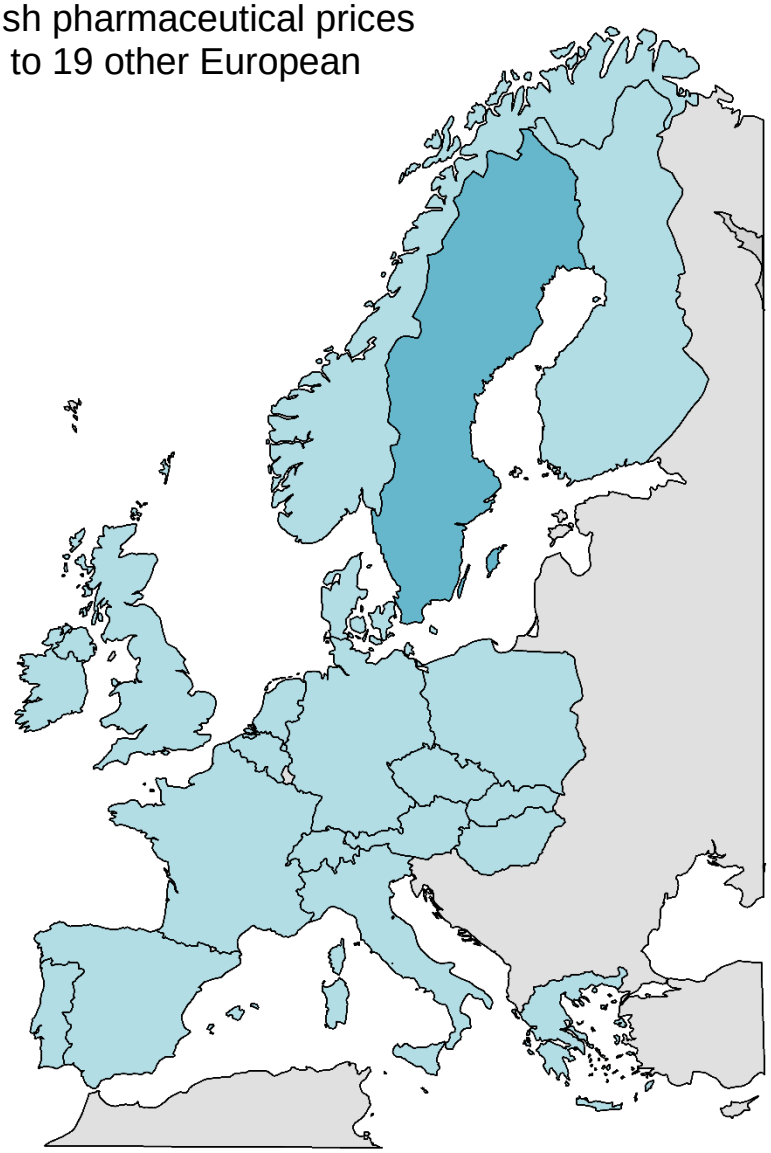
TANDVÅRDS- OCH
LÄKEMEDELSFÖRMÅNSVERKET

International price comparison 2019

An analysis of Swedish pharmaceutical prices and volumes 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 each year between 2014 and 2019 in Sweden in comparison with 19 other European countries. The segments analysed are pharmaceuticals not exposed to competition and pharmaceuticals exposed to competition, with the latter including all pharmaceuticals available as substitutable medicines in the Swedish generic substitution system (product-of-the-month) as per March 2019.

The report should be viewed as a basis for further continuous monitoring of the dynamics of Swedish prices and price changes compared to that seen in other countries.

Agneta Karlsson
Director-General

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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. The report is the sixth report of its kind.

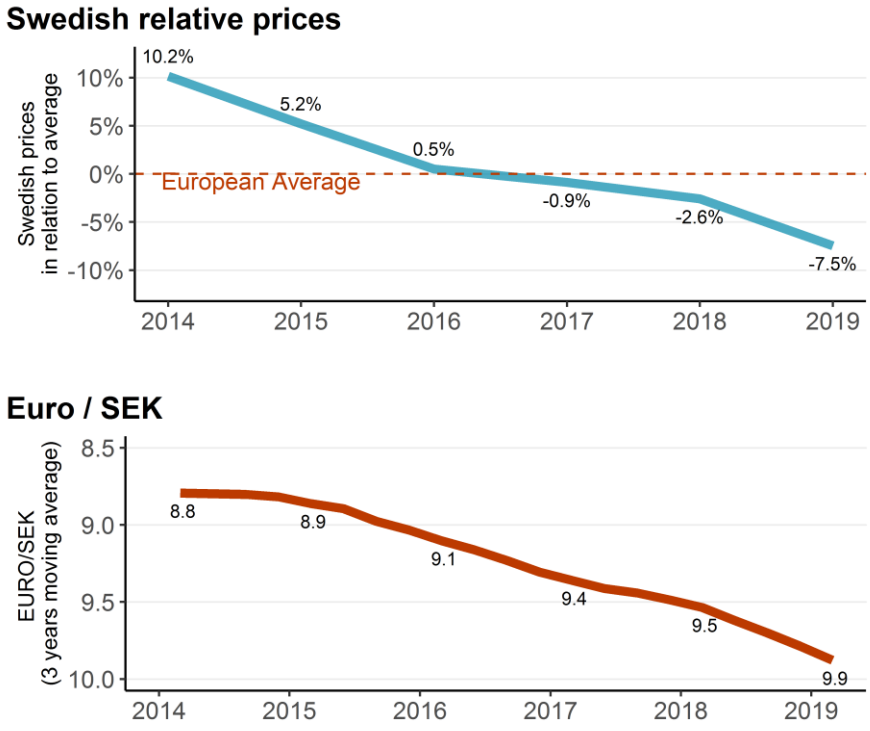
Price comparisons of pharmaceuticals between countries is a tool for healthcare, pricing and reimbursement authorities, and companies to gain knowledge about how a country's pharmaceutical prices relate to other countries. In recent years, various forms of agreements have been established for several pharmaceuticals in European countries, ultimately resulting in the cost being lower than if the cost were to be calculated based solely on list prices. In Sweden, these agreements are referred to as managed entry agreements. The report shows that, even when pharmaceuticals with Swedish managed entry agreements are excluded, the overall results remain the same.

The analysis is based on prescription human pharmaceuticals. For the analysis, TLV uses price and sales statistics from IQVIA. The prices refer to prices that applied during the first quarter of each year in each country. The volumes refer to a rolling 12 months in Sweden up to and including the first quarter of each year between 2014 and 2019. Prices in Sweden are compared with prices in 19 other European countries. The report is based on national prices at the pharmacy purchasing price (AIP) level. Only public prices are included in the comparison since only these can be collected in a standardised manner.

For comparison, a three-year rolling average is applied to the exchange rate for each quarter, which means the results are less sensitive to temporary currency changes. The pharmaceuticals have been divided into two segments based on the conditions for competition in Sweden. Pharmaceuticals that are not substitutable are included in the segment for pharmaceuticals not exposed to competition, while products that are substitutable and included in the generic substitution system (product-of-the-month) for the period are included in the segment for pharmaceuticals that are exposed to competition.

The results for Swedish pharmaceutical prices 2019 have changed in comparison with 2018. Pharmaceuticals not exposed to competition have dropped in price in relation to the report's comparison countries. For the first quarter of 2018, Swedish pharmaceutical prices were 2.5 per cent below the average, while for the first quarter of 2019 they had fallen to 7.3 per cent below the average. A strong contributing factor behind Sweden's relative price reduction may be weakening of the Swedish krona in relation to the euro. Figure 1 below shows Sweden's relative price development and the development of the euro/SEK for the period 2014 to 2019.

Figure 1. Sweden's relative prices in relation to the average per year, calculated as cross-section



Source: IQVIA, Eurostat and TLV analysis.

Note: Pharmaceuticals not exposed to competition, running 3-year average exchange rate for the respective year. Development of the Swedish krona relative to the euro for the same period.

The figure shows that Sweden's relative prices, as part of a 20-country comparison, largely follow the development of the krona's value in relation to the euro. This is because pharmaceuticals not exposed to competition have set prices in SEK that do not vary greatly over time. If the Swedish krona has a lower value in euros, the price will appear to be lower compared to a country with the euro, even though the prices have remained unchanged locally. However, it is not just the currency that has affected Sweden's relative position. Reductions in the list price, i.e. the set prices in Sweden (AIP), have also contributed. From 2014 to 2016, the relative price reduction can largely be attributed to the effects of reviews and regulated price reductions of pharmaceuticals that are 15 years old or older. Together, currency and price dynamics have contributed to Sweden moving from being the country with the five highest prices in 2014 to having the five lowest prices in 2019.

Within the pharmaceuticals exposed to competition segment, Sweden has consistently had lower prices in relation to other countries in Europe. During the period 2014 to 2019, Sweden has been in the group with the lowest prices, together with Denmark and the Netherlands, which also has a generic exchange at pharmacies.

For pharmaceuticals exposed to competition, the possibility to adjust prices are greater as a result of the design of Sweden's product-of-the-month system. The prices are allowed to vary under a ceiling price. This means that if the value of the Swedish krona drops, pharmaceutical companies can raise their prices to compensate for exchange rate losses. A weaker krona does not lead to relative price reductions in the same way for Sweden's part of the segment pharmaceuticals exposed to competition. Sweden's relative prices have increased during the period. However, this relative price increase has not resulted in Sweden losing its position as the country with the lowest relative prices in this segment.

This year's report also analyses price differences for a number of defined pharmaceutical groups. The largest sales are in the pharmaceutical groups oncology, TNF inhibitors and hepatitis C. For these groups, Sweden has relatively low list prices. For certain medicines in these three groups, there are managed entry agreements, and the actual costs in Sweden are thereby lower than the list prices used in the analysis. The pharmaceutical groups IL inhibitors, antiepileptics and obstructive airway diseases all have high sales in Sweden. The Swedish prices for these pharmaceutical groups are higher or in line with the European average. Since the Swedish prices are currently relatively low due to a weak currency, it is likely that the relative prices would increase and become higher than the European average if the Swedish krona becomes stronger again. For these three groups, there are no managed entry agreements, and the list prices thereby mirror the actual pharmaceutical costs in Sweden.

In the segment pharmaceuticals exposed to competition, the analysis shows that the pharmaceutical groups ADHD and antiepileptics have relatively high prices in Sweden. One possible explanation is that Sweden's product-of-the-month system is limited for these groups for various reasons.

Part of TLV's mandate is to shed light on Sweden's pharmaceutical prices over their life cycle. This year's results are in line with previous years' analyses. New pharmaceuticals are priced in line with the average for the countries in the study. When products have been on the market for 5 to 15 years, Sweden's prices are relatively higher than the average. This is because prices in other countries drop during this period, while Sweden's set prices remain largely unchanged. When the patent runs out after about 15 years, and generic competition usually arises, Sweden's pharmaceutical prices drop clearly below the average.

Terms and concepts

ATC – *Anatomical Therapeutic Chemical Classification, (ATC*) is a system for classifying pharmaceuticals. The ATC system consists of 14 main groups into which pharmaceuticals are classified based on their main indication.

A Alimentary tract and metabolism
B Blood and blood-forming organs
C Heart and cardiovascular system
D Dermatological medicines
G Genitourinary system and reproductive hormones
H Systemic hormonal preparations, excluding reproductive hormones and insulins
J Antiinfectives for systemic use
L Antineoplastic and immunomodulating agents
M Musculoskeletal system
N Nervous system
P Antiparasitic products, insecticides and repellents
R Respiratory system
S Sensory organs
V Various ATC structures

AIP - Pharmacy purchase price –the pharmacy operator's purchase price in SEK. Set by TLV.

AUP - Pharmacy selling price –the pharmacy operator's selling price in SEK. Set by TLV.

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

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

Ex factory – sales price from the marketing authorisation holder. Costs for transport from the factory plus taxes and mark-ups will be added.

Generic pharmaceutical – pharmaceuticals containing the same active substance, in the same dosage form and with the same strength, and which give the same medicinal effect.

EPR - International reference price (IRP, EPR, ERP) – pricing method where the price(s) of a pharmaceutical in one or more countries is considered in the national pricing of pharmaceuticals. Common synonyms are international reference pricing (IRP), *external price reference* (EPR) or *external reference pricing* (ERP). It could also be called simply reference pricing. The pricing method can be formal or informal/supporting, in combination with another method (e.g. assessment of 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.

ERP – see *EPR*

INN – Generic name – 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.

IRP – see *EPR*

List price – Price that is formally paid, regardless of discounts or rebates. Equivalent to set prices in the form AIP in Sweden. When countries, including Sweden, are named as a group, list prices are also used to describe Sweden's prices (AIP).

Pharmaceutical benefits scheme – a pharmaceutical included in the pharmaceutical benefits scheme is subsidised and included in the high-cost protection system.

Managed entry agreement – collective name for agreements reduce the cost for using the pharmaceutical, such as risk-sharing agreements, discount and rebate agreements.

Managed introduction – in Sweden called *National managed introduction of new pharmaceutical products* and is developed by the NT Council. Sweden's county councils and regional authorities are collaborating on which new pharmaceutical products should be introduced in health care.

Originator pharmaceutical product – 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 until patent protection expires.

Product-of-the-month – the generic substitutable pharmaceuticals that have the lowest price and that the pharmacies must offer their customers when they replace one pharmaceutical with another. Each month, the product in each package size group that has the lowest unit sales price and that the pharmaceutical company has confirmed can be provided to the entire market with a sufficient sustainability for the entire pricing period price becomes the product-of-the-month. Officially named *Periodens Vara-systemet* (*PV-systemet*) in Swedish.

PV system – see *Product-of-the-month*.

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

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

Cross-sectional price index – the same product needs to be available in several countries to be included in any of the countries' price indices. The threshold, referred to as degree of matching, 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. In those countries that do not have one year's worth of sales of a pharmaceutical that is available in Sweden, Swedish prices are used instead.

Discount – see Rebate

Relative prices – prices in relation to average prices. If relative prices in Sweden increase, this means that Sweden has become more expensive in relation to average prices. This may be because Sweden's prices have increased, or that other countries have lowered their prices and Sweden has remained at the same level.

Risk sharing agreement – agreement where the final cost for use of a pharmaceutical product depends on future outcomes. Often used for new expensive pharmaceutical products where the therapeutic benefit is uncertain.

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.

Segment pharmaceuticals exposed to competition (in the Product-of-month) – includes all pharmaceuticals available as substitutable pharmaceuticals for the product-of-the-month per year as per March.

Collateral agreement – see *Managed entry agreement*. In Sweden, these agreements are concluded between the pharmaceutical companies and the county councils.

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

Substitutable pharmaceuticals – pharmaceuticals that the Swedish Medical Products Agency has determined are exchangeable with one another because they contain the same active substance in the same dosage form and with the same strength and that they give the same medical effect.

Rebate – a form of reimbursement that is paid retrospectively. In Sweden, manufacturers pay rebates to county councils based on the provisions of the managed entry agreements. Internationally it is often referred to as a discount.

1 Introduction

1.1 Mandate

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 tasks is to develop value-based pricing in order to ensure that the cost of pharmaceuticals is reasonable throughout the entire life cycle. Part of this work involves setting Sweden's pharmaceutical prices and use in an international perspective. The regulation (2007:1206) with instructions to TLV, amongst other things, states 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. This report is part of the ongoing work and is the sixth report of its kind.

The comparison covers pharmaceuticals not exposed to competition as well as pharmaceuticals exposed to competition. The report describes how the prices of prescription pharmaceuticals in Sweden relate to 19 other countries in Europe. For all countries, see the table below.

Table 1. Countries included in the analysis

Belgium	Portugal
Denmark	Switzerland
Finland	Slovakia
France	Spain
Greece	United Kingdom
Ireland	Sweden
Italy	Czech Republic
Netherlands	Germany
Norway	Hungary
Poland	Austria

The purpose of the report is to analyse the Swedish prices in an international perspective. In addition, the dynamics are examined in terms of price, volume and exchange rate, factors that affect the Swedish prices in relation to other countries.

1.1.1 Delimitation and explanation of terms

The mandate does not include determining whether Swedish pharmaceutical prices are at the desired level or suggesting changes to potentially reach a desired level. This report primarily analyses the outpatient market. Pharmaceuticals sold within inpatient care therefore have limited coverage in this report. The proportion of pharmaceuticals that are dispensed within inpatient care varies significantly between countries.

In Sweden, price and cost analyses are based on fixed prices (AIP, pharmacy purchase price)[1]. The statistics analysed in this report are based on the list prices of other countries, making list prices the starting point of the analyses in this report. In Sweden, list prices are defined as prices set by TLV.

The purpose of this report is to analyse Sweden's pharmaceutical prices compared to other countries. In Sweden, there are agreements between regions and pharmaceutical companies, managed entry agreements, that entail rebate of parts of the pharmaceutical costs from the companies to the regions. The pharmaceutical costs are thus affected by rebates from managed entry agreements. The effect is not captured when the analysis focuses on price comparisons of list prices. Since the analysis is carried out over time and focuses on the development of price, a comparison of price differences remains important and relevant. However, it is interesting to also analyse how much rebates from managed entry agreements affect the analysis of Sweden's pharmaceutical prices compared to other countries. For this reason, a comparison of this type is found in section 3.2.2.

The analyses in this report are mainly based on pharmaceutical prices within outpatient care, which means that the pharmaceuticals are picked up from a pharmacy. In some countries, some pharmaceuticals are largely managed within inpatient care, while in Sweden the majority are handled via prescription in outpatient care.

The report only uses exchange rates calculated as a rolling average of three years. This is to prevent overestimation of the effect of exchange rate fluctuations, and it gives a fair picture of how prices between Sweden and other countries vary; see further in section 2.1.1. The prices used are the prices for the first quarter of each year of the time period, and the volume weightings are rolling for 12 months from the first quarter each year.

1.2 Outline

Under the heading *Methodology and data*, there is a summary of the report's methodology, choice of exchange rate period and data sources. A more comprehensive description of the methodology, sensitivity analyses and previous studies can be found in *Appendix 1: Sensitivity analysis and methodology*. This is followed by a section on the pharmaceuticals market in general, and information on the pricing and reimbursement system for countries in the sample. In *Appendix 2: Pricing and reimbursement* systems, there are detailed descriptions of the systems in all countries that provides additional valuable knowledge about differences and similarities between countries and price systems.

The *Results* section is divided into three sections. First, there is an in-depth study on the life cycle of pharmaceuticals, where prices are analysed according to the age of the pharmaceutical. Then there is a more detailed description of pharmaceuticals

[1] or fixed prices to AUP (pharmacy selling price)

not exposed to competition (outside the generic substitution system) and then pharmaceuticals exposed to competition (within the generic substitution system).

The report concludes with a discussion on the key findings of this year's study and information on continued work.

1.3 Methodology and data

1.3.1 Description of data sources

Method and data selection are briefly described here, and in greater detail under *Methodology* in *Appendix 1*.

The dataset consists of the prescription pharmaceuticals in Sweden showing the highest sales and covered by pharmaceutical benefits scheme. In addition, there are substances with the highest sales in Europe and new, innovative substances[2]. By supplementing the sample with top seller in Europe, the comparison becomes fairer as more relevant pharmaceuticals are compared. In total, there are 813 substances and 10,641 pharmaceuticals in the data set[3]. The market has been divided into pharmaceuticals that are not exposed to competition and pharmaceuticals that are exposed to competition. Exposed to competition means that the pharmaceutical has generic competition and is substitutable at pharmacies. This means that the pharmaceutical is part of the Swedish Product-of-the-month system (Swedish: *Periodens-vara systemet* or *PV-system*), which means that the pharmaceutical is substitutable at pharmacies in Sweden. Divided according to this definition, 2019 contains[4]:

- **Pharmaceuticals not exposed to competition**
  225 substances and 577 pharmaceuticals
- **Pharmaceuticals exposed to competition**
  810 substances and 10,064 pharmaceuticals

In Sweden, pharmaceuticals not exposed to competition accounted for about 82 per cent of total sales (AIP) in quarter 1 2019, while pharmaceuticals with competition account for about 18 per cent. IQVIA's data covers about 97 per cent of the sales in Sweden for 2019. The price comparison is based on prices in other countries and Sweden. In Sweden, the prices are set prices in the form of pharmacy purchase price (AIP), but Sweden's prices are also referred to as list prices in comparison with other countries. Discounts on list price in other countries and rebates from managed entry agreements in Sweden are not included in the data set. A product is defined as a pharmaceutical with the same substance, dosage form and strength. The price is calculated as cost per counting unit[5].

[2] EFPIA's WAIT Indicator. https://www.efpia.eu/media/412747/efpia-patient-wait-indicator-study-2018-results-030419.pdf (2019-11-10)
[3] A pharmaceutical is defined as a combination of substance, dosage form and strength.
[4] A substance can be found in both segments, i.e. exposed to competition or not exposed to competition. This is because different forms and strengths of the same substance can have a different competition status.
[5] According to IQVIA's definition of sales volume in counting units

TLV has used price and sales statistics from IQVIA for the first quarters of 2014, 2015, 2016, 2017, 2018 and 2019. The price level in Sweden is compared with 19 other European countries.

1.3.2 Method

One challenge with price comparisons between countries is that not all countries use the same pharmaceuticals as Sweden. The proportion of pharmaceuticals used in two countries that are compared is called degree of matching. The report is mainly based on two methods for comparisons as they show different things. The methods of price comparison in the report are:

- **Bilateral comparison**
  Compares prices of *only* the pharmaceuticals found in a particular country and in Sweden. For example, if Finland uses 59 per cent of the pharmaceuticals that Sweden uses, the price comparison only covers 59 per cent of the pharmaceuticals found in Sweden. Pharmaceuticals with very low sales in relation to the Swedish market have been excluded.

- **Cross-sectional comparison**
  Assumes that *all* countries in the study have *all* of the pharmaceuticals used in Sweden. If a country does not use a pharmaceutical, it is assumed that the country's price is the same as the average price of that pharmaceutical in the countries that use it. To ensure that a sufficient number of countries use a pharmaceutical, it must have sales in at least eight countries to be included in the comparison.

One advantage of the cross-sectional analysis is that all countries have all pharmaceuticals, making it possible to calculate an average. The bilateral price comparison instead describes an exact price comparison between a specific country and Sweden. Thus, it is not possible to calculate an average for all countries, and it is not possible to compare with e.g. Denmark and Norway when only the pharmaceuticals that are found both there and in Sweden are used.

Both the bilateral and cross-sectional price comparison are based on Swedish volumes of the respective pharmaceutical. Only prices of pharmaceuticals are compared between countries. For more detailed information on the method, see the section *Sensitivity analysis*, subheading *Methodology,* for more information.

2 The pharmaceuticals market

2.1 Market overview

The purpose of the sections on market overview, pricing models and facts about the countries in the study is to provide a background to the context in which the results of the international comparison of pharmaceutical prices should be viewed. Some of the countries in the study have major similarities in their healthcare systems and systems for pricing pharmaceuticals, while others differ more widely. For example, this may relate to transparency regarding list prices and whether discount systems are institutionalised and included in pharmacy purchase prices or other agreements mean that certain official list prices do not fully reflect the actual price of a pharmaceutical.

Globally, pharmaceuticals had sales of around SEK 8,672 billion in 2019, calculated as the price from the manufacturer. North America dominates the pharmaceutical market and represents about 49 per cent of the world market. Europe in its broadest sense represents about 23 per cent. Africa, Asia and Australia together account for just over 17 per cent, Japan represents just over 7.4 per cent of the world market and Latin America just over 3 per cent.[6]

The total population of the 20 countries in the study amounts to about 483 million inhabitants[7]. The five largest countries in terms of population (Germany, France, the UK, Italy and Spain) together account for almost 66 per cent of the population base. These five countries account for about 69 per cent of the total sales in the analysis at pharmacy purchase price (AIP) level. Sweden's share of the population is 2 per cent, and its share of the total sales is just under 4 per cent.

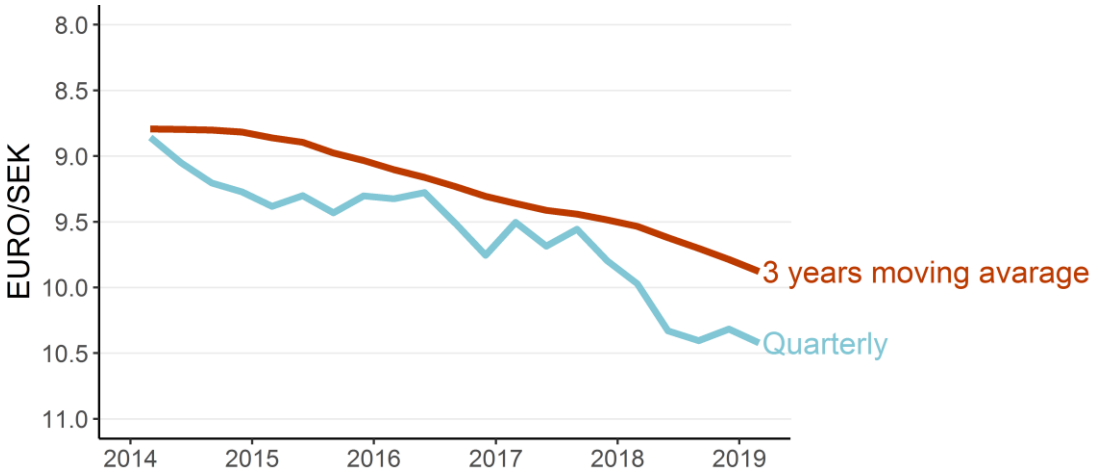
2.1.1 Exchange rate

Development of the Swedish krona has been weak in recent years, with the trend continuing in 2019. In order to obtain a more balanced overview of the Swedish relative prices, exchange rates have therefore been calculated as a three-year rolling average. This is the same method as used in the 2018 report, but differs from the reports from 2014 to 2017.

The diagram below shows the Swedish krona's development quarterly and as a rolling three-year average in order to clarify the difference depending on which method is used.

[6] EFPIA, The Pharmaceutical Industry in Figures 2019, states that global sales amount to EUR 845,235 million. Conversion to SEK according to the average exchange rate (10.26) in 2018.
EFPIA (2019) The Pharmaceutical Industry in Figures, Key data 2019.
https://www.efpia.eu/media/413006/the-pharmaceutical-industry-in-figures.pdf
[7] Eurostat (2015)

Figure 2. Swedish krona's development quarterly and in a rolling 3-year average, 2014–2019



Source: Eurostat

Note: euro/SEK; the number of Swedish krona per euro.

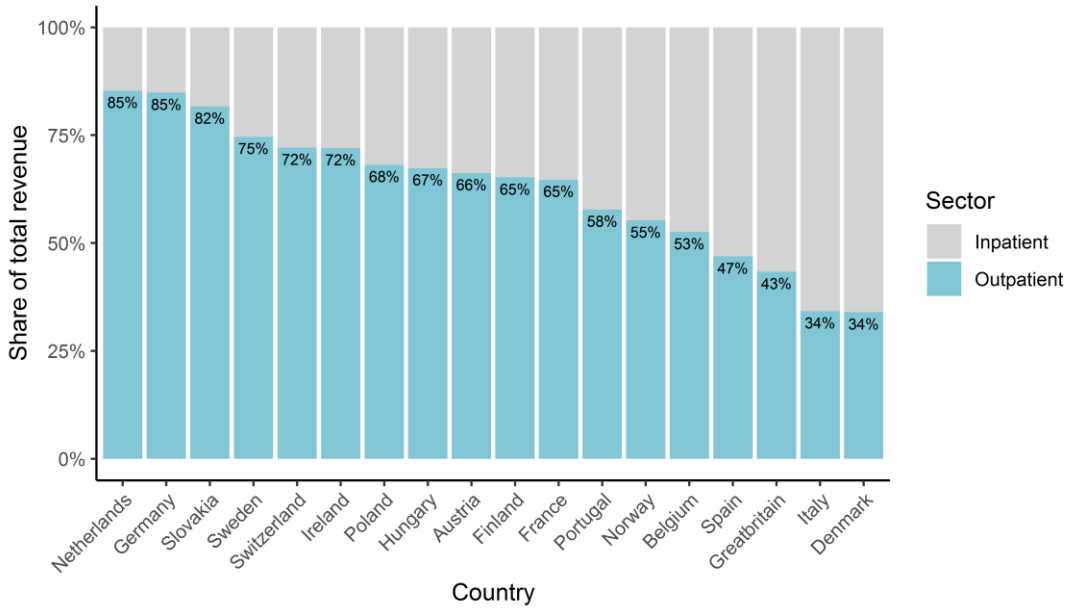
The weakening of the Swedish krona against the euro means that a pharmaceutical with an unchanged price in SEK becomes relatively cheaper in euro. The development of the Swedish krona compared to euro becomes more conservative with a 3-year rolling average and is more in line with historic levels. This gives a fairer picture of how prices between Sweden and other countries vary, and reflects fundamental causes rather than the weak exchange rate. The difference between the rolling three-year average and the quarterly exchange rate has increased between 2018 and 2019. See the section *Sensitivity analyses* and subheading *Exchange rate* for more information. The sensitivity analysis also examines the outcome with other exchange rates.

2.1.2 Outpatient and inpatient care

The analyses in this report are mainly based on pharmaceutical prices within outpatient care, which means that the pharmaceuticals are picked up from a pharmacy. In some countries, some pharmaceuticals are largely managed within inpatient care, while in Sweden the majority are handled via prescription in outpatient care. Some caution should be exercised when comparing data from outpatient care only. The choice of pharmaceutical management, i.e. by prescription in outpatient care or at a hospital with inpatient care, makes this kind of comparison difficult without knowledge of specific national conditions regarding pharmaceutical management.

The figure below shows the percentage of outpatient and inpatient management by sales value. On average, these 19 countries manage over 60 per cent of the total sales within the context of outpatient care. Denmark, Italy, the UK and Spain are the countries that have a relatively small sales value within outpatient care and a significantly higher relative percentage that is managed within inpatient care. In Sweden, approximately three quarters are managed by prescriptions within outpatient care, and one quarter is managed within inpatient care.

Figure 3. Percentage of sales value in AIP sold within inpatient and outpatient care per country



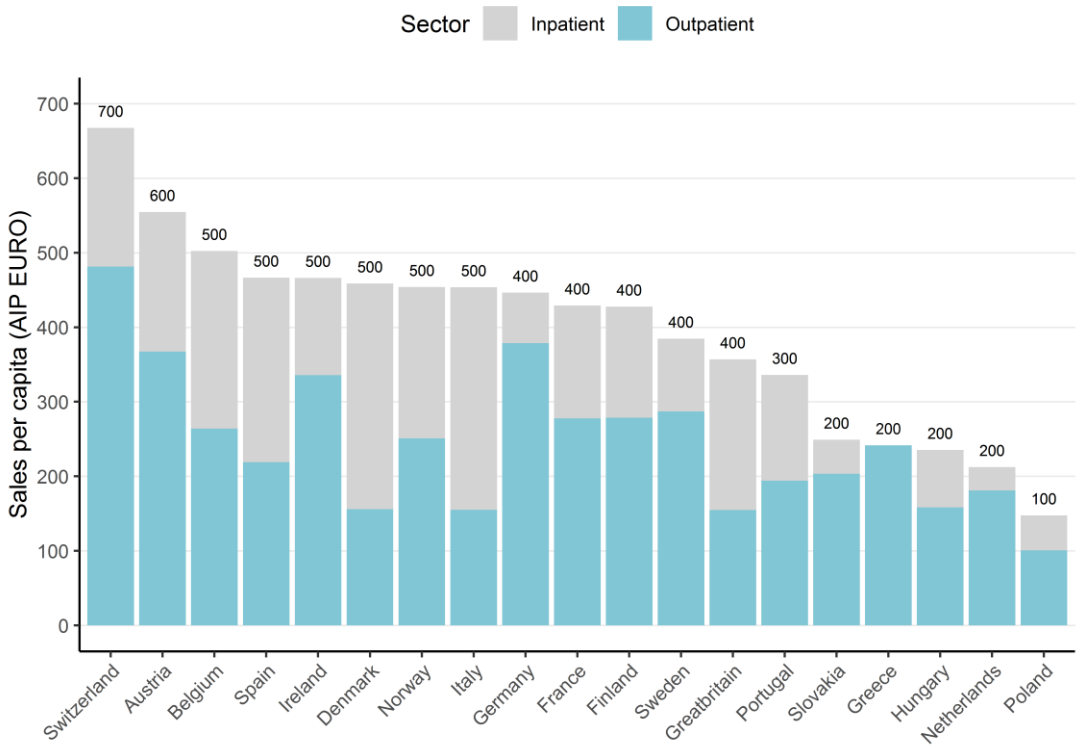
Source: IQVIA and TLV analysis.

Note: Data regards rolling 12 months through March 2019. Greece is excluded because inpatient care data is missing.

The following figure shows outpatient and inpatient pharmaceutical sales per capita in Europe. The average amounts to approximately SEK 3,500. The total sales value per inhabitant is highest in Switzerland (approximately SEK 6,600 per inhabitant), followed by Austria (SEK 5,500 per inhabitant). Sweden has the twelfth highest sales of all countries with approximately SEK 3,800 per capita.

Based on total sales value per capita, our Nordic neighbours Denmark, Norway and Finland have slightly higher costs compared to Sweden. See Figure 4 below.

Figure 4. Sales value in SEK AIP sold within inpatient and outpatient care per country



Source: IQVIA and TLV analysis.

Note: Data regards rolling 12 months through March 2019, rounded to even hundreds. Greece is excluded because inpatient care data is missing.

The analysis only includes products with sales within the Swedish outpatient care. The sample was limited to prescription pharmaceuticals within outpatient care because it is these pharmaceuticals that TLV sets prices for. The products in inpatient care also have less transparent prices, which makes this type of analysis more difficult.

There may be variations in how healthcare in different countries chooses to treat the same disease. One difference could be how they handle what is distributed through prescription and what is managed within the context of inpatient care. Another difference could be variations in drug therapies, which could mean that a disease is treated with different pharmaceuticals than those used for treatment in Sweden. In addition, not all pharmaceuticals are approved or introduced in all countries.

This means that the pharmaceuticals included in the analysis based on a Swedish perspective are not necessarily found to the same extent in the comparison countries. The calculation of the weighted price comparison covering all countries is affected by the mix of pharmaceuticals available in the different countries. Products sold by prescription in Sweden may not be sold by prescription in other countries. Such products will then not be included in the calculation.

2.1.3 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 level in several reference countries (reference pricing) or to base pricing on appraised values or profitability.

Table 2. Different pricing systems

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 (IRP)	**a)** Formal	**b)** Informal in combination with another method (e.g. assessment of benefit or value)	

Reference pricing, which is the most common method in Europe, can be formal or informal/supporting. This means that the average, the median or the maximum price that is calculated governs the set price either directly, or it constitutes a level that is considered during negotiation, during procurement or that forms part of a wider supplementary health-economic assessment.

The number of countries in a price basket varies greatly within Europe, from 3 to 31 countries. Consequently, this affects what effect an individual country's price or price range will have on a price basket in another country. The direct or indirect strength of the price impact also varies depending on whether the country applies some form of supplementary assessment in addition to international reference pricing. Also, of great importance is whether a country considers the lowest price or the average price among the prices in a reference basket. For a more detailed description of the pricing system, see *Appendix 2*: Pricing and reimbursement systems.

2.1.4 Generic substitution

There are several variants for generic substitution systems linked to the lowest price over a period of time. Examples of this are as follows:

- Denmark uses periods of two weeks,
- Sweden, with the Product-of-the-month system, has a period of one month,
- The Netherlands has a period of 3, 6, 12 or 24 months and
- Finland has a system with price tendering that applies for three months. The lowest bid wins the tendering. Other players can then lower their price to this price to become substitutable.

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 stepped pricing model for generic pharmaceuticals. 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, which connect price reduction of the originator and generic pharmaceuticals to certain periods of time after competing pharmaceuticals have entered the market.

Most of the countries have some form of supplementary pricing and reimbursement management in addition to traditional pricing. In some cases, this applies to the entire pricing through general discounts, but it is more common for measures to be applied to specific products. What in Sweden is referred to as "sidoöverenskommelser" ("collateral agreements") falls under the broader concept of *managed entry agreements* (MEA) internationally. An MEA can be anything from special financial agreements with refunds, rebates, discounts, price-volume agreements and risk sharing to different variants of managed introduction.

Portugal, Germany and Spain are examples of countries with general discount systems that are not seen in list prices. Lack of complete information on discounts is a weakness in all price surveys. However, analysis of change over time and – specifically in this report – a comparison of the development of the same products between 2014 and 2019 is a clear advantage. Assuming that any discounts are at about the same level from one year to the next gives a good comparison of the relative price development between different countries.

For further information about the pricing models, please see Appendix 1 and 2, which are intended to improve understanding of the pricing and reimbursement systems in the 20 countries analysed in TLV's international price comparison.

2.2 Descriptive statistics

The table below shows how much of Sweden's sales are covered by the data that forms the basis for the analysis. The data set for this report comes from IQVIA.

Table 3. Coverage of sales values

Year	Total AIP IQVIA	Total AIP eHm	Coverage
2014	4.09	4.57	90%
2015	4.74	4.81	98%
2016	4.68	5.07	92%
2017	4.74	5.42	87%
2018	5.76	5.8	99%
2019	6.15	6.26	98%

Note: in data from IQVIA in relation to data from the Swedish eHealth Agency (eHm). Sales of pharmaceuticals in quarter 1 between 2014 and 2019. Totals at AIP level.

The sales value does not cover the total prescription sales of pharmaceuticals in Sweden in the outpatient market. Only the substances with the highest sales in Sweden and Europe are included.

3 Price comparisons

In this chapter, the results of the comparison of Sweden's pharmaceutical prices are presented in relation to other countries. The results are presented in three sections:

- **Price over the pharmaceutical's life cycle**
- **Pharmaceuticals not exposed to competition**
- **Pharmaceuticals exposed to competition**

A pharmaceutical's life cycle has been analysed from the time when the pharmaceuticals received market approval. The division of pharmaceuticals between exposed and not exposed to competition is made against the background that many countries treat pharmaceutical pricing differently depending on their potential for substitution. In Sweden, a pharmaceutical is defined as substitutable if it is included in the Product-of-the-month system. The fact that a pharmaceutical is not substitutable may be due to the temporary monopolies that patents provide, or that the pharmaceutical is not considered substitutable on medical grounds. Examples of pharmaceuticals that are generally not considered substitutable even though they lack patent protection are biopharmaceuticals, such as pharmaceuticals with the substances adalimumab and etanercept[8], and synthetic pharmaceuticals that are not deemed therapeutically equivalent.

3.1 Prices over the pharmaceutical's life cycle

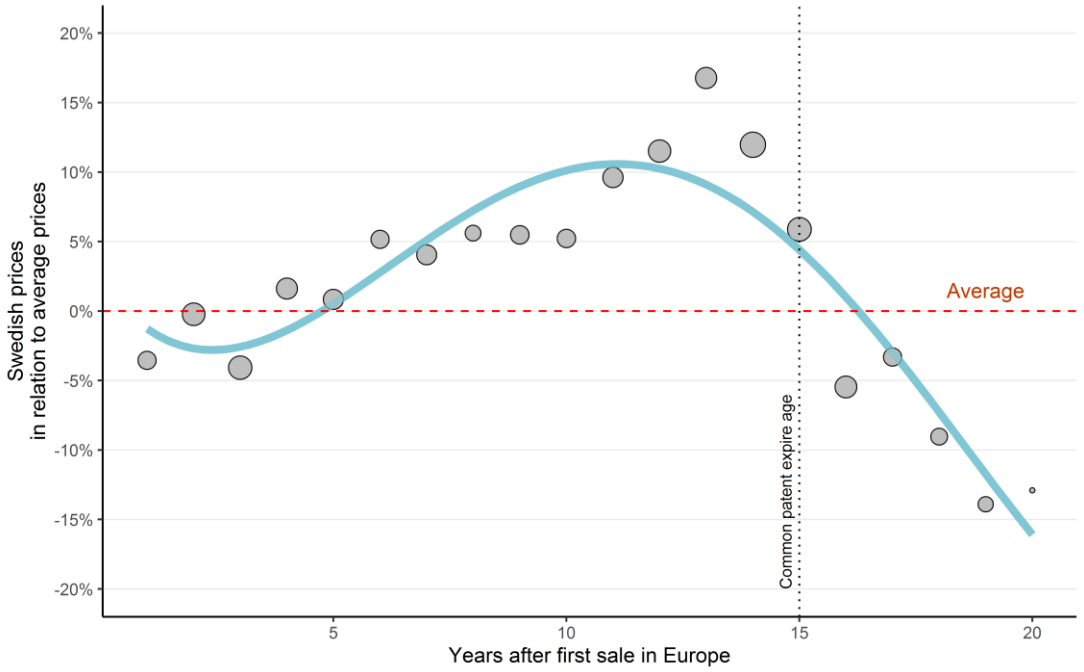
This section examines how Sweden's price development compares with the prices in other European countries based on the year of launch in Europe. This analysis covers the entire period from 2014 to 2019 and includes pharmaceuticals both exposed to and not exposed to competition. To understand a pharmaceutical's total cost over its life cycle, it is important to consider the price over time, not just at the time of launch. The fact that the price of older pharmaceuticals is falling may have a major impact on the total pharmaceutical costs. Falling prices mean that innovations will benefit consumers as they can get a better product at the same price or the same product at a lower price.

Figure 5 below shows Sweden's pharmaceutical prices for each year after their first launch in Europe, compared with the average in the comparison countries (up to 20 years after launch). The figure shows that Sweden's pharmaceutical prices are in line with, or slightly below, the average of the comparison countries during the first five years. Between years 5 and 15, Sweden has more expensive pharmaceuticals.

[8] Originator and reference pharmaceutical Humira and Enbrel.

After year 15, marked with a vertical dotted line, Swedish prices fall to below the average.

Figure 5. Sweden's relative pharmaceutical prices compared to the average price for the report's 20 European countries, per year after market approval

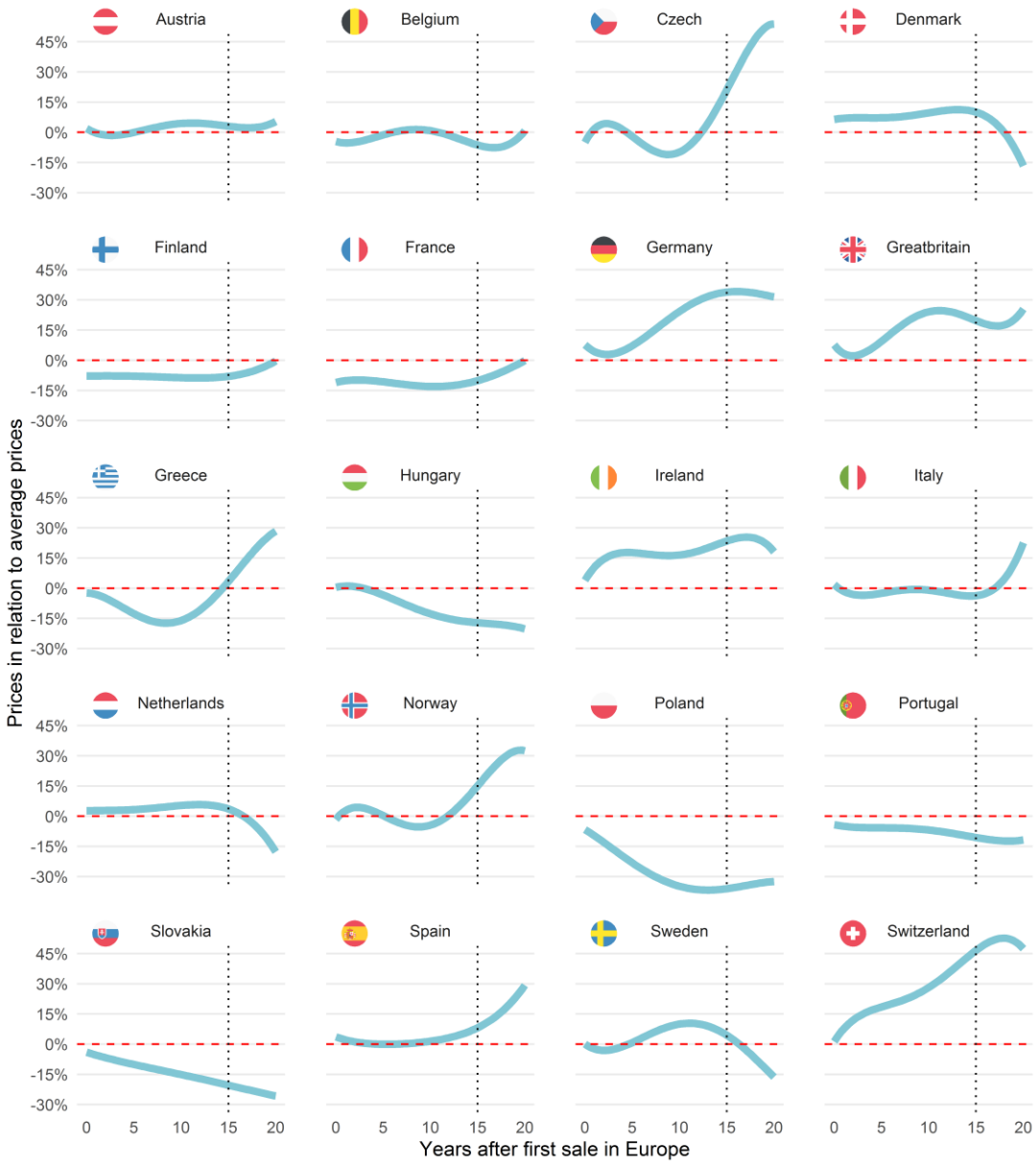


Source: IQVIA and TLV analysis.
Note: The red line shows the average prices for 20 European countries. The positions of the circles show the actual deviation from the average prices, and their size shows how large the sales value is in Sweden for pharmaceuticals of that age. The blue line is an approximate calculation to show the trend over the life cycle. Sales data for years 2014–2019.

The size of the circles indicates the sales value for the pharmaceuticals in the age grouping. The age grouping is based on market approval and not introduction in Sweden. Pharmaceuticals that are 10 to 15 years old account for relatively large expenditure in Sweden (larger circles). The figure shows that Sweden has relatively competitive prices at launch and for a few years afterwards. After five years, Swedish relative prices start to rise to become higher than average. This is not because Sweden raises its prices, but rather that prices in other countries drop more than Sweden's prices. After 15 years on the European market, generic competition usually arises, and Sweden's Product-of-the-month system presses prices to about 15 per cent below the average for the period with pharmaceuticals are 15 to 20 years old.[9] For pharmaceuticals that are not judged to be substitutable, despite genetic competition, Sweden applies what is known as the 15-year rule, which lowers the set price by 7.5 per cent.

[9] The actual price reduction can be more than 15 per cent of the list price, but as several countries reduce the list prices simultaneously, the relative reduction is lower.

Figure 6. All countries' relative list prices compared to the average price for the report's 20 European countries, per year after market approval



Source: IQVIA and TLV analysis
Note 1: Norway and the Czech Republic should be interpreted with caution for pharmaceuticals older than 15 years. This is because the structure of their substitution system causes list prices and transaction prices to differ significantly. The observations in this figure show list prices only.
Note 2: The red line shows the average prices for 20 European countries. The blue line is an approximate calculation to show the trend over the life cycle. Sales data for outpatient pharmaceuticals, years 2014–2019.

Figure 6 above shows the relative price level in relation to the pharmaceutical's age distributed among all countries in the report. Sweden's development over the life cycle with a hump, with more expensive pharmaceuticals for the age interval 5 to 15 years, is not found in many countries. Several countries have regulations that regulate prices of pharmaceuticals after they have been on the market for a few years. One example is Finland, which has a subsidy decision that applies for

maximum three years. Finland also has lower prices than Sweden for pharmaceuticals that are between 5 and 15 years old. Another example is France, which reviews price and reimbursement status after five years. Like Sweden, the UK has value-based pricing, which may explain why their life cycle is similar to the Swedish one with higher relative prices for pharmaceuticals 5 to 15 years old.

In countries with generic substitution at pharmacies, prices of pharmaceuticals drop after 15 years on the market. This can be seen clearly in Figure 6 for Sweden, Denmark and the Netherlands. Norway's results for pharmaceuticals older than 15 years should be interpreted with caution. For more information on the Nordic countries, see the 2018 report and the section *Nordic overview*.

3.2 Pharmaceuticals not exposed to competition

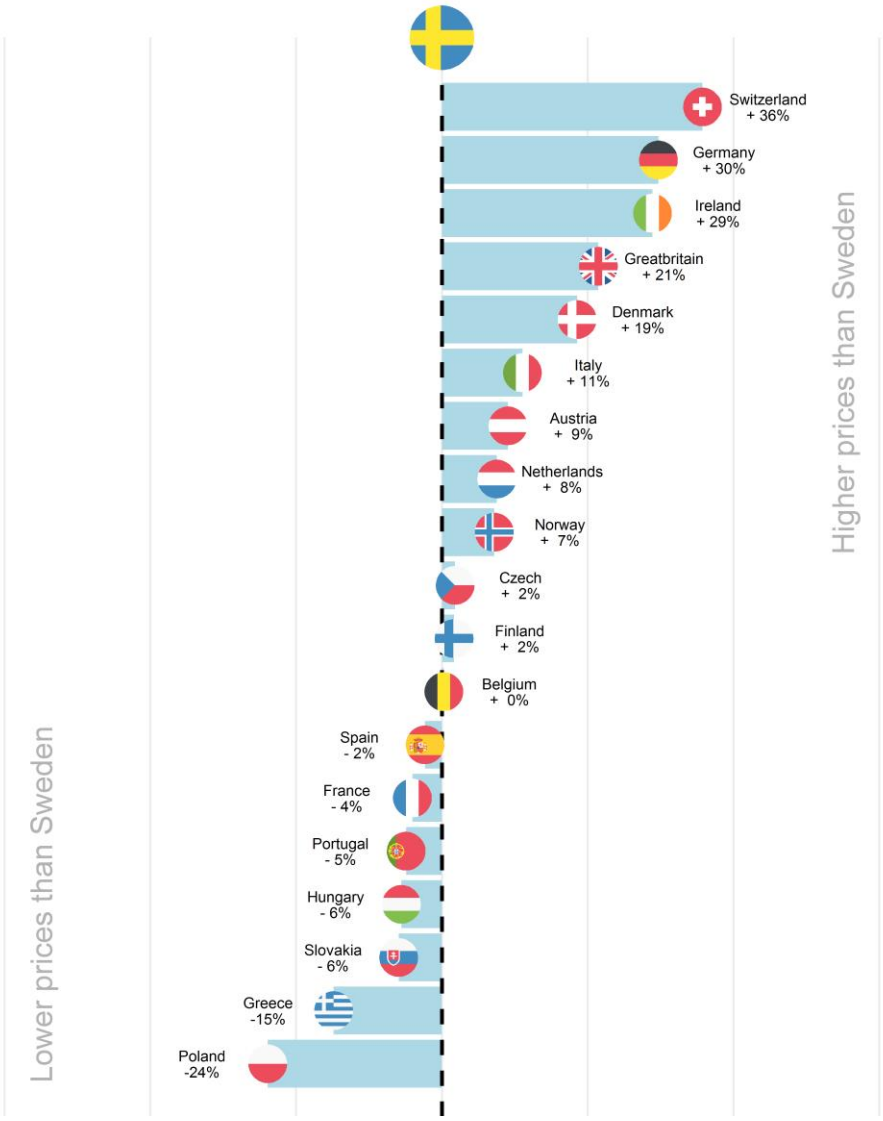
Pharmaceuticals that are considered non-substitutable by the Swedish Medical Products Agency are included in the segment for pharmaceuticals not exposed to competition. Sweden and other countries have different pricing systems to control the costs of pharmaceuticals, which is necessary because the use of pharmaceuticals is largely financed with public funds. In Sweden, so-called value-based pricing is used, which means that TLV makes health-economic evaluations of pharmaceuticals before they are subsidised within the framework of the high-cost protection scheme. Several countries, including Sweden, use different types of agreements that reduce the actual costs of pharmaceuticals compared to list prices.

3.2.1 Bilateral price comparison 2019

Analysis of prices of pharmaceuticals not exposed to competition reveals that there are significant differences between the countries included in the comparison. Figure 7 presents a bilateral price comparison, where Sweden's prices during the first quarter of 2019 are compared to the prices of other countries during the same period. The comparison is done in pairs, which means that pharmaceuticals with sales in both Sweden and the individual country are included in the comparison. As a result, different pharmaceuticals are compared for different countries, and some comparisons with other countries are thereby not possible.[10]

[10] For example, it is not possible to say that Germany has higher prices than Ireland as it is not certain that the same pharmaceuticals were compared.

Figure 7. Bilateral price comparison for pharmaceuticals not exposed to competition, 2019



Source: IQVIA and TLV analysis.

Note: Prices during Q1 2019. Volumes for running 12-month period through March 2019. 3-year average exchange rate

The price different in the above figure should be interpreted to mean that the UK has 21 per cent higher pharmaceutical prices than the pharmaceuticals not exposed to competition that are found in both Sweden and the UK. Sweden has lower prices than 11 of the countries, higher prices than seven of the countries, and no difference in price compared to one country (Belgium).

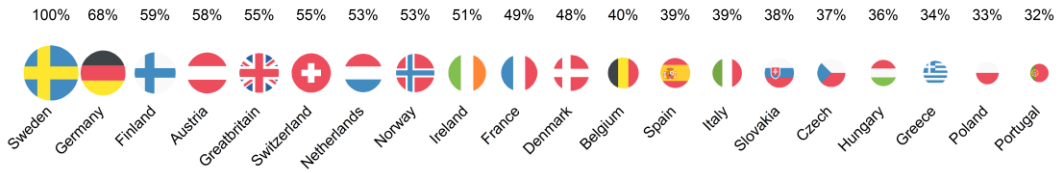
The bilateral comparison shows what *the Swedish pharmaceutical use, with Swedish volumes, would have cost if purchased at other countries' prices.*

The analysis shows that twelve countries have higher prices than Sweden for the pharmaceuticals used in Sweden and the respective individual country. Poland has the lowest prices compared to Sweden, with an average price that is 23 per cent lower than that of Sweden. Switzerland has the highest prices compared to Sweden, with an average price that is 36 per cent higher than that of Sweden. In total, seven countries have a lower average price compared to Sweden. However, these countries have a relatively low degree of matching[11] against Swedish use, which means that the results should be interpreted with caution. Countries with a higher price than Sweden generally have a higher degree of matching, which is described in the next section.

3.2.1.1 Degree of matching

The degree of matching illustrates what proportion of the pharmaceuticals in the sample are available in both Sweden and other countries. The focus here is only pharmaceuticals that are available in both Sweden and other countries. Pharmaceuticals with significantly lower sales per capita than Sweden are excluded from the comparison.

Figure 8. Swedish degree of matching for pharmaceuticals not exposed to competition



Source: IQVIA and TLV analysis.

Sweden has a total of 577 pharmaceuticals in the sample for this segment. These pharmaceuticals are used as the base in the comparison with the prices in other countries. Sales of pharmaceutical forms in other countries that do not match those found in Sweden have therefore been excluded (even if the substance itself is found in other countries). The number of pharmaceuticals that are available in Sweden (counted as substance, dosage form and strength) is therefore the maximum number of pharmaceuticals.

On average, the degree of matching is highest in Germany (68 per cent), followed by Finland, Austria, the UK, Switzerland and the Netherlands, with a degree of matching between 55 and 59 per cent. The lowest degree of matching is with countries such as Portugal, Poland, Greece and Hungary, with about 35 per cent.

[11] For more information on degree of matching, see section 3.2.1.1 Degree of matching.

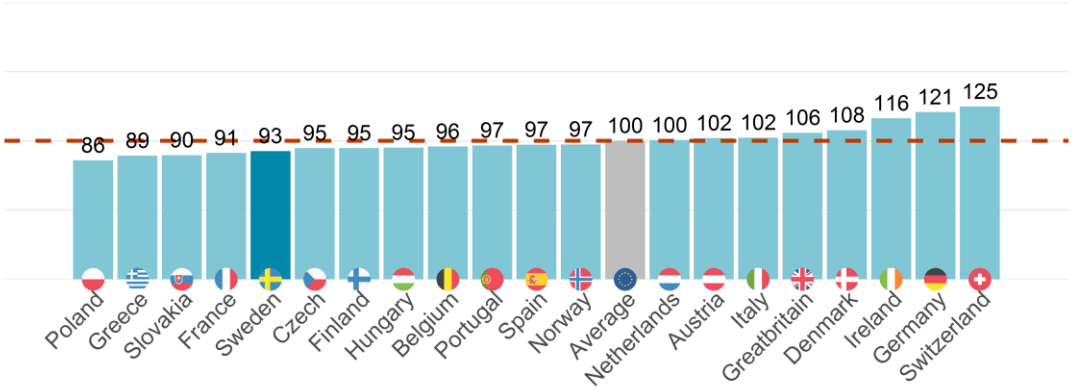
The degree of matching with our Nordic neighbours, Denmark and Norway, is about 50 per cent. A comparison between Germany and Sweden is thus based on 68 per cent of the pharmaceuticals found in Sweden, while a comparison with Portugal is based on only 32 per cent. Bilateral price comparisons can therefore only compare the respective country with Sweden, not compare the countries to each other.

It may be important to consider differences in the degree of matching between countries when examining differences in a bilateral price comparison more closely. A high degree of matching and a pharmaceutical use similar to Sweden means that the price comparison becomes more robust. Comparisons with countries with very low degrees of matching will be more difficult to generalise, since the comparison is only relevant for the few products that are common.

3.2.2 Cross-sectional comparison

With a price comparison made using cross-sections, all countries are assumed to have all pharmaceuticals with sales in Sweden for the respective year. This differs from the bilateral index, where a comparison between Sweden and another country only includes pharmaceuticals that are found in both countries. In cases where price data for a pharmaceutical is missing in a country, the pharmaceutical's average price level in Europe is used. Figure 9 shows a cross-sectional index for all countries. An index of 100 corresponds to the average prices of all countries (European average).

Figure 9. Cross-sectional index for pharmaceuticals not exposed to competition, 2019



Source: IQVIA and TLV analysis.

Note: Prices during Q1 2019. Volumes for running 12-month period through March 2019. 3-year average exchange rate.

European average = index 100.

Unlike the bilateral comparison, the cross-sectional comparison makes it possible to make comparisons between countries to a certain degree[12]. The sample of

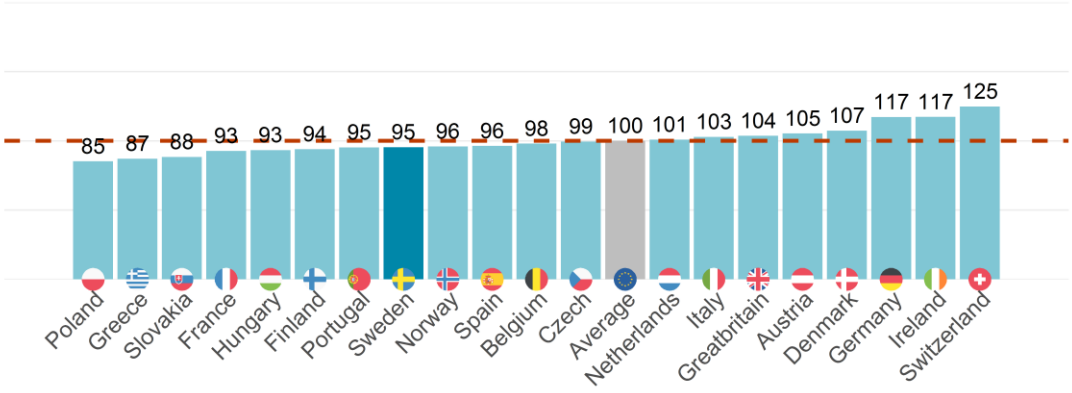
[12] However, the degree of matching affects what percentage of the pharmaceuticals have been replaced with average prices according to the cross-section methodology.

pharmaceuticals is still those used in Sweden, but also includes the pharmaceuticals that have low use in Sweden but higher use in other countries. The average price level in Europe is used as base, with index 100. An index higher than 100 indicates a pharmaceutical price higher than the average price in Europe. A pharmaceutical must be found in at least eight countries to be included in the comparison. Figure 9 above indicates that Sweden has an index of 93. This means that Sweden has about seven per cent lower prices than the average of the countries in the report. The figure also shows that e.g. Austria and Italy have a similar price level for the sample of pharmaceuticals.

The differences in method and pharmaceutical sample result in Sweden having a relatively low position compared to the bilateral comparison. Only four countries have average prices that are lower than Sweden's Note, however, that the sample of pharmaceuticals included in the analysis are those used in Sweden, and that the analysis is based on list prices, which do not include any discounts.

A common criticism of price comparisons at list prices is the existence of non-public (hidden) prices. In Sweden, there are *managed entry agreements*, where the rebate level is classified. The figure below shows the cross-sectional index for pharmaceuticals, with the difference that all pharmaceuticals with managed entry agreements in Sweden have been removed from the sample of pharmaceuticals.

Figure 10. Cross-sectional index for pharmaceuticals not exposed to competition and without managed entry agreement, 2019



Source: IQVIA and TLV analysis.

Note: Prices during Q1 2019. Volumes for running 12-month period through March 2019. 3-year average exchange rate.

Excludes pharmaceuticals with managed entry agreements in Sweden. European average = index 100.

Figures 9 and 10 show that countries' position and price level are not significantly changed by excluding pharmaceuticals with managed entry agreements. This indicates that managed entry agreements in Sweden do not affect the general comparison of Sweden's pharmaceutical prices in relation to other countries[13]. One

[13] Other countries may have hidden actual prices for pharmaceuticals that do not have managed entry agreements in Sweden, which means that the prices in other countries may be lower. In Sweden, managed entry agreements provide a rebate that makes the actual cost of the pharmaceutical lower than the set price.

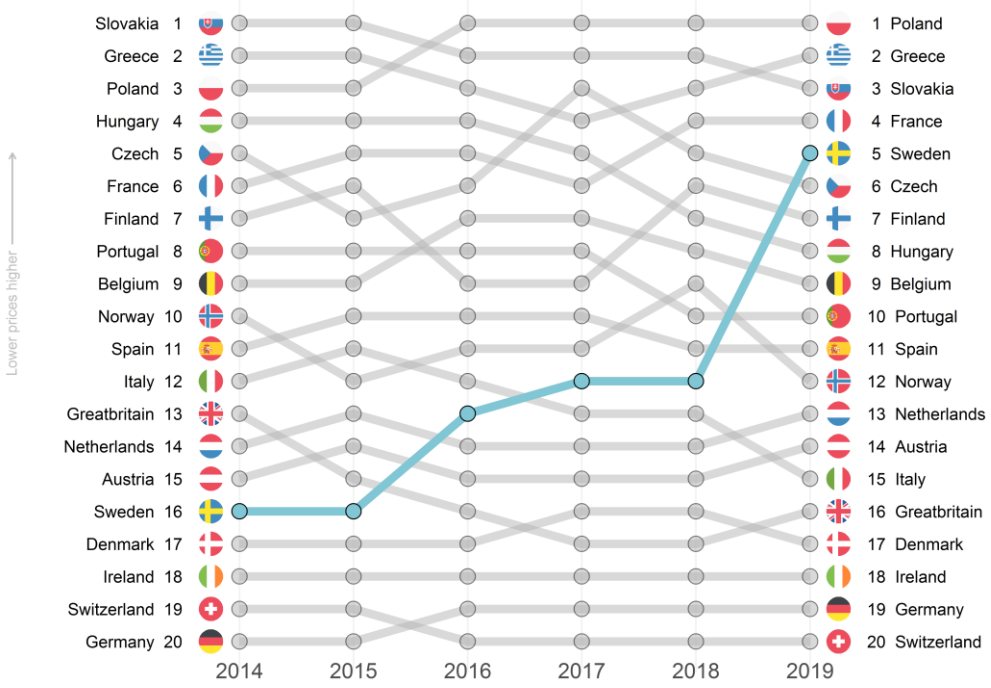
advantage of excluding pharmaceuticals with hidden prices is that the comparison is based on pharmaceuticals with list prices without hidden discounts to a greater extent. A disadvantage is that about 24 per cent of the sales value is not included in the analysis.

If pharmaceuticals that are covered by a managed entry agreement in Sweden are excluded, the Swedish cross-sectional index is instead 96, compared to 93 for pharmaceuticals not exposed to competition including managed entry agreements. This means that Sweden's relative price level is slightly lower than pharmaceuticals covered by managed entry agreements, and slightly higher for pharmaceuticals not covered by managed entry agreements.

3.2.3 Historical development

Sweden's prices in pharmaceuticals not exposed to competition have declined in relation to other countries. In 2019, Sweden is in fifth position in the ranking, as four countries have lower prices and eight countries have higher prices. In 2014, Sweden was in 16th position, with only four countries having higher prices. This means that prices in Sweden have decreased since 2014, since a country climbs in the ranking list when prices fall in relation to other countries. Figure 11 shows the development between 2014 and 2019 for all countries included in the comparison.

Figure 11. Development of the price comparison over time as cross-section, 2014 – 2019



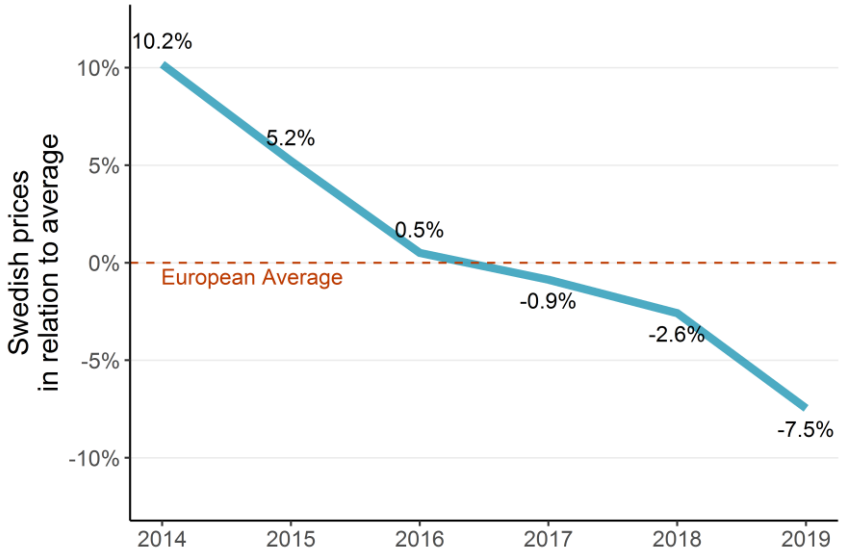
Source: IQVIA and TLV analysis.

Note: Rank 1 means that the country has the lowest prices. Running 3-year average exchange rates per year.

Four countries have lower average prices than Sweden in 2019. This is a change compared to 2018, when eleven countries had lower prices compared to Sweden. The change may seem large, but since several countries have a price level that is relatively close to the Swedish one, a small price change percentage-wise results in a relatively large shift in the ranking in the figure. As previously mentioned, Swedish prices have fallen mainly as a result of a weak exchange rate for the Swedish krona in recent years. Should Swedish currency increase in value again compared to the currency of other countries while the set prices remain the same, this could have a major effect on the ranking. The percentage difference in price level between countries is small in many cases. In such case, Sweden's placement may move downwards, i.e. Swedish relative prices will increase. Generally speaking, it can be noted that the countries whose currency is not linked to the euro have greater variation in placement compared to others.

Figure 11 shows that Sweden's prices have fallen compared with other countries since 2014. In order to get a better picture of the development, it is also interesting to look at the size of this change. Figure 12 shows the percentage deviation between the prices in Sweden and the average prices in other countries.

Figure 12. Sweden's relative prices in relation to the average per year, calculated as cross-section. Pharmaceuticals not exposed to competition



Source: IQVIA and TLV analysis.

Note: Calculation based on cross-section. Running 3-year average exchange rate for the respective year.

The figure shows that Sweden's prices in 2014 were 10.2 per cent higher than the average for all countries. Over time, Sweden's prices have gradually decreased by about 17 percentage points through the first quarter of 2019, when Sweden's prices were instead 7.3 per cent lower than the average. The change is largely attributable to the exchange rate change. However, from 2014 to 2016, the relative price decrease was mainly driven by reviews and the introduction of regular price reductions for pharmaceuticals that are 15 years and older. As previously mentioned, Swedish prices are likely to rise if the Swedish krona increases in value

again. A more detailed description of the background to price development is found in section 3.2.4.

3.2.4 Drivers of relative price

There are several factors that influence Sweden's relative prices for pharmaceuticals compared to the rest of Europe. As previously mentioned, it is clear that the Swedish exchange rate contributes greatly to the Swedish price level being relatively low. This section has been broken down into the factors that contribute to the price change that occurred in Sweden between 2014 and 2019, relative to the rest of Europe. The breakdown is for three different types of changes, namely price, currency and volume composition. The analysis only includes the pharmaceuticals in the sample that have had positive sales and have not been exposed to competition (in Sweden) throughout the entire period 2014–2019. Thus, the price change resulting from new pharmaceuticals being added and others disappearing is not included in the analysis. The pharmaceuticals included accounted for 60 per cent of the total sales volume during the first quarter of 2019. An explanation of the three categories of the breakdown is found below.[14]

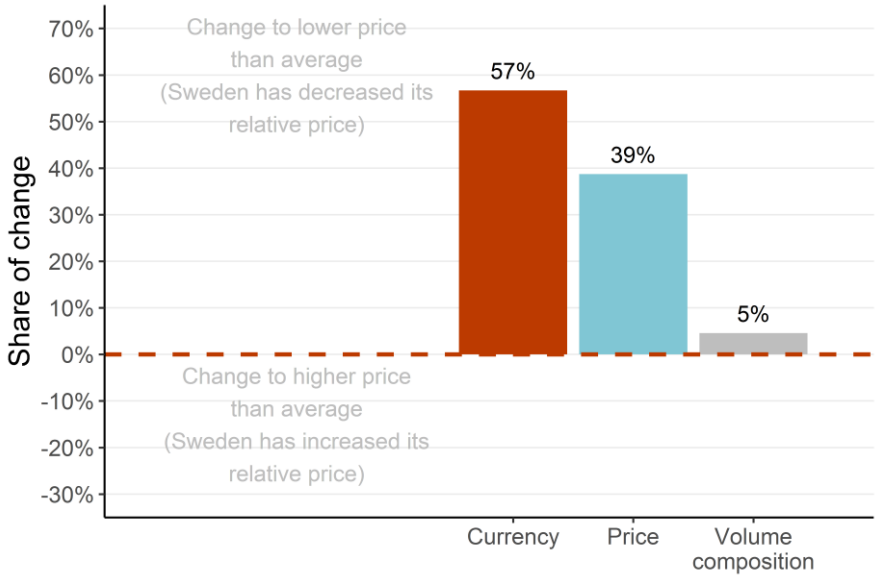
Price changes: The category price changes is the part of the relative price that occurred as a result of Sweden, or other countries, changing their actual pharmaceutical prices. When calculating this category, a constant exchange rate and pharmaceutical use are used to isolate the part that constitutes actual price changes, regardless of use and currency fluctuations. For example, if the price per unit rises from SEK 100 to SEK 120 in Sweden, and at the same time remains unchanged in other European countries, the price change is 20 per cent.

Currency changes: This category explains the part of the change in relative prices that occurred as a result of exchange rate fluctuations. If the price per unit has remained unchanged in Europe, but the Swedish exchange rate has dropped from SEK 8/EUR to SEK 10/EUR, the currency change is -25 per cent.

Volume composition changes: The last category explains how the overall price picture has changed as a result of change in the volume distribution between the pharmaceuticals used. If, over time, Sweden shifts its use to products whose prices are lower in Sweden compared to other countries, Sweden's index will decrease. Note that this category only includes pharmaceuticals that have had sales and have not been exposed to competition throughout the entire period 2014–2019. The fact that the relative prices change as a result of new pharmaceuticals being added and others completely disappearing is not captured in this category.

[14] A more detailed description of the exact method used to calculate the different components is found in the section about Methodology in Appendix 1.

Figure 13. Percentage change, in cross-section, broken down by price, currency and volume composition change, 2014 – 2019. Pharmaceuticals not exposed to competition



Source: IQVIA and TLV analysis.

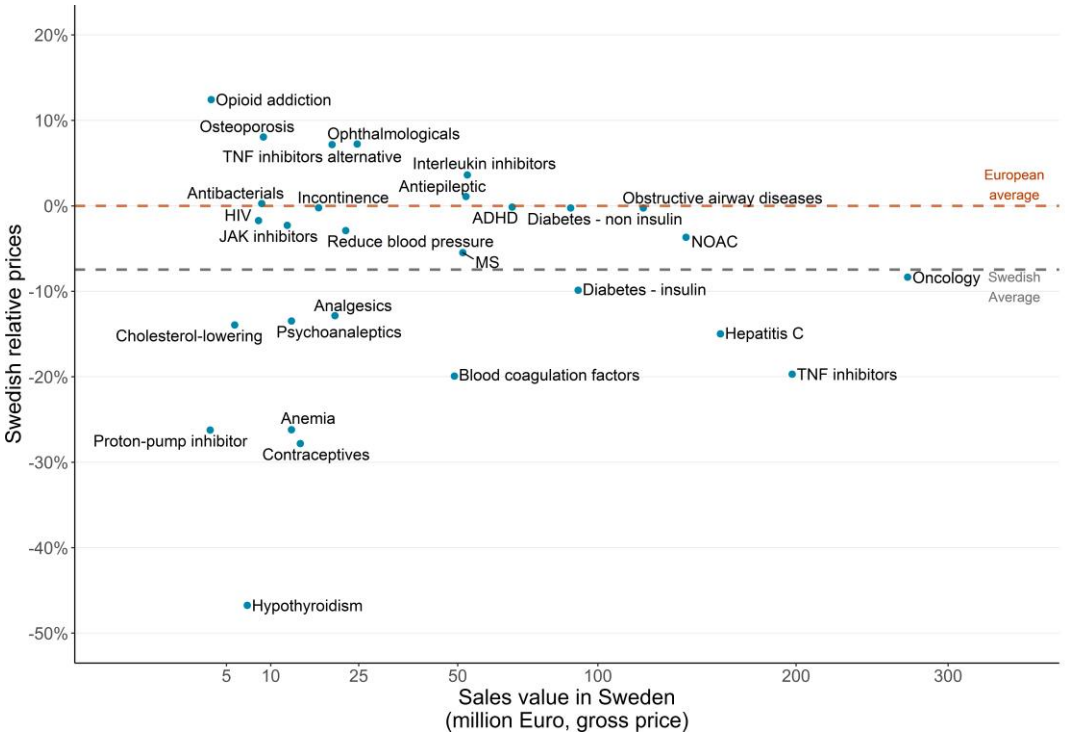
Figure 13 shows the percentage of the total, relative price change 2014–2019 that is made up of the various subcomponents. Although the above analysis only includes one subset of the pharmaceuticals sold in Sweden, the figure makes it clear that the factor with the greatest impact on the Swedish pharmaceutical prices, relative to Europe, is a falling Swedish exchange rate (57 per cent). This, in turn, means that relative prices are likely to increase if the exchange rate were to return to the level that applied in 2014. It is also clear that the price changes applied in Sweden and other countries to the pharmaceuticals being analysed contribute to Sweden having a lower average relative price in 2019 compared to 2014. Between 2014 and 2016, the lower relative prices mainly occurred when more extensive reviews[15] were carried out. However, the effect of a change volume composition is low. All three components have had a relatively negative effect on Sweden's relative prices, so they have all contributed to Sweden having a *lower* average price relative to Europe today compared to 2014. A more detailed discussion of the impact of the different components, with a description over time, is presented in the section on *Methodology* in *Appendix 1*.

3.2.5 Pharmaceutical groups

To examine differences in price at a more detailed level, Figure 14 shows Sweden's prices in comparison with Europe, as well as sales in Sweden in 2019[16], broken down into different pharmaceutical groups[17].

[15] TLV can review, i.e. re-evaluate a pharmaceutical or pharmaceutical group. This can lead to a lower set price.
[16] The sales value is calculated as the price interval during quarter 1 2019, multiplied by the volume for the respective pharmaceutical between quarter 2 2018 and quarter 1 2019.

Figure 14. Swedish prices for pharmaceutical groups compared to the European average AIP, 2019. Pharmaceuticals not exposed to competition



Source: IQVIA and TLV analysis.

Note: Note that the x-axis intervals increase exponentially. This is done so that all pharmaceutical groups can be shown together.

The figure shows that, for example, the pharmaceutical groups oncology, TNF inhibitors and hepatitis C have high sales in Sweden, but relatively low list prices. the pharmaceutical groups IL inhibitors, antiepileptics, obstructive airway diseases, diabetes excluding insulin, and ADHD all have high sales in Sweden. The Swedish prices for these groups are higher or in line with the European average. Since the Swedish prices are currently relatively low due to a weak currency, it is likely that the prices would increase and become higher than the European average if the Swedish krona becomes stronger again. For these three groups in particular, there are no managed entry agreements, only set prices (list prices). The pharmaceutical groups NOAC and diabetes excluding insulin have high sales and lower relative prices compared to Europe. However, the price level for these groups is high relative to the Swedish average. These pharmaceutical groups would probably become more expensive than the European average if the Swedish krona were to increase in value. For pharmaceuticals within these groups, there are no managed entry agreements in Sweden. There are managed entry agreements for pharmaceuticals within a number of groups, including oncology, TNF inhibitors, hepatitis C, and blood coagulation factors.

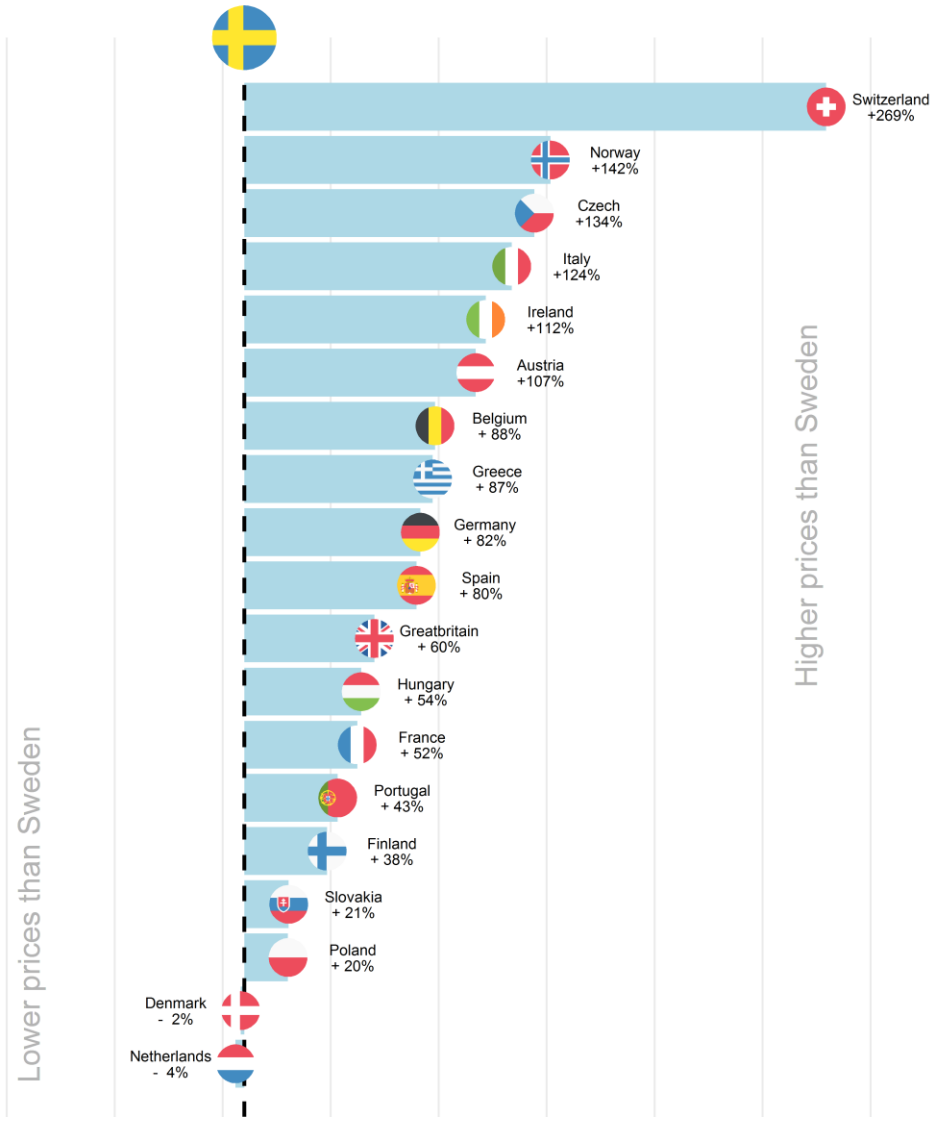
[17] For more information about pharmaceutical groups, see *Appendix 1* under the subheading *Pharmaceutical groups*.

3.3 Pharmaceuticals exposed to composition

3.3.1 Bilateral price comparison 2019

The countries in this report show significant differences in prices within pharmaceuticals exposed to competition. The relative prices vary more than in pharmaceuticals not exposed to competition, which were reported in the previous section.

Figure 15. Bilateral price comparison for pharmaceuticals exposed to competition, 2019



Source: IQVIA and TLV analysis.

Note: Prices during Q1 2019. Volumes for running 12-month period through March 2019. 3-year average exchange rate.

Figure 15 presents a bilateral price comparison for pharmaceuticals exposed to competition, where Sweden's prices during the first quarter of 2019 are compared to

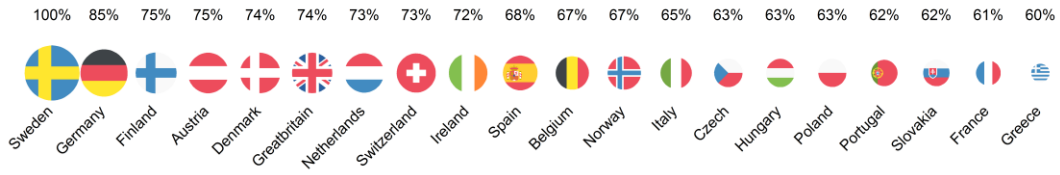
the prices of other countries during the same period. The comparison is done in pairs, which means that pharmaceuticals with sales in both Sweden and the individual country are included in the comparison between Sweden and the country in question. From the figure, one can see that for the pharmaceuticals used in both Sweden and Spain, the Swedish prices would have increased by 79 per cent if Spanish prices had applied.

In the bilateral price comparison for Sweden and the other 19 countries, only Denmark and the Netherlands have lower prices relative to Sweden. Both of these countries have generic substitution at pharmacies that creates competition between generic packages of the same pharmaceutical. Switzerland is significantly higher in price than Sweden, If Sweden were to have Swiss prices yet use the same volumes as today, Sweden's prices for pharmaceuticals exposed to competition would be two and a half times higher than today.

3.3.1.1 Degree of matching

The degree of matching illustrates what proportion of the pharmaceuticals in the sample are available in both Sweden and other countries. The focus here is only pharmaceuticals that are available in both Sweden and other countries.

Figure 16. Swedish degree of matching for pharmaceuticals exposed to competition



Source: IQVIA and TLV analysis.

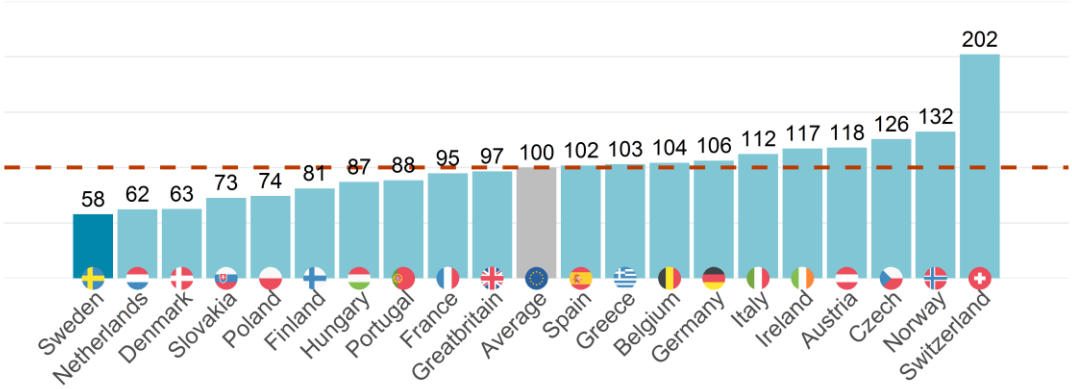
Pharmaceuticals sold below a so-called bagatelle limit abroad have been excluded. Sweden has a total of 10,064 pharmaceuticals in the sample for this segment. These pharmaceuticals are used as the base in the bilateral comparison with other countries. In the segment pharmaceuticals exposed to competition, the degree of matching is generally significantly higher than for pharmaceuticals not exposed to competition.

3.3.2 Cross-sectional comparison 2019

With a price comparison made using cross-sections, all countries are assumed to have all pharmaceuticals for the respective year. If a country does not use a pharmaceutical, it is assumed to have the average price in Europe for that pharmaceutical. The advantage of the cross-sectional method, as compared to the bilateral method, is that all countries can be compared with each other. Figure 17

shows a cross-sectional index for all countries. An index of 100 corresponds to the average prices of all countries (European average).

Figure 17. Cross-sectional index for pharmaceuticals exposed to competition, 2019



Source: IQVIA and TLV analysis.

Note: Prices during Q1 2019. Volumes for running 12-month period through March 2019. 3-year average exchange rate.

European average = index 100

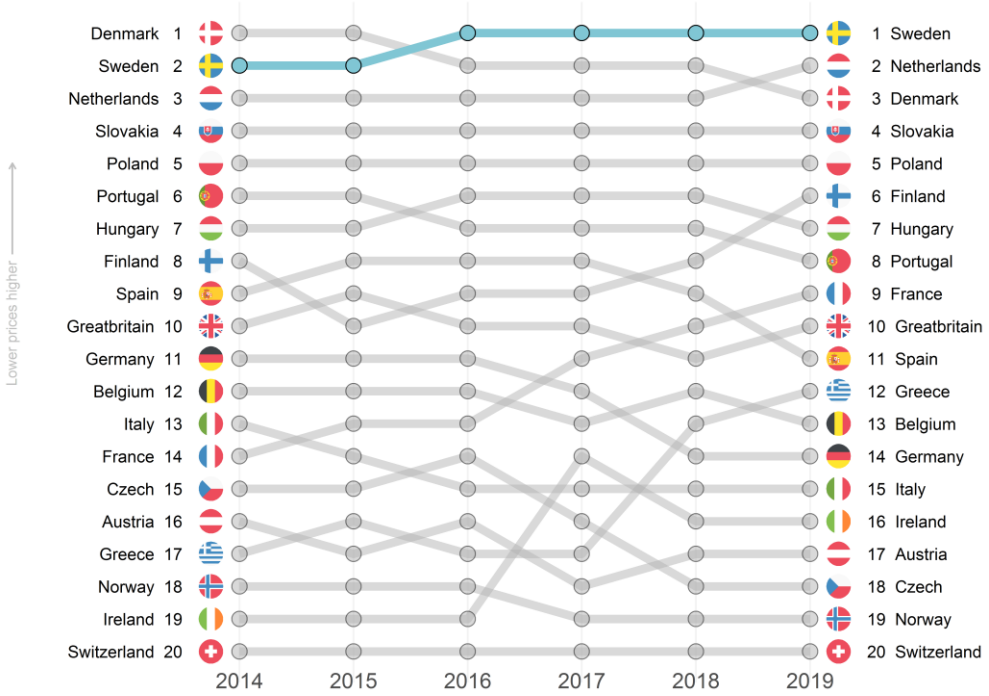
Figure 17 above indicates that Sweden has an index of 58. This means that Sweden has about 42 per cent lower prices than the average of the countries in the report. In this Figure, it is possible to compare all countries[18]. This means that e.g. Greece and Spain have a similar price level as the average for the pharmaceuticals included in the sample.

3.3.3 Historical development of pharmaceutical prices

Sweden's prices within pharmaceuticals exposed to competition have been among the lowest during the years 2014 to 2019. In 2019, Sweden had the lowest prices in the segment. Figure 18 shows the ranking trend for each country in the comparison. Rank one means that the country has the lowest prices. Denmark and the Netherlands are the two countries that changed rankings with Sweden during the years 2014 to 2019. Three countries that have seen major relative price reductions between 2014 and 2018 are Ireland, Greece and France.

[18] However, the degree of matching affects what percentage of the pharmaceuticals have been replaced with average prices according to the cross-section methodology.

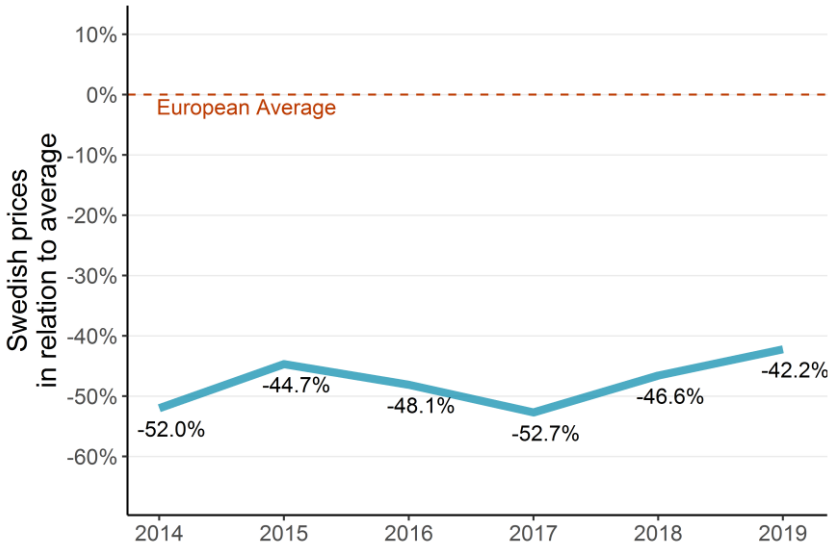
Figure 18. Development of the price comparison over time as cross-section, 2014 – 2019 Pharmaceuticals exposed to competition



Source: IQVIA and TLV analysis.

The ranking over time, as presented in Figure 18, shows that Sweden continues to have amongst the lowest prices in relation to other countries since 2014. However, it does not show how much the pharmaceutical prices have changed in relation to other countries. Figure 19 below shows how Sweden's prices in the segment pharmaceuticals exposed to competition are in proportion to the average of all countries in the report.

Figure 19. Sweden's relative prices in relation to the average per year, calculated as cross-section. Pharmaceuticals exposed to competition



Source: IQVIA and TLV analysis.

Note: Calculation based on cross-section. Running 3-year average exchange rate for the respective year.

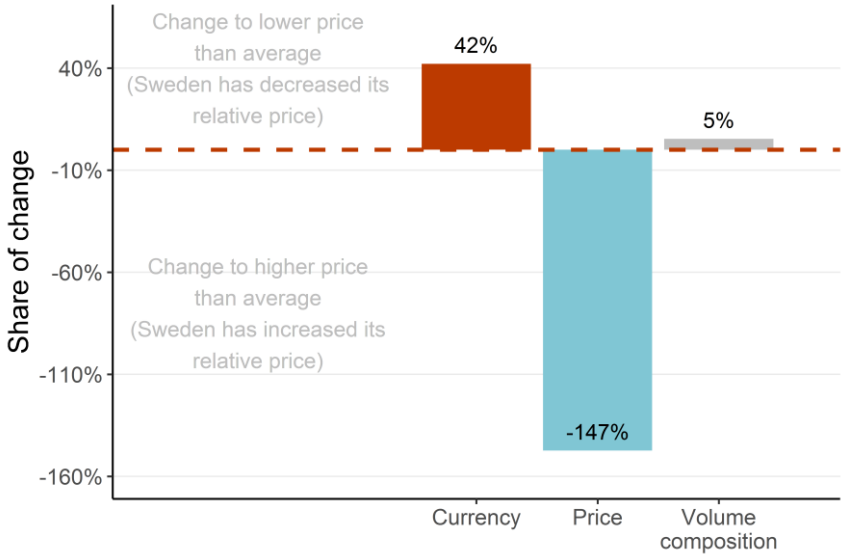
The figure above should be interpreted as showing that in 2014, Sweden's prices for pharmaceuticals exposed to competition were 52 per cent lower than the average for the 20 countries included in this report. In 2019, Sweden’s pharmaceutical prices increased to 42.2 per cent below the average. Here, we see the other side of the corn of the Swedish krona being weaker. The PV system allows price increases as a result of getting paid less in euros. It is the competitive situation in the segment that affects the price level and is, in turn, affected by the international price situation.

3.3.4 Drivers of relative price

Figure 20 shows how the total change in Sweden's relative price level, during the period 2014–2019, is driven by three different effects. The price change captures the part of the relative price that is affected by actual price changes; the currency change captures the relative price change that occurred as a result of the falling Swedish currency. Finally, the volume composition shows how Sweden's relative price has changed as a result of the shift in use to or from pharmaceuticals with a different price level relative to the European average. A more detailed description of these effects is found in section 3.2.4 and in the section *Methodology* in *Appendix 1*. Only the pharmaceuticals that have had sales and have been exposed to competition throughout the entire period 2014–2019 are included in the data set. These accounted for 62 per cent of the total sales during the first quarter of 2019. Changes in relative prices that are affected by new products being added and others disappearing are thereby not captured.

The Swedish pharmaceutical prices for pharmaceuticals exposed to competition have increased relative to Europe in general. The figure shows that the price increase is driven solely by a change in actual prices. The falling exchange rate and volume composition both contribute to a reduction in the negative price change effect. Please note that the prices for pharmaceuticals in the PV system, in practice, are renegotiated on a monthly basis. As a result, changes in the SEK exchange rate are compensated through a corresponding change in price, which can occur relatively quickly. This is likely to be the main reason why the effect of currency changes is relatively less here, compared to pharmaceuticals not exposed to competition (see Figure 13).

Figure 20. Percentage change, in cross-section, broken down by price, currency and volume composition change, 2014 – 2019. Pharmaceuticals exposed to competition

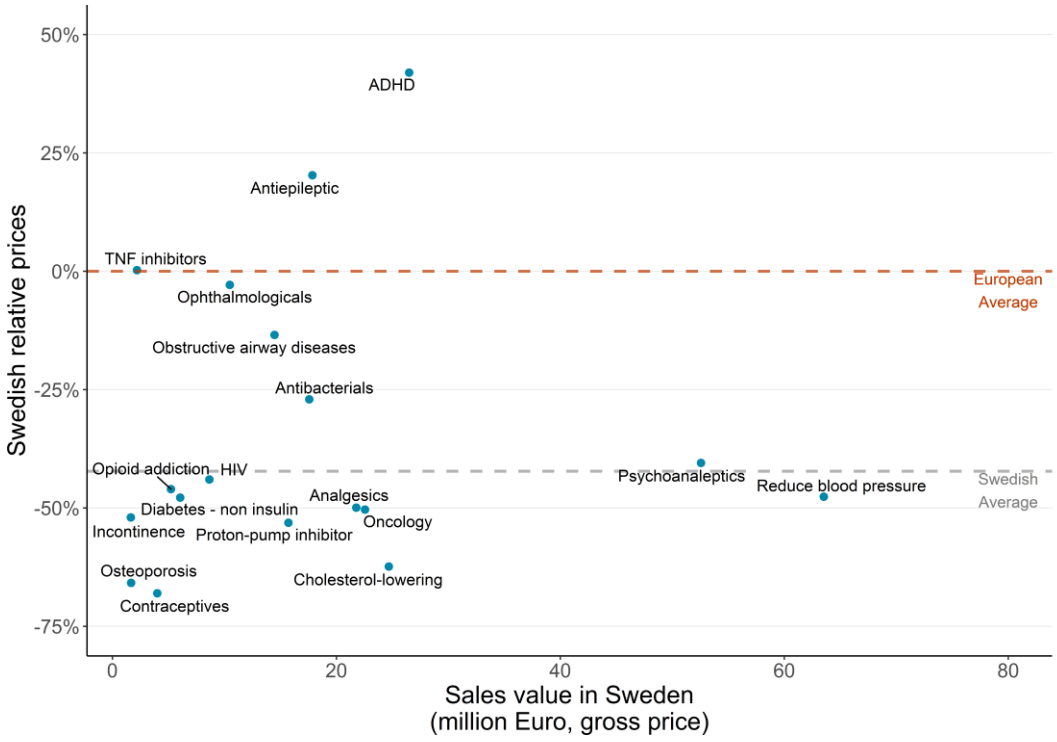


Source: IQVIA and TLV analysis.

3.3.5 Pharmaceutical groups

Figure 21 shows Sweden's prices compared with Europe, and sales in Sweden in 2019[19] broken down into different pharmaceutical groups.

Figure 21. Swedish prices for pharmaceutical groups compared to the European average AIP, 2019. Pharmaceuticals exposed to competition



Source: IQVIA and TLV analysis.

As the Swedish prices for pharmaceuticals exposed to competition are low, it can be seen in the figure above that the majority of pharmaceutical groups have prices below the European average. Only two of the defined pharmaceutical groups have prices over the European average. For the pharmaceutical group antiepileptics, substitution in the PV system[20] is likely to be limited because some pharmaceuticals are not considered substitutable with all pharmaceuticals within the same product group. Substitution in the PV system is also limited in the pharmaceutical group ADHD. However, this is mainly because prescribers oppose substitution of the prescribed pharmaceutical with other products within the substitution group. For the pharmaceutical groups ophthalmologicals, obstructive airways diseases, and antibacterials, the prices in Sweden are lower than the European average. However, the prices for these groups are higher than the Sweden average (42 per cent).

[19] The sales value is calculated as the price interval during quarter 1 2019, multiplied by the volume for the respective pharmaceutical between quarter 2 2018 and quarter 1 2019.
[20] https://lakemedelsverket.se/Alla-nyheter/NYHETER---2005/Lamotrigin--original-och-generika-inte-utbytbara/ (2019-11-13)

4 Discussion

In this report, pharmaceutical prices have been analysed in different segments and levels. A clear result is that exchange rates between countries are a strong contributing factor to the development of relative prices. The Swedish krona has fallen in value compared to the euro in recent years, with a marked weakening between 2018 and 2019. Since the prices of pharmaceuticals in Sweden are set in local currency, the Swedish relative prices drop when the Swedish krona drops.

For *pharmaceuticals not exposed to competition*, Sweden is ranked fifth out of 20 countries, which is a move from twelfth place in 2018. Sweden's change in position from twelfth to fifth place between 2018 and 2019 is due to a relative price reduction of five percentage points. In general, the price levels in the different countries are similar, when it comes to pharmaceuticals not exposed to competition. About 60 per cent of Sweden's relative price change can be attributed to currency changes, and 40 per cent to changes in list prices. IL inhibitors, antiepileptics, and pharmaceuticals for obstructive airway diseases are three pharmaceutical groups where Sweden's relative prices and sales are high.

For *pharmaceuticals exposed to competition*, Sweden, Denmark and the Netherlands have the lowest prices in the comparison. In these countries, regulations steer use towards the cheapest alternative of substitutable pharmaceuticals. For Sweden, this has contributed to pharmaceuticals exposed to competition making up about 60 per cent of the sales volume, but only one-fifth of the sales value. Unlike pharmaceuticals not exposed to competition, the set prices can rise. This means that companies can increase prices to compensate for losses if the krona becomes weaker. Such a trend can be seen in Sweden for the period 2014 to 2019. For certain pharmaceutical groups, where substitution within the Product-of-the-month is limited, Sweden has relatively high prices compared to other countries.

In this report, the price dynamics across the age of a pharmaceutical has been analysed for the years 2014 to 2019. The prices of new pharmaceuticals in Sweden are in line with other countries at launch. However, during the period when pharmaceuticals are between 5 and 15 years old, Sweden's prices are higher than average. This is because the prices during this period drop in other countries, but not in Sweden. For pharmaceuticals that are 15 years and older, and thus usually included in the Product-of-the-month, Sweden's relative prices are significantly lower than the average. For pharmaceuticals that are not considered substitutable and thus are not included in the Product-of-the-month, the prices do not fall to the same extent. The 15-year rule is thereby an important tool for lower the prices of these pharmaceuticals. To manage pharmaceuticals that are age 5 to 15, reviews and ongoing health-economic evaluation can be important tools.

TLV will continue to monitor pharmaceutical prices from an international perspective. A priority area is to report pricing dynamics for a pharmaceutical

throughout the life cycle. A further ambition is to perform deeper analyses of the time it takes for new pharmaceuticals to be launched in Sweden, and how this affects the launch price. As countries in Europe apply different types of discounts or risk-sharing systems for pharmaceuticals not exposed to competition, one ambition is to be able to capture these aspects as well. It should be mentioned that most pharmaceuticals do not have hidden prices, and that comparisons to list prices between countries are therefore relevant. Price comparisons based on list prices highlight differences in countries' pricing systems.

In summary, Sweden has among the five lowest prices of the report's comparison countries for pharmaceuticals exposed and not exposed to competition in 2019. The Product-of-the-month creates good competition for pharmaceuticals with generic competition. In a European perspective, the price development over a pharmaceutical's life cycle and its competition are two key elements of Sweden relative pharmaceutical prices. These factors become important to monitor if Sweden wants to retain its position in the event the krona gains strength.

Appendix 1: Sensitivity analysis and methodology

Sensitivity analyses

Exchange rate

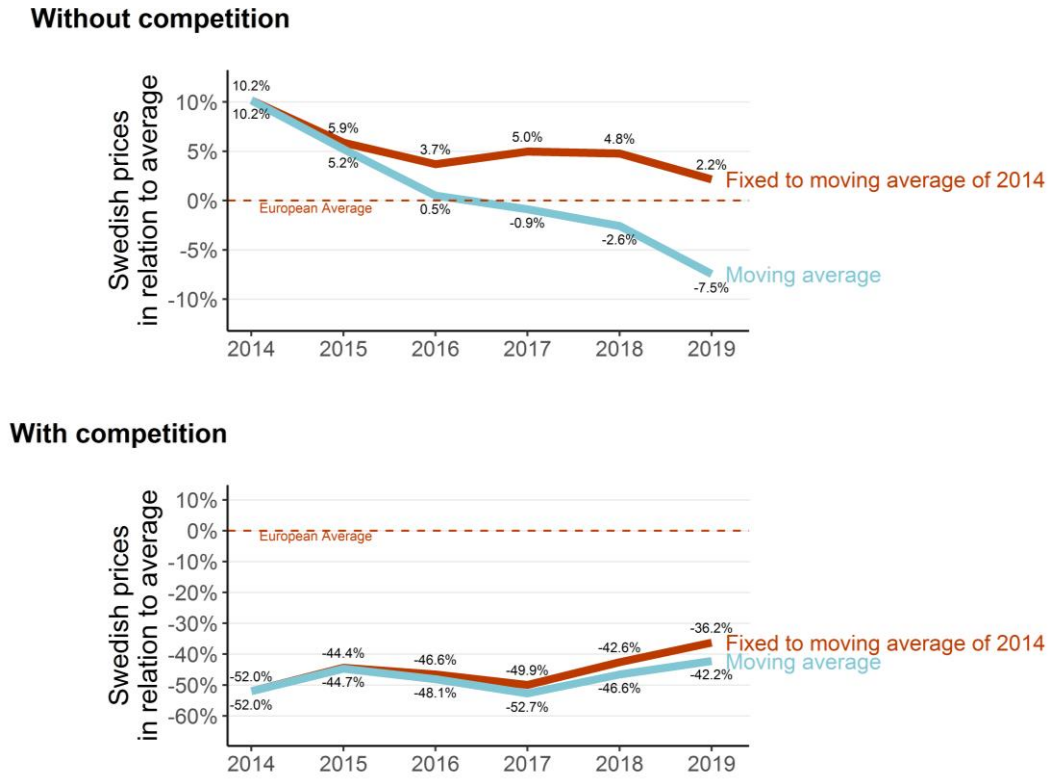
Currency changes affect relative prices compared to other countries. If the currency strengthens in one country, prices in other countries appear to have decreased, even though they are nominally unchanged in the respective country's currency. A weaker Swedish krona, all else being equal, means that Swedish prices appear to be lower than if the krona were strong.

The exchange rate's significance for relative prices remains important in the 2019 report because the Swedish krona is currently weaker than it has been for a long time. During the first quarter of 2019, the krona weakened against the euro, which is a continuation of a trend that began in 2014. An important explanation is that the Riksbank is Sweden is one of the central banks that lowered the interest rate the most, and the tender (repo) interest rate has been negative since February 2015.

One way to show the exchange rate's significance to Sweden's relative price development is to fix the currency to 2014[21] The figure below shows Sweden's relative prices of pharmaceuticals exposed and not exposed to competition between 2014 and 2019, broken down into a rolling exchange rate and fixed to 2014.

[21] Quarter 1's rolling three-year average exchange rate.

Figure 22. Sweden's relative prices in relation to the average per year, calculated as cross-section. Pharmaceuticals not exposed to and exposed to competition



Note: Exchange rate broken down into 3-year running average for the respective year and fixed 3-year running average for 2014.

The figure above shows how Sweden's pharmaceutical prices have developed between 2014 and 2019, depending on whether the currency has fluctuated over the years or was fixed at the 2014 exchange rate. Fixing at the 2014 exchange rate should be interpreted as changing all years to the exchange rate that the Swedish krona had against the respective currencies in Europe in 2014. For pharmaceuticals not exposed to competition with variable exchange rate, Sweden's relative prices have gone from about ten per cent above the average in 2014 to about seven per cent below the average in 2019. If the currency is instead fixed to 2014's rolling exchange rate, Sweden's relative prices drop to two per cent above the average. The difference is about half of Sweden's relative price reduction during the time period.

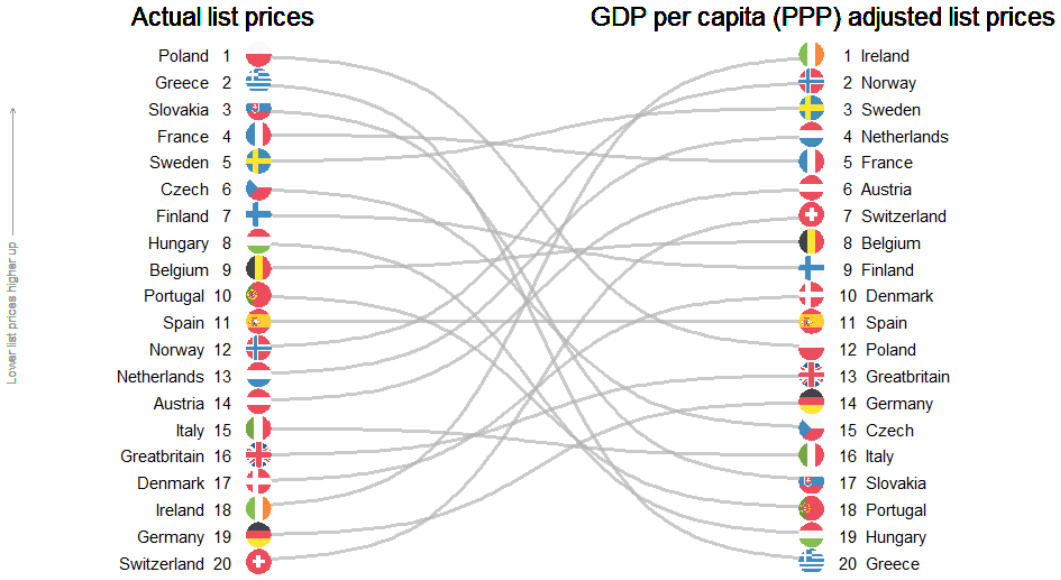
All else being equal, Swedish prices would be just over two per cent above the average for all countries if the exchange rate were to return to the 2014 level.

Purchasing power adjustment of prices

The countries of the report have a relatively large spread in purchasing power-adjusted GDP per capita. Some countries may have just under three times the

purchasing power of another country.[22] Figure 23 shows how the ranking for all countries changes if the prices are adjusted according to purchasing power-adjusted GDP level.

Figure 23. Change in the price comparison at normal pharmaceutical prices and adjusted pharmaceutical prices after purchasing power-adjusted GDP per capita. Pharmaceuticals not exposed to competition, 2019



Source: IQVIA, IMF and TLV analysis.

Note: Rank 1 means that the country has the lowest prices. Running 3-year average exchange rates per year.

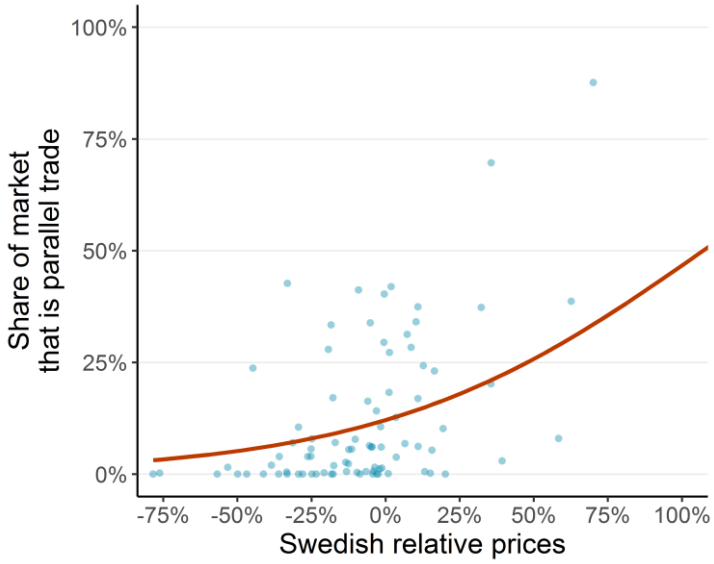
The figure above shows major position changes if the purchasing power-adjusted prices are used. Many of the countries with low relative pharmaceutical prices nominally have high relative prices if adjusted for purchasing power. The same applies in the other direction. Ireland is ranked 18 out of 20 with nominal list prices, which means high relative prices. If Ireland's prices are purchasing power adjusted, it looks to have the lowest prices in Europe. Greece, on the other hand, has the second lowest nominal relative prices, but appears to have the highest relative prices if these are adjusted for purchasing power.

Parallel trade

Within the European Union, there is a right to export pharmaceuticals to other countries, which is called parallel trade. Parallel traders can purchase a pharmaceutical in one country and sell it in another country where prices are higher, and get a margin in between. A sensitivity analysis for this report may thus be that the percentage of parallel trade increases when the price of the pharmaceutical in Sweden is higher.

[22] This means that the country with high purchasing power can purchase about three times as many goods for an average salary in their own country, compared to the country with lower purchasing power.

Figure 23. Correlation between percentage of parallel trade and relative prices in Sweden, 2019



Source: IQVIA and TLV analysis.

Note: The regression coefficient (Sweden's prices in relation to the average) is significant at 90% significance level. The relative price in Sweden (compared to other countries in the report) for Q1 2019 is calculated as the cross-reference. 3-year running exchange rate average. All pharmaceuticals are grouped at ATC3 level.

Figure 23 above shows the correlation between Sweden's relative price level for each pharmaceutical group at the third ATC level. The higher the relative prices in Sweden, the greater the amount of sales of parallel imported (or parallel distributed) pharmaceuticals.

Methodology

Segmentation depending on competition status

The pharmaceuticals have been divided into segments based on the conditions for competition in Sweden. Pharmaceuticals that can be substituted with generics are considered to be exposed to competition. These segments are:

- Pharmaceuticals not exposed to competition (outside of the Product-of-the-month)
- Pharmaceuticals exposed to competition (within the Product-of-the-month)

The segment pharmaceuticals not exposed to competition includes products where competition between at least 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 occurred. As a rule, biosimilars are also

included in this segment since these are not directly substitutable with the reference product. The reason why these pharmaceuticals are included in the same segment is that the Swedish Medical Products Agency considers these pharmaceuticals as originator pharmaceutical products and that the conditions for the price formation then become the same as for originator pharmaceutical products. However, the competitive conditions may differ between the countries in the comparison. The segment pharmaceuticals exposed to competition (within the Product-of-the-month) includes all pharmaceuticals that were included in the generic substitution within the Product-of-the-month of the respective year in March up through 2019.

Data set and pharmaceutical sample

The starting point of the analysis is the highest-selling prescription pharmaceuticals in Sweden that are part of the pharmaceutical benefits scheme. This year's data set has been supplemented with the pharmaceuticals with the highest sales in Europe and new pharmaceuticals between 2015 and 2017, which were included in EFPIA's WAIT study on time-to-market in different countries.

Prior to TLV's first report in 2014, IQVIA[23] was commissioned to provide data for 200 substances within the "protected pharmaceuticals" segment, 180 substances within the segment "unprotected originator pharmaceutical products not exposed to competition" and 200 substances within the segment "unprotected pharmaceuticals exposed to competition" with the highest sales. Each year thereafter, the data material was updated and expanded with new pharmaceuticals that demonstrated high sales. In this year's report, the sample contains 225 substances in the segment "protected originator", 810 substances in the segment "unprotected pharmaceutical" (Product-of-the-month).

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

Pharmaceutical matching method

This price comparison analyses weighted prices for different "price baskets" of pharmaceuticals. What is defined as a product can be interpreted differently. Pharmaceutical matching can be performed in different ways, with different consequences for precision and in how many countries a pharmaceutical is included 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 pack size, since the choice of pack size used differs depending on the country.

[23] IQVIA was called IMS Health prior to November 2017.

In Sweden, pharmaceuticals are normally dispensed by pharmacies for a three-month period, while a one-month period is the norm in Southern Europe. Thus, larger pack sizes are sold in Sweden compared to countries in which prescriptions are filled at shorter intervals. If the pack sizes that are usually sold have a lower price than those with lower sales volumes, it would mean that large pack sizes would be given greater weight and would thus benefit Sweden in a price index. To correct for this, the price has been calculated as cost per unit for a particular substance, dosage form and strength. This makes it possible to compare different pack sizes with each other, making the price indices more accurate. This practice increases the degree of matching with other countries, although the precision of the comparison is somewhat lower than when matching at the pack level.

An alternative would be matching at the pack level, which means that exactly the same pack in terms of substance, dosage form, strength and size must 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 in terms of packaging. At the same time, there is a greater risk that a specific pack will not be available in very many countries. Pack size often correlates to dispensing frequency. The longer the time between dispensing, the greater the probability that larger pack sizes are more common, and vice versa.

Another option would be to measure the costs incurred by each country for a specific therapy group, regardless of which pharmaceuticals are used, and then weigh these costs together to see what the country pays to treat various diagnoses. The problem with this type of price comparison is difficulties in qualifying which pharmaceuticals belong to a specific therapy group, and that treatment traditions may differ between countries.

Pharmaceuticals with very low volumes in a country are excluded

Some countries that have matching with a product in Sweden may exhibit sales volumes considerably lower than in Sweden. If the volume per capita is less than 0.5 per cent of the Swedish equivalent, the pharmaceutical is excluded from the bilateral index calculation for that year. This practice is done to avoid attributing a product that has very little use in the comparison country a disproportionate weighting in the price comparison and thereby potentially overestimating the relative price level. Data on volume over a running 12-month period through March 2019 is used for calculation.

Sales volumes and weighting

It is common practice to weight the various product prices in a price index by volume. 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 there are two periods (period 0 and period t) and n products, a price index is generally written as:

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

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 one 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 either be sales volume in a foreign country or sales volume in Sweden. The choice affects whether the price index should be interpreted from a Swedish perspective or not. The convention for price analyses is to calculate the Laspeyres price index, i.e. with the country from whose perspective the price differences should be seen as base – in this case Sweden:

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

Where p^U refers to the price in the foreign country and q^S is the quantity in Sweden. If the price is the same in Sweden and in the foreign country, the index has a value of 100. If the index is <100 (or >100), the product has a lower (or higher) price in the foreign country than in Sweden. Several figures in the report use a percentage instead of an index to e.g. show that a country has a price that is a number of percentage points above the average. In such case, an average index for all countries is calculated, and an individual country's index is then divided by the average index. For example, if Sweden has an index of 100 and the average of the countries is 107, Sweden has just under seven per cent lower prices than the average.

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 prices, 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 introduction of competing products and improvements to existing ones, is also important.

The price index gives a good overview of how the price level in comparable countries correlates to the price level in Sweden during the period in question. However, the absolute price index should be interpreted with caution since it is influenced by both volume and currency effects. However, this study uses a rolling exchange rate for the last three years throughout. This also applies to the index data reported for 2014, 2015, 2016, 2017, 2018 and 2019.

If another country's volume weight is used as a base instead of the home country, the absolute level of the price index is adjusted, but not necessarily the relative order between the countries.

Definition of “price basket”

To calculate a price index, whether it is bilateral or cross-sectional, the “price basket” must be defined. For a bilateral price index, the same product needs to be in Sweden and in the comparison country to be included in the price comparison for that country.

For a cross-sectional price index, the same product needs to be available in several countries to be included in any of the countries' price indices. The threshold, referred to as degree of matching, 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. To create the same basket for all countries, in cases where a country does not have sales of a particular product, the average price of the countries that do have sales is applied.

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 more stringent the matching requirement applied, the lower the amount of data that needs to be filled out, but this means that fewer pharmaceuticals are eligible for comparison. A less stringent matching requirement increases the number of pharmaceuticals in the comparison, but requires that more data be filled out with Swedish data, which tends to even out the differences between the 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 maximises the number of pharmaceuticals included in the comparison and makes it unnecessary to fill out with average values when a pharmaceutical is not available in another country. The dilemma is that the mix of pharmaceuticals varies between countries. It is therefore not possible to compare price levels between countries, only the respective country’s relation to Sweden’s index.

To see how different choices of price baskets (based on countries other than Sweden) affect the price comparison, please see the information in *Appendix 1* in the report for 2018.

Drivers of relative price

The Swedish pharmaceutical prices relative to the rest of Europe are affected by several factors. In order to determine which effects have the greatest impact on the relative price level, the effects are divided into three different factors, namely price, currency and volume composition. These are calculated by applying the cross-sectional index formula (see section 1.3.2) to an adjusted variant of the data material, where the three components exchange rate, price per unit and volume[24]

[24] Defined as the number of packs sold.

are kept constant at the level observed in 2014, for all countries. The total relative price difference ($P_{s,y}^{rel}$) for country s during year y, compared to the average for all countries $c \in C$, where C is the number of countries included in the comparison[25], is calculated as follows:

$$\mathrm{P}_{\mathrm{s,y}}^{\mathrm{rel}} = \frac{\sum_{\mathrm{i}\in\mathrm{I}} \mathrm{p_{i,y,s}} \cdot \mathrm{z_{y,s}} \cdot \mathrm{q_{i,y,s}}}{\frac{\sum_{\mathrm{c}\in\mathrm{C}} \sum_{\mathrm{i}\in\mathrm{I}} \mathrm{p_{i,y,c}} \cdot \mathrm{z_{y,c}} \cdot \mathrm{q_{i,y,s}}}{|\mathrm{C}|}}$$

Where I is the number of individual pharmaceuticals[26] in the comparison material. $z_{y,c}$ denotes the exchange rate for country $c \in C$ (in SEK) and $q_{i,y,c}$ denotes the sales volume for pharmaceutical $i \in I$, during year y in country $c \in C$.

The (total) difference in relative price between two years, y_1 and y_2, is thus calculated as follows:

$$P_{s,y_2}^{rel} - P_{s,y_1}^{rel}$$

The effect of an individual component is calculated by holding the two remaining components constant, and then calculating the difference compared to the base year (2014). For example, the effect of the exchange rate is calculated by locking the price per unit and volume to the 2014 level, thereby capturing the effect, on the cross-sectional index, of the exchange rate in isolation. The change Δ_d of each individual component $d \in D$, during the period $y_1 - y_2$ is calculated as follows:

$$\Delta_{Price\,y_1,y_2} = \frac{\sum_{\mathrm{i}\in\mathrm{I}} \mathrm{p_{i,y_2,s}} \cdot \mathrm{z_{y_1,s}} \cdot \mathrm{q_{i,y_1,s}}}{\frac{\sum_{\mathrm{c}\in\mathrm{C}} \sum_{\mathrm{i}\in\mathrm{I}} \mathrm{p_{i,y_2,c}} \cdot \mathrm{z_{y_1,c}} \cdot \mathrm{q_{i,y_1,s}}}{|\mathrm{C}|}} - \frac{\sum_{\mathrm{i}\in\mathrm{I}} \mathrm{p_{i,y_1,s}} \cdot \mathrm{z_{y\_1,s}} \cdot \mathrm{q_{i,y\_1,s}}}{\frac{\sum_{\mathrm{c}\in\mathrm{C}} \sum_{\mathrm{i}\in\mathrm{I}} \mathrm{p_{i,y_1,c}} \cdot \mathrm{z_{y_1,c}} \cdot \mathrm{q_{i,y_1,s}}}{|\mathrm{C}|}}$$

$$\Delta_{Currency\,y_1,y_2} = \frac{\sum_{\mathrm{i}\in\mathrm{I}} \mathrm{p_{i,y_1,s}} \cdot \mathrm{z_{y_2,s}} \cdot \mathrm{q_{i,y_1,s}}}{\frac{\sum_{\mathrm{c}\in\mathrm{C}} \sum_{\mathrm{i}\in\mathrm{I}} \mathrm{p_{i,y_2,c}} \cdot \mathrm{z_{y_2,c}} \cdot \mathrm{q_{i,y_1,s}}}{|\mathrm{C}|}} - \frac{\sum_{\mathrm{i}\in\mathrm{I}} \mathrm{p_{i,y_1,s}} \cdot \mathrm{z_{y\_1,s}} \cdot \mathrm{q_{i,y\_1,s}}}{\frac{\sum_{\mathrm{c}\in\mathrm{C}} \sum_{\mathrm{i}\in\mathrm{I}} \mathrm{p_{i,y_1,c}} \cdot \mathrm{z_{y_1,c}} \cdot \mathrm{q_{i,y_1,s}}}{|\mathrm{C}|}}$$

$$\Delta_{Volume\ comp.\,y_1,y_2} = \frac{\sum_{\mathrm{i}\in\mathrm{I}} \mathrm{p_{i,y_1,s}} \cdot \mathrm{z_{y_1,s}} \cdot \mathrm{q_{i,y_2,s}}}{\frac{\sum_{\mathrm{c}\in\mathrm{C}} \sum_{\mathrm{i}\in\mathrm{I}} \mathrm{p_{i,y_1,c}} \cdot \mathrm{z_{y_1,c}} \cdot \mathrm{q_{i,y_2,s}}}{|\mathrm{C}|}} - \frac{\sum_{\mathrm{i}\in\mathrm{I}} \mathrm{p_{i,y_1,s}} \cdot \mathrm{z_{y\_1,s}} \cdot \mathrm{q_{i,y\_1,s}}}{\frac{\sum_{\mathrm{c}\in\mathrm{C}} \sum_{\mathrm{i}\in\mathrm{I}} \mathrm{p_{i,y_1,c}} \cdot \mathrm{z_{y_1,c}} \cdot \mathrm{q_{i,y_1,s}}}{|\mathrm{C}|}}$$

The significance of each component, in relation to the total change, is then calculated by comparing the Euclidean distance in the relative price change, between 2014 and 2019, with the corresponding distance in total change for the same period:

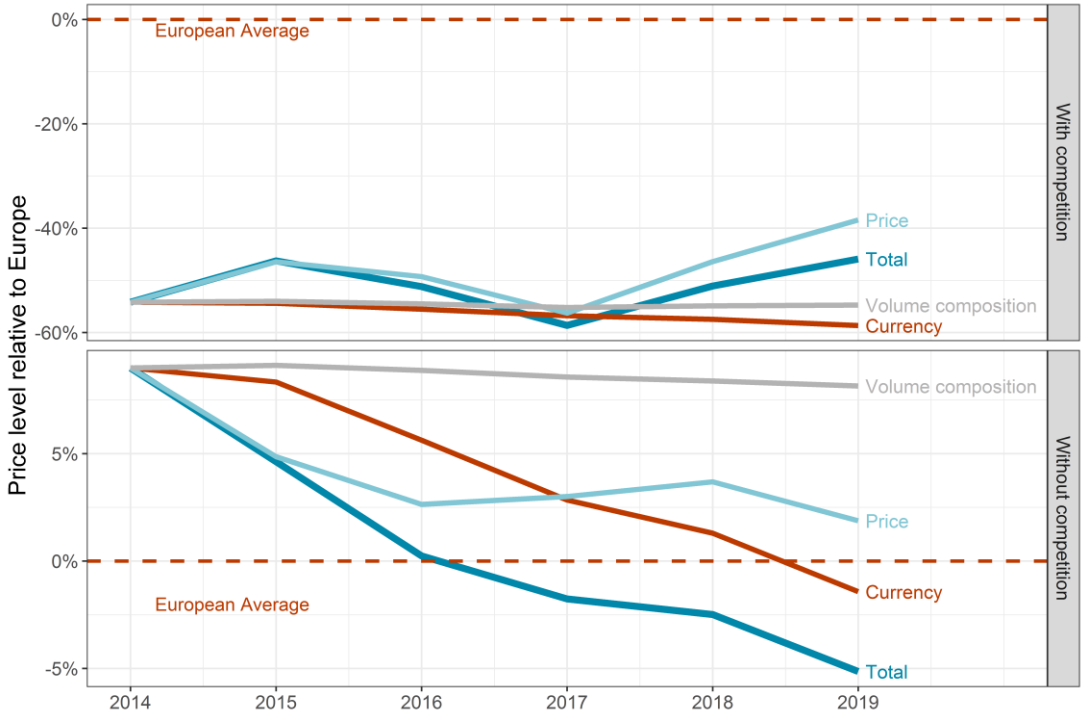
$$Proportion\ \Delta_d = \frac{\Delta_d}{\sum_{i\in D} \Delta_i}$$

[25] Note that $s \in C$

[26] Defined as a unique combination of a specific substance, dosage form and strength.

Only pharmaceuticals that have had the same competition status, and positive sales, during the entire period 2014–2019 are included in the analysis. This is because pharmaceuticals that are added and disappear between years are affected by current, price and volume effects. The analysis is simplified by the exclusion of these products, not least because this ensures that the same comparison is made between different years. Figure 24 shows the effect of each individual effect over time, both for pharmaceuticals exposed to competition and those not exposed.

Figure 24 Change in cross-section index over time, broken down by price, current and volume composition. Pharmaceuticals not exposed to competition and pharmaceuticals exposed to competition.



Note: Only pharmaceuticals with positive sales and unchanged competition status for the period 2014–2019.

Pharmaceutical groups

A list of the defined pharmaceutical groups is found below, along with which substances are found in each group. The list is based on the grouping made by the National Board of Health and Welfare in connection with the pharmaceutical cost forecast. TLV then revised the grouping, mainly categorising additional pharmaceuticals.

Table 4. Definition of pharmaceutical groups

Group	Substances
ADHD	Atomoxetine, Guanfacine, Lisdexamfetamine, Methylphenidate
Analgesics	Codeine,Paracetamol, Eletriptan, Fentanyl, Hydromorphone, Morphine, Naloxone,Oxycodone, Oxycodone, Rizatriptan, Sumatriptan, Tapentadol, Tramadol, Zolmitriptan, Dihydroergotamine, Ketobemidone, Acetylsalicylic Acid, Caffeine, Codeine
Anaemia	Darbepoetin Alfa, Epoetin Beta, Epoetin Zeta
Antibacterials	Amoxicillin, Amoxicillin,Clavulanic Acid, Avibactam,Ceftazidime, Azithromycin, Aztreonam, Cefadroxil, Ceftazidime, Ceftolozane,Tazobactam, Ceftriaxone, Ciprofloxacin, Clarithromycin, Clindamycin, Colistin, Daptomycin, Doxycycline, Erythromycin, Flucloxacillin, Levofloxacin, Linezolid, Meropenem, Moxifloxacin, Penicillin V, Pivmecillinam, Sulfamethoxazole,Trimethoprim, Telithromycin, Tobramycin, Trimethoprim, Lymecycline, Mecillinam
Antiepileptic	Brivaracetam, Carbamazepine, Clonazepam, Eslicarbazepine Acetate, Ethosuximide, Gabapentin, Lacosamide, Lamotrigine, Levetiracetam, Oxcarbazepine, Perampanel, Pregabalin, Rufinamide, Topiramate, Valproic Acid, Vigabatrin, Zonisamide, Stiripentol
Blood coagulation factors	Albutrepenonacog Alfa, Efmoroctocog Alfa, Eftrenonacog Alfa, Emicizumab, Lonoctocog Alfa, Nonacog Beta Pegol, Octocog Alfa, Rurioctocog Alfa Pegol, Simoctocog Alfa, Turoctocog Alfa, Nonacog Gamma
Cholesterol-lowering	Alirocumab, Atorvastatin, Bezafibrate, Colesevelam, Colestyramine, Evolocumab, Ezetimibe, Ezetimibe,Simvastatin, Fenofibrate, Fluvastatin, Gemfibrozil, Rosuvastatin, Simvastatin, Colestipol
Contraceptives	Desogestrel, Dienogest,Estradiol, Dienogest,Ethinylestradiol, Drospirenone,Ethinylestradiol, Drospirenone,Ethinylestradiol Betadex, Estradiol,Nomegestrol Acetate, Ethinylestradiol,Levonorgestrel, Ethinylestradiol,Norgestimate, Etonogestrel, Levonorgestrel
Diabetes - insulin	Insulin Aspart, Insulin Aspart,Insulin Aspart Protamine Crystalline, Insulin Degludec, Insulin Degludec,Liraglutide, Insulin Detemir, Insulin Glargine, Insulin Glargine,Lixisenatide, Insulin Glulisine, Insulin Human Base, Insulin Human Base,Insulin Human Isophane, Insulin Human Isophane, Insulin Lispro, Insulin Lispro,Insulin Lispro Protamine, Insulin Aspart, Insulin Aspart Protamine
Diabetes - non-insulin	Acarbose, Alogliptin, Canagliflozin, Dapagliflozin, Dapagliflozin,Metformin, Dulaglutide, Empagliflozin, Empagliflozin,Linagliptin, Empagliflozin,Metformin, Exenatide, Glibenclamide, Glimepiride, Glipizide, Linagliptin, Linagliptin,Metformin, Liraglutide, Lixisenatide, Metformin, Metformin,Pioglitazone, Metformin,Saxagliptin, Metformin,Sitagliptin, Metformin,Vildagliptin, Pioglitazone, Repaglinide, Saxagliptin, Sitagliptin, Vildagliptin, Semaglutide
Hepatitis C	Daclatasvir, Elbasvir, Grazoprevir, Glecaprevir,Pibrentasvir, Ledipasvir, Sofosbuvir, Ombitasvir, Paritaprevir, Ritonavir, Sofosbuvir, Sofosbuvir, Velpatasvir, Sofosbuvir, Velpatasvir, Voxilaprevir
HIV	Abacavir, Abacavir, Dolutegravir, Lamivudine, Abacavir, Lamivudine, Atazanavir, Cobicistat, Darunavir, Darunavir, Dolutegravir, Efavirenz, Efavirenz, Emtricitabine, Tenofovir Disoproxil, Emtricitabine, Rilpivirine, Tenofovir Disoproxil, Emtricitabine, Tenofovir Disoproxil, Lamivudine, Lopinavir, Ritonavir, Nevirapine, Raltegravir, Rilpivirine, Tenofovir Disoproxil, Cobicistat, Darunavir, Emtricitabine, Tenofovir Alafenamide, Atazanavir, Cobicistat
Hypothyroidism	Levothyroxine Sodium, Liothyronine
Incontinence	Fesoterodine, Mirabegron, Oxybutynin, Solifenacin, Tolterodine, Darifenacin
Interleukin inhibitors	Brodalumab, Guselkumab, Ixekizumab, Sarilumab, Secukinumab, Tocilizumab, Ustekinumab
JAK inhibitors	Baricitinib, Tofacitinib
MS	Cladribine, Dimethyl Fumarate, Fampridine, Fingolimod, Glatiramer Acetate, Interferon Beta-1a, Interferon Beta-1b, Natalizumab, Peginterferon Beta-1a, Teriflunomide
Neuroleptic	Alprazolam, Aripiprazole, Chlorprothixene, Clozapine, Diazepam, Flupentixol, Haloperidol, Hydroxyzine, Levomepromazine, Lorazepam, Melatonin, Midazolam,

Group	Substances
	Nitrazepam, Olanzapine, Paliperidone, Paliperidone Palmitate, Quetiapine, Risperidone, Sertindole, Ziprasidone, Zolpidem, Zopiclone, Zuclopenthixol, Clomethiazole, Zaleplon, Lurasidone, Perphenazine, Propiomazine
NOAC	Apixaban, Dabigatran Etexilate, Edoxaban, Rivaroxaban
Obstructive airway diseases	Aclidinium Bromide, Aclidinium Bromide,Formoterol, Beclometasone, Beclometasone, Formoterol, Beclometasone, Formoterol, Glycopyrronium, Benralizumab, Budesonide, Budesonide, Formoterol, Fluticasone, Fluticasone Furoate, Vilanterol, Fluticasone, Formoterol, Fluticasone,Salmeterol, Formoterol, Glycopyrronium, Glycopyrronium, Indacaterol, Indacaterol, Ipratropium Bromide, Ipratropium Bromide, Salbutamol, Mepolizumab, Montelukast, Olodaterol, Omalizumab, Roflumilast, Salbutamol, Salmeterol, Terbutaline, Tiotropium Bromide, Umeclidinium Bromide
Oncology	Abiraterone Acetate, Afatinib, Anagrelide, Anastrozole, Axitinib, Bevacizumab, Bexarotene, Bicalutamide, Bosutinib, Brigatinib, Buserelin, Busulfan, Cabozantinib, Capecitabine, Ceritinib, Chlorambucil, Dabrafenib, Dasatinib, Enzalutamide, Erlotinib, Estramustine, Everolimus, Exemestane, Filgrastim, Fludarabine, Fulvestrant, Gefitinib, Gimeracil,Oteracil,Tegafur, Goserelin, Histrelin, Ibrutinib, Idarubicin, Idelalisib, Imatinib, Ixazomib, Lenalidomide, Lenvatinib, Letrozole, Leuprorelin, Lipegfilgrastim, Medroxyprogesterone, Melphalan, Mercaptopurine, Methotrexate, Methyl-5-Aminolevulinic Acid, Midostaurin, Mitotane, Nilotinib, Nintedanib, Olaparib, Osimertinib, Palbociclib, Pazopanib, Pegfilgrastim, Pomalidomide, Ponatinib, Regorafenib, Ribociclib, Ruxolitinib, Sorafenib, Sunitinib, Tamoxifen, Temozolomide, Topotecan, Trametinib, Trastuzumab, Vemurafenib, Venetoclax, Vinorelbine, Tioguanine
Ophthalmologicals	Aflibercept, Bimatoprost, Bimatoprost, Timolol, Brimonidine, Brimonidine, Brinzolamide, Brimonidine, Timolol, Brinzolamide, Brinzolamide, Timolol, Chloramphenicol, Dexamethasone, Dorzolamide, Dorzolamide, Timolol, Latanoprost, Latanoprost, Timolol, Nepafenac, Ranibizumab, Tafluprost, Timolol, Timolol, Travoprost, Travoprost, Olopatadine, Tafluprost
Opioid addiction	Buprenorphine, Methadone
Osteoporosis	Alendronic Acid, Denosumab, Ibandronic Acid, Risedronic Acid, Strontium Ranelate, Teriparatide
Proton-pump inhibitor	Esomeprazole, Lansoprazole, Omeprazole, Pantoprazole
Psychoanaleptics	Agomelatine, Amitriptyline, Bupropion, Citalopram, Clomipramine, Donepezil, Duloxetine, Escitalopram, Fluoxetine, Galantamine, Idebenone, Memantine, Mirtazapine, Moclobemide, Modafinil, Paroxetine, Piracetam, Reboxetine, Rivastigmine, Sertraline, Venlafaxine, Vortioxetine
Reduce blood pressure	Amlodipine, Amlodipine, Hydrochlorothiazide, Olmesartan Medoxomil, Amlodipine, Hydrochlorothiazide, Valsartan, Amlodipine, Valsartan, Atenolol, Atorvastatin, Ezetimibe, Bisoprolol, Candesartan Cilexetil, Candesartan Cilexetil, Hydrochlorothiazide, Carvedilol, Diltiazem, Doxazosin, Enalapril, Enalapril, Hydrochlorothiazide, Eprosartan, Felodipine, Hydrochlorothiazide, Irbesartan, Hydrochlorothiazide, Losartan, Hydrochlorothiazide, Quinapril, Hydrochlorothiazide, Telmisartan, Hydrochlorothiazide,Valsartan, Irbesartan, Isradipine, Lercanidipine, Lisinopril, Losartan, Metoprolol, Pindolol, Propranolol, Quinapril, Ramipril, Sacubitril,Valsartan, Sotalol, Telmisartan, Timolol, Valsartan, Verapamil, Eprosartan, Hydrochlorothiazide
TNF inhibitors	Adalimumab, Certolizumab Pegol, Etanercept, Golimumab, Infliximab
TNF inhibitors alternative	Abatacept, Apremilast, Belimumab

Appendix 2: Pricing and reimbursement systems

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 level in several reference countries (reference pricing) or to base pricing on appraised values or profitability.

Table 5. Pricing models

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 (IRP)	**a)** Formal	**b)** Informal in combination with another method (e.g. assessment of benefit or value)	

Reference pricing, which is the most common method in Europe, can be formal or informal/supporting. This means that the average, the median or the maximum price that is calculated governs the set price either directly, or it constitutes a level that is considered during negotiation, during procurement or that forms part of a wider supplementary health-economic assessment.

The method for selecting reference countries varies. In some cases, the method is described, such as the countries having to be similar in terms of certain characteristics, like economy and geographical proximity. However, in most cases the reason why some countries are selected as reference countries is not given.

The number of countries in a price basket varies greatly within Europe, from 3 to 31 countries. Consequently, this affects what effect an individual country’s price or price range will have on a price basket in another country. With average value pricing, an individual country's weighting may vary from 3 per cent up to approximately 30 per cent. The direct or indirect strength of the price impact also varies depending on whether the country applies some form of supplementary assessment in addition to international reference pricing.

Exchange rate fluctuations affect pricing in countries that use reference pricing. The rules vary whether prices can not only decrease but also increase in response to exchange rate fluctuations. Thus, these changes affect the dynamics in the prices of other countries. The Netherlands and Norway use international reference pricing and adjust a fixed price ceiling in response to factors such as exchange rate changes in the reference countries, but at a predetermined time interval. Norway adjusts price both upwards and downwards. Ireland also adjusts the set reference price in response to exchange rate changes, but only downwards (this was introduced from

2017 together with the changed composition of the country basket for price comparisons). 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 is adjusted automatically in countries with reference pricing. The price is readjusted between three months to five years after a pricing decision.

Denmark, Sweden and the UK apply a different pricing method than reference pricing. Up until 2011, Germany also applied a different method, but has since transitioned to considering reference prices as part of a more extensive assessment of new pharmaceuticals.

Value-based pricing is used in Sweden and the UK. Denmark uses free pricing at the AIP level, while AUP (pharmacy selling price) is regulated nationally, which means that the same prices are found in pharmacies across the country. In the UK, price is regulated through voluntary PPRS (Pharmaceutical Price Regulation Scheme) agreements 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.

Table 6. Pricing systems in the countries included in the analysis

	Country	Pricing model (pharmaceuticals not exposed to competition)	# of countries	Reference countries	Method	Time until new price adjustment (months)
1	Denmark	No IRP. Competition/ price notification	-	.	-	-
	United Kingdom	No IRP. Indirect price control	-	-	-	-
	Sweden	No IRP. VBP	-	-	-	-
2a Formal IRP	Greece	IRP, formal	27	Other EU	Average of 3 lowest	3/6
	Ireland	IRP, formal	14	Austria, Belgium, Denmark, Spain, Finland, France, Netherlands, the UK, Sweden, Portugal, Luxembourg, Greece and Italy	Average	12
	Netherlands	IRP, formal	4	Belgium, Germany, France, the UK	Average	6
	Norway	IRP, formal	9	Belgium, Denmark, Finland, Ireland, Netherlands, the UK, Sweden, Germany and Austria	Average of 3 lowest	12
	Portugal	IRP, formal	3	Spain, France, Italy	Average	12
	Switzerland	IRP, formal	9	Belgium, Austria, Germany, Denmark, Finland, France, Netherlands, Sweden and the UK	Average	36
	Slovakia	IRP, formal	27	Other EU	Average of 3 lowest	6
	Czech Republic	IRP, formal	*28/19	Rest of EU for subsidy decisions. For price decision decisions: Belgium, Germany, Spain, Finland, France, Netherlands, Croatia, Ireland, Italy, Lithuania, Latvia, Hungary, Poland, Portugal, Greece, Slovakia, Slovenia, Sweden, the UK	Average of 3 lowest	36
	Hungary	IRP, formal	31	EU and EEA	Lowest price	-
	Austria	IRP, formal	27	Other EU	Average	-
2b Informal/ supporting IRP, in combination with another method	Belgium	IRP, informal/ supporting	27	Other EU	Average	-
	Finland	IRP, informal/ supporting	29	EEA (Other EU + Norway and Iceland)	Not determined/ average	60
	France	IRP, informal/ supporting	4	The UK, Italy, Spain and Germany	Average/ “close” price	60
	Italy	IRP, informal/ supporting	24	Other countries in the EURIPID database	Not determined/ lowest price	24
	Poland	IRP, informal/ supporting	31	EU and EFTA	Not determined/ average	24
	Spain	IRP, informal/ supporting	*18/3	Euro countries but greater emphasis on three countries: France, Italy and Portugal	Lowest price	12
	Germany	IRP, informal/ supporting	15	Austria, Belgium, Cyprus, Denmark, Greece, Spain, Finland, France, Ireland, Italy, Netherlands, Portugal, Sweden, Slovakia, the UK	Weighting by market and purchasing power	-

Pricing systems in Europe

In order to set the results of the price comparison in context, this section provides a description of the reimbursement and pricing systems in participating countries. For a more in-depth look at the pricing and reimbursement systems in Germany, France and the UK, please see the 2018 report.[27]

Sweden

TLV determines which pharmaceuticals should be included in the pharmaceutical benefits scheme. In 2018, the cost of pharmaceuticals in the benefits scheme amounted to approximately SEK 31.3 billion, based on AUP, including patient co-payments. The cost of prescription pharmaceuticals without benefit amounted to SEK 4.3 billion. In addition, the cost of pharmaceuticals for inpatient care, referred to as requisitioned pharmaceuticals, amounted to SEK 9.0 billion.[28]

For pharmaceuticals with no generic competition, value-based pricing is applied.[29] For generics, the period-of-the-month system is applied.

TLV's assessments are based on an ethical platform with three basic principles:
1. Human dignity principle – healthcare should respect that all people are equal in value,
2. Need and solidarity principle – those with the greatest medical need should be entitled to more of the healthcare resources,
3. Cost-effectiveness principle – the cost should be reasonable from a medical, humanitarian and socio-economic perspective.

For a pharmaceutical to be subsidised, a pharmaceutical company must first submit a reimbursement application to TLV. TLV then assesses whether the cost is reasonable for the pharmaceutical to be included in the pharmaceutical benefits scheme. The decisions are made by the Pharmaceutical Benefits Board, which is TLV's decision-making body.

Managed entry agreements

A managed entry agreement is a contract between the county councils and a pharmaceutical company that may be considered by TLV when deciding on pricing and reimbursement status. New pharmaceuticals are becoming introduced earlier, and some pharmaceuticals are sometimes associated with uncertainties regarding use and efficacy in clinical practice. With managed entry agreements, the risk can be shared and facilitate early use, even when there is considerable uncertainty about medical effect and cost effectiveness.[30]

Managed entry agreements can also be a tool for creating price competition, which lowers the costs within established pharmaceutical areas where no competition or

[27] TLV (2018a)
[28] TLV (2019a) p. 21 and p. 15
[29] See e.g. TLV (2018e), TLV (2018f) and TLV (2018g)
[30] TLV (2018d).

downward pressure on prices has occurred for various reasons. One example is biopharmaceuticals, where price competition rarely occurs despite the existence of biosimilars.

At the end of the first half of 2019, there were 46 pharmaceuticals in outpatient care that were covered by current managed entry agreements. The total cost for the pharmaceutical areas subject to managed entry agreements accounts for approximately 19 per cent in AIP of the total costs for pharmaceuticals included in the benefits scheme. The total cost of pharmaceuticals within the benefits scheme was just over SEK 30 billion in 2019.[31]

Table 6. Pharmaceuticals that have or previously had managed entry agreements

Area	Number of pharmaceuticals	Sales at set prices (TSEK)
Cancer	11	1,354,920
Hepatitis C	6	2,072,373
Factor VIII	11	573,664
JAK inhibitors	2	99,365
PCSK9	2	36,480
TNF inhibitors	8	2,051,514
Other	6	135,247
Total	46	6,323,563

Source: TLV (2019a) p. 39
Note: Statistics per area, plus total sales (set prices) January-December 2018, thousands of SEK.

Most agreements are found within the areas of cancer and Factor VIII. Within the area of cancer, new and costly pharmaceuticals are often introduced at an early stage and with a high degree of uncertainty.

High-cost protection

The cost of pharmaceuticals within the pharmaceutical benefits scheme is included in the patient's high-cost protection. The patient pays maximum SEK 2,250 in co-payments per 12-month period for pharmaceuticals included in the scheme. The county councils pay the rest. The national government pays annual grants to the county councils for the pharmaceutical benefits.

Since 2016, pharmaceuticals in the benefits scheme are free of charge for children under the age of 18.

Since 1 January 2017, contraceptives in the benefits scheme are free of charge for young adults under the age of 21.

Generic substitution

Generic substitution was established in Sweden in 2002, and since 2009 TLV has been responsible for what is known as the product-of-the-month system, where the manufacturers compete on price through a monthly auction procedure. Generic

[31] TLV (2019a) p. 21

substitution leads to lower prices, and there may eventually be significant differences in price between substitutable pharmaceuticals. TLV then lowers the maximum accepted sales price within the pharmaceutical 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. TLV sets a ceiling price when the prices in a group of substitutable pharmaceuticals have dropped to at least 70 percent of their pre-competition price and when generic competition has occurred for at least six months. If the criteria are met, a ceiling price of 35 per cent of the original price of the originator pharmaceutical product is introduced.[32] Setting ceiling prices in this manner reduces the price differences between substitutable pharmaceuticals within the benefits scheme. It also results in even lower costs beyond the effect of generic substitution itself.

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

Some older pharmaceuticals have no or only weak generic competition. This could be because, for example, it is not possible to substitute an originator pharmaceutical product with a generic one or the pharmaceutical is a biopharmaceutical. In January 2014, a price reduction was introduced for pharmaceuticals that are more than 15 years old, are included in the pharmaceutical benefits scheme, and have no or only weak generic competition. The price reduction equals 7.5 per cent of the price that applied in October 2012.[33]

For prescription pharmaceuticals that are not included in the benefits scheme, free pricing applies. Patients either pay the entire cost themselves or, in some cases including pharmaceuticals for infectious diseases, the county council covers the entire cost.

Finland

Finland applies informal reference pricing. Since 2014, the reference countries are EU 27 and Norway and Iceland. In addition to reference prices, factors such as

[32] TLV (2018h).
[33] TLV (2018i).

therapeutic value, benefit and price of similar products are taken into consideration.[34]

Originator pharmaceutical products: time-limited benefits
When pricing new pharmaceuticals, the following factors are considered:

1) the prices in Finland of the corresponding pharmaceutical preparations used for the treatment of the same disease,
2) the prices of the pharmaceutical preparation in other countries of the European Economic Area,
3) the healthcare costs that the use of the pharmaceutical preparation entails and the benefit that can be achieved for the patient and the total costs in the health and social care,
4) the benefits and costs of other available alternative treatment methods,
5) the funds available for reimbursement.

Research and development costs can also be considered in the price assessment.

For pharmaceuticals with new substances, price and reimbursement status are decided for a period of maximum three years. After this period, the company needs to reapply for the pharmaceutical to be included in the benefits scheme. For other products, the decision applies for a period of maximum of five years.[35]

Reference price groups with "price-of-the-period"
In Finland, there is a system of price bidding in reference price groups that has some similarities to the product-of-the-period systems in the Netherlands, Sweden and Denmark. However, in Finland, the supply period is three months instead of one month as in Sweden. The price of other substitutable pharmaceuticals in the substitution group can be changed during the three-month period.[36]

The system means that pharmaceuticals at the ATC-5 level (pharmaceuticals with the same substance) are divided into reference groups. A reference price group assumes that there is at least one generic, parallel imported or parallel distributed pharmaceutical. The bidding process is thus applied not only to generics but also to pharmaceuticals traded in parallel.

For generic pharmaceuticals in Finland, the first subsequent product of an originator pharmaceutical product is priced at least 50 per cent lower than the originator. The price of any subsequent generic pharmaceutical may not exceed the set price. For certain products, the level is 40 per cent. One change introduced for originator pharmaceutical products from 2016 is that the original price must be reduced by 40 per cent nine months after it is first exposed to generic competition in order to retain reimbursement status.

[34] HILA (2018)
[35] Kela (2017)
[36] COWI (2014), p. 9.

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 a new substitution period begins, Kela (Social Insurance Institution of Finland) submits information to the pharmaceutical companies about which price applies at the start of the three-month period. The reference price is calculated based on the pharmaceutical companies' price notifications by adding 0.50 euro to the price of the product with the lowest price in each substitution group (substance and biological equivalent). The calculated reference price is a maximum price used to calculate degree of subsidy. If the price of the pharmaceutical is less than the calculated price, the subsidy calculation is deducted from the pharmaceutical price.[37]

For the first two weeks of the three-month period, the price set by Kela applies. However, a pharmaceutical company may adjust the price of the pharmaceutical when the database is updated with a new publication of the price list. If the pharmaceutical is not part of the benefits scheme, the pharmaceutical company can set the price freely. The price of any pharmaceutical in the benefits scheme may not exceed the price set by the Pharmaceuticals Pricing Board.

Due to 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-period"*.[38]

High-cost protection

In Finland, the general rule is that all patients receive financial compensation for pharmaceuticals where the Pharmaceuticals Pricing Board has decided that reimbursement applies. The ceiling for co-payments amounts to EUR 572 per year. In 2016, a stepped system for co-payments was introduced. This means that all patients over the age of 18 pay 50 euros before any subsidy is applied.[39]

There are three categories of pharmaceutical subsidies:

Table 7.Subsidy levels in Finland and proportion of benefits, 2017

	Subsidy level	Proportion of benefit	Diseases
Basic reimbursement	40%	22.4%	
Lower special	65%	17.4%	11 chronic diseases

[37] Kela (2017)
[38] Kela (2018a).
[39] Kela (2019).

reimbursement			
Higher special reimbursement	100%	49.3%	34 chronic diseases
(Other subsidies)	-	10.9%	

Source: Kela (2017)

Basic reimbursement covers 40 per cent of the pharmaceutical's price or calculated reference price (22.4% of the benefits scheme cost). The lower special reimbursement covers 65 per cent of the pharmaceutical's price or calculated reference price (11 chronic diseases) (17.4%). The higher special reimbursement covers 100 per cent (34 serious chronic diseases) (49.3%), but the patient then pays 4.50 euros each time the prescription is filled.[40] The remaining 10.9% of the benefits scheme cost is attributable to payment of other subsidies.[41]

The dispensing fee is 2.50 euros per prescription during the year that a patient has exceeded the co-payment ceiling.

Managed entry agreements
Risk sharing/managed entry agreements were introduced in outpatient care in 2017. A total of 7 agreements were concluded during the year. Since 2017, prescribers have also been required to prescribe the option with the lowest cost when biosimilar products are available, or to explain the choice of a more expensive pharmaceutical in the medical record. The changes are expected to result in savings of EUR 134 million for outpatient pharmaceuticals.[42]

Norway

In Norway, the price of outpatient pharmaceuticals is set in relation to the price level in other countries through formal reference pricing, and the ceiling price for prescription pharmaceuticals is regulated by the Norwegian Medicines Agency (Statens Legemiddelverk).[43] Norway's reference countries are Belgium, Denmark, Finland, Sweden, Ireland, the UK (NHS), Germany, Netherlands and Austria. The system was implemented in 2002. The calculation is made at the AIP level. The ceiling price is set by taking the average market price for the product in the three countries with the lowest price and then adding a fixed trade margin. The focus of comparison is the price for the same product, and the comparison is made regardless of whether the product is marketed under different names in the reference countries. The calculation uses the exchange rate for at least the average of the last six months according to the compilation by central bank of Norway (Norges Bank).

The timing of price reviews is predetermined and takes place on a regular basis, which means that price adjustments for specific ATC groups are implemented every

[40] Kela (2016b).
[41] Kela (2017) p. 80
[42] Kela/Fpa (2018)
[43] Norwegian Medicines Agency (2018a).

month. It is also possible for companies to apply for price review. The prices of the 250 substances with the highest turnover are adjusted according to price changes in the comparison countries or to address major changes in exchange rates, however this is done no more than once per 12-month period. The pharmaceuticals included in this annual price review represent about 70–80 per cent of the market.

Generics: Stepped pricing model with volume component
Generic pharmaceuticals are subject to the *trinnprismodellen* (the Norwegian stepped pricing model), which was introduced in 2005 and regulates the maximum sales price at the pharmacies.

The price is decreased in steps depending on sales volume.[44] When generic competition arises, the price of the originator pharmaceutical product is reduced by 35 per cent when the patent expires. The second step in the model occurs six months after this. The maximum price is then 59 to 81 per cent lower than the price of the originator pharmaceutical product at the time of patent expiry. The third sept occurs 18 months after generic competition has arisen. The maximum price is then 69 to 90 per cent lower than the price of the originator pharmaceutical product at the time of patent expiry. A larger price reduction is applied to substances with high turnover.[45]

Table 8. Trinnprismodellen/Norwegian stepped pricing model

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

Source: Norwegian Medicines Agency (2018b).

The system for setting the ceiling price and the stepped pricing model apply to both parallel imported and directly imported pharmaceuticals.

Pharmacies can negotiate purchase prices with the manufacturers. In practice, there is only negotiation in relation to generic pharmaceuticals. Negotiation of purchase prices for originator pharmaceutical products is more limited.

Pharmacies are expected to switch to the cheapest pharmaceutical when there are several options on the *Byttelistan* (substitution list).[46] If a patient does not accept generic substitution, they must pay the additional cost.[47]

[44] Norwegian Medicines Agency (2018b).
[45] Norwegian Medicines Agency (2015).
[46] Norwegian Medicines Agency (2018d).

Since April 2017, there have been managed entry agreements within the framework of outpatient care. Separate agreements have been entered into for two products: Repatha and Praluent.[48]

H-prescriptions
In addition to the prescribing of common outpatient prescriptions, Norway also has what is known as H-prescriptions, which make it possible for some inpatient pharmaceutical to be collected at regular pharmacies. The H-prescription system has existed since 2006 and has been extended several times. There is a joint procurement organisation for inpatient care products, Hospital Purchases (Sykehusinnkjøp), whose function is similar to that of Amgros in Denmark with the aim of obtaining discounts on inpatient pharmaceuticals.

The objective of reducing costs has also led to the gradual transfer of purchases and management of certain pharmaceutical groups in Norway from outpatient care to inpatient care. TNF-alpha inhibitors have been managed within inpatient care since 2006. MS pharmaceuticals 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 and clotting factors, and growth hormones was transferred to inpatient care in 2016.[49, 50] Additional pharmaceutical groups have been subsequently transferred to management via H-prescription, including medicines for the treatment of pulmonary arterial hypertension (PAH) from January 2017 and many oncology medicines from May 2017.[51]

High-cost protection

The degree of subsidy is generally 61 per cent of the cost of the pharmaceutical, but different conditions apply. The degree of subsidy is 100 per cent for children under the age of 16 and pensioners with low incomes, as well as for pharmaceuticals for treating infectious diseases such as tuberculosis, hepatitis C and HIV. However, a limit has been set so patient co-payments are maximum NOK 520 per prescription. A ceiling for co-payments is set each year. The 2019 ceiling is NOK 2,380.

Denmark

Denmark applies free pricing for list prices at the AIP level. This applies to both originator pharmaceutical products and pharmaceuticals exposed to competition. Prices of pharmaceuticals are reported to the Danish Medicines Agency (Lægemiddelstyrelsen), which in turn publishes the sales price and the subsidised price. The pharmacy selling price (AUP) is regulated through fixed dispensing fees and a percentage margin on the AIP. In Denmark, however, it has become more

[47] Norwegian Medicines Agency (2018c).
[48] Norwegian Medicines Agency (2018e)
[49] Norwegian Society for Medical Informatics (2016).
[50] Norwegian Medicines Agency (2016a).
[51] Norwegian Directorate of Health (2018).

common for pharmaceuticals to be bought up through Amgros, the hospital system's acquisition organisation, and to be handled within the framework of inpatient care. The role of free pricing in the price of pharmaceuticals has therefore decreased.

Prices are set every other week
Denmark has a substitution system similar to the Swedish product-of-the-month system. Pharmaceutical producers can announce price and product range changes as often as every fourteen days. The product with the lowest price in the respective group automatically becomes the highest amount that is subsidised.[52]

Products-of-the-period in Denmark become class A products during the period in question. Pharmaceuticals are categorised as class B if they are within a so-called bagatelle limit of class A products. If a doctor has prescribed a class B product, the pharmacy is not required to replace it with an A class product. However, the subsidy is limited to the subsidy of the relevant class A product. The bagatelle limit is between DKK 5 and 20 depending on the pharmaceutical's price.[53] Class C products that exceed the bagatelle limit must be substituted unless otherwise specified to the pharmacist by the doctor or patient.

The Danish Association of the Pharmaceutical Industry, the government and the regions in Denmark have entered into price-capping agreements for pharmaceuticals for a number of years. The current agreement runs from 2019 to 2023. This means that the reference price model for list prices within inpatient care must undergo a conversion, resulting in a price reduction of 12.5 per cent over a four-year period.[54] The agreement also ensures that the price of new inpatient pharmaceuticals does not exceed the average price in Sweden, Norway, Finland, the UK, the Netherlands, Belgium, Germany, Ireland and Austria.

High-cost protection

Pharmaceutical companies apply for benefits scheme status with the Danish Medicines Agency.[55] Reimbursement can be general or individual. Individual reimbursement can be granted for pharmaceuticals without general reimbursement. In such cases, the doctor applies for reimbursement on behalf of the patient. The subsidy is 80 per cent of the price. General reimbursement is a positive list and can be limited to an indication group or a patient group.[56]

The general reimbursement and co-payment thresholds are as follows 2018: 0 per cent of the cost up to DKK 965, 50 per cent of costs between DKK 965 and 1,595, 75 per cent of costs between DKK 1,595 and 3,455, and 85 per cent of costs over DKK

[52] Danish Medicines Agency (2018a).
[53] COWI (2014), p. 32.
[54] Ministry of Health and Elderly Affairs (2019). http://sum.dk/Aktuelt/Nyheder/Medicin/2019/marts/Medicinpriserne-saenkes-i-DK.aspx
[55] Danish Medicines Agency (2018c).
[56] Danish Medicines Agency (2018d).

3,455. Co-payment is capped at DKK 4,030 per year. Children under the age of 18 are subject to different degrees of subsidy than adults.[57]

Since 2015, pharmacists have been allowed to open up to seven pharmacies within a 75-kilometre radius. The increase in the number of pharmacies is intended to give patients greater access to pharmacies.

Germany

In Germany, there is a price and reimbursement system that combines free pricing, reference pricing and value-based pricing. The reference pricing component is informal/supporting, and price information is collected at "actual" ex-factory level (before transport and other distribution costs and after discounts and rebates).[58] [59] Most of the German population (90%) is covered by a mandatory statutory health insurance (SHI). The rest is covered by private insurance. Private health insurance companies usually have the same products as SHI, but they have the ability to limit or expand the benefits.

All approved pharmaceuticals entering the German market are included in health insurance funds, except those not covered by a specific law (e.g. OTC) or a decision by the Federal Joint Committee (Gemeinsamer Bundesausschuss – G-BA). The patients are generally obliged to contribute to the cost of pharmaceuticals by means of a 10% contribution (minimum 5 euros and maximum 10 euros per prescription).

AMNOG – Arzneimittelmarkt-Neuordnungsgesetz (Act on the Reform of the Market for Medicinal Products) – is an act that came into force on 1 January 2011 that regulates the pricing of new pharmaceuticals. Under AMNOG, manufacturers freely set prices for pharmaceuticals when launched on the market.[60] However, they must submit documentation with necessary information for assessing the additional therapeutic benefit of the pharmaceutical. AMNOG states that a formal assessment of the "additional therapeutic benefit" for new pharmaceuticals must be made by G-BA.[61] The price is subject to negotiation based on the assessed additional therapeutic benefit within twelve months after the launch of the product on the German market. The purpose of AMNOG was to limit rising pharmaceutical costs while retaining early access to new pharmaceuticals and incentives for innovation.[62]

Additional therapeutic benefit is assessed against a suitable comparator (care standard) within 6 months. The assessment is usually performed by the Institute for

[57] Danish Medicines Agency (2018e). The maximum annual cost for children under the age of 18 is DKK 4,030. 60% subsidy for costs between DKK 0-965, 60% for costs between DKK 965-1,595, 75% for costs between DKK 1,595-3,455.
[58] Silke Baumann and Karam Abulzahab, Federal Ministry Of Health, contributed information for the description of the German system, 9 November 2017.
[59] GKV-Spitzenverband contributed information for the description of the German system, 1 June 2018.
[60] VFA, How does a new drug enter the market?
[61] Between 2011 and 2014, 66 pharmaceuticals were evaluated, of which 27 did not show any additional therapeutic benefit compared to already existing pharmaceuticals.
[62] German Federal Ministry of Health, Die Spreu vom Weizen trennen Das Arzneimittelmarktneuordnungsgesetz (AMNOG).

Quality and Efficiency in Health Care (IQWiG).[63] The decision (assessment) about additional therapeutic benefit is based on this assessment and the results of a public inquiry after publication of the evaluation. G-BA's decision on additional therapeutic benefit determines the benefits scheme price after the first year with free pricing. If the pharmaceutical has not shown any additional therapeutic benefit, the pharmaceutical is included in a reference price cluster. Based on G-BA's decision, the manufacturer and the National Association of Statutory Health Insurance Funds (GKV-SV) negotiate a benefits scheme price within six months. If the parties cannot reach an agreement, the price is determined through arbitration.

AMNOG's evaluation and price negotiation apply to all new pharmaceuticals with new active substances introduced on the German market after 1 January 2011. Exceptions exist for pharmaceuticals with annual sales within SHI of less than EUR 1 million. For orphan pharmaceuticals, additional therapeutic benefit is assumed by virtue of marketing authorisation without reference to a suitable comparator in Germany, provided that annual sales within SHI are below EUR 50 million. When this threshold is exceeded, the orphan pharmaceutical is evaluated, and the price is negotiated the same way as all other pharmaceuticals.

No direct pricing is applied to pharmaceuticals introduced before 2011. However, for the generic market and the *me-too* market, there are several instruments that affect the (benefits scheme) prices for these pharmaceuticals and/or steer doctors towards a more rational prescribing behaviour (e.g. to prescribe a generic alternative).

Most generics and some other pharmaceuticals are included in G-BA's reference price clusters. These include pharmaceuticals (1) with the same active substance and similar use, (2) with comparable therapeutic or pharmacologically active substances (usually at ATC4 level), and (3) with comparable therapeutic effect (usually used for fixed combinations).

Pharmaceuticals in a reference price cluster are assigned a maximum benefits scheme amount. If the price of the pharmaceutical exceeds the amount, the patients pay the difference. Companies often lower their prices to match the maximum reimbursement amount. If they do not, the patients may ask their prescriber for an alternative.

Within the health insurance system, it is common to see discounts on the list price, especially for generic pharmaceuticals. Individual health insurance funds can draw up agreements on discounts on the pharmaceutical company's list price through public procurement. The prices of pharmaceuticals given to hospital patients are negotiated between pharmaceutical companies and hospitals, hospital chains or group purchasing organisations, while the official price for outpatient care acts as a ceiling price.

[63] Federal Institute for Drugs and Medical Devices (BfArM), AMNOG (Act on the Reform of the Market for Medicinal Products).

The pharmaceutical companies provide a statutory discount of 7% off the list price for patented pharmaceuticals that are not grouped in reference price groups.[64] There are also discounts for generic pharmaceuticals. The discount is normally 6 per cent for pharmaceuticals exposed to competition, unless the price is at least 30 per cent below the reference price.[65]

In addition to the statutory discounts, GKV-SV negotiates a refund rate (Erstattungsbetrag) with the manufacturers. These refund rates may replace the statutory discount in whole or in part. After seven years with AMNOG, the statutory discount is retained in fifty per cent of the cases, while the others are replaced by other (higher) discounts that are negotiated.[66] Refund rates and their discounts (statutory) are available in the German price database.[67] In addition to the discounts negotiated by GKV-SV, local health insurance funds can negotiate additional discounts. This occurs with e.g. generics and diabetes pharmaceuticals, where competition is fierce. These discounts are not visible in the price database.

The legislation also stipulates a price freeze at the price level that applied on 1 August 2009. This was extended to 2022. From and including 2018, prices can be adjusted according to inflation.

Substitution at pharmacies is an important tool for holding down rising pharmaceutical costs. Pharmacists should substitute with a cheaper pharmaceutical with the same substance. If the patient's health insurance fund has an agreement for a discount on a product with the same substance as the prescribed product, the pharmacy is obliged to dispense the product for which the discount applies. However, in certain therapeutic areas, substitution is not allowed, e.g. thyroid hormones, antiepileptics and pharmaceuticals for certain heart diseases. In all other cases, prescribers can exclude substitution for medical reasons.

At the regional level, there are agreements between health insurance funds and doctor associations on additional rules for prescribing in order to hold back cost development and stimulate more rational prescribing behaviour, e.g. quotas for biosimilars. It is also possible to issue sanctions if doctors do not comply with these rules or other legislation.

United Kingdom

In the UK, almost all healthcare, including pharmaceutical subsidies, takes place through the state healthcare system. Healthcare is funded through taxes.

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[64] Discounts to 2010 inclusive, ex-factory, amounted to 6 per cent on new innovative pharmaceuticals. The discount for that category increased to 16 per cent during the period 1 August 2010 – 31 December 2013. (KBV (2018) and Ruggeri, K. and Nolte, E. (2013) p. 42.)
In 2014 it was decided that the mandatory discount on subsidised pharmaceuticals would be reduced from 16 per cent to seven per cent (Portugal (2016), p. 20).
[65] KBV (2018).
[66] GKV (2018).
[67] Lauer-Fischer (2018).

Pricing of new pharmaceuticals takes place with value-based pricing which is reminiscent of the Swedish system. Manufacturers are free to set prices at market launch. Subsidy is regulated through a negative list of pharmaceuticals that may not be prescribed with the benefits scheme. Most new pharmaceuticals are granted full subsidy in connection with market launch and price being approved. However, in order for the pharmaceutical to be prescribed in larger quantities it must be recommended by NICE (National Institute for Health and Care Excellence), and its price must be below the ceiling price that NICE determines in a health economic assessment. At launch, manufacturers can request evaluation of the new pharmaceutical by NICE. In the application, they state a requested price. NICE carries out an evaluation where value-based pricing is performed, using quality-adjusted life-years and the establishment of ceiling prices.

If NICE determines that the pharmaceutical is cost-effective at the requested price, this is addressed in the recommendations for the NHS. The NHS must then provide the pharmaceutical at the requested price. The NHS Constitution from 2012 gives patients legal rights to pharmaceuticals recommended by NICE. NICE recommendations take precedence over local or regional recommendations. If NICE has recommended a pharmaceutical, then local or regional boards will not make any modifications or changes to this. NICE recommendations must be incorporated into local or regional regulations within 90 days.

There is free pricing for generic pharmaceuticals in the UK, provided that the pharmaceutical is priced below the ceiling price that applied at the time the originator pharmaceutical product's patent expired. Generic prescribing (INN) is voluntary, but widely used.

France

In France, there is a compulsory state health insurance system. National health insurance is the main payer of healthcare, including pharmaceuticals (to about 70 per cent). 97 per cent of the French have supplementary insurance that pays the remainder[68].

France has been applying formal/informal reference pricing since 2003. The prices (ex-factory) should be *close to* the prices in the reference countries (Germany, Spain, Italy and the UK). Price review within the reference price component takes place every 60 months.

It is the pharmaceutical companies who provide information on pricing in other countries. The price that is set is fixed for five years. After this time, the list price can be renegotiated. Reference pricing is not the main method at the time of renegotiation.

[68] HST (2015), p. 70. Source: 2018 report

When a manufacturer wants to launch a pharmaceutical with subsidy, it must be evaluated by the Economic Committee for Health Care 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 pharmaceutical's therapeutic value and the pharmaceutical's additional therapeutic value compared to alternative treatments. A four-level scale is used, where 1 means major improvement, new therapeutic area, reduced mortality, and 4 means no improvement. CEPS then negotiates price with the manufacturer. For pharmaceuticals rated 1-3 (major to some improvement), reference prices are only one component of the assessment. The pharmaceuticals are also subject to HTA evaluation.

Pricing of older pharmaceuticals

France has a special system for pricing older pharmaceuticals, where discounts are converted into list price reductions.[69] Paragraph 21 of the three-year framework agreement, which governs the negotiations between CEPS and the manufacturers, states the following:

> At the end of a period of price guarantee [five years for innovative pharmaceuticals] or, by default, at the end of a period of three years after the pharmaceutical has obtained benefits scheme approval, CEPS will request a full or partial conversion of agreed discounts [remise conventionelle] given according to the Social Services Act, L. 162-18.

Thus, CEPS has a strong framework to lean on when negotiating when the manufacturers. The procedure is as follows:

- Each year, the National Assembly defines a savings target on health expenses, including on the reduction of pharmaceutical prices.
- Given pricing rules and market dynamics, CEPS sends an agreement to the manufacturer to reduce the price of a pharmaceutical.
- The manufacturer has one month to respond, but can also request consultations.
- The process continues until CEPS and the manufacturer have agreed on a new price.
- Ultimately, by law CEPS has the right to unilaterally determine the price.

A pharmaceutical graded with a value of I-III on the ASMR scale has a price guarantee that the price will not be below the lowest price in France's reference basket. However, this does not mean that the price cannot change during the first five years.[70]

In France, generic pharmaceuticals are priced at least 60 per cent lower than the originator pharmaceutical product. The price of the originator is reduced by 20 per

[69] Jonathan Rodrigues, CEPS, contributed information for the description of the French system, 1 June 2018.
[70] One example is Opdivo, whose list price began to fall after one year (CEPS 2018).

cent, and then reduced by a further 12.5 per cent 18 months later.[71] 18 months after expiry of the originator pharmaceutical product's patent, the price of generics is reduced by a further 7 per cent.

Biosimilars are priced 40 per cent lower than the biological originator. The price of the biological originator is reduced by 20 per cent. After 18–24 months, the price is further reduced depending on the pharmaceutical's market share. A market share of 60–100 per cent results in a price reduction of 15 per cent. A market share of 40–60 per cent results in a price reduction of 10 per cent. A market share of 0–40 per cent results in a price reduction of 5 per cent.

From 1 January 2015, generic prescribing (INN) is mandatory. However, it is permitted to add a brand name to the prescription in addition to generic prescribing.

The degree of subsidy is dependent on how the disease is classified: 100 per cent subsidy for pharmaceuticals for severe chronic diseases, 65 per cent subsidy for pharmaceuticals with high clinical efficacy on severe diseases, 30 per cent subsidy on pharmaceuticals with less clinical efficacy, and 15 per cent subsidy on pharmaceuticals with weak clinical efficacy.[72]

In France, there are discounts linked to growth, similar to the system in Italy.[73] 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 actual price is lower than the list price after certain volume steps are achieved for some pharmaceuticals.

Netherlands

It is mandatory for people living and working in the Netherlands to have a basic health insurance. The content of this insurance is determined by the state and is equal for everybody. Most of the healthcare costs are covered by the basic health insurance, and it is funded through fixed insurance premiums paid by everybody over the age of eighteen. There are essentially two financial schemes for health insurance; either the insurance company covers all costs for the collection of prescriptions, or the policy holder pays the outlay and submits a claim for reimbursement at the end of the insurance period. The state decides which pharmaceuticals will be included in the benefits scheme (Geneesmiddelenvergoedingssysteem (GVS)). The Dutch Ministry of Health, Welfare and Sport sets ceiling prices twice a year according to the Medical Products Award Act (Wet Geneesmiddelen prijs (WGP)).[74]

[71] Pricing and Reimbursement Questions p. 43.
[72] Rémuzat, C., Toumi, M., Falissars, B. (2013).
[73] QuintilesIMS (2014).
[74] SFK (2017)

Reference pricing to set the ceiling price is applied to all pharmaceuticals in both outpatient and inpatient care. The Netherlands includes Belgium, France, Germany and the UK in its reference price basket. A price review takes place every six months, taking into account price development in the reference countries as well as exchange rate changes.[75] Internal reference pricing is carried out each month.

The Dutch Ministry of Health, Welfare and Sport can continue to set ceiling prices for pharmaceuticals after 2012, but is not obliged to do so.[76] Since 2005, there is greater emphasis on health economic assessments for certain types of pharmaceuticals. The pharmaceuticals must undergo a cost-effectiveness evaluation before a decision about reimbursement is made. Pharmaceuticals that are managed within outpatient care and have an expected budget impact of over EUR 2.5 million must undergo a health economic evaluation.

Managed entry agreements
Risk sharing agreements have become more common in the Netherlands in recent years. Such pharmaceuticals are usually managed within inpatient care, although risk sharing agreements exist within outpatient care, such as for Hepatitis C. Since 2012, TNF-alpha inhibitors are only managed within inpatient care to more effectively reduce pharmaceutical costs.[77] The change was implemented to enable inpatient care, together with insurance companies, to act with more bargaining power as a procurer, thereby reducing prices. Hospitals also partner with each other to get discounts from manufacturers.

Generics
The insurance companies negotiate "*products-of-the-period*" in different pharmaceutical groups through different approaches:

Disclosed preference policy (manufacturer's lowest published price)
Non-disclosed preference policy (manufacturer's lowest confidential price)

Insurance companies can choose to only subsidise the "*product-of-the-period*" at the pharmacies. A pharmaceutical that has the lowest price within the pharmaceutical group becomes the "preferred product". This applies for a fixed time period which lasts between 1 and 24 months. However, there are insurance companies that apply even longer periods. The insurance companies apply different variants of the *preference policy* for preferred products, "product(s)-of-the-period". The only rule is that there must be at least two pharmaceuticals within the same grouping according to substance, dosage form and strength.

[75] Medicijnkosten (2018).
[76] There are several regulations in the Netherlands that aim to limit and control state spending on prescription pharmaceuticals. Medicine Price Act (Wet Geneesmiddelenprijzen (WGP)) and the reimbursement system (Geneesmiddelenvergoedingssysteem (GVS)).
[77] In 2014, an insurance company partnered with 12 hospitals to purchase TNF-alpha medicines together to keep costs down.
See more in the Government of the Netherlands document Medicines Policy Plan: New drugs available to patients fast at an acceptable cost, 29 January 2016.
https://www.government.nl/topics/medicines/documents/letters/2016/03/07/medicines-policy-plan-new-drugs-available-to-patients-fast-at-an-acceptable-cost

Pharmaceuticals are prescribed generically. The pharmacist at the pharmacy where the product is dispensed decides which package is dispensed. Prescribers can cite medical need and indicate that they object to substitution. If a patient does not want the preferred product, they must pay the entire cost, except in cases of special medical need.

The price of pharmaceuticals dispensed at pharmacies can vary depending on which insurance company the patient is insured with. Either the lowest price is applied according to the G standard, or the list price is used and the pharmacy receives a rebate/discount according to a special agreement with the insurance company from the manufacturer.[78]

In 2008, several insurance companies (Menzis, VGZ, CZ and Agis) announced their intention to expand application of *preference policies*. The first national tender process by the insurance companies was carried out in June 2008 and led to a price war between generic pharmaceutical suppliers. In connection with this process, the price of generic pharmaceuticals with high sales fell by about 90 per cent.[79]

The price pressure of the tender process generated extra earnings for the insurance companies, which led to the Dutch Ministry of Health, Welfare and Sport reducing the financial grant the state gave to the insurance companies in 2009. In response to this, the insurance company VGZ developed a hidden pricing model in 2009. In this model, the pharmaceutical manufacturer could maintain a high list price while offering VGZ a negotiated discount. This approach is still met with criticism because the benefit received by the insurance company as buyer was not transparent to outsiders, while pharmacies dispensed certain pharmaceuticals that were more expensive than the lower-cost generic pharmaceuticals available.

Belgium

Originator pharmaceutical products
Belgium has been using informal/supporting reference pricing since 2001. The reference countries consist of the EU27. The manufacturer is required to disclose the sales price (ex-factory) in other European countries where available. A national price comparison is carried out as a complement. The total economic impact of the pharmaceutical and the price level of similar pharmaceuticals in Belgium are also examined. The set price is a ceiling price for the manufacturer. The maximum mark-ups and margins are then set for distributors and pharmacies based on national regulation of both the margin (in per cent) and the total maximum mark-up on distributor (wholesaler) purchase prices and within the pharmacy chain.

Generics
Generic pharmaceuticals are also subject to price regulation in Belgium. The price is reduced immediately when generics enter the market (in a reference cluster). The

[78] Ruggeri, K. and Nolte, E. (2013) and Zuidberg, C. (2010).
[79] SFK (2015) p. 19-20.

highest price for a generic product cannot exceed the price of the most expensive product in the same reference cluster. The price of the first generic product is set 43.64 per cent lower (without reference cluster) or 51.52 per cent lower (ex-factory), depending on the reimbursement category.

With generic prescribing, pharmacies substitute the cheapest alternative for pharmaceuticals included in the reference price system.

The pricing of combination pharmaceuticals (pharmaceuticals with more than one active substance) was adapted in March 2017. Combination pharmaceuticals that have an expired patent but are not included in the benefits scheme are reviewed when one of the pharmaceutical's active substances is included in the benefits scheme. The price and subsidy level of the combination pharmaceutical can never exceed the sum of the corresponding monosubstances.

Managed entry agreements exist for a large number of innovative new pharmaceuticals.

Austria

Austria applies formal reference pricing. Price information is collected at the ex-factory level. The price of outpatient pharmaceuticals in the benefits scheme is regulated nationally at the DIP level (distributor purchase price). Price review is carried out after 6, 24 and 48 months from the pharmaceutical's entry onto the market.

Price is determined after price negotiations between the manufacturer and the Ministry of Health (BMG) in consultation with the national pricing committee. In these negotiations, the average price within the EU27 constitutes a ceiling price. In order to calculate the average price, the manufacturer needs to provide information about the pharmaceutical's availability in other EU markets and state the prices in these countries.

Pharmaceuticals are categorised in different colour schemes for benefits: green, orange, yellow and red. For pharmaceuticals in the green category, the price must be below the average price in the reference countries. For the yellow and red categories, the price must be less than or equal to the average price in the reference countries. Pharmaceuticals deemed to be of additional benefit, as well as essential pharmaceuticals, are categorised in the orange category. In order for a reference price to be calculated, there must be price information from at least two other countries. Statutory discounts, for example in Germany, Ireland and Greece, are taken into account. Exchange rates are calculated as the average for the last month.

Generics
Since April 2017, Austria distinguishes between subsequent generic products and biosimilars in terms of how prices are adjusted after new competitors enter the market. Previously, rules for generic pharmaceuticals also applied to biosimilars.

To retain benefits scheme status, the price of the originator pharmaceutical product must be reduced by 30 per cent within three months of the date a first generic enters the market. The first subsequent product is priced at least 28.6 per cent lower than the originator's reduced price. The second subsequent product is priced 18 per cent lower than the first subsequent one. If there is a third subsequent product, it is priced 15 per cent lower than the second subsequent product. Thereafter, all comparable products must have the same price level as the third subsequent product within three months.[80]

For biosimilars, the price of the originator pharmaceutical product must be reduced by 30 per cent after the first biosimilar enters the market in order to retain its benefits scheme status. The first biosimilar is priced at least 11.4 per cent lower than the biological originator's reduced price. The second subsequent biosimilar is priced 15 per cent lower than the first subsequent one. If there is a third subsequent biosimilar, it is priced 10 per cent lower than the second subsequent biosimilar.[81]

In order for products to retain their benefits scheme status, both the originator and the subsequent products must apply the price of the third generic product or biosimilar.

Patients pay a fee per prescription at the time of dispensing. The fee is adjusted annually, and amounted to 5.85 euros in 2017. Co-payment is capped at 2 per cent of a patient's annual income.

Ireland

Ireland applies reference pricing.[82] Manufacturer prices are set based on the average price in the reference countries (ex-factory), adjusted for exchange rate differences.

Framework agreement

Price review takes place every year, with reference pricing serving as the main criterion. Under the new agreement, the first time was 1 August 2016.[83] Thereafter, it is set for 1 July 2017[84], 2018[85] and 2019. Exchange rate fluctuations are also given consideration in the price review. Prices are only adjusted downwards.

The agreement also specifies that the discount (*PCRS (Community Schemes) Rebate*) on pharmaceuticals currently amounts to 5.25 per cent in sales value, an increase from 4 per cent compared to 2016. The discount increases by 0.25 percentage points to 5.5 per cent from 1 August 2018.

[80] PPRI (2015a).
[81] Herzig (2017).
[82] Health Service Executive (2018).
[83] HSE (2016)
[84] HSE (2017)
[85] HSE (2018)

The agreement also specifies a new discount for inpatient pharmaceuticals. It amounts to 5.25 per cent of the sale value from 1 June 2016 and increases to 5.5 per cent from 1 August 2018.

Generics

Ireland has introduced generic substitution at the ATC 5 level and reference pricing in order to reduce the overall cost of pharmaceuticals.

In Ireland, generic pharmaceuticals are priced 50 per cent below the price of the originator pharmaceutical products. When a generic pharmaceutical enters the market, the price of the originator pharmaceutical product is reduced by 30 per cent within 60 days and by a further 20 per cent the following year.[86]

Biopharmaceuticals (*Patent-Expired Non-Exclusive Biologic Medicine*) are priced 20 per cent below the previous price of the biological originator. When a biosimilar enters the market, a discount must of 12.5 per cent be given on the reduced price.[87]

There are essentially four systems for the benefits scheme.[88]

- General Medical Services (GMS) – 2.50 euros co-payment per product and 25 euros per family and month.
- Drugs Payment Scheme (DPS) – ceiling for co-payment amounting to 134 euros per month.[89]
- Long-term Illness Scheme (LTI) – 16 medical conditions have special coverage. The degree of subsidy amounts to 100 per cent for individuals.[90]
- High Tech Scheme (HT) – pharmaceuticals prescribed in hospitals but dispensed at pharmacies.[91] Examples are rejection inhibitors and pharmaceuticals used in conjunction with chemotherapy or growth hormones. Patient co-payment amounts to 62.03 euros when pharmaceuticals are collected at a pharmacy when dispensed and 30.26 euros during months when no pharmaceuticals are collected. Patients who collect pharmaceuticals for medical conditions under LTI are exempt from co-payment, including for pharmaceuticals within High Tech. For others, there is a co-payment ceiling of 134 euros per month under the DPS.

100 per cent subsidy applies after a special direct payment has been made.

Italy

Italy adopted informal reference pricing in 2001. Reference pricing is not the main criterion, but it does support the decision-making process and is used in

[86] COWI (2014), p. 110
[87] Paragraph 8.1.3 of the Framework Agreement (IPHA (2017).
[88] HSE (2018b)
[89] HSE (2018c).
[90] HSE (2018d).

[91] High tech list February 2017.
http://www.hse.ie/eng/staff/PCRS/items/Feb%202017%20High%20Tech%20Listing.pdf

negotiations with the price committee. In negotiations with the price committee, issues taken into consideration include the following:[92]

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 efficacy,
Assessment of the economic impact on the national healthcare system,
Data on price and use in other European countries. Reference price information is collected at the ex-factory level. Price review within the reference price component takes place every 24 months.

It is possible for pharmaceutical companies to apply for a premium price for innovative products.[93]

Italy has implemented far-reaching decentralisation of responsibility within healthcare, and it began regionalisation in 2001. The different regions in Italy have the freedom to determine the levels of patient co-payments and can thereby control their costs and budget outcomes.

Co-payments vary between regions (varies from 1 to 8 euros). There is no percentage degree of subsidy.

In Italy, generic pharmaceuticals are priced at least 20 per cent lower than the reference price of the originator pharmaceutical product.

Generic prescribing (INN) is mandatory in Italy. Pharmaceutical names may only be stated if specific medical reasons exist.

Portugal

Portugal adopted formal reference pricing in 2003. The reference countries are Spain, France and Italy. Price information is collected at the ex-factory level. Price review within the reference price component takes place every 12 months.

During the period from the second half of 2010 to March 2013, a 6 per cent reduction of the maximum price for pharmaceuticals accepted in the benefits scheme was implemented. A price reduction of 7.5 per cent was implemented in 2011, but only for specific biopharmaceuticals. Official list prices at that time should not have taken this discount into account, according to Vogler et al (2011).

Degrees of subsidy

The degree of subsidy is 100 per cent for pharmaceuticals for specific defined diseases such as HIV and Alzheimer's disease. For other prescriptions, the level is

[92] ISPOR Italy Pharmaceuticals.
[93] ISPOR Italy Pharmaceuticals.

90 per cent for critical pharmaceuticals for chronic diseases, 69 per cent for critical pharmaceuticals for *serious* diseases, 37 per cent for non-priority pharmaceuticals with therapeutic benefit, and 15 per cent for new pharmaceuticals whose therapeutic benefit has not been established.

Generics
In Portugal, generic pharmaceuticals are priced up to 50 per cent lower than the originator pharmaceutical product. If the price of the reference product is below 10 euros, the generic pharmaceutical is priced 25 per cent lower than the originator.

A new law on generic prescribing (INN) entered into force in 2015.

Switzerland

Switzerland applies formal reference pricing in combination with value-based pricing ("national therapeutic comparison"). The average price of pharmaceuticals in nine countries is used as reference. Price information is collected at the ex-factory level.[94] In 2015, the number of reference countries increased from six to nine through the addition of Belgium, Finland and Sweden.[95] The other countries are Denmark, the Netherlands, France, Germany, the UK and Austria. The countries were chosen because they are considered similar in terms of economic conditions and treatment traditions. Price review within the reference price component takes place every 36 months.

Swissmedic handles marketing approval and the Federal Office of Public Health (FOPH) deals with reimbursement and pricing. When submitting an application to the FOPH, the pharmaceutical companies must present a positive recommendation from Swissmedic. Price is decided in the List of pharmaceutical specialities (SL).[96] Conditions for inclusion in the SL list include Swissmedic approving the pharmaceutical and it being deemed cost-effective. The cost analysis assesses international reference prices and there is also a therapeutic comparison to similar products. 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. There is also an innovation bonus (for better efficacy, fewer side effects) of 1–20 per cent that may be applied in the therapeutic comparison.[97]

Prices are weighted with a 2/3 weighting according to the average for the international reference price and a 1/3 weighting for the national therapeutic comparison. There is a limit of five per cent if the national therapeutic comparison

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[94] FOPH (2016a).
If ex-factory is not available, then wholesaler or pharmacy price can be used. FOPH approximates margins as follows: *Wholesaler margins have to be: Denmark: 6.5% of the pharmacy price, UK: 12.5% of the NHS price The Netherlands: 6.5% of the pharmacy price, Finland: 3% of the pharmacy price, Sweden: 2.7% of the pharmacy price*
[95] Interpharma, Price comparison with other countries.
[96] FOPH (2016b).

[97] FOPH (2016a).

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 pharmacy margin is regulated. For prescription pharmaceuticals, it is CHF 4–240 plus a percentage margin of 0–12 per cent that is added to the ex-factory price.

The price of generic pharmaceuticals should be at least 20 per cent lower than the price of the originator pharmaceutical product[98]. An exception to this is generics with a small market share. Ceiling prices of generic pharmaceuticals are set differently depending on the sales of the originator pharmaceutical product four years before patent expiry. The price of the first subsequent product is set at least 10 per cent lower than the originator's price if the originator's sales value was below CHF 4 million. If the sales value of the originator was CHF 4–8 million, the price is set to 20 per cent below that of the originator. If the sales value of the originator was CHF 8–16 million, the price is set to 40 per cent below that of the originator. If the sales value of the originator was CHF 16–25 million, the price is set to 50 per cent below that of the originator. If the sales value exceeded CHF 25 million, the price of the subsequent product is set 60 per cent lower than the originator.

The price of biosimilars is set to 25 per cent below the price of the originator pharmaceutical product.

Switzerland plans to introduce a reference price system for generic pharmaceuticals as well, but the time point of this measure has not been determined.

Private health insurance is compulsory for everyone living in Switzerland. The insurance cover includes the costs of pharmaceuticals obtained by prescription from a doctor. Co-payment amounts to CHF 300 annually. A further 10 per cent of the remaining cost amounting to maximum CHF 700 per year is added to this. If a generic alternative to the pharmaceutical is available but not selected, the patient's additional cost instead amounts to 20 per cent of the remaining cost of treatment.

Spain

Spain applies informal/supporting reference pricing based on lowest price. Price review within the reference price component takes place every 12 months. Price information is collected at the ex-factory level.

Spain has implemented a far-reaching decentralisation of responsibility for healthcare. Since 2003, 17 regions have full budgetary responsibility for healthcare. The price in Spain must 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.[99]

[98] FOPH (2016a).
[99] Ruggeri, K. and Nolte, E. (2013).

Prices for generic pharmaceuticals are set 40 per cent lower than the price of the originator pharmaceutical product. When a reference cluster group is created, the price of the originator 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 shall be implemented in pharmacies in all cases where prescriptions are issued with generic prescribing.

During the first half of 2010, a discount of 7.5 per cent on originator pharmaceutical products and 4 percent on orphan pharmaceuticals was implemented. Official list prices should take this discount into account. At the same time, a 30 per cent price reduction was also implemented for generic pharmaceuticals.[100] A discount system linked to the size of the pharmaceutical companies' investment in research and development in Spain is in place.

Greece

Greece adopted formal reference pricing in 2006. Prices (ex-factory) are based on an average of the lowest three prices of the other 27 EU countries. A price must be available in at least three countries for reference price calculation to be possible. As of 2016, a price review takes place twice a year, in May and November. Decisions on new products are made four times a year.

Pricing for generic pharmaceuticals has been amended several times in recent years. Since April 2016, the prices of generic pharmaceuticals have been linked to the price of originator pharmaceutical products after patent expiry. Prior to this, they were linked to the price before or at the time of patent expiry.

The pricing mechanism for generic pharmaceuticals was amended in September 2015. Generic pharmaceuticals are priced 32.5 per cent lower than the originator's price before patent expiry – it was previously 20 per cent. Pharmaceuticals whose sales price does not exceed 4.5 euros and for which the patient's daily 24-hour dose does not cost more than 0.15 euros are exempt from mandatory price reduction for generic pharmaceuticals (as per January 2017).[101] From July 2017, the levels have been adjusted to a sales price of less than 1 euro and a daily price of less than 0.02 euro.

As of August 2015, generic prescribing is once again mandatory. Previously, it was permitted to add a brand name to the prescription in addition to generic prescribing. Targets have been set for the proportion of generic pharmaceuticals a doctor should prescribe at the ATC4 level. If the target is not met, i.e. if a doctor prescribes originator pharmaceutical products at too great an extent, they may suffer financial consequences.

[100] Vogler et al (2011).
[101] Previously, the sales levels for exemptions were higher, e.g. the limits were 12 euros and 0.40 euros per daily dose 2015.

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

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

Hungary

Hungary applies formal reference pricing using the lowest price of 31 countries (EU and EEA). Price information is collected at the ex-factory level. The intention is for a reference price review for the products with the highest sales volume within the benefits scheme to take place annually, but it is not yet implemented.

For generic pharmaceuticals in Hungary, the first subsequent product is priced at least 40 per cent below the price of the originator pharmaceutical product. The second subsequent generic product is priced 20 per cent lower than the first subsequent product. The third subsequent product is priced 10 per cent lower than the second subsequent product. The fourth through sixth subsequent product is priced five per cent lower than the preceding one. After this, subsequent products are only priced lower than the preceding one, without specification of minimum level. For biopharmaceuticals, the first subsequent product is priced 30 per cent lower than the price of the reference pharmaceutical, and the second and third product are priced 10 per cent lower than this.[102]

The degrees of subsidy are 85 per cent, 55 per cent and 25 per cent depending on therapeutic value and the severity of the disease. For some specific diseases, a stepped subsidy up to 100 per cent may apply.

Czech Republic

The Czech Republic applies formal reference pricing for both reimbursement and pricing. The reference countries are the entire EU, with the exception of Cyprus, Estonia, Malta, Luxembourg, Germany, Romania and Austria.[103] Greece no longer serves as a reference country as of 1 January 2018.

When deciding on reimbursement status, i.e. whether the pharmaceutical should be included in the benefits scheme, the lowest price of the reference countries is determined. If the lowest price is more than 20 per cent lower than the second lowest price, the average of the second and third lowest price is calculated. Price

[102] Kawalec et al (2017).
[103] SÚKL (2017).

information is collected at the ex-factory level. When deciding on price, the average of the countries with the three lowest prices is calculated. The price is a ceiling price. Price review within the reference price component takes place every 36 months.

Pharmaceuticals deemed to be “highly innovative” can receive temporary reimbursement status for a two-year period, which can be extended by one year. The pharmaceutical must exhibit a sufficiently high benefit and have already achieved reimbursement status in at least two of the reference price countries. The average price for these countries is used to calculate a price.

For generic pharmaceuticals in the Czech Republic, the first subsequent pharmaceutical is priced 32 per cent lower than the price of the originator pharmaceutical product (30 per cent for biopharmaceuticals). The same lowest price reduction is applied to the entire reference group.

The co-payment is the difference between the fixed subsidised price and the sales price. The patient also pays a prescription dispensing fee of CZK 30 (approximately 1.20 euros).

From 2018, use of e-prescriptions is mandatory.

Slovakia

Slovakia applies formal reference pricing using prices from 27 countries. With the change in pricing introduced in 2008, the price in the six countries with the lowest price in Europe is compared. Since 2011, price is calculated as the average of three of the countries with the lowest price for a product.[104] Price review within the reference price component takes place every 6 months. Price information is collected at the ex-factory level.

Pharmaceuticals classified as new and innovative undergo health-economic evaluation with a ceiling price according to life-years (QALY). The limit is set at the average annual work income in Slovakia for the previous two years.

The degree of subsidy is either 100 per cent or a partial amount.

Generic prescribing has been mandatory since 2011. At the time of dispensing, pharmacies are obliged to provide information on which pharmaceutical within the substitution group has the lowest price. For generic pharmaceuticals in Slovakia, the first subsequent product is priced at least 35 per cent lower than the originator pharmaceutical product (at least 20 per cent for biosimilars).

Poland

[104] Psenkova et al (2017).

Poland applies informal/supporting 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. Price review within the reference price component takes place every 24 months. Poland has six countries that constitute a reference group for HTA assessments (Estonia, Latvia, Lithuania, Hungary, Croatia and Slovakia).

Every other month, the Ministry of Health publishes a list of pharmaceuticals that are subsidised. Depending on whether the length of treatment is more than or less than 30 days, the overall degree of subsidy for the pharmaceuticals in the benefits scheme is 50 or 70 per cent. The degree of subsidy is 100 per cent for certain diseases as well as for war veterans. Co-payments for certain pharmaceuticals (defined on the *S-list*) used by pensioners over 75 years of age were discontinued on 1 September 2016.

For generic pharmaceuticals, the subsequent pharmaceutical is priced at maximum 75 per cent of the reference price of the originator pharmaceutical product. The first price decision applies for two years, and thereafter in three-year and five-year periods respectively.

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