PRICE ANALYSIS OF HOSPITAL PHARMACEUTICALS IN SEVEN EUROPEAN COUNTRIES

AMGROS

SUMMARY

This report presents the results of an analysis concerning pharmaceutical prices. The purpose of the analysis was to investigate the price level of a selected group of pharmaceuticals that in Denmark are mainly used in the hospital sector and therefore classified as hospital pharmaceuticals.

The price analysis was performed bilaterally between Denmark and each of the six European countries; Norway, Sweden, England, Belgium, the Netherlands, and Germany. Both list prices and contract prices are included.

The main result of the analysis is illustrated in table 1. As the analysis was performed bilaterally between Denmark and all the other countries, Denmark is always defined by index 100. An index higher than 100 indicates higher prices for pharmaceuticals in the respective country, whereas an index lower than 100 indicates a saving if pharmaceuticals are purchased at the respective country's prices.

The table indicates that Denmark has higher prices than Norway (87), Sweden (90), England (90), and Belgium (91). Danish and Dutch (101) list prices are at a similar level, and the German (108) prices are 9 % higher than the Danish.

The price indices for the contract prices are quite different from the list price indices. Only England (62) and Norway (88) have lower prices than Denmark. The Swedish (104) prices are slightly higher than the Danish, while Denmark receives considerably lower prices than Belgium (112) and Germany (118). Since it was not possible to receive Dutch contract prices, the analysis between Denmark and the Netherlands is limited to a comparison of list prices.

Table 1: Main result - Bilateral price indices between Denmark and the respective countries, 2017.

Country	Index for list prices	Index for contract prices
Denmark	100	100
Norway	87	88
Sweden	90	104
England	90	62
Belgium	91	112
Netherlands	101	-
Germany	108	118

Besides the price indices for total turnover for the selected pharmaceuticals, the analysis consists of an analysis in which the pharmaceuticals are divided according to therapeutic areas (ATC groups). The result of this analysis is in the results section in this report.

CONTENTS

INTRODUCTION

Expenditure on hospital pharmaceutical has been increasing over recent years in Denmark, and there are no signs of this changing. Most recently, expenditure went up by 7.5 % from 2016 to 2017. Thus, there is great interest in knowing the price level for pharmaceuticals in Denmark as well as in comparable countries, to ensure that pharmaceutical prices are at the same level and Denmark is getting the best value for its money.

At request of the Ministry of Health and Danish Regions (DR), Amgros has analysed the price level of a selection of what in Denmark are categorised as hospital pharmaceuticals.

The purpose of the analysis was to obtain knowledge about the price levels in Denmark and similar countries of the pharmaceuticals mainly used in the Danish hospital sector. The analysis investigates both list price and contract price level. In addition, the analysis highlights several factors that can affect the individual country's prices.

Besides Denmark, the selected countries are; Norway, Sweden, England, Belgium, the Netherlands, and Germany.

The report contains an analysis of the price level for a selection of pharmaceuticals in the selected countries. The analysis investigates both the total price level for the chosen pharmaceuticals and the price level for different therapeutic areas across the seven countries. In addition, relevant parameters in the different countries' structural setup that may affect the pharmaceutical prices are described. The descriptions are based on the report, *Analyse af priser på sygehusmedicin i fem lande* by COWI from 2016. Existing descriptions have been updated, and descriptions of the English and German system have been added, as these countries were not included in the 2016 report (These are described in appendix a).

METHODS AND DATA

The following chapter contains a review of the methods used, the choices made, and the data on which the analysis is based.

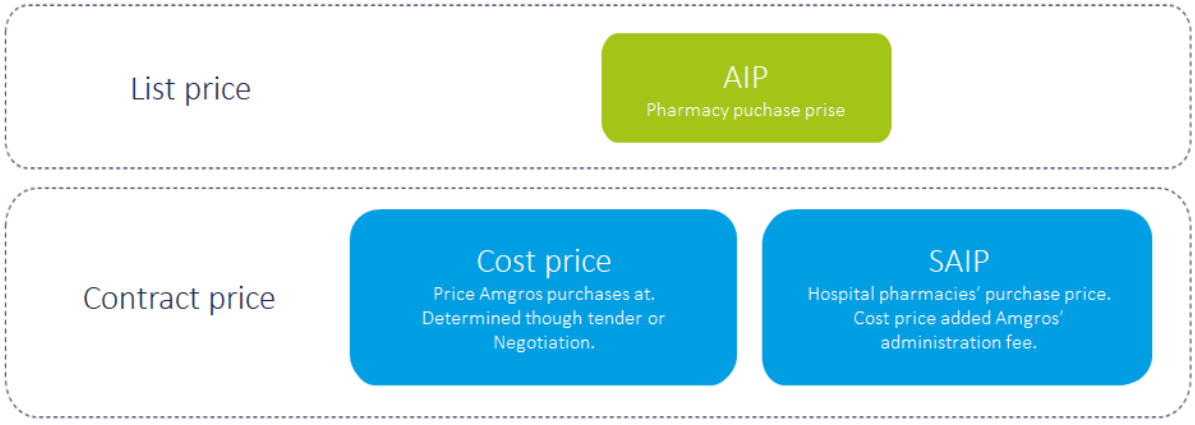
Countries

In addition to Denmark, the analysis includes six countries: Norway, Sweden, England, Belgium, the Netherlands, and Germany. The countries have been chosen according to a criterion of comparability to Denmark, and because they are reference countries in the current price cap agreement. A description of the organisational setup and pricing of pharmaceuticals in the selected countries is included in appendix a. Four of the selected countries were included in the report *Analyse af priser på sygehusmedicin i fem lande* by COWI from 2016 and they are also described in this report. Since no major changes have been made since the 2016 report, the descriptions from the 2016 report have been included in this report. As England and Germany were not included in the 2016 report, corresponding descriptions have been made for these countries, and these are also in appendix a.

Price terminology

The analysis was performed using both list prices and contract prices. List prices are the pharmacies' purchase price (AIP). In Denmark, hospital pharmaceuticals are purchased via a centralised procedure. This takes place though the regional government's pharmaceutical procurement organisation Amgros, who purchase pharmaceuticals at a price reached through either a tender procedure or negotiation. Before resale to the hospital pharmacies, a small administration fee is added, which together with the cost price represents the purchase price paid by hospital pharmacies (SAIP). In some cases, the hospital pharmacies purchase the pharmaceuticals at the list price. This occurs when no discount agreement has been made with the pharmaceutical company or if the price exceeds the list price when the Amgros administration fee is added to the cost price (see figure 1).

Figure 1: Graphic presentation of pharmaceutical terms used in Denmark and their meaning.



When list prices and contract prices are mentioned throughout this report, reference is made to AIP and SAIP, respectively.

Selection of pharmaceuticals

The analysis is based on Amgros' sales figures for the Danish hospital pharmacies in 2017. Only pharmaceuticals that accounted for the majority of sales in 2017 are included. They were selected according to the following criteria:

1. The 50 active substances (ATC 5 level) that accounted for most turnover in 2017 for Amgros in sales to the Danish hospital pharmacies.

2. The most traded packages, which together accounted for at least 50 % of the sales of each of the ATC groups selected were included.

These criteria provided a list of 67 pharmaceutical packages within the 50 ATC groups (see appendix b).

As shown in table 2, the 50 selected pharmaceuticals accounted for 62 % of all sales from Amgros to the hospital pharmacies in 2017. For many of the ATC groups, only a single package accounted for most of the turnover. To limit the extent of the analysis, only those packages accounting for at least 50 % of the turnover were included.

Table 2: The total turnover for pharmaceuticals purchased by the hospital pharmacies from Amgros, top 50 turnover, and turnover for pharmaceutical packages included in the analysis, 2017.

Sales from Amgros to the hospital pharmacies, 2017	Turnover for the contract prices [DKK]	Share of the total turnover
Total turnover	8,441,389,111	100 %
Top 50 pharmaceuticals	5,213,040,107	62 %
Packages selected for the analysis	3,982,733,807	47 %

The turnover for the selected pharmaceuticals is not evenly distributed between the therapeutic areas, as large percentages are limited to a few areas. Table 3 shows the turnover forming the basis for the analysis and how it distributes between the different therapeutic areas. The turnover is listed as both list prices and contract prices. In addition, the number of ATC groups and packages included for each of the areas is displayed.

Pharmaceuticals in L01 and L04 account for most of the turnover to the pharmaceuticals included in the analysis. Overall, the two groups constitute 69 %.

Analytical methods

In the analysis, several price indices were calculated to determine the price level for the respective countries. The comparisons between Denmark and the other countries were made bilaterally, i.e. in pairs between Denmark and the respective countries.

The product list for the analysis consisted of 67 pharmaceutical packages, and the comparison was made between identical packages. Usually, the pharmaceutical packages with the highest turnover in Denmark will be those where a pharmaceutical company has given the lowest price in the area concerned.

In some cases, other products may account for most of the turnover in another country due to differentiated pricing. Thus, the same pharmaceuticals do not necessarily have the lowest price in all countries. For some pharmaceuticals it is possible that no contract price was available, as the pharmaceutical used in Denmark is not the cheapest in the country compared to and thus not used in that country. In cases where a pharmaceutical package with the same trade name was found, but the volume of the package varied, linear extrapolation was used to provide a basis for the analysis.

Therefore, data included in the bilateral comparisons varies between countries, as the datasets are based on the prices obtainable in the different countries. The data will be described later in this chapter.

The price indices accounting for the total price level and the price level for the different therapeutic areas were calculated by weighting the different packages within the therapeutic areas in relation to the Danish turnover in 2017. In cases where no price was available in a country, the price was also removed for Denmark in the comparison.

Denmark is always defined by index 100, as the analyses were made bilaterally between the individual countries and Denmark. An index above 100 indicates that additional costs are associated with purchasing the selected pharmaceuticals at the country's prices, while an index below 100 indicates a saving when purchasing the selected pharmaceuticals at the country's prices.

Table 3: Total turnover and underlying data for selected ATC groups, 2017.

ATC groups	Turnover in contract prices [DKK]	Turnover in list prices [DKK]	Share of contract price turnover	Number of ATC groups (number of packages)
B02 Antihemorrhagics B03 Antianemic preparations	163,420,350	246,276,700	4 %	3 (11)
H01 Pituitary and hypothalamic hormones	70,295,569	82,512,514	2 %	2 (2)
J01 Antibacterials for systemic use J05 Antivirals for systemic use J06 Immune sera and immunoglobulins	347,098,508	602,817,998	9 %	5 (7)
L01 Antineoplastic agents	1,378,423,254	1,523,134,282	35 %	19 (21)
L02 Endocrine therapy L03 Immunomodulating agents	210,331,253	332,845,043	5 %	3 (4)
L04 Immunosuppressive agents	1,365,903,966	1,679,136,417	34 %	14 (18)
M05 Drugs for treatment of bone diseases N07 Other nervous system drugs R03 Anti-asthmatics S01 Ophthalmologicals	447,260,906	663,426,704	11 %	4 (4)
Selected pharmaceutical in total	**3,982,733,807**	**5,130,149,658**	**100 %**	**50 (67)**

Exchange rates

Pharmaceutical prices were received in the countries' own currency. Prices were converted into DKK by applying the annual average exchange rate for 2017, see table 4. This approach was chosen as the pharmaceutical contracts entered into force at different times during the year.

A supplementary analysis, illustrating the significance of the exchange-rate fluctuations through 2017 for the calculated price indices, is included in the results section.

Table 4: Exchange rates, 2017 average, DKK per 100 units of currency.

SEK	NOK	EUR	GBP
77.23	79.82	743.86	848.63

Source: The Danish National Bank.

Data basis for the selected countries

Amgros' international network assisted in the data collection, and a request was sent to the network for both list prices and contract prices for the selected pharmaceuticals. Additional data was collected through desk-research, where information concerning the countries' organisational setup, pricing mechanisms and list prices was obtained. The data collection was also supplemented through dialogue meetings with selected contacts.

The results from the price analysis were aggregated according to therapeutic areas. In one case, several therapeutic areas were combined into one group (ATC groups M05, N07, R03, and S01). These areas would otherwise consist of a single product, which would breach confidentiality agreements made with the contacts from the different countries.

In the period 2016 to 2017, patents expired for two of the pharmaceuticals included in the analysis. The effect of excluding these was investigated during the analysis and proved to have limited effect on the results.

Table 5 shows the amount of data included in the analysis for each country, and the proportion it represents of the complete product list.

It was not possible to receive contract prices for individual packages from England. Instead, prices were received in an aggregated form, which made the comparison possible without revealing the price for each product. Consequently, the English contract prices are not weighted in relation to Danish consumption at product level as they are in comparisons between Denmark and all the other countries.

It was not possible to receive contract prices from the Netherlands. This means the comparison between Denmark and the Netherlands is limited to list prices.

Both list prices and contract prices are included in the analysis for all other countries.

Table 5: Available price information from the selected countries.

	List prices				Contract prices			
	Pharmaceuticals	Share	Packages	Share	Pharmaceuticals	Share	Packages	Share
Denmark	50	100 %	67	100 %	50	100 %	67	100 %
Norway	50	100 %	67	100 %	37	74 %	51	76 %
Sweden	50	100 %	67	100 %	32	64 %	44	66 %
England	48	94 %	63	94 %	50	100 %	66	99 %
Belgium	49	98 %	65	97 %	49	98 %	65	97 %
Netherlands	48	96 %	65	97 %	0	0 %	0	0 %
Germany	50	100 %	66	99 %	21	42 %	27	40 %

Data providers

The following section describes the prices received from the different countries.

If any profits or fees are added to the price before sale to the hospital pharmacies, these are included in the pharmacy purchase price. All prices are without VAT.

Denmark: All Danish prices are provided by Amgros and apply nationwide. The contract price is the price paid by the hospital pharmacy when purchasing the pharmaceuticals i.e. the cost price plus Amgros' administration fee. The list price is the price the pharmaceuticals are purchased at, if no other price agreement has been made. Prices represent a weighted average of prices from 2017.

Norway: The Norwegian prices apply nationwide and are the prices at which the hospital pharmacies purchase the pharmaceuticals. The list price is a maximum price set through international price references. Maximum prices are set as the average of the three lowest prices in the reference countries. The pharmaceuticals are purchased at maximum price, if no other price agreement has been made.

Sweden: Purchases of pharmaceuticals in Sweden are decentralised. Thus, prices may vary between the different Swedish regions (*län*). Prices were obtained from 17 out of the 21 län. The amount of data from the different *län* varied. In those cases where the prices from the different Swedish län were not identical, an average has been calculated. The list prices apply nationwide and are

supplied by the *Tandvårds- och läkemedelsförmånsverket's (TLV)* list of reimbursable pharmaceuticals. Prices of pharmaceuticals not found on the TLV list were calculated from the pharmacies' price list.

England: English prices were supplied by the National Health Service (NHS). Due to confidentiality, contract prices were not delivered at product level. The contract prices include prices negotiated by the Commercial Medicines Unit (CMU) at the NHS and prices from PharmaEx, which is a system to collect data on the prices at which hospitals purchase pharmaceuticals where the CMU has not negotiated a contract. List prices originate from the BNF (British National Formulary) and are at package level.

Belgium: Contract prices apply nationwide and represent the price at which the hospital pharmacies can purchase the pharmaceuticals. It is possible for the Belgian hospitals to negotiate with suppliers locally, thus, prices may for at some hospitals be lower if an agreement has been made with the supplier. List prices are the price pharmaceuticals are purchased at, if no other agreement has been made.

Netherlands: Dutch list prices were supplied by *Nederlandse Zorgautoriteit (NZa)*, the national health authority. The price is set by the company that holds the marketing authorization for the product. However, there are cases where a maximum price fixed by NZa represents the list price.

Germany: German prices were supplied by a purchasing organisation. Therefore, the agreement prices apply only to those hospitals where medicines are purchased by this organisation, while list prices are nationally applicable. Supplementary list prices were obtained through *Deutsches Institut für Medizinische Dokumentation und Information's (DIMDI)* ABDA database. The list price indicates the country's official maximum subsidy, which is the amount the pharmacies will be refunded for the sale.

RESULTS

The purpose of the analysis was to investigate and compare the price level for pharmaceuticals in Denmark with the six countries: Norway, Sweden, England, Belgium, the Netherlands and Germany. Price level refers to both list price and contract price level.

This section presents the results of the analysis. First, the bilateral price indices for both list and contract prices are presented, followed by the turnover basis used to calculate these. This analysis shows the total Danish turnover for the selected pharmaceuticals, and what the turnover would have been if the same quantities were purchased at the respective countries prices. Turnover is calculated for both list and contract prices. The bilateral price indices are presented by therapeutic area (ATC groups). Finally, the importance of the exchange rate fluctuations is investigated, as well as the importance of the variation in the Swedish contract prices, as these are areas that might influence the outcome of the analysis.

Overall price indices

The main result of the analysis is illustrated in table 6. The overall price indices for both list prices and contract prices are displayed.

Table 6: Bilateral price indices for Denmark compared with the six countries, for both list prices and contract prices, 2017

Country	Indices for list prices	Indices for contract prices
Denmark	100	100
Norway	87	88
Sweden	90	104
England	90	62
Belgium	91	112
Netherlands	101	-
Germany	108	118

Overall Denmark has higher list prices than Norway (87), Sweden (90), England (90) and Belgium (91). The Danish and Dutch (101) list prices are at a similar level and the German (108) list prices are 9 % higher than the Danish.

The picture is slightly different, for the contract price indices. Denmark has higher prices than England (62) and Norway (88). The analysis indicates that Swedish (104) contract prices, are slightly higher than the Danish, while Danish prices are significantly lower than the Belgian (112) and German (118).

As no Dutch contract prices were available, no bilateral comparison has been made between Denmark and the Netherlands for these.

The analysis shows that England (62) has the lowest contract prices compared to Denmark, followed by Norway (86). An explanation for this may be the prioritisation of pharmaceuticals practiced in these countries for several years. This allows them to limit the use of pharmaceuticals where the price is not considered to reflect the efficacy of the pharmaceutical. In addition, Norway has an international pricing model, where pharmaceutical prices are set as an average of the three lowest prices in the reference countries.

The remaining countries all have higher contract prices than Denmark. In Belgium (112), however, it is possible for individual hospitals to negotiate with pharmaceutical companies for lower purchase prices. Therefore, price levels

may in fact be lower than the Danish if some of the hospitals have local agreements for the pharmaceuticals included in the analysis.

International reference pricing is used in some of the countries. The structure of this pricing model varies between the countries. In Norway, prices are determined as an average of the prices in the three reference countries with the lowest prices. In contrast, the Netherlands sets prices as an average of all prices available from the reference countries. In some countries the reference price is only determined at the launch time for the pharmaceuticals while others continuously revise the prices. Thus, it is desirable for a pharmaceutical company to introduce products early in the countries with high prices and which are often included as reference countries.

Germany (118) has the highest prices in the analysis regarding both list and contract prices. The high level for list prices might be due to the large number of countries which include Germany as a reference when using international price referencing. England as well is often included as a reference country, but in this case high pricing can lead to pharmaceuticals not being recommended. This is not the case for Germany, where pharmaceutical companies are free to set the price as they please for the first 12 months without affecting the later cost-effectiveness assessment conducted by the countries.

Turnover and theoretical savings potential

The analysis was based on a calculation of the total turnover for the selected pharmaceuticals in Denmark in 2017, and a corresponding calculation of the total turnover, if the pharmaceuticals were purchased at the prices paid in Norway, Sweden, England, Belgium, the Netherlands, and Germany, respectively. The analysis was performed with list prices and contract prices. The total turnover calculation only included packages found in the country Denmark is being compared to. Due to the difference in the data between countries, the tables should only be read horizontally.

Listed in table 7 are the overall list price indices, the related theoretical turnovers, and the resulting savings or additional costs.

Table 7: Total turnover with Danish consumption and the respective country's prices and the actual Danish turnover. Calculations are based on list prices.

Country	Price index	Total turnover at the respective country's list prices [DKK]	Total Danish turnover at the Danish list prices [DKK]	Theoretical saving/ additional cost [DKK]
Denmark	100	5,130,149,658	5,130,149,658	-
Norway	87	4,487,404,194	5,130,149,658	-642,745,464
Sweden	90	4,608,436,111	5,130,149,658	-521,713,547
England	90	4,124,803,204	4,593,268,780	-468,465,576
Belgium	91	4,593,254,552	5,039,165,194	-445,910,642
Netherlands	101	5,040,969,174	5,005,748,658	35,220,516
Germany	108	5,543,494,101	5,130,149,658	413,344,443

In the bilateral comparison with Norway, which has the lowest list prices of all the selected countries, the total list price turnover for the pharmaceuticals would be approximately DKK 643 million lower if the same quantities were purchased at Norwegian list prices as were purchased in Denmark in 2017 at Danish list prices. If pharmaceuticals were bought at German list prices instead, which are the highest in comparison, the turnover would be approximately DKK 413 million higher than in Denmark.

As Denmark as well as the other countries included in the analysis mostly buy at contract price and not list price, a calculation of the theoretical savings or additional costs is more relevant when based on contract prices. Table

8 shows the overall contract price indices, the related theoretical turnovers, and the resulting savings or additional costs.

Table 8: Total turnover with Danish consumption and the respective country's prices and the actual Danish turnover. Calculations are based on contract prices.

Country	Price index	Total turnover at the respective country's contract prices [DKK]	Total Danish turnover at the Danish contract prices [DKK]	Theoretical saving/ additional cost [DKK]
Denmark	100	3,982,733,807	3,982,733,807	-
Norway	88	2,772,735,402	3,241,252,827	-382,280,966
Sweden	104	2,543,833,905	2,442,944,601	100,889,304
England	63	2,466,933,728	3,921,775,705	-1,454,841,977
Belgium	112	4,376,175,189	3,896,108,132	480,067,057
Netherlands	-	-	-	-
Germany	118	2,136,720,925	1,809,543,981	327,176,944

In the bilateral comparison with England, which has the lowest contract prices of all the selected countries, the overall contract price turnover for the pharmaceuticals would be approximately DKK 1.5 billion lower if the same quantities purchased in Denmark in 2017 were purchased at English contract prices.

In comparison with Norway, which has the second lowest contract prices of the countries, the total contract price turnover on the selected pharmaceuticals would be approximately DKK 382 million lower if the same quantities purchased in Denmark in 2017 were purchased at Norwegian contract prices.

If the pharmaceuticals were instead purchased at German contract prices, which are the highest in the comparison, the turnover would be approximately DKK 327 million higher than it was in Denmark in 2017.

Price indices for therapeutic areas

To determine whether the price level could be affected by the area of disease in which the pharmaceuticals are being used, results are also presented according to therapeutic areas.

ATC groups L, which contain pharmaceuticals for the treatment of cancer and pharmaceuticals for the immune system (primarily biological pharmaceuticals for the treatment of rheumatological diseases), is by far the most comprehensive group in this analysis. For a complete list of pharmaceutical packages and ATC groups divided by therapeutic area, see appendix c.

table 9 shows the bilateral list price indices for the therapeutic areas (ATC group).

Norway is the only country that receives lower prices than Denmark in all therapeutic areas. This could be a result of the international pricing model used in Norway and its positive impact on pharmaceutical prices.

Except for a single area (the mixed group M05, N07, R03, S01), both Sweden and England have lower prices than Denmark in all cases. For Belgium and the Netherlands, the price level for the therapeutic areas exceeds the Danish level in two and three cases, respectively.

Germany has four areas where the price level exceeds the Danish, and Germany also has the highest price index. This is for the Pituitary hormones area, where the price index for German list prices is 173. However, this area has less significance for total turnover, as it only accounts for 2 % of total turnover.

Although, most of the countries' price indices are below 100, both the Netherlands and Germany have a price index for total turnover that is higher than the Danish. This is due to the large proportion of the Danish turnover within the L04 group, where Denmark receives significantly lower prices than the Netherlands and Germany.

There is a certain variation across the therapeutic areas. The results indicate that Danish list prices are particularly high in the areas J01, J05 and J06. On the other hand, the results also indicate that, in relation to the mixed group M05, N07, R03, and S01, Denmark has relatively low list prices compared to Sweden and England.

Table 9: Bilateral list price indices for therapeutic areas.

ATC groups	Denmark	Norway	Sweden	England	Belgium	Netherlands	Germany
B02 Antihemorrhagics B03 Antianemic preparations	100	79	84	79	106	113	121
H01 Pituitary and hypothalamic hormones	100	79	91	79	73	118	173
J01 Antibacterials for systemic use J05 Antivirals for systemic use J06 Immune sera and immunoglobulins	100	63	68	67	60	91	80
L01 Antineoplastic agents	100	97	99	90	101	95	99
L02 Endocrine therapy L03 Immunomodulating agents	100	86	82	95	92	98	100
L04 Immunosuppressive agents	100	90	86	92	93	107	126
M05 Drugs for treatment of bone diseases N07 Other nervous system drugs R03 Anti-asthmatics S01 Ophthalmologicals	100	88	104	108	84	100	103

Table 10 displays the bilateral contract price indices for the different therapeutic areas (ATC groups). Similar to the list price indices, there appears to be a certain variation across the therapeutic areas for the contract prices.

The results show that England has the lowest contract prices of all countries included in the analysis. All the price indices for therapeutic areas are lower than the corresponding Danish indices. As the English prices are delivered in aggregated form (see method section), unlike the remaining countries, there is greater uncertainty associated with this result. It is not possible to establish whether there are specific pharmaceuticals where very favourable agreements have been received, thereby affecting the price level for the entire group, or whether more favourable agreements are generally reached for all the pharmaceuticals.

The Norwegian contract price indices are lower than the Danish for all therapeutic areas. As described earlier, this may be due to the prioritising of pharmaceuticals practiced in Norway, like in England, where treatments not considered to be cost-effective will not be recommended. Another reason could be the international pricing model practiced in Norway.

The Swedish contract prices are lower for some of the therapeutic areas, specifically the areas B02 and B03 as well as J01, J05 and J06. As these areas together make up 13 % of the total turnover, this has less significance for the overall price index. The Swedish contract prices are higher than the Danish in both groups L01 and L04, and this has more significance for the overall price index, as these are areas with the highest turnover in Denmark.

Belgium is one of the countries whose contract price indices are mostly above the Danish level. Despite this, the total turnover index is no more than 112, since L01, antineoplastic agents, weighs most in the analysis because of its turnover, and the Belgian prices are only 7 % higher for this area than the Danish.

Due to confidentiality, the German data providers were not allowed to share contract prices received as a result of negotiation with the pharmaceutical companies. Because of this, the German dataset only contains 27 packages

and 21 ATC groups. It is possible that the price indices would be lower if the negotiated prices from Germany were included, as it seems likely that these pharmaceuticals achieve the greatest discounts. Inclusion of the negotiated price may have taken the result in another direction. At German hospitals, in some cases, volume discounts are given on purchases of large quantities, but these cannot be attributed to a direct discount on the various pharmaceutical packages, even though the price is in fact lower than stated.

Table 10: Bilateral contract price indices for therapeutic areas.

ATC groups	Denmark	Norway	Sweden	England	Belgium	Netherlands	Germany
B02 Antihemorrhagics B03 Antianemic preparations	100	92	93	45	157	-	167
H01 Pituitary and hypothalamic hormones	100	91	104	86	82	-	190
J01 Antibacterials for systemic use J05 Antivirals for systemic use J06 Immune sera and immunoglobulins	100	95	71	31	109	-	22
L01 Antineoplastic agents	100	84	108	57	107	-	101
L02 Endocrine therapy L03 Immunomodulating agents	100	64	-	67	140	-	-
L04 Immunosuppressive agents	100	83	104	72	109	-	145
M05 Drugs for treatment of bone diseases N07 Other nervous system drugs R03 Anti-asthmatics S01 Ophthalmologicals	100	109	118	79	119	-	115

The Netherlands was the only country where it was not possible to obtain contract prices. The Dutch system is structured such that the individual hospitals alone or smaller purchasing organisations, locally procure medicines, and then a fixed amount is reimbursed from the patient's insurance company. Thus, by negotiating low prices with pharmaceutical companies, hospitals can earn profits on individual pharmaceuticals when they are reimbursed by insurance companies. The structure of the system means that in the Netherlands there is an unusually high degree of confidentiality about drug prices, since the hospitals do not want their contract prices to become generally known so that they lose the opportunity to profit from the reimbursement they receive for pharmaceuticals.

Evaluation of factors which can affect the results

Data basis

The data for the analysis consists of 67 pharmaceutical packages within 50 ATC groups. All countries supplied at least 94 % of the list price information requested and for several 100 % was obtained. The almost complete amount of list price information strengthens the results of the analysis, as the risk of an unknown price could have led the results in another direction.

The level of contract price information was in general lower. This was to be expected as a consequence of the great confidentiality surrounding some of the prices in several countries as well as Denmark. The different organisational setups in different countries also have a part in this, as Denmark has a relatively large proportion of pharmaceuticals restricted for hospital use only and, thus, has a contract price. In other countries, the selected pharmaceuticals are often used in both the primary sector and hospital sector, and therefore the price

mechanisms are different. The expected amount of pharmaceuticals sold in a sector influences the price, as consumption in both sectors permits the pharmaceutical companies to generate profits through the spill-over effect. Based on this, the pharmaceutical companies will often postulate that a high price in one sector will be evened out by a low price in the other sector. In the comparison with England and Norway, on the other hand, this is not the case, as both countries have a lower price level than Denmark for both list prices and contract prices. In relation to these two perspectives, a large number of contract prices were received, and this helps to strengthen the conclusions of the analysis.

With the Netherlands as an exception, the smallest number of contract prices were received from Germany. Germany is also the only country where data supplier informed that there are contract prices for some pharmaceuticals that have not been supplied because of extended confidentiality on prices agreed up on due to negotiation. Therefore, the German result for contract prices are associated with the greatest uncertainty. The German price level is higher than the Danish, but as the prices not included from Germany are those obtained through negotiation, it is fair to expect that the German price level would be closer to the Danish, if all prices had been included.

Patent expiration has a great effect on the pharmaceutical market and pricing. Only two patent expirations occurred for the selected pharmaceuticals during 2016 and 2017 and these concerned Glivec® and Xolair®. The effect of removing the two pharmaceuticals from the analysis only has little effect on the results. The greatest change is for the German indices. The patent expiries have no influence on the overall conclusions of the report.

Impact of currency fluctuations

All price data was provided in the respective country's currency, so prices had to be converted into DKK to allow a direct comparison. Currency conversion was made as an average of exchange rates throughout 2017.

Since the NOK, SEK and GBP are not linked to the DKK via fixed exchange-rate policies, sensitivity analyses were performed to determine the importance of the overall price indices and price indices for the therapeutic areas in order to assess the importance of currency fluctuations. The sensitivity analyses were based on the lowest, the average (base scenario) and the highest exchange rate in 2017, respectively.

In both table 11, which illustrates the importance of exchange rate fluctuations over 2017 on the list price indices, and table 12, which illustrates the importance of exchange rate fluctuations over 2017 on the contract price indices, the average price indices appear first, followed by a parenthesis with price indices based on lowest and highest exchange rate in 2017.

The sensitivity analyses illustrate that exchange rate fluctuations had a marginal impact on the Belgian, Dutch and German price indices, which is to be expected as the DKK is linked to the EUR through fixed-rate policies and thus only small exchange rate variations occur between the two currencies.

Exchange rate fluctuations through 2017 had a larger impact on the price indices between Denmark and Norway. The overall list price index varies between 82 and 92, and the overall agreement price index varies between 83 and 93.

Exchange rate fluctuations also affected the price indices between Denmark and Sweden. In this comparison, exchange rate fluctuations throughout 2017 affected the overall list price index in such a way that it varies between 86 and 92, and the overall contract price index varies between 100 and 106.

The comparison between Denmark and England is also affected by larger fluctuations in the GBP against the DKK. In this comparison, exchange rate fluctuations throughout 2017 led to the overall list price index varying between 85 and 94, and the overall contract price index varying between 58 and 65.

Table 11: Price indices calculated using the respective country's list prices. The price has been converted into DKK using both the minimum and maximum exchange rate for 2017. Price indices based on minimum and maximum exchange rates are listed in the parentheses in the table.

ATC groups	Denmark	Norway	Sweden	England	Belgium	Netherlands	Germany
B02 Antihemorrhagics B03 Antianemic preparations	100	79 (75:84)	84 (81:86)	79 (74:83)	106 (106:106)	113 (113:113)	121 (121:121)
H01 Pituitary and hypothalamic hormones	100	79 (74:83)	91 (87:93)	79 (75:83)	73 (73:73)	118 (118:119)	173 (173:173)
J01 Antibacterials for systemic use J05 Antivirals for systemic use J06 Immune sera and immunoglobulins	100	63 (59:66)	68 (66:70)	67 (63:70)	60 (60:60)	91 (91:91)	80 (80:80)
L01 Antineoplastic agents	100	97 (91:102)	99 (95:101)	90 (85:94)	101 (101:101)	95 (95:96)	99 (99:99)
L02 Endocrine therapy L03 Immunomodulating agents	100	86 (81:91)	82 (79:84)	95 (90:100)	92 (92:93)	98 (98:98)	100 (100:100)
L04 Immunosuppressive agents	100	90 (84:95)	86 (83:88)	92 (87:97)	93 (93:93)	107 (107:107)	126 (126:126)
M05 Drugs for treatment of bone diseases N07 Other nervous system drugs R03 Anti-asthmatics S01 Ophthalmologicals	100	88 (83:93)	104 (100:106)	108 (101:113)	84 (84:84)	100 (100:100)	103 (103:103)
Indices for total turnover	100	87 (82:92)	90 (86:92)	90 (85:94)	91 (91:91)	101 (101:101)	108 (108:108)

The pharmaceutical company's country of origin can have a great impact on price variations over time. Many major pharmaceutical companies are American and Swiss, which means that exchange rate fluctuations between the US dollar and the Swiss franc in relation to the DKK may affect the pricing of pharmaceuticals, as pricing policy is typically determined for the company's headquarters. An extreme example of these significant exchange rate fluctuations was in early 2015, when the Swiss Central Bank removed the exchange rate cap of 1.20 Swiss franc per EUR, which led to prices increasing by over 15 % from one day to the next. The rates have today fallen to a level not far above the rate before the exchange rate cap was removed. The removal of the exchange rate cap and the exchange rate development since is an example of the significance for the price level of when a pharmaceutical's pricing policy is set, and when a pharmaceutical is launched.

Therefore, it is possible that part of the price difference that may exist on certain pharmaceuticals across countries, can be attributed to varying launch times across the different countries.

Table 12: Price index calculated using the respective country's contract prices. The price has been converted into DKK using both the minimum and maximum exchange rate for 2017. Price indices based on minimum and maximum exchange rates are listed in the parentheses of the table.

ATC groups	Denmark	Norway	Sweden	England	Belgium	Netherlands	Germany
B02 Antihemorrhagics B03 Antianemic preparations	100	92 (87:97)	93 (89:95)	45 (43:47)	157 (157:157)	-	167 (167:167)
H01 Pituitary and hypothalamic hormones	100	91 (86:96)	104 (100:106)	86 (81:91)	82 (82:82)	-	190 (190:191)
J01 Antibacterials for systemic use J05 Antivirals for systemic use J06 Immune sera and immunoglobulins	100	80 (76:85)	71 (68:72)	31 (29:33)	109 (108:109)	-	22 (22:22)
L01 Antineoplastic agents	100	81 (76:85)	108 (104:111)	57 (54:60)	107 (107:107)	-	101 (101:101)
L02 Endocrine therapy L03 Immunomodulating agents	100	64 (60:68)	-	72 (68:76)	140 (139:140)	-	-
L04 Immunosuppressive agents	100	83 (78:88)	104 (100:106)	68 (65:72)	109 (109:109)	-	145 (145:145)
M05 Drugs for treatment of bone diseases N07 Other nervous system drugs R03 Anti-asthmatics S01 Ophthalmologicals	100	109 (103:116)	118 (113:121)	79 (75:83)	119 (119:119)	-	115 (115:115)
Indices for total turnover	100	86 (82:91)	104 (100:106)	62 (58:65)	112 (112:112)	-	118 (118:118)

Variation in Swedish contract prices

Purchases of pharmaceuticals in Sweden are decentralised as the different regions purchase locally. Some regions have merged into larger purchasing units to achieve greater market power and reduce administrative expenses (see appendix a for a more detailed description). Since procurement is decentralised, the different regions receive varying discounts and thus different contract prices.

Table 13 illustrates the variation in the contract prices achieved by the different Swedish regions compared to Danish contract prices. The average contract price index in the column to the right is the price index referred to earlier in the report. Lowest contract price is a contract price index based on the lowest package price for each pharmaceutical package. The same applies for the contract prices where the highest contract price is a contract price index based on the highest package price for each pharmaceutical.

Thus, the analysis does not refer to the region which collectively has obtained the lowest or highest package price, but instead the analysis is based on the individual package. If the analysis were based on the total prices of each region, the variation would be significantly lower.

Table 13: Contract price index based on lowest, highest, and average Swedish contract price.

ATC groups	Average contract price (lowest contract price: highest contract price)
B02 Antihemorrhagics B03 Antianemic preparations	93 (80:121)
H01 Pituitary and hypothalamic hormones	104 (104:104)
J01 Antibacterials for systemic use J05 Antivirals for systemic use J06 Immune sera and immunoglobulins	71 (59:80)
L01 Antineoplastic agents	108 (101:111)
L02 Endocrine therapy L03 Immunomodulating agents	-
L04 Immunosuppressive agents	104 (94:141)
M05 Drugs for treatment of bone diseases N07 Other nervous system drugs R03 Anti-asthmatics S01 Ophthalmologicals	118 (96:141)
Indices for total turnover	104 (93:118)

Considering the variation at package level, there is a relatively large variation between 93 and 118 and the average of 104 for the overall contract price index. Within therapeutic area L04 in particular, there is a large variation from index 94 to 141. Since L04 also weighs relatively high in the calculation of the overall price indices, the variation greatly affects the overall result.

Aggregation of English prices

As pharmaceutical prices are an area surrounded by great confidentiality, there was some difficulty in obtaining contract prices. This led to an aggregation of ATC groups M05, N07, R03, and S01, which otherwise would have consisted of single pharmaceutical packages and thereby breached the confidentiality agreements made with the different data suppliers. The high level of confidentiality has resulted in no contract prices from the Netherlands, which is why no analysis has been possible.

The English package prices were all aggregated into one price for each ATC group. Therefore, there is greater uncertainty than for the rest of the results. It is possible that a single or few prices could affect the price level for an entire area in a certain direction. This is not possible to determine as it was not possible to weight at package level according to the Danish consumption, as was done for the other countries. Therefore, all package prices were weighted equally in the groups, even though the consumption of the products in reality was different.

Appendices

APPENDIX A

The general setup for four countries, Norway, Sweden, Belgium and Netherlands, was previously described in the 2016 report; *Analyse af priser på sygehusmedicin i fem lande*. As no major changes were found in relation to the 2016 report, the descriptions of these four countries have been included in this report as well. The descriptions from the 2016 report are indicated by quotation marks and in italics. A minor addition has been made to the section concerning Norway as the only change. Since England and Germany were not included in the 2016 report, similar descriptions have been made for these two countries. In addition, a section describing the latest changes in the Danish pharmaceutical system has been added.

Denmark

Organisation of the healthcare system

The Danish healthcare system is universal and based on the principles of free and equal access to healthcare for all citizens. The healthcare system offers high-quality services, the majority of which are financed by general taxes.

Approximately 84 % of healthcare expenditure is publicly financed (2015). The remaining 16 % are financed primarily through patient co-payments.

The healthcare system operates across three political and administrative levels: the state, the regions and the municipalities (national, regional and local levels):

- The Ministry of Health is responsible for establishing the overall framework for the provision of health and elderly care. This includes legislation on the organisation and provision of health and elderly care services, patients' rights, healthcare professionals, hospitals and pharmacies, medicinal products, vaccinations, maternity care and child healthcare. The legislation covers the tasks of the regions, municipalities and other authorities within the area of health.
- The regions are responsible for hospital care, including emergency care, psychiatry, and for health services provided by GPs and specialists in private practice.
- The municipalities are responsible for a number of health and social services. Local health and elderly care services include disease prevention and health promotion, rehabilitation outside hospital, home nursing, school health services, child dental treatment, child nursing, physiotherapy, alcohol and drug abuse treatment, home care services, nursing homes, and other services for elderly people.

Medicines must be authorised by the Danish Medicines Agency or by the European Commission before they can be placed on the Danish market.

Pricing systems

In Denmark, pharmaceutical companies are free to set the official prices of medicine. However, members of the Danish Association of the Pharmaceutical Industry (Lif) are subject to a price-cap agreement between the Association, the Ministry of Health and the Danish Regions.

Medicines with no directly competing products that have been granted reimbursement by the Danish Medicines Agency are included in the price-cap agreement between the Danish Association of the Pharmaceutical Industry, the Danish Regions and the Ministry of Health. While medicines used in public hospitals are provided free of charge, there is a comprehensive reimbursement system that entitles patients to reimbursement when they buy medicine from a private pharmacy.

The Danish Medicines Agency decides whether a medicine is eligible for public reimbursement. The decisions are based on recommendations given by the Danish Reimbursement Committee.

The procurement and pricing procedures differ between the hospital sector and the primary healthcare sector.

Hospital sector: In Denmark, 99 % of all medicines used at public hospitals are purchased through the pharmaceutical procurement service Amgros, which is owned by the five regions. Amgros carries out tendering

procedures and purchases medicines for all public hospitals. All hospital medicines are paid for by the regions, and all treatments in public hospitals, including medicines, are provided free of charge to the patient.

The Danish Medicines Council was established on January 1, 2017 by the board of Danish Regions. The Council is based on experiences from the Danish Council for the Use of Expensive Hospital Medicines (RADS) and "Koordineringsrådet for ibrugtagning af sygehusmedicin" (KRIS).

The Medicines Council evaluates new pharmaceuticals and indications in terms of efficacy, price and existing treatment, after which it is decided whether the pharmaceutical can be recommended as standard treatment. In addition, the Medicines Council also prepares common regional treatment guidelines, which advise on which pharmaceuticals are most suitable for different therapeutic areas.

Primary healthcare sector: The actual pricing of medicines for the primary healthcare sector varies depending on whether there are directly competing products. The prices of directly competing medicines from the generic industry are set by 14-day auctions. Following each tender, the pharmaceutical companies will report their prices for the following two weeks to the Danish Medicines Agency. This information is communicated to all pharmacies, which means that prices are the same throughout Denmark. The system has proven to ensure price-transparency and market competition.

Norway

Organisation of the healthcare system

"The Norwegian healthcare system is based on a principle of equal access, decentralisation and free choice between hospitals. Health services are primarily financed through taxes, with dentists as an exception. In Norway, all citizens are covered by a national health insurance scheme and patients do not pay for the pharmaceuticals they receive during hospitalisation.

The healthcare system in Norway is organised on three levels:

- *The state.* Helse- og Omsorgsdepartementet *is responsible for overall health legislation and allocation of funds to the health area. The Norwegian Directorate of Health (*Social-og Helsedirektoratet*) oversees the health legislation. The Norwegian Medicines Agency (*Statens Legemiddelverk (SLV)*) is the key player in terms of approval, information, marketing rules and supervision in the pharmaceutical field.*
- *Four regional* helseforetak *are responsible for the hospital sector and the specialised health services, including psychiatrics. They are also responsible for the overall financial and planning efforts at regional hospitals. Underlying the regional* helseforetak *are several local* helseforetak *which are responsible for the hospitals in their local area.*
- *428 municipalities which deliver health services to the primary healthcare sector*

*In Norway, the pharmaceutical area is regulated by two laws; the Pharmaceuticals Act (*legemiddelloven*) and the Pharmacy Act (*Lov om apotek*).*

There is no specific definition of hospital pharmaceuticals in Norway, but there is a distinction between prescription pharmaceuticals (blue and white prescriptions) and the pharmaceuticals prescribed in hospital regimes. The boundaries between the two are partially fluid, i.e. hospital pharmaceuticals can be obtained from pharmacies in the primary sector. This is for geographical reasons, in that there can be long distances to hospitals.

Pricing systems

Pricing systems based on external and internal price references are used in Norway.

External price references

According to Norwegian law, other European Economic Area (EEA) countries' pharmaceutical prices must be taken into consideration when prices for prescription pharmaceuticals are determined. The maximum purchase price for the pharmacies is based on an average of the three lowest market prices for same product in a number of countries: Sweden, Finland, Denmark Germany, the United Kingdom, the Netherlands, Austria, Belgium and Ireland.

The maximum price determination was implemented in 2002 and this defines the list price. The price is revised by SLV once a year for the most sold products, while other products are more rarely revised. A price is notified to SLV when the pharmaceutical manufacturers intend to launch a new product. External price reference is used when products have no generic competition i.e. patented products. The maximum-price system has been developed to limit the growth in expenditure on pharmaceuticals in the primary sector, but hospital pharmaceuticals are also purchased at list price if no other price is agreed on.

Pharmaceutical manufacturers in the different countries disclose the prices that are used for external reference pricing.

Internal price references

*A special pricing model (*trinprismodellen*) applies for the generic pharmaceuticals. It was introduced in 2005 and last changed in 2014. Adjustments are made step by step through a predefined rate when a product loses its patent protection and is thus exposed to generic competition. The reduction depends on turnover and the length of time that has passed since the competition was established. The Norwegian Medicines Agency publishes a list of the generic pharmaceuticals included in the system."*

Addition to the 2016 Report:

The *Nye Metoder* (new methods) system was introduced in Norway in 2013. The regional *helseforetak*, the Norwegian Institute of Public Health (*Folkehelseinstituttet*), the Norwegian Medicines Agency (SLV), the Norwegian Radiation Protection Authority (*Statens Strålevern*) and the Norwegian Directorate of Health (*Helsedirektoratet*) established the system. These bodies work on behalf of *Helse- og omsorgsdepartementet* to ensure methods introduced in the Norwegian healthcare system are evaluated in terms of efficacy and safety. Any new method is assessed in relation to existing treatment to determine any additional value.

For pharmaceuticals, SLV conducts a method assessment. The pharmaceuticals division (LIS) at *Sykehusinnkjøp HF* (the specialist procurement service for the specialist health services) negotiates with the pharmaceutical supplier in cases where a lower price is required for a product to be classified as cost-effective. Negotiations are also conducted in cases where the pharmaceutical is cost effective, but the use of the treatment will have major budget implications. The final decision to initiate the use of the method or pharmaceutical is taken by the four CEOs of the regional *helseforetak*.

Sweden

Organisation of the healthcare system

"Like in Denmark and Norway, the health care system in Sweden is mainly tax-financed and access to health services is in principal free as required, but more services are subject to user charges than in Denmark. At an individual level, however, the user payment is limited, as there is a cap on the total annual user payment per person. Sweden is divided into 21 Län*/regions, which are responsible for health and hospital services, dental care and other areas. Political decisions in the regions are made by elected members of the regional governments (*Landstinget*). In comparison with Denmark, the organisation is more decentralised, but the present Swedish government has a goal to reduce the number of* landsting*.*

The primary sector in Sweden is quite differently organised than the Danish system. In Sweden, the term Öppenvård *is used for (outpatient) clinics at hospitals, while private medical practice – as we know from Denmark – has a less important role. Among other things, this means, that some pharmaceuticals, which in Denmark are considered hospital pharmaceuticals, are prescribed in* öppenvård *with subsidies.*

Pricing systems

*In principle, there is free pricing of pharmaceuticals in Sweden. However, pricing is influenced by principles of value-based pricing, which are applied in connection applications for subsidies (primary sector) and in the preparation of recommendations under "*ordnat indförande*".*

Prescription drugs not used in hospital treatment may be subsidised upon application to the Dental and Pharmaceuticals Benefits Agency (TLV). Normally, drug manufacturers apply for subsidies, as this ensures a greater market share. For many years, TLV has been using value-based pricing when assessing applications for subsidies. This means that the price is assessed in relation to the treatment effect in a health-economic analysis. All price changes for pharmaceuticals in the subsidies system must be approved by TLV. TLV may lower list prices

for original pharmaceuticals by 7.5 % when the marketing authorisation is older than 15 years if there is little or no generic competition.

There is no formal requirement to apply for subsidies for pharmaceuticals which are mainly used to treat patients at hospital. Nevertheless, pharmaceutical manufacturers often apply for subsidies to obtain a national seal of approval for a new products' competitive advantages in relation to older products. In each region, practice regarding the approval of new pharmaceuticals for hospital treatment has varied. The introduction of the national ordnat införande *has provided a system that sets the framework for the assessment of new hospital pharmaceuticals and ensures uniform assessment across all regions.* Ordnat införande *means that health-economic assessments of the pharmaceuticals can be included. It is decided from case to case whether this is necessary.*

Horizon scanning is included in ordnat införande*. This is a systematic process designed to identify new treatments that in the near future will require assessment of evidence, impact, and financial aspects.*

The health-economic assessment can lead to negotiation of the price of the pharmaceutical. Based on principles of value-based pricing, risk-sharing agreements are made between the payer and the manufacturer. Direct negotiations with the manufacturer at decentral level have resulted in varying models for risk-sharing. Treatment response and number of treatments are usually elements in a risk-sharing agreement. These agreements can be confidential."

England

Organisation of the healthcare system

Like in Denmark, the English healthcare system is mainly financed through taxes. Additionally, part is financed through national insurance contributions and a smaller part through user fees, for example dental care and prescription fees. Access to hospital treatment is only available by referral from a medical practitioner, except for acute treatment.

The Department of Health & Social Care (DH) has overall responsibility for strategic management and financing of healthcare. At arm's length to the DH, the National Health Service (NHS) England is an independent body responsible for resource distribution and supervision. The public hospitals are run by NHS trusts, which must ensure high-quality treatment and the efficient use of funds.

The Commercial Medicines Unit (CMU) is a department under NHS England. The CMU is responsible for pharmaceutical tenders, which can either be in the ten regional pharmaceutical purchasing groups in the four NHS England regions, or nationally for England, depending on the pharmaceutical's characteristics.

Pricing systems

The National Institute for Health and Clinical Excellence (NICE) delivers evidence-based guidelines for NHS England. These include the Technology appraisal guidance, which assesses the clinical effect and cost-effectiveness of pharmaceuticals and other health technologies. Hospitals under the NHS trust are obligated to follow these guidelines. NICE uses quality-adjusted life years (QALY) to measure cost-benefit.

There is free pricing for pharmaceuticals, but the subsidy price is regulated by value-based pricing. Pharmaceuticals which are used as standard treatment in NHS England must be assessed by NICE. This gives the pharmaceutical companies incentive to price their pharmaceuticals in a manner that reflects the effects, if they want the pharmaceutical to be recommended for treatment in hospitals.

Since NHS England has a fixed budget, all recommendations of new pharmaceuticals are at the expense of other treatments. If it is not found that a pharmaceutical's price is reflected in its effect, it will not be recommended for use, as it will rob too many resources from other treatments.

In England, there is no list of pharmaceuticals entitled to subsidy, instead there is a negative list of pharmaceuticals without subsidy.

The non-generic drugs purchased by NHS England are regulated through the Pharmaceutical Price Regulation Scheme (PPRS). This is a voluntary agreement between the DH and the Association of the British Pharmaceutical Industry, and it aims to regulate the profit the pharmaceutical manufacturer achieves from trading with NHS England.

It is possible for the pharmaceutical company to offer the so-called Patient Access Schemes (PAS) in cases where a pharmaceutical is not recommended by NICE for routine use based on the list price. In this context, the pharmaceutical company can reduce the price or enter into a risk-sharing agreement.

As the PPRS is voluntary, pharmaceutical companies may choose not to participate. This will mean that they are subject to an alternative called the statutory scheme, where PAS is not an option. As a result, most companies choose to participate in PPRS.

In 2011, the English government introduced the Cancer Drug Fund (CDF), which included an objective to give patients early access to expensive new cancer pharmaceuticals by financing these while examining the cost effectiveness. In 2016, the system was reviewed and changed. Subsequently, a new assessment process was introduced for NICE. They are now assessing all new cancer pharmaceuticals that are expected to receive marketing authorisation, and then deciding whether the pharmaceutical should be recommended for routine use generally, for routine use within the CDF, or not recommended at all. Once sufficient information has been collected, pharmaceuticals financed through the CDF will be re-assessed, after which they will either be recommended for routine use or not be recommended at all.

Belgium

Organisation of the healthcare system

"The Belgian health service is insurance-based, with mandatory health insurance for all citizens. The regulatory framework for the system dates back to 1944, with the latest major revision in 1994.

Citizens are entitled to a wide range of healthcare services, which are determined centrally. There are six private (non-profit) health insurance funds and one public, which collectively covers all citizens. It is through these funds that providers are reimbursed for benefits received by citizens. Healthcare services are delivered through private as well as public suppliers, which act as an integrated part of the insurance-based healthcare system. Belgium has around 200 hospitals; approximately 70 are psychiatric hospitals and the rest are somatic hospitals. Of the somatic hospitals, 16 are teaching hospitals.

The National Institute for Health and Disability Insurance is under the Ministry of Social Affairs and Health. The institute is responsible for the general organisation and management of the mandatory health-insurance scheme. The institute sets the reimbursement/subsidy criteria and monitors the budgets. The budgets are determined centrally and are approved by the government. A buffer system is incorporated In the budget system, and this is financed by the pharmaceutical companies. The system is activated if pharmaceutical expenses prove to be higher than planned, and this helps balance the public budgets if the costs of drugs turn out to be significantly higher than planned.

In the Belgian system, there is no final definition of hospital pharmaceuticals, but like in Denmark, hospital pharmaceuticals can mean pharmaceuticals for treating patients admitted to hospital or in outpatient treatment. Since 2006, hospitals have received a total amount to cover the cost of pharmaceuticals, and this has stimulated hospitals to more rational drug use. However, some types of pharmaceuticals are fully refundable from the health insurance funds.

Pricing systems

When a pharmaceutical has marketing authorisation, the Minister for Economic Affairs will decide on a maximum price for the pharmaceutical based on advice from two committees. Thus, pricing is not free in Belgium. At the same time as a maximum price is set for the pharmaceutical, the Subsidy Committee under the National Institute for Health and Disability Insurance assesses whether the pharmaceutical should be covered by the system of reimbursement in the health insurance system and the type of subsidy/reimbursement to be given. Based on the Subsidy Committee's assessment, the Minister for Social Affairs finally decides on the status for the subsidy/reimbursement.

The maximum price is set through both a reference price system and the relative value of the pharmaceutical, and this is part of the Subsidy Committee's assessment process. Assessment criteria include therapeutic effectiveness and cost-effectiveness.

External price references in several European countries are used as part of the assessment process for new pharmaceuticals. There is no ongoing updating of the reference prices, and these are only used in the assessment process. Internal price reference is also used for similar products (generics).

Prices are also regulated through negotiations with the pharmaceutical companies. This results in a large number of managed entry agreements or risk-sharing agreements.

The sickness funds reimburse hospitals with a total treatment cost, including pharmaceutical expenses. However, as mentioned above, there is a scheme in which the cost of special pharmaceuticals is reimbursed in addition to this."

The Netherlands

Organisation of the healthcare system

"After a new law concerning mandatory health insurance for all citizens in the Netherlands, the Dutch healthcare system underwent a major restructuring in 2006.

Since the new act was adopted, all citizens have been entitled to a comprehensive basic package of health services purchased from private health-insurance companies. The package includes coverage of all emergency hospital treatment, primary healthcare from GPs and services from specialists. It also covers expenses for pharmaceuticals and various devices.

Healthcare in the Netherlands is provided through private suppliers in the primary sector as well as the hospital sector. The Dutch hospitals have traditionally been owned and operated by private non-profit organisations. Like in Denmark, practitioners act as gatekeepers for the hospitals.

Health-insurance companies buy health services from different suppliers and are free to enter into agreements with the hospitals. Negotiations regarding price and quality are regulated by the state and only a limited part of the services is actually influenced by price negotiations.

Citizens choose themselves which insurance company they wish to enter into an agreement with. The health insurance market is dominated by four companies that have 90 % of the market.

The Ministry of Health, Welfare and Sport is responsible for the overall health legislation and decides which pharmaceuticals are covered by grants in the primary sector, while pharmaceuticals in the hospital sector are automatically covered if they meet a number of standard requirements. The National Health Care Institute (ZiN) advises the ministry and is responsible for assessing new pharmaceuticals.

In the Dutch system, there is no final definition of hospital pharmaceuticals, but like in Denmark, hospital pharmaceuticals can mean pharmaceuticals for treating patients admitted to hospital or in outpatient treatment. In recent years, several pharmaceuticals have been moved from the primary sector to the hospital sector to ensure better control of ordination and expenses.

Pricing systems

In the Netherlands, the Pharmaceutical Price Act establishes the regulatory framework for the pricing of pharmaceuticals - except for non-prescription pharmaceuticals.

A key element of the Act is the fixing of maximum prices (AIPs) for the pharmaceuticals. This is based on a reference price system consisting of countries (Belgium, Germany, England and France) where the maximum price represents a numerical average of the prices in the four countries referred to. Prices are regulated twice a year.

The Ministry of Health, Welfare and Sport has stated that several pharmaceuticals with a high budget impact (> EUR 2.5 million) should not automatically be approved for use but must be assessed by the National Health Care Institute (ZIN). Depending on the assessment, the minister may choose to exclude the pharmaceuticals from subsidies or withdraw them from the market.

In addition, the Ministry of Health, Welfare and Sport is in negotiations with the pharmaceutical companies and has, to date, concluded a number of nationwide agreements of different nature, which can generally be characterised as different types of financial risk sharing agreements. A total of 17 agreements have been concluded, but only two of these concern hospital pharmaceuticals.

Insurance companies reimburse hospitals in accordance with a total treatment fee (DRG-based), which includes pharmaceutical expenses. There is a scheme for particularly expensive pharmaceuticals, where insurance companies reimburse hospitals 80 % of the cost of the pharmaceutical."

Germany

Organisation of the healthcare system

The German healthcare system is financed through statutory health insurance (SHI), and approximately 70 million citizens are covered by the scheme. Only a minority is covered by private health insurance (PHI). When hospitalised, the services are financed through the patient´s health insurance, but there is a self-payment of EUR 10 per day.

- The German ministry of health, *Das Bundesministerium für Gesundheit (BMG)* is the supreme authority in the German health system. The ministry aims to further develop quality in the health system, strengthen patient interest and ensure economic efficiency.
- *Gemeinsamer Bundesausschuss (G-BA)* is the supreme decision-making authority. It is a common organisation for the autonomous institutions. It performs assessments of new pharmaceuticals and establishes guidelines and substitution groups for these. *G-BA is financed* through contributions from its members.
- *Gesetzlichen Krankenversicherung (GKV)* is an association of all statutory health insurers. It sets prices for substitution groups and negotiates prices with pharmaceutical companies.

German hospitals can be owned by private non-profit or for-profit organisations, or they can be publicly owned. Open EU procurement is not used, but instead pharmaceuticals are purchased locally, either by individual hospitals or in purchasing organisations which represent several hospitals.

The German definition of hospital pharmaceuticals differs from the Danish. In Germany, pharmaceuticals received during outpatient treatment are subject to the same regulation and funding as those used in the primary sector. Therefore, the definition of hospital pharmaceuticals will include pharmaceuticals used for inpatient treatment. Because of this difference in the pharmaceuticals used to treat outpatients, the systems regulating the prices in the primary sector will also influence the pharmaceuticals we in Denmark categorise as hospital pharmaceuticals.

Pharmaceutical expenses are financed through DRG rates, which are determined by G-BA and refunded by the insurance funds. To ensure access to new expensive hospital pharmaceuticals, some pharmaceuticals are financed through a separate supplement to the DRG rate, which in German is referred to as *Zusatzentgelte (ZE)*.

As in England, pharmaceuticals without subsidy are listed on a so-called negative list. All pharmaceuticals are initially approved for subsidy in the first 12 months following marketing authorisation. Then the subsidy is reassessed through the early benefit assessment and it is decided whether the pharmaceutical should keep its subsidy status. It is possible for the pharmaceutical company to set a price higher than the amount of the subsidy, in such a case the patients are required to finance the difference themselves.

Pricing systems

Early benefit assessment:

During the first 12 months following marketing authorisation, there is free pricing of pharmaceuticals in Germany. Following this, a new price is negotiated based on the assessment performed by G-BA. Here, the new treatment is compared with the existing standard treatment in the area.

- If no additional value is proven, the pharmaceutical is placed in a substitution group with similar pharmaceuticals and receives the same subsidy price.
- If an added value is detected, GKV and the pharmaceutical company negotiate an additional amount added to the subsidy price for the substitution group the pharmaceutical falls under.
- If there is no substitution group in which the pharmaceutical can be placed, a subsidy price will be negotiated, and the pharmaceutical will constitute a group on its own. Other similar pharmaceuticals entering the market later may be placed in this group.

Since the individual hospitals themselves can purchase medicines, they can negotiate with the pharmaceutical companies for discounts. Thus, decisions made by G-BA have less significance for their prices.
Hospitals are reimbursed a fixed amount, either through the DRG or ZE supplement, and thus can generate profits by using the pharmaceuticals for which they have the lowest contract prices. This also gives pharmaceutical companies incentives to offer low prices to hospitals, as it will lead to more patients being treated with their products and in turn patients will become familiar with these products so that, in many cases, they will continue the same treatment after hospitalisation. This enables pharmaceutical companies to increase

their profits by providing favourable prices to hospitals but maintaining prices at a higher level in the primary sector. This means that the so-called spill-over effect is very important for the pricing of pharmaceuticals in Germany.

APPENDIX B

Product list

Table 14: Product list with pharmaceuticals selected for the analysis.

ATC groups	ATC name	Product name	Strength	Package size
B02BD02	Octocog alfa	Advate	2000 IE	1 set (5 ml)
B02BD02	Octocog alfa	Advate	3000 IE	1 set (5 ml)
B02BD02	Moroctocog alfa	ReFacto® AF	2000 IU	1 pc.
B02BD02	Octocog alfa	Helixate NexGen	2000 IE	1 pc.
B02BD04	Nonacog alfa	Benefix®	3000 IE	1 set
B02BD04	Nonacog alfa	Benefix®	2000 IE	1 pc.
B03XA02	Darbepoetin alfa	Aranesp®	300 µg	1 x 0.6 ml
B03XA02	Darbepoetin alfa	Aranesp®	500 µg	1 ml
B03XA02	Darbepoetin alfa	Aranesp®	40 µg	4 x 0.4 ml
B03XA02	Darbepoetin alfa	Aranesp®	150 µg	4 x 0.3 ml
B03XA02	Darbepoetin alfa	Aranesp®	300 µg	0,6 ml
H01CB02	Octreotid	Sandostatin® Lar	30 mg	1 vial
H01CB03	Lanreotid	Ipstyl® Autogel	120 mg	1 pc.
J01CR05	Piperacillin and beta-lactamaseinhibitor	Piperacil/ Tazobactam	4 g+500 mg	10 pcs.
J05AP55	Sofosbuvir and velpatasvir	Epclusa, komb.	400 mg +100 mg	28 pcs.
J05AR18	Emtricitabine, tenofovir alafenamide, elvitegravir and cobicistat	Genvoya, komb.	200 mg+10 mg+ 150 mg +150 mg	30 pcs.
J06BA01	Human normal immunoglobulin	Gammanorm®	165 mg/ml	10 x 20 ml
J06BA01	Human normal immunoglobulin	Hizentra	200 mg/ml	20 ml
J06BA02	Human normal immunoglobulin	Privigen	100 mg/ml	200 ml
J06BA02	Human normal immunoglobulin	Privigen	100 mg/ml	400 ml

L01BA04	Pemetrexed	Alimta®	500 mg	1 vial
L01BC07	Azacitidine	Vidaza®	25 mg/ml	100 mg
L01CD04	Cabazitaxel	Jevtana®	60 mg/1.5 ml	1,5 ml
L01XC02	Rituximab	Mabthera®	500 mg	1 pc.
L01XC03	Trastuzumab	Herceptin®	600 mg/5 ml	1 pc.
L01XC07	Bevacizumab	Avastin®	25 mg/ml	1 x 16 ml
L01XC11	Ipilimumab	Yervoy®	5 mg/ml	40 ml
L01XC13	Pertuzumab	Perjeta	420 mg	1 pc.
L01XC17	Nivolumab	Opdivo	100 mg/10 ml	1 pc.
L01XC18	Pembrolizumab	Keytruda®	25 mg/ml	4 ml
L01XC24	Daratumumab	Darzalex	20 mg/ml	20 ml
L01XE01	Imatinib	Glivec®	400 mg	3 x 10 pcs.
L01XE18	Ruxolitinib	Jakavi	5 mg	56 pcs.
L01XE18	Ruxolitinib	Jakavi	20 mg	56 pcs.
L01XE23	Dabrafenib mesylate	Tafinlar	75 mg	120 pcs.
L01XE25	Trametinib	Mekinist	2 mg	30 pcs.
L01XE25	Trametinib	Mekinist	2 mg	30 pcs.
L01XE27	Ibrutinib	Imbruvica	140 mg	90 pcs.
L01XE33	Palbociclib	Ibrance	125 mg	21 pcs.
L01XX32	Bortezomib	Velcade	3.5 mg	1 vial
L01XX45	Carfilzomib	Kyprolis	60 mg	1 pc.
L02BB04	Enzalutamide	Xtandi	40 mg	112 pcs.
L02BX03	Abiraterone acetate	Zytiga	500 mg	56 pcs.
L03AB07	Interferon beta-1a	Avonex®	30 µg	4 x 0.5 ml
L03AB07	Interferon beta-1a	Avonex®	30 µg	4 x 0.5 ml
L04AB01	Etanercept	Benepali	50 mg	4 pcs.
L04AB01	Etanercept	Benepali	50 mg	4 pcs.
L04AB02	Infliximab	Remsima	100 mg	1 pc.

L04AB04	Adalimumab	Humira	40 mg/0.4 ml	2 pcs.
L04AB05	Certolizumab pegol	Cimzia®	200 mg	2 pcs.
L04AB06	Golimumab	Simponi	50 mg	1 pc.
L04AC05	Ustekinumab	Stelara®	90 mg	1 syringe (1 ml)
L04AC07	Tocilizumab	RoActemra	162 mg	4 pcs.
L04AC10	Secukinumab	Cosentyx	150 mg	2 pcs.
L04AX04	Lenalidomide	Revlimid®	25 mg	21 pcs.
L04AX04	Lenalidomide	Revlimid®	25 mg	21 pcs.
L04AX04	Lenalidomide	Revlimid®	15 mg	21 pcs.
L04AX06	Pomalidomide	Imnovid®	4 mg	21 pcs.
L04AA23	Natalizumab	Tysabri®	300 mg	15 ml
L04AA27	Fingolimod hydrochoride	Gilenya	0.5 mg	28 pcs.
L04AA31	Teriflunomide	Aubagio	14 mg	84 pcs.
L04AA31	Teriflunomide	Aubagio	14 mg	28 pcs.
L04AA33	Vedolizumab	Entyvio	300 mg	1 pc.
M05BX04	Denosumab	Xgeva	120 mg	1 pc. (1.7 ml)
N07XX09	Dimethyl fumarat	Tecfidera	240 mg	56 pcs.
R03DX05	Omalizumab	Xolair®	150 mg	1 syringe
S01LA05	Aflibercept	Eylea	40 mg/ml	1 pc.

APPENDIX C

Data from selected countries

Table 15: Number of list prices identified for each ATC group and (package) in the different countries.

ATC groups	Denmark	Norway	Sweden	England	Belgium	Netherlands	Germany
B02 Antihemorrhagics B03 Antianemic preparations	3 (11)	3 (11)	3 (11)	3 (11)	3 (10)	3 (11)	3 (11)
H01 Pituitary and hypothalamic hormones	2 (2)	2 (2)	2 (2)	2 (2)	2 (2)	1 (1)	2 (2)
J01 Antibacterials for systemic use J05 Antivirals for systemic use J06 Immune sera and immunoglobulins	5 (7)	5 (7)	5 (7)	5 (7)	4 (6)	4 (6)	5 (6)
L01 Antineoplastic agents	19 (21)	19 (21)	19 (21)	17 (19)	19 (21)	19 (21)	19 (21)
L02 Endocrine therapy L03 Immunomodulating agents	3 (4)	4 (4)	4 (4)	4 (4)	4 (4)	4 (4)	4 (4)
L04 Immunosuppressive agents	14 (18)	14 (18)	14 (18)	13 (16)	14 (18)	14 (18)	14 (18)
M05 Drugs for treatment of bone diseases N07 Other nervous system drugs R03 Anti-asthmatics S01 Ophthalmologicals	4 (4)	4 (4)	4 (4)	4 (4)	4 (4)	4 (4)	4 (4)
Total	50 (67)	50 (67)	50 (67)	48 (63)	49 (65)	48 (65)	50 (66)

Table 16: Number of contract prices identified for each ATC group and (package) in the different countries.

ATC groups	Denmark	Norway	Sweden	England	Belgium	Netherlands	Germany
B02 Antihemorrhagics B03 Antianemic preparations	3 (11)	3 (11)	3 (11)	3 (11)	3 (10)	0	1 (5)
H01 Pituitary and hypothalamic hormones	2 (2)	2 (2)	2 (2)	2 (2)	2 (2)	0	1 (1)
J01 Antibacterials for systemic use J05 Antivirals for systemic use J06 Immune sera and immunoglobulins	5 (7)	2 (3)	3 (5)	5 (7)	5 (6)	0	1 (1)
L01 Antineoplastic agents	19 (21)	12 (13)	13 (13)	19 (21)	19 (21)	0	11 (12)
L02 Endocrine therapy L03 Immunomodulating agents	3 (4)	1 (2)	0	3 (4)	3 (4)	0	0
L04 Immunosuppressive agents	14 (18)	14 (18)	8 (10)	14 (17)	14 (18)	0	5 (6)
M05 Drugs for treatment of bone diseases N07 Other nervous system drugs R03 Anti-asthmatics S01 Ophthalmologicals	4 (4)	3 (3)	3 (3)	4 (4)	4 (4)	0	2 (2)
Total	50 (67)	37 (51)	32 (44)	50 (66)	49 (65)	0	21 (27)

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