, among other things, is also taken into account. Price and reimbursement is decided for a maximum of three years, after which the pharmaceutical company needs to re-apply for a pharmaceutical to be included in the benefits scheme.

Finland, product-of-the-month system with price variation

For generic pharmaceuticals in Finland, the first subsequent product for an original pharmaceutical will be priced at least 50 percent lower than the original. Prices of

²⁸ TLV (2016f).

²⁹ TLV (2016g).

subsequent generic pharmaceuticals cannot exceed this stipulated price. However, for some products the level is 40 percent. One change introduced for original pharmaceuticals from 2016, is that the original price shall be reduced by 40 percent nine months after generic competition in order to retain subsidy status.

Finland has a system for the product-of-the-month similar to that of the Netherlands, Sweden and Denmark. In Finland, the applicable period is three months, but the price of other substitutable pharmaceuticals in the substitution group can be changed during the three-month period.³⁰

The exchange group or the reference price group is determined by the Finnish Medicines Agency Fimea. Since 2016, pharmacies are required to inform customers about which pharmaceuticals have the lowest price in the substitution group when dispensing products.

21 days before the substitution period, pharmaceutical companies inform Kela what prices are applicable at the start of the three-month period.³¹ The reference price is calculated based on the pharmaceutical companies' price notifications by adding € 1.50 to the price of the product with the lowest price in each substitution group. If the price of the product with the lowest price is at least € 40, € 2 will be added to the price.³²

For the first two weeks of the three-month period, the price remains as notified. A pharmaceutical company can, however, adjust the price of the pharmaceutical when the database is updated with the new publication of the price list. If the pharmaceutical is not within the benefits scheme, the pharmaceutical company can freely set the price. However, the price of pharmaceuticals in the benefits scheme may not be higher than the price set by the Pharmaceuticals Pricing Board.

Because of price competition, prices of many pharmaceuticals change two weeks after the reference prices come into force (the 15th of January, April, July and October). What usually happens is that products with prices exceeding the reference price are lowered to the reference price level and the products with prices below the reference price are raised to the reference price level. In practice, this means a system of several '*products-of-the-month*'.³³

Co-payment within the high-cost protection threshold

In Finland, the general rule is that all patients receive financial compensation for pharmaceuticals where the Pharmaceuticals Pricing Board has decided that reimbursement applies. In 2016, the ceiling for the patient's own contribution is € 610.³⁷ From 2016, a step-wise model is implemented. This means that all patients over 18 years pay € 50 before any subsidies come into force.³⁴

³⁰ COWI (2014), p.9.

³¹ Kela (2016c).

³² Kela (2016c).

³³ Kela (2016d).

³⁴ Kela (2016a).

There are three categories of pharmaceutical subsidies; Basic compensation covers 40 percent of the pharmaceutical's price. The lower special compensation covers 65 percent of the pharmaceutical's price (11 chronic diseases) and the higher special allowance covers 100 percent (34 serious chronic diseases), but in this case, the patient pays € 4.50 per dispatch.³⁵ Handling charges amount to € 2.50 per prescription in the year that patients have exceeded the amount for their own contribution.

Norway

The Norwegian price of outpatient pharmaceuticals is related to the price level in other countries through formal reference pricing. In Norway, the State Medical Products Agency regulates the ceiling price for prescription pharmaceuticals.³⁶ Norway's reference countries are: Belgium, Denmark, Finland, Sweden, Ireland, United Kingdom (NHS), Germany, the Netherlands and Austria. These countries have been chosen because of geographical proximity. The system was implemented in 2002. The calculation is made on the AIP level. Ceiling price is set to the average of the market price for the product in the three countries with the lowest price and to that is added a fixed trading margin. It is the price for the same product that is compared and the comparison is made regardless of whether or not the product is marketed under different names in the reference countries. The calculation uses the exchange rate for at least the past six months' average according to the Norwegian central bank.

The timing of price revisions is predetermined and ongoing, which means that price adjustments are implemented for specific ATC groups every month. It is also possible for companies to apply for a price review. Prices for the 250 substances with the highest turnover are adjusted according to price changes in the comparison countries or to major changes in exchange rates, nevertheless on a maximum of one occasion per 12-month period. Pharmaceuticals that are covered by this annual price revision represent about 70-80 percent of the market.

Step-wise model with volume component

For generic pharmaceuticals, the Norwegian step-wise model applies. This was introduced in 2005. The price is lowered in stages depending on sales volume.³⁷ When generic competition occurs, the price at the patent expiry of the original pharmaceutical is lowered by 35 percent. The second step in the model occurs six months thereafter. The maximum price is then 59 to 81 percent lower than the price of the original pharmaceutical at patent expiry. The third step occurs 18 months after generic competition arose. The maximum price is 69 to 90 percent lower than the price of the original pharmaceutical at patent expiry. Substances with a high turnover receive a greater price reduction.³⁸

³⁵ Kela (2016b).

³⁶ Statens legemiddelsverk / Norwegian Medicines Agency (2016a).

³⁷ Statens legemiddelsverk / Norwegian Medicines Agency (2016b).

³⁸ Statens legemiddelsverk / Norwegian Medicines Agency (2015).

Table 21. Norwegian step-wise model

Turnover generic competition	before	Step 1 (Immediate)	Step 2 (after 6 months)	Step 3 (after 18 months at the earliest)	
Under 100 MNOK		35%	59%	Turnover >15 MNOK	69%
Over 100 MNOK		35%	81%	Turnover >30 MNOK	88%
				Turnover >100 MNOK	90%

Source: Statens legemiddelsverk / Norwegian Medical Products Agency (2016b).

The system for determining the ceiling price and the step-wise pricing model applies to both parallel imported pharmaceuticals as well as to directly imported pharmaceuticals.

Pharmacies can negotiate purchase prices with the manufacturers. In practice, the negotiations apply to generic pharmaceuticals. Negotiating the purchase price of original pharmaceuticals is more limited.

Pharmacies are tasked to substitute the prescribed pharmaceutical to the pharmaceutical within the substitute group with the lowest price whenever there is an alternative on the substitute list (Byttelistan).³⁹ In the event that patients oppose generic substitution, they pay the full cost themselves.⁴⁰

Co-payment within the high-cost protection threshold

Generally, the subsidy level is 62 percent of the cost of the pharmaceutical, but different conditions apply. The subsidy level is 100 percent for children under 16 and pensioners with low incomes, as well as for pharmaceuticals for treating infectious diseases such as tuberculosis, hepatitis C and HIV. However, patients pay at the most an own contribution of 520 NOK per prescription. The annual ceiling for own contributions is 2 185 NOK per year.

H-prescriptions

There is a common procurement organization for inpatient care products; Lekemiddelinkøbssamarberid (Pharmaceutical procurement cooperation LIS). Like Amgros in Denmark, it works to obtain discounts on inpatient pharmaceuticals. Some examples of transferred therapy groups. TNF-alpha inhibitors have been handled in inpatient care since 2006 and MS medicines were transferred to inpatient care in 2008. Some oncology medicines were transferred to inpatient care in 2014. Financial responsibility for pharmaceuticals to treat hepatitis C, blood coagulation factors and growth hormones was transferred to inpatient care during in 2016.

In addition to the prescribing of common prescriptions, Norway has what is known as H-prescriptions, which allows some inpatient pharmaceutical to be collected at regular pharmacies. The system of H-prescriptions has existed since 2006 and been

³⁹ Statens legemiddelsverk / Norwegian Medicines Agency (2016e).

⁴⁰ Statens legemiddelsverk / Norwegian Medicines Agency (2016c).

extended several times. From January 1, 2016, the system has been further extended to include, for example, hepatitis C and growth hormones.^{41 42}

Denmark

Denmark applies free pricing for list prices at the pharmacy purchase price level (AIP). This applies to both original medicines and pharmaceuticals with competition. Prices of pharmaceuticals are reported to the Danish Medicines Agency, which in turn publishes the sale price and subsidized price. The pharmacy retail price (AUP) is regulated by fixed handling fees and a percentage margin on the wholesale price level.

Price is set every second week

Denmark has a substitution scheme that is similar to the Swedish product-of-the-month system. Pharmaceutical producers may announce price and assortment changes as often as every 14 days. The product with the lowest price in each respective group will automatically become the highest remuneration that is subsidised.⁴³

Products-of-the-month in Denmark are A-marked products during the actual period. B-marked products have a price difference to A-marked products that is not considered sufficiently large enough to be taken into consideration. If a doctor has prescribed a B-product, pharmacies are not obliged to change it to an A product. The subsidy is, however, limited to the equivalent that an A-product would have. The 'bagatelle range' is between 5 and 20 Danish crowns, depending on the pharmaceutical's price.⁴⁴ C-products exceeding the 'bagatelle range' shall be substituted unless the doctor or patient informs the pharmacist otherwise.

The Pharmaceutical Industry Association, the government and the regions in Denmark have signed a price-capping agreement on pharmaceuticals.⁴⁵ The first agreement concerned the period 2012-2014. The agreement was later extended in stages, first for the period 1 January 2015 until 1 July 2016 and thereafter for the period July 2016 to December 2018.

On April 1, 2016, the Danish regions, the national health authority, the department of the elderly and the Danish Pharmaceutical Industry Association signed an agreement which means that the reference price model for list prices in inpatient care must undergo a conversion resulting in a price reduction of 10 percent over a three-year period.⁴⁶ The agreement applies April 1, 2016 - March 31, 2019. The agreement also ensures that the price of new inpatient pharmaceuticals may not exceed the average price in Sweden, Norway, Finland, UK, Netherlands, Belgium, Germany, Ireland and Austria.

⁴¹ Norsk Helseinformatikk (2016).

⁴² Statens legemiddelverk (2016d).

⁴³ Lægemedelstyrelsen (2016a).

⁴⁴ COWI (2014), p.32.

⁴⁵ COWI (2014), p. 57.

⁴⁶ Sundheds- och äldredepartementet (2016a).

Co-payment within the high-cost protection threshold

Pharmaceutical companies apply for benefit status with The Danish Medicines Agency⁴⁷. The subsidy may be general or individual. Individual subsidization can be given for pharmaceuticals without general subsidy. In these cases, the doctor applies for the subsidy on behalf of the patient. Compensation is 80 percent of the price. The general subsidy is a positive list and can be limited to an indication or patient group.⁴⁸

General reimbursement and own contributions amount to the following for 2016⁴⁹: 0 percent of the cost up to 935 Danish crowns, 50 percent of costs between 935-1 535 Danish crowns, 75 percent for costs between 1 535-3 325 kronor and 85 percent for costs over 3 325 Danish crowns. For chronic diseases, the compensation is 100 percent for expenses greater than 17,975 Danish crowns. Patients with special chronic grants pay a maximum own contribution of 3 880 Danish crowns, provided that the patient chooses the product with the lowest price.

From 2015, pharmacists are allowed to open up to seven pharmacies within a 75-kilometer radius. The purpose of the increase in the number of pharmacies is to give patients greater accessibility to pharmacies.

Rest of Europe

Netherlands

Reference pricing regarding setting a price ceiling is applied to all pharmaceuticals. The Netherlands has Belgium, France, Germany and United Kingdom in its reference price basket. A price review takes place every six months, taking into account price changes in the reference countries as well as exchange rate changes. Price ceilings are officially published twice a year.⁵⁰

Pharmaceuticals that are prescribed by brand name will be automatically changed to the generic name (INN, substance name) by an electronic prescribing system.

The healthcare system is publicly funded and operated through insurance companies. Since 2006, all Dutch citizens are required to have their own health insurance. The insurance companies act as the healthcare 'buyer'. There are essentially two economic arrangements for health insurance; either the insurance company covers all the costs when the pharmaceuticals are collected or it makes an economic outlay and files a claim for reimbursement at the end of the insurance period.

The insurance companies negotiate the 'product-of-the-month' by two approaches:

- Disclosed preference policy (lowest published price at the manufacturer)
- Non-disclosed preference policy (confidential minimum price at the manufacturer)

⁴⁷ Lægemedelstyrelsen (2016c).

⁴⁸ Lægemedelstyrelsen (2016d).

⁴⁹ Lægemedelstyrelsen (2016e).

⁵⁰ Medicijnkosten (2016).

A product can only become a preferred product when the lowest price on the official list price is within five percent of the lowest price of a medicines cluster. The product can then become the preferred product for a specified period of time, usually six months, but this can vary between one and twelve months.

Insurance companies may choose to only subsidize *'products-of-the-month'*.

If the manufacturer cannot deliver the product in sufficient quantities, or if the price is increased during the period, it is no longer the product of choice. If patients do not want the preferred product, they pay the difference, except for certain specific medical needs.

The price of pharmaceuticals collected from a pharmacy may vary depending on the insurance company to which the patient is affiliated. That is to say, a pharmaceutical can have four or five prices depending on which insurance company entered into agreement with the pharmacy. (Currently there are four insurance companies that have 90% of the total market, even though significant regional differences do occur. In some regions, one or two companies basically have the entire market).⁵¹

In 2008, several insurance companies (Menzis, VGZ, CZ and AGIS) notified their intention to extend the application of the *preference policies*. The first national tender by the insurance companies conducted in June 2008 led to a price war between suppliers of generic pharmaceuticals. In connection with this process, the price of generic pharmaceuticals (those pharmaceuticals with high sales) decreased by about 90 percent.⁵²

As a result of the price-suppressing effect of the tender procedure leading to insurance companies making additional earnings, the Dutch Ministry of Health in 2009 decreased the financial assistance the state gave to the insurance companies. In the same year, the insurance company VGZ developed a hidden pricing model in which the pharmaceutical manufacturer was able to maintain a high list price while offering VGZ a negotiated discount. This procedure was met with criticism because the benefit that the insurance company received as a buyer was unclear to outsiders, while pharmacies dispensed certain pharmaceuticals that were more expensive than the lower-cost generic pharmaceuticals available.

Since 2012, the Dutch Ministry of Health has continued to set price ceilings on pharmaceuticals, but is not obliged to do so.⁵³ Since 2015, greater emphasis is placed on health economic evaluations for certain types of pharmaceuticals. This particularly applies to special pharmaceuticals with expected high costs, such as oncology pharmaceuticals. These pharmaceuticals need to undergo an evaluation of

⁵¹ Ruggeri, K. och Nolte, E. (2013) and Zuidberg, C. (2010).

⁵² SFK (2015) p. 19-20.

⁵³ There are several regulations in the Netherlands aimed at restricting and controlling government spending on prescription pharmaceuticals. Medicine Price Act (Wet Geneesmiddelenprijzen (WGP)) and the subsidy system (Geneesmiddelenvergoedingssysteem (GVS)).

cost effectiveness before the decision about subsidy is taken. Manage entry agreements have become increasingly common in the Netherlands in the last couple of years.

Manage entry agreements with price and volume components are often confidential in nature and contain hidden discounts that make the real price of these pharmaceuticals less than the list price. These pharmaceuticals, however, are usually handled within inpatient care. Since 2012, TNF-alpha inhibitors are only handled within inpatient care. The purpose behind this change was that inpatient care (with insurance companies) can act more forcefully as a procurement agent and thus bring down prices. Hospitals also cooperate with each other to get discounts from manufacturers.

Insurance companies have introduced a variant of 'clawbacks' in the agreements reached between insurance companies and pharmacies.

United Kingdom

The United Kingdom applies indirect price control through an evaluation of health economic aspects, e.g. cost effectiveness, and with regard to the pharmaceutical industry's profitability. A study from 2014 shows that cost effectiveness weighs heavily in the evaluation and was the single factor in explaining the outcome in 82 percent of NICE's decisions.⁵⁴

In the UK, the pricing of original pharmaceuticals is regulated by voluntary agreement with the pharmaceutical industry. Ceiling prices of original drugs must be set so that they meet the voluntary Pharmaceutical Price Regulation Scheme 2014 (PPRS) agreement or other regulation.⁵⁵ Prior to launch, pharmaceutical manufacturers must agree a maximum price with the Department of Health. New active substances according to European and national definitions are subject to free pricing. PPRS 2014 applies until 2018 and aims to provide stability in the pricing of original pharmaceuticals.⁵⁶

Reference prices, cost projections and clinical needs are taken into account when making pricing agreements. Following up manufacturers' profitability can lead to the adjustment of prices and reimbursement levels. Manufacturer follow-up regulates, including how much of the state reimbursement shall go to research and development, marketing, etc.

Pharmaceutical companies compensate the Department of Health according to a specific percentage of all pharmaceutical costs that exceed the agreed level. This is done quarterly.⁵⁷

⁵⁴ Dakin et al (2014).

⁵⁵ Department of health (2014).

⁵⁶ Department of health (2016).

⁵⁷ Department of health (2015).

Free pricing of generic pharmaceuticals applies in the UK provided that the pharmaceuticals are priced below the ceiling price applicable at the original pharmaceutical's patent expiry. Generic prescribing (INN) is voluntary but widely used.

Subsidies are regulated via a negative list of pharmaceuticals that may not be prescribed with benefits. Most new pharmaceuticals are granted full subsidy in connection with market entry and price approval.

Germany

Germany has a pricing and subsidies system that combines free pricing, reference pricing and value-based pricing. The reference pricing part is informal and price information is collected at ex-factory level.

The law on the reorganization of the pharmaceutical market (AMNOG), which regulates pricing, came into force on 1 January 2011 and led to changes in the pricing and reimbursement of medicines. The purpose of AMNOG was to limit rising pharmaceutical costs within the framework of the health insurance system.⁵⁸ In Germany, subsidy decisions are taken at the same time as market entry is granted. Once a pharmaceutical is approved, it can be prescribed to the patient. At market launch, free pricing applies during a short period that can be up to twelve months.⁵⁹

Using a pharmaceutical's value creation based on evidence is a relatively new aspect of the pricing model for new pharmaceuticals. The manufacturer may apply for a review of additional value.⁶⁰ The manufacturer can then assert that there is a therapeutic benefit over existing treatments for a particular indication and, therefore, that it has the right to individual pricing in relation to the value creation effect.⁶¹ The pharmaceutical's benefits are first evaluated by the Federal Joint Committee (G-BA). G-BA is responsible for assessment and decision-making in outpatient and inpatient care.

G-BA decides whether the IQWiG (Institute for Quality and Effectiveness in Healthcare) shall carry out a full cost-benefit analysis of additional benefits / value. IQWiG may decide that the product provides great benefits, significant benefits, non-quantifiable benefits, or no benefit. IQWiG does not make an assessment based on QALY.⁶²

For products without additional benefit or value, the maximum subsidy rate should be set to not exceed the cost of comparable treatment. If the product is deemed to provide further medical value, its price should be decided through negotiations between the SHI (Gesetzliche Krankenversicherung / National Association of Statuto-

⁵⁸ Bundesministerium für gesundheit, Die Spreu vom Weizen trennen Das Arzneimittelmarktneuordnungsgesetz (AMNOG).

⁵⁹ VFA, How does a new drug enter the market?

⁶⁰ Between 2011 and 2014, 66 pharmaceuticals were evaluated, of which 27 showed no additional benefit over existing pharmaceuticals.

⁶¹ Ruggeri, K. och Nolte, E. (2013).

⁶² Bundesinstitut für Arzneimittel und Medizinprodukte, BfArM, AMNOG (Act on the Reform of the Market for Medicinal Products).

ry Health Insurance Funds) and the pharmaceutical company. Within six to twelve months from the decision on market authorization, the pharmaceutical company must agree on what SHI system prices and discounts shall apply in the future. Negotiations may also result in retroactive refunds.⁶³

If a negotiated price agreement is not possible, the matter is referred to an arbitration institute. During its deliberations, the product's price is limited to the level in force in a number of European reference countries.

Subsidized pharmaceuticals that do not have prices set according to the reference-pricing model have their price levels fixed to the price level of August 2009. According to a new agreement of April 1, 2014, 2009 price levels shall continue to apply until 31 December 2017.⁶⁴ The agreement means that pharmaceutical prices of pharmaceuticals already on the market cannot be adjusted for inflation, for example.

All German citizens are entitled to healthcare funded through the health insurance system (GVK). GVK consists of 134 sickness funds financed by employers and employees. In addition to GVK, approximately eleven percent of citizens have private insurance. Health insurance funds are non-profit and act as insurance companies covering doctor visits and prescription pharmaceuticals. In turn, health insurance funds negotiate with pharmaceutical companies and the Medical Association regarding pharmaceutical prices and doctor visits.

Germany is trying to steer prescribing over to biosimilars (from biological originals). Regions apply different quota systems concerning the amount that can be prescribed and penalties ensue if these are not followed.

The patient pays the difference between the reference price and the selling price. Pharmaceuticals are grouped into three categories: 1) products with the same active ingredient and similar use, 2) products with comparable therapeutic or pharmacologically active substances, and 3) products with comparable therapeutic effect.

Pharmaceutical manufacturers are free to set the prices of generic pharmaceuticals. However, the degree of subsidy is regulated. The patient pays the difference between the reference price and the selling price.

Substitution in pharmacies is an important tool in holding down rising pharmaceutical costs. Pharmacists should switch to a cheaper pharmaceutical if the prescribed pharmaceutical is included in the agreement *SHI discount contract*. In some areas, however, substitution is not permitted, e.g. thyroid hormones, anti-epileptic pharmaceuticals, or pharmaceuticals for certain heart diseases.

⁶³ Henschke, C., Sundmacher, L. och Busse, R., (2013).

⁶⁴ VFA (2014).

Within the health insurance system, discounts on the list price are common. The discount up to and including 2010 was, ex factory, six percent for innovative new pharmaceuticals. The discount for this category increased to 16 percent during the period 1 August 2010 to 31 December 2013.⁶⁵ In 2014, it was decided that the mandatory discount of subsidized pharmaceuticals would be reduced from 16 percent to seven percent.⁶⁶ Discounts are also available for generic pharmaceuticals; six percent for pharmaceuticals with competition outside the reference price system. Generics and parallel imports are discounted an additional ten percent unless the price is at least 30 percent below the reference price.⁶⁷

Pharmaceutical companies with turnovers of less than one million EUR per year, or pharmaceuticals that are used only in hospitals, are exempt from the pricing system. Orphan drugs for rare diseases are exempt as long as their turnover in the state health insurance system is less than EUR 50 million.⁶⁸

Belgium

Belgium has had informal reference pricing since 2001. In 2014, it increased the number of reference countries from 24 to 27. The manufacturer is required to disclose the selling price (ex-factory) in other European countries where available. As a complement, a national comparison is also conducted. The pharmaceutical's total economic impact and the price levels for similar pharmaceuticals in Belgium are also examined. The set fixed price is a ceiling price for the manufacturer. Distributors' and pharmacies' maximum mark-ups and margins are then determined on the basis of a national regulation of both the margin in percentage and the total maximum mark-up of distributors' (wholesalers') purchase prices and within the pharmacy chain.

A general price reduction of all pharmaceuticals was carried out in April 2012. Manufacturers had to choose between lowering prices by 1.95 percent for all products or lowering prices on products of their choice to bring about the corresponding savings. In March 2015, a price reduction of six percent on pharmaceuticals included in the reference price system and whose cluster group had existed for at least six years was implemented. The price cuts affected about 85 percent of generic pharmaceuticals.

Price regulation is also found for generic pharmaceuticals in Belgium. In March 2016, the pricing of generics was simplified. The price is reduced immediately when generics enter the market (in a reference cluster) rather than being successively lowered after two, four and six years. The highest price for a generic product cannot exceed the price of the most expensive product in the same reference cluster. For the first follow-up product, the price is set 43.64 percent lower (without a reference cluster) or 51.52 percent lower (ex-factory), depending on subsidy category.

⁶⁵ KBV (2016) och Ruggeri, K. and Nolte, E. (2013) p. 42.

⁶⁶ Tillväxtanalys (2016), p. 20.

⁶⁷ KBV (2016).

⁶⁸ Tillväxtanalys (2016) p. 20.

When generics are prescribed (INN), pharmacies substitute the cheapest alternative for medicines included in the reference price system.

Managed entry agreements exist for some innovative new pharmaceuticals.

France

France adopted formal / informal reference pricing in 2003. Prices (ex-factory) shall be close to the prices in the reference countries. The price is not set lower than the lowest price of the four reference countries; Germany, Spain, Italy and Britain. Reference price reviews take place every 60th month.

Some pharmaceutical companies make available prices in other countries. The price that is determined is fixed for five years. Thereafter, the list price can be renegotiated. Reference pricing is the main method used at the time of renegotiation.

Manufacturers wanting to launch a pharmaceutical with a subsidy must have it evaluated by the Economic Committee for Healthcare Products (Comité Economique des Produits de Santé, CEPS). The transparency commission of the French High Authority for Health (Haute Autorité de Santé, HAS) assesses the therapeutic value of the pharmaceutical as well as the additional therapeutic value when compared with alternative treatments. The assessment scale uses four stages where 1 means great improvement, new therapeutic area or reduced mortality and 4 means no improvement. CEPS then negotiates price with the manufacturer. Reference pricing is only a part of the evaluation of the pharmaceutical and is assessed as 1 to 3 (great to some improvement). The pharmaceuticals are also subject to an HTA (Health Technology Assessment) evaluation.

In France, generic medicines are priced at least 60 percent lower than the original. Thereafter, the price of the original is lowered by 20 percent and 18 months later the price will be further reduced by 12.5 percent.⁶⁹ Prices of generic pharmaceuticals will be reduced by 7 percent 18 months after the patent expiry of the original pharmaceutical.

Biosimilars are priced at least 30 percent lower than the biological original. Prices of biological originals are reduced by 15 percent after 18 months.

From January 1 2015, generic prescribing (INN) is mandatory. However, as an addendum to generic prescribing, it is permissible to also specify a brand name on the prescription.

In France, about 95 percent of the population is covered by private health insurance. The degree of subsidization depends on how the disease is classified: 100 percent reimbursement for pharmaceuticals for severe chronic illnesses, 65 percent for pharmaceuticals with substantial clinical effects on severe diseases, 30 percent for

⁶⁹ Pricing and Reimbursement Questions p. 43.

pharmaceuticals with lesser clinical efficacy, and 15 percent for pharmaceuticals with a weak clinical effect.⁷⁰

France has discounts related to growth similar to the system in Italy.⁷¹ The discounts are not known in advance and are not included in the list price. There are also managed entry agreements linked to price, volume and various risks. This means that the real price deviates downwards from the official list price after certain volume steps have been achieved for some pharmaceuticals.

Greece

Since 2006, Greece has applied formal reference pricing. Prices (ex-factory) are based on an average of the lowest three prices of the other 27 EU countries. In 2016, it was decided that price reviews will take place in May and November each year. Pricing for generic pharmaceuticals has been amended several times in recent years. Since April 2016, the prices of generic pharmaceuticals are linked to the price of original pharmaceuticals after patent expiry. Prior to this, they were linked to the price before or at patent expiry.

The pricing mechanism for generic pharmaceuticals was amended in September 2015. Generic pharmaceuticals are priced 32.5 percent lower than the original was prior to patent expiry. (Previously it was 20 percent).

From August 2015, generic prescribing is once again mandatory. Previously, it was permitted to add a brand name to the prescription in addition to the INN. Targets have been set for the proportion of generic pharmaceuticals a doctor should prescribe at the ATC4 level. If this is not met, i.e. doctors prescribe originals to too great an extent, they may suffer financially.

Prior to 2016, patients were responsible for the entire amount that exceeded the cheaper pharmaceutical (reference price) per therapeutic reference price group. Since 2016, patients and industry now share the cost between the excess amount and the cheapest pharmaceutical in the group. A limitation meaning that patients pay at most € 20 extra per pharmaceutical has also been introduced. Previously, the limit was € 50 extra per pharmaceutical.

The degree of subsidy is dependent on the disease: 100 percent subsidy for pharmaceuticals for serious diseases, and 90 percent for pharmaceuticals for chronic conditions and pharmaceuticals for pensioners with low incomes. There is also a regular reimbursement level of 75 per cent.

Ireland

Ireland applies reference pricing.⁷² Manufacturers' prices are set according to a currency-adjusted average price in the reference countries (ex-factory). Price revision occurs every 36 months, with reference pricing the main criterion.

⁷⁰ Rémuzat, C., Toumi, M., Falissars, B. (2013).

⁷¹ IMS Health (2014).

⁷² Health Service Executive (2016).

In order to reduce the total cost of pharmaceuticals, Ireland has introduced generic substitution at ATC 5 level and reference pricing. This reform was conditional to Ireland receiving aid under the EU / IMF financial assistance programs. Reference prices have been gradually introduced from November 2013.

A study of the reform's impact on 15 active substances (41 pharmaceuticals) between August 2013 and May 2014 showed that it led to an average 53 percent cost saving. The greatest effect was measured for atorvastatin, whose total costs fell by 71 percent. Generic use increased by 44 percent during the same period.⁷³

Generic pharmaceuticals are priced 50 percent below the price of original pharmaceuticals. At the same time as a generic pharmaceutical enters the market, the original pharmaceutical price is reduced by 30 percent within 60 days and a further 20 percent the following year.⁷⁴

There are essentially four systems for the benefits scheme:⁷⁵

- General Medical Services (GMS) - € 2.50 own fee per product.
- Drugs Payment (DP) - ceiling for own fee amounts to € 144 per month
- Long-Term Illness (LTI) - 16 medical conditions have special coverage. The subsidy level amounts to 100 percent for people in LTI and people with *Hepatitis C and Health Amendment Act Cards*.
- High Tech Drugs (HTD) - is managed within inpatient care but pharmaceuticals can be collected at the pharmacy.

A 100 percent level of subsidization applies after a special direct payment has been made.

Discounts are also found. According to IMS Health, Ireland has a similar discount arrangement as Germany, i.e. about four percent.

Italy

Since 2001, Italy has applied formal / informal reference pricing. Reference pricing is not the main criterion, but it does support the decision-making process and is used in negotiations with the price committee. In negotiations with the price committee, issues taken into consideration include the following:⁷⁶

- Cost-effectiveness of the pharmaceutical in the absence of other effective therapies,
- Risk / benefit compared with alternative pharmaceuticals for the same indication,
- Therapeutic cost per day compared to products with the same effect,
- Assessment of the economic impact on the national healthcare system,

⁷³ Spillane (2015).

⁷⁴ COWI (2014), p. 110.

⁷⁵ Spillane (2015).

⁷⁶ ISPOR Italy Pharmaceuticals.

- Data on price and use in other European countries. IRP data are collected at ex-factory level. IRP price reviews take place every 24 months.

It is possible for pharmaceutical companies to apply for a premium price for innovative products.⁷⁷

Italy has implemented far-reaching decentralization of responsibility within healthcare and it began regionalization in 2001. The different regions in Italy have the freedom to determine the levels of patients' own fees and can thereby control their costs and budget outcomes.

Own fee contributions vary between regions within the range 1-8 €. There is no percentage degree of subsidization.

In Italy, generic medicines are priced at least 20 percent lower than the original pharmaceutical reference price. Generic prescribing (INN) is mandatory. Pharmaceutical names can be stated only if specific medical reasons exist.

Portugal

Portugal has applied formal reference pricing since 2003. In April 2013, two changes were made regarding reference countries: Slovakia was replaced with Slovenia and Italy was replaced with France. As previously, Spain remains a reference country. Price data are collected at ex-factory level. Reference price reviews take place every 12 months.

During the period from the second half of 2010 to March 2013, a reduction of the maximum price for granting subsidized pharmaceuticals of 6 percent was implemented. In 2011, a price decrease of 7.5 percent was made, but only for specific biological pharmaceuticals. Official list prices at that time shall not take account of that discount, according to Vogler et al 2011.

The degree of subsidization is 100 percent for pharmaceuticals vital to life: 90 percent for critical pharmaceuticals for chronic diseases, 69 percent for critical pharmaceuticals for serious diseases, 37 percent for non-priority pharmaceuticals with therapeutic benefit, and 15 percent for new pharmaceuticals with non-established therapeutic benefits.

In Portugal, generic pharmaceuticals are priced 20-50 percent lower than the original. A new law on generic prescribing (INN) entered into force in 2015.

Switzerland

Switzerland applies formal reference pricing. The average price of pharmaceuticals in nine countries is used as reference. Price information is collected on the ex-factory level.⁷⁸ In 2015, the number of reference countries increased from six to

⁷⁷ ISPOR Italy Pharmaceuticals.

⁷⁸ FOPH (2016a)

If ex-factory is not available, wholesaler or pharmacy prices can be used. FOPH approximates wholesale margins.

nine as Belgium, Finland and Sweden were added.⁷⁹ Other countries are Denmark, the Netherlands, France, Germany, Britain and Austria. Countries have been chosen because they are considered similar regarding economic conditions and healthcare structure. Reference prices are used in combination with national therapeutic comparisons. Reference price reviews take place every 36 months.

Swissmedic handles marketing approval and the Federal Office of Public Health (FOPH) deals with subsidies and pricing. Upon application to the FOPH, pharmaceutical companies need to demonstrate a positive recommendation from Swissmedic. Price is decided in the List of pharmaceutical specialties (SL).⁸⁰ Conditions for inclusion in the SL-list include Swissmedic approving the pharmaceutical and that it is deemed cost-effective. The cost analysis assesses international reference prices and a therapeutic comparison to similar products is also made. This involves a comparison with other products that already have subsidy status in Switzerland for the same or similar indication, and a comparison of treatment costs per day or total treatment cost. An innovation bonus (for better efficacy, fewer side effects) of 1-20 percent that may apply in the therapeutic comparison is also found.⁸¹

Prices are weighted with a 2/3 weighting according to the international reference price and a 1/3 weighting for the national therapeutic comparison. There is a limit of 5 percent if the national therapeutic comparison gives a higher value than the international reference price. In the absence of data on international reference prices (for example, if the pharmaceutical is not on the market in other countries), only the national therapeutic comparison is used.

The margin for distribution is regulated and for prescription pharmaceuticals is 4-240 CHF plus a relative margin of 0-12 percent that is added to the ex-factory price.

The prices of generic pharmaceuticals should be at least 20 percent lower than the price of the original.⁸² Exceptions can, however, be made for generic pharmaceuticals with small market shares. Ceiling prices of generic pharmaceuticals are set differently depending on the sales of the original pharmaceutical four years before patent expiry. The price of the first subsequent product is set to at least 10 percent lower than the original price if the original sales value was below 4 million CHF. If the original sales value was 4-8 million, price is set to 20 percent below the original. If the original sales value amounted to 8-16 million, the price is 40 percent lower than the original. If the sales volume amounted to between CHF 16-25 million, price is 50 percent lower than the original. If the sales value exceeded 25 million CHF, the price of the subsequent product is set to 60 percent lower than the original.

⁷⁹ Interpharma, Price comparison with other countries.

⁸⁰ FOPH (2016b).

⁸¹ FOPH (2016a).

⁸² FOPH (2016a).

Generics are obliged to enter the market at a discounted price to the original (after the patent expiry re-evaluation), depending on turnover of the original: 60% price discount, if turnover > CHF 25 mio. 50% price discount, if turnover > CHF 16-25 mio. 40% price discount, if turnover > CHF. 8-16 mio. 20 % price discount, if turnover > CHF. 4-8 mio. 10 % price discount, if turnover < CHF. 4 mio.

Prices of biosimilars are set to 25 percent below the price of the original pharmaceutical. Switzerland plans to introduce a reference price system even for generic pharmaceuticals but the timing of this measure is not established.

Private health insurance is compulsory for everyone living in Switzerland. The insurance includes the costs of pharmaceuticals prescribed on prescription by a doctor. The own-fee contribution amounts to 300 CHF on an annual basis. A further 10 percent of the remaining costs amounting to a maximum of 700 CHF per year will be added. If a generic alternative to the medicine is available but not chosen, the patient's additional cost instead amounts to 20 percent of the remaining cost of treatment.

Spain

Spain applies informal reference pricing on the basis of lowest price. Price reviews take place every 12 months. Price data are collected at ex-factory level.

Spain has implemented a far-reaching decentralization of responsibility for healthcare and since 2003, 17 regions have full budgetary responsibility for healthcare. The price in Spain shall be below the lowest price available in the Euro zone countries in those cases where the cost-effectiveness is considered less favourable, or when a pharmaceutical is expected to have a large budgetary impact.⁸³

Prices of generic pharmaceuticals are set at 40 percent lower than the price of the original. When a reference cluster group is created, the price of the original is lowered to the same level as the subsequent products.

Generic prescribing is encouraged in Spain. Substitution to the pharmaceutical with the lowest price in the group should be implemented in pharmacies in all cases where prescriptions are prescribed with the INN.

During the first half of 2010, a discount of 7.5 percent on original pharmaceuticals and 4 percent on orphan pharmaceuticals was implemented. Official list prices shall take account of this discount. At the same time, even a 30 percent price reduction on generic pharmaceuticals was made.⁸⁴ A discount system linked to the size of the pharmaceutical companies' investment in research and development in Spain is in place.

Austria

Austria applies formal reference pricing. Price data is collected at ex-factory level. The price of outpatient pharmaceuticals in the benefits scheme is regulated nationally on a distributor purchase price or pharmaceutical company selling price level.

Price is determined after price negotiations between producers and the Ministry of Health (BMG) in consultation with the national pricing committee. In these negoti-

⁸³ Ruggeri, K. and Nolte, E. (2013).

⁸⁴ Vogler et al (2011).

ations, the average price in the EU constitutes a ceiling price. To calculate the average price, manufacturers need to provide information about the pharmaceuticals' availability in other EU markets and state the prices in these countries.

Austria makes no distinction between subsequent generic products or biosimilars. The only aspect regulated is that price is adjusted after that a '*subsequent*' enters the market. The first subsequent product is priced at least 48 percent lower than the price of the original. In turn, the price of the original product shall be reduced by 30 percent within three months of the first subsequent entering the market. The second subsequent product is priced 15 percent lower than the first subsequent. If a third subsequent enters, its price is set 10 percent lower than the second subsequent. Subsequently, all comparable products are to have the same price level as the third subsequent product within three months.⁸⁵

The fee per prescription amounts to € 5.55. Own contributions can amount to a maximum of 2 percent of a patient's annual income.

Hungary

Hungary applies formal reference pricing using the lowest price of 31 countries (EU and EEA). Price data is collected at ex-factory level.

For generic pharmaceuticals in Hungary, the first subsequent product is priced at least 40 percent below the original price. The second subsequent generic product is priced 20 percent lower than the first subsequent product. Third subsequent product is priced 10 percent lower than the second subsequent product. The fourth to sixth subsequent products' prices are five percent lower than the preceding. Subsequently, subsequent products are merely priced lower than the preceding without specified minimum levels being given.

Degrees of subsidization amount to 85 percent, 55 percent and 25 percent depending on therapeutic value and disease severity. For some specific diseases, subsidy up to 100 percent may apply.

Czech Republic

The Czech Republic applies formal reference pricing for both subsidization and pricing. When deciding on subsidization, if the pharmaceutical is to be included in the benefits scheme, the lowest price of the reference countries (the entire EU) is calculated. In cases where the lowest price is more than 20 percent lower than the second lowest price, the average of the second and third lowest price is calculated. Price data are collected at ex-factory level. When making pricing decisions, the average price of the three countries with the lowest prices is calculated. Reference price revisions take place every 36 months.

⁸⁵ PPRI (2015a).

The patient's own fee contribution comprises the difference between the determined subsidized price and the selling price. In addition, the patient pays a prescription dispensing fee of 30 CZK (around 88 SEK).

For generic pharmaceuticals, the first subsequent pharmaceutical is priced 32 percent below the original price (15 percent for biologicals). The same lowest price reduction is applied to the entire reference group.

Slovakia

Slovakia applies formal reference pricing using prices from 27 countries. Price is calculated as the average of the three countries with the lowest price for a product. Reference price reviews take place every 6 months. Price information is collected at ex-factory level.

Pharmaceuticals classified as new and innovative are investigated to see if their efficacy is equivalent to the limit set for quality-adjusted life years (QALYs). The limit is set at the average working earnings for the previous two years.

The degree of subsidization is either 100 percent or a partial figure depending on criteria.

For generic pharmaceuticals, the first subsequent pharmaceutical is priced at least 35 percent lower than the original (at least 20 percent for biosimilars). Generic prescribing is compulsory since 2011. However, it is possible for doctors to also specify a trade name or brand on the prescription.

Poland

Poland applies informal reference pricing using prices from 31 countries (EU and EFTA). Price information (ex-factory) is used in conjunction with the Economic Commission's price negotiations. Reference price reviews take place every 24 months. Poland has six countries that constitute a reference group for HTA assessments (Estonia, Latvia, Lithuania, Hungary, Croatia and Slovakia).

Every second month, the Ministry of Health publishes a list of pharmaceuticals that are subsidized. Depending on whether the length of treatment is more than or less than 30 days, the overall degree of subsidization for the pharmaceuticals in the benefits scheme is 50 or 70 percent. The degree of subsidization is 100 percent for certain diseases and also for war veterans. Own fee contributions for certain pharmaceuticals (defined on the subsidized list) used by pensioners over 75 years were taken away on September 1, 2016.

For generic pharmaceuticals, subsequent pharmaceuticals are priced at the most at 75 percent of the reference price of the original. The initial price decision applies for two years and thereafter for three- and five-year periods.