Evaluation of procurement prices in Ukraine across 12 programmes 2015-2016/

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CROWN AGENTS

Contents

Executive summary

The present report analyses changes in prices of pharmaceuticals and medical dvices under twelve Crown Agents procurement programmes in Ukraine from 2015-2016. For pharmaceuticals, the analysis takes into account fluctuations in external factors which can influence prices, and compares prices obtained in Ukraine in 2016 with other countries in the region. For medical devices, where international comparison is mostly not feasible, the analysis focuses on price and procurement volume changes from 2015-2016 in Ukraine only.

The external factors considered for pharmaceutical products are exchange rates, quality of finished products, cost of Active Pharmaceutical Ingredients and the volume of goods procured. The impact of these factors on price changes in Ukraine from 2015 to 2016 is analysed with regression models. Furthermore, pharmaceutical prices are compared with list prices and procurement prices in five countries in the same region: Moldova, Romania, Slovenia, Armenia and Kazakhstan.

The analysis shows that the majority of pharmaceuticals procured via Crown Agents in Ukraine are subject to price decreases between 2015-2016, mostly up to -30%. The distribution of price changes is overall skewed towards reductions, and a small number of products exhibit large changes in price (non-normal distribution with outliers).

Due to the nature of the data, therefore, the overall price change across procurement programmes is summarised by the median rather than the average. The median price reduction across all procurement programmes is -8%. The largest reductions were observed in programme 19 (cardiovascular and cerebrovascular), while moderate increases were observed in programme 28 (bleeding).

The majority of pharmaceutical products procured are considered highest quality, and prices are not systematically different across the quality scale. No effect of volume or API cost changes is observed on finished product price. Pharmaceutical prices in Ukraine generally compare favourably with other countries in the region, with a few specific exceptions.

Unit prices of medical devices across all procurement programmes decreased by a median of -18%. Price increases were only seen in programme 21 (Endoprostheses) and for reagents for one type of HIV-1 diagnostic test under programme 26. These price changes were not due to changes in volume of goods procured in Ukraine between 2015-2016.

The exchange rate of Ukrainian Hryvna (UAH) to the US dollar (USD) did not impact the analysis, as prices were examined in USD. However, a substantial depreciation in the UAH:USD rate between 2015-2016 means the budget of the Ministry of Health in Ukraine overall is characterised by decreased buying power in 2016 compared with the previous year.

Analysis of historical rates also suggests within-year depreciation can impact the overall purchasing power of the procurement budget. Overall, the present analysis suggests pharmaceuticals and medical devices are procured with high efficiency in the majority of cases.

Abbreviations

AMD	Armenian Dram
API	Active Pharmaceutical Ingredient
ATC	Anatomical Therapeutic Classification
EMA	European Medicines Agency
EUR	Euro
FDA	Food & Drug Administration
GMP	Good Manufacturing Practice
KZT	Kazakh Tenge
MDL	Moldovan Lei
RON	Romanian Leu
SRA	Stringent Regulatory Authority
UAH	Ukrainian Hryvna
USD	United States Dollar

Background

In 2016, Crown Agents commissioned an independent evaluation of its oncology procurement programme in Ukraine for the years 2014 to 2015 (Yadav 2016). In this work, Yadav analysed the prices of oncology medicines procured via Crown Agents and found prices were generally reduced in 2015 compared with the previous year, and that the difference was not substantially attributable to changes in input prices, currency fluctuation or product quality.

In the present report, a similar evaluation is undertaken for the years 2015 to 2016, focusing on medicines and medical devices procured under twelve programmes in which

Crown Agents are involved:

- IV (4): Blood donation and associated components
- XIX (19): Cardiovascular and cerebrovascular disease
- XX (20): Peritoneal dialysis
- XXI (21): Endoprostheses and implantation instruments
- XXIII (23): Consumables to determine glucose levels in the blood
- XXIV (24): Hepatitis B and C
- XXVI (26): HIV diagnostics
- XXVII (27): Reproductive health: Contraceptives for women with serious diseases
- XXVIII (28): Reproductive health: Emergency medical care in case of bleeding
- XXIX (29): Reproductive health: Neonatal respiratory distress
- XXXIII (33): Pediatric dialysis
- XXXVII (37): Substitution maintenance therapy

The present analysis evaluates changes in prices from 2015 to 2016, as well as changes in variables that could influence finished product prices in Ukraine: Exchange rate fluctuation, cost of Active Pharmaceutical Ingredients (API), quality of finished products, volume of finished product procured.

In addition, the analysis compares 2016 prices in Ukraine with list prices and net prices including discount (where available) in a series of countries in the Eastern European and Central Asian region. For this exercise, the authors note that transparency of medicines pricing is a controversial issue, and the trend in recent years has been towards decreasing price transparency. This makes it difficult in many cases to obtain net price data from most countries. Attempts to make prices widely available to the public have been made, but have not been updated regularly (e.g. www.cedd.oep.hu most recent data from 2010). Furthermore, prices from international procurement bodies such as the IDA Foundation

(www.idafoundation.org) and Durbin (www.durbinglobal.com) are confidential and only made available to suppliers. Other major international actors in the procurement space (e.g. www.medeor.de) do publish catalogue prices but procure a limited range of products which are not relevant to the present evaluation.

Consequently, the regional comparison is based on best available data, and where list prices are used, the reader should bear in mind that typical discounts are in the range of 10-30% of the list price, although higher discounts also occur (Morgan, Vogler, and Wagner 2017).

Methods

Exchange rates

Price comparisons are undertaken in United States Dollars (USD). Effective exchange rates from Ukrainian Hryvna (UAH) to USD for all programmes (except 24 and 26) are the rates on tender closing date provided by the Ministry of Health. Programmes 24 and 26 were transferred to Crown Agents from United Nations Development Programme in 2015, however no price data was disclosed. For these programmes, reference prices are therefore taken from the technical specification received from the Ministry of Health in Ukrainian Hryvna, converted to USD using the period average exchange rate for 2015.

Period average exchange rates between USD and all study currencies (Moldova MDL, Armenia AMD, Europe EUR, Romania RON, Kazakhstan KZT) for 2016 were obtained from World Bank (World Bank 2017). Historical daily exchange rates between USD and UAH were obtained from the National Bank of Ukraine (Ukraine 2017).

Quality

Manufacturers for the 2016 procurement programmes were rated according to the following scale:

1. Stringent Regulatory Authority[1] (SRA) approval for product in question
2. SRA in a developed market of another product, or a Good Manufacturing Practice (GMP) certificate of the product in question
3. All others

Manufacturer and regulatory portfolio information was obtained from PharmaCom-

[1] Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Sweden, The Netherlands, United Kingdom, United States and Japan

pass www.pharmacompass.com, manually through online searches for the manufacturer name in combination with the medicine name, and through searches of the European Medicines Agency (EMA) and Food and Drug Administration (FDA) databases. Among the procurement items studied are iodine-containing radiopaque substances and medical patches, which are assumed to be subject to the same registration requirements as other pharmaceuticals (Widmark 2007; FDA 2015). Differences in price changes between 2015 to 2016 stratified by product quality were assessed using the non-parametric Mann-Whitney U-test at a 5% significance level.

Regional and global procurement data

The authors attempted to acquire list and net price data from all Eastern European countries with a shared border with Ukraine and Central Asian countries. Details on institutions contacted are listed in Appendix A by country, along with a brief discussion of country specific procurement arrangements and challenges where appropriate.

Officials were contacted in a total of 13 countries (Slovenia, Poland, Hungary, Moldova, Belarus, Bulgaria, Romania, Slovak Republic, Czech Republic, Latvia, Armenia, Kyrgyzstan, Kazakhstan), mostly within Ministries of Health and WHO country offices. The data obtained for regional comparison is listed in Table 1.

Table 1 Regional data sources for analysis

Country	Type	Year(s)	URL
Moldova	Public tenders (2016)	2016	www.capcs.md/licitatii-desfasurate/
Moldova[2]	Regulated ex-factory price	Most recent	www.amed.md/ro/catalogul-national
Romania	Regulated price	Most recent	www.preturi.ms.ro/interogare.php
Slovenia	Regulated price	Most recent	www.cbz.si (lookup by Anatomical Therapeutic Classification (ATC) codes)
Slovenia	Hospital procurment	2017	Data provided in confidence
Armenia	Public tenders (2016)	2016	www.armeps.am/ppcm/public/procurements
Kazakhstan	Supply price	2016	Data provided by Crown Agents

[2] For Moldova, the National Catalogue ex-manufacturer price (excl. VAT) was adjusted by 15% to account for supply chain mark-up (see www.who.int/medicines/areas/coordination/Moldova_PSCPNarrativeQuestionnaire_23052011.pdf).

In many cases, although some procurement results data is made publicly available, there is not sufficient granularity for the data to be used in the present analysis, for example because only aggregated spend or volume but not unit costs are reported (e.g. Bulgaria, Romania, Latvia). In other countries, formal authorisation is required before any purchasing data can be shared (Belarus), which is a lengthy process beyond the scope of the present evaluation.

The authors explored several alternative sources of procurement data, most of which were not appropriate for different reasons. These included the Common European Drug Database (www.cedd.oep.hu/, not updated since 2010) and the IDA Foundation (which was unable to share data for the present work). None of these were considered appropriate for inclusion.

The most recent data of the Management Sciences for Health Drug Price Indicator Guide was from 2015, and very few products corresponded to the Ukraine procurement list. However, the database was included for comparison with the caveat that prices are one year out of date. An additional approximation used in this dataset was substitution of G03AA09 estradiol+gestogen with the cheapest product in G03FA (Progestogens and estrogens, fixed combinations). Apart from the online database, the WHO drug price guide based on the MSH data was also checked (www.apps.who.int/medicinedocs/documents/s23203en/s23203en.pdf) but no additional information was identified.

Active Pharmaceutical Ingredient prices

Global average prices for imports and exports of API were sourced from the Indian database Zauba (www.zauba.com). Along with China and Bangladesh, India produces a high proportion of global API, and this methodology of price collation has proven successful for most of the pharmaceutical products studied.

Prices in Indian Rupees were recorded on a month-by-month basis between 2015 and 2016, expressed as price/kg for small molecule medicines. For biologic medicines and nuclear medicines, price per unit was used as these do not utilise a traditional API. API prices per month were then averaged to determine price per year.

Price change over time was expressed in Indian rupees to avoid influence of foreign exchange rate movements over time. Very small volume purchases have been excluded to minimise volume effects. The export volumes for API and finished products were not as high as would be expected in primary care areas. This is likely because of the more specialist nature of the pharmaceutical products studied. Best available data was used for the present analysis, and products for which API price changes could not be reliably calculated are outlined in Results.

Analysis

Changes in procurement price from 2015 to 2016 were modelled as a function of changes in procurement volume and API cost in univariate models separately, and correlation coefficients (R2) were derived. A 5% significance level was applied.

Results

Procurement of pharmaceuticals

Among the items evaluated in the present report, 45 were pharmaceuticals or other non-device products (e.g. medicated patches and radiopaque substance) with ATC codes. These are evaluated separately from medical devices in order to control for fluctuations in parameters that are specific to pharmaceutical products (API costs, product quality). Volume and exchange rate effects are considered for both categories of products.

Year-on-year unit price changes

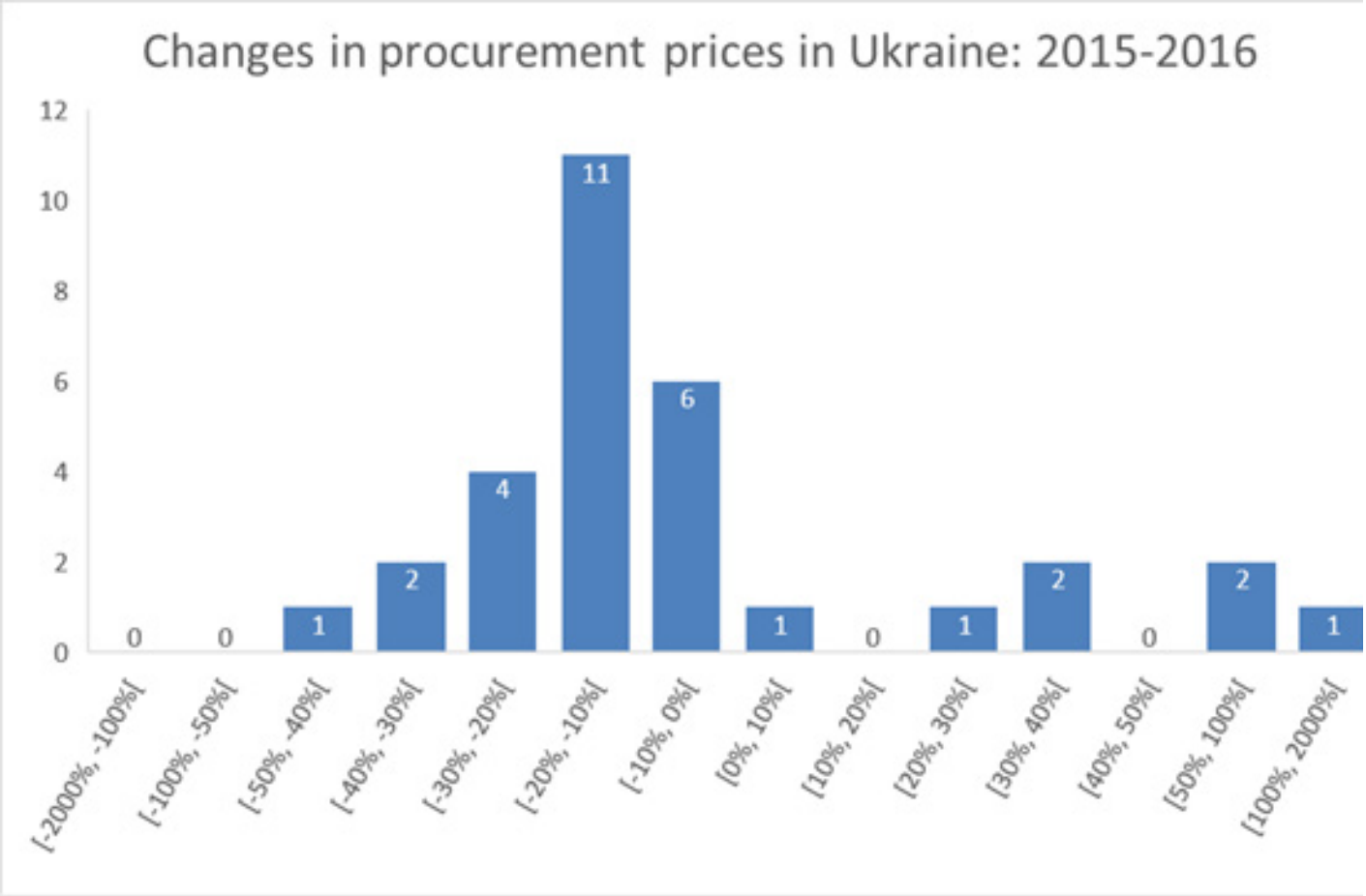

Figure 1 Year-on-year unit price changes for pharmaceuticals in Ukraine 2015-2016

Figure 1 Year-on-year unit price changes for pharmaceuticals in Ukraine 2015-2016. The relative increase/decrease in price between 2015 and 2016 is shown in Figure 1 for all medicines where prices were available for both years (n=31). The histogram shows the majority of prices (n=24, 77%) have decreased since 2015, with most prices (n=21, 68%) decreasing by up to 30%. Under a quarter of prices (n=7, 23%) increased from 2015 to 2016, most of these (n=5) by less than 30%.

The majority of price changes were within a range of -30% to +30%. However, eight outliers with larger increases or decreases were also observed. Most of these were Pegylated Interferon alpha (Programme 24, items 6 and 12), which increased by +30.3%, and Pegylated Interferon alfa-2b 80mcg to 120mcg doses (Programme 24, items 8, 9, 10), which decreased in price by -38 to -41%. Relatively large price increases were observed for Streptokinase (programme 19, item 1) at +67%, Lamivudine (Programme 24, item 7) at +75% and Ribavirin (programme 24, item 13) by 865%.

Median prices were reduced in all programme categories except programme 28 (emergency care for bleeding) where the median change was 0% (Table 2). Across all programmes the median price reduction was -8%. The dispersion of unit price changes across programmes is illustrated in Figure 2, which shows the greatest range of price changes is observed in programme 24 (hepatitis) followed by programme 28 (bleeding).

Table 2 Price differences observed between 2015-2016 in Ukraine by programme category

Prog.	Programme components	Price difference observations (n)	Mean difference	Median difference	Lowest difference	Highest difference
19	Medicines for cardiovascular and cerebrovascular disease Iodine radiopaque substance Hemostatic patches	12	-8%	-17%	-25%	67%
24	Hepatitis B and C	11	-4%2	-13%	-41%	865%
27	Contraceptives	1	-5%	-5%	-5%	-5%
28	Emergency medical care for bleeding	4	4%	0%	-12%	29%
29	Neonatal respiratory distress	3	-12%	-12%	-18%	-7%
37	Substitution maintenance therapy	01	N/A	N/A	N/A	N/A
All		31	-5%2	-12%	-41%	865%

Notes: [1]No 2015 comparator observed.

[2]The mean is substantially impacted by the Ribavirin outlier value of 865%, consequently means are reported without this data point. Including Ribavirin brings the mean in programme 24 to 75% and for the total sample to 23%.

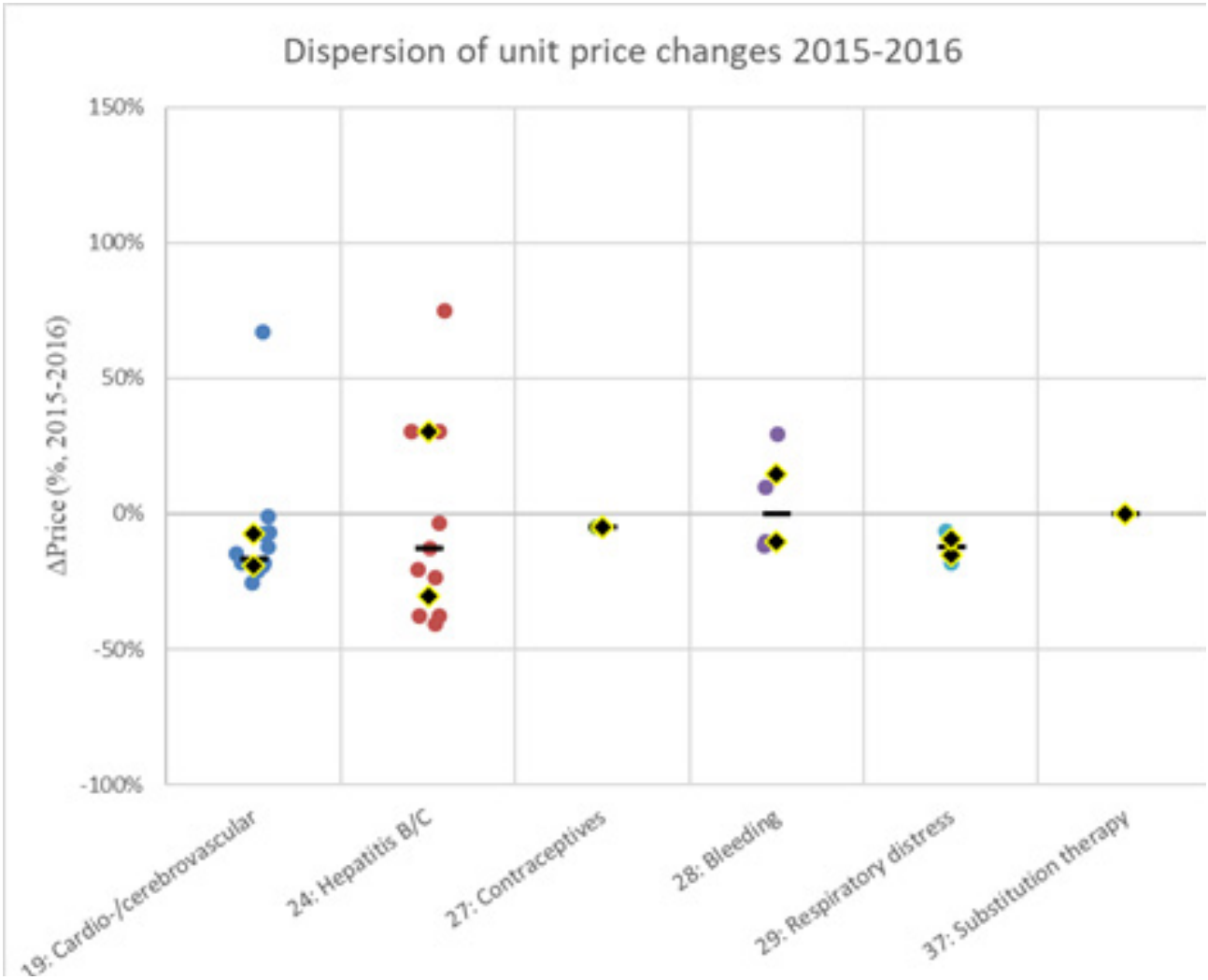

Figure 2 Dispersion of unit price changes of pharmaceuticals by programme

Note: Median values are represented by black horizontal bars, 25th and 75th percentile by black diamonds.

Vertical axis is truncated at 150%, one value is recorded above this (Ribavirin, programme 24, 865%).

In summary, median unit prices were reduced across all but one programme, and overall more than three quarters of medicines were procured at a lower unit cost in 2016 than in 2015. A small subsample of medicines (Streptokinase, Lamivudine and Ribavirin) were subject to a disproportionate price increase, warranting specific attention to the causes of this. In contrast, particularly large price reductions were achieved for Pegylated Interferon alfa-2b.

Quality

The product quality, as determined by Stringent Regulatory Authority (SRA) approval and Good Manufacturing Practice (GMP) status, was overall high. Out of 34 items, 22 (65%) were categorised as highest quality (Table 3), based on SRA approval of the same product by the same manufacturer in a developed market, chiefly the USA, Canada, UK and EU.

All of the 12 items (35%) categorised as tier 2 were on the basis of GMP certification of the relevant products, which were supplied by four different domestic manufacturers in Ukraine.

Table 3 Quality distribution of procurement items

Quality tier	**n =**	**%**
1. Stringent Regulatory Authority (SRA) approval in a developed market of the product in question	22	65%
2. SRA in a developed market of another product, or a Good Manufacturing Practice (GMP) certificate of the product in question	12	35%
3. All others	0	0%

Overall the distribution of price changes from 2015 to 2016 (Figure 3) was not significantly different between the tier 1 and tier 2 quality categories (Mann-Whitney U, p=0.97/p=0.60 without/with the Ribavirin outlier), although the median price change was empirically higher for tier 2 quality products (+16%/+57% without/with Ribavirin outlier for tier 2 as opposed to -8% for tier 1).

Although the difference is not statistically significant, it is interesting to note that the small sample of domestically sourced products (tier 2) are generally associated with numerically greater price changes between 2015 and 2016, and the median price change is

higher in this group. These products are all supplied by domestic manufacturers, so it is feasible the higher median change is related to the weakening of UAH against the USD from 2015 to 2016.

Quality assessment was only undertaken for the 2016 procurement round, and consequently changes in quality of procured items are not taken into account in the quantitative model further below.

However, if procurement price reductions were to be attributable to decreased product quality, one would expect a trend towards lower prices in lower quality categories.

As there was no statistically significant difference in the price change distribution between tier 1 and tier 2 quality products, and indeed the observed trend was in the opposite direction, a potential contribution of quality to price fluctuations is not considered likely.

Figure 3 Distribution of price changes by quality

Note: The outlier of 865% in Tier 2 is Ribavirin

Volume effects

No effect of purchase volume on price was observed when the Ribavirin outlier was removed (Figure 4, R2=0.0005, p=0.71, n=30), and this did not change materially when Ribavirin was included. Overall, volume was unchanged between 2015 and 2016 in more than half of procurement items (n=16), although prices did change in all of these (reduction in price in 13, and an increase in price in 3 items). Consequently, changes in purchase volume does not appear to have influenced changes in procurement price.

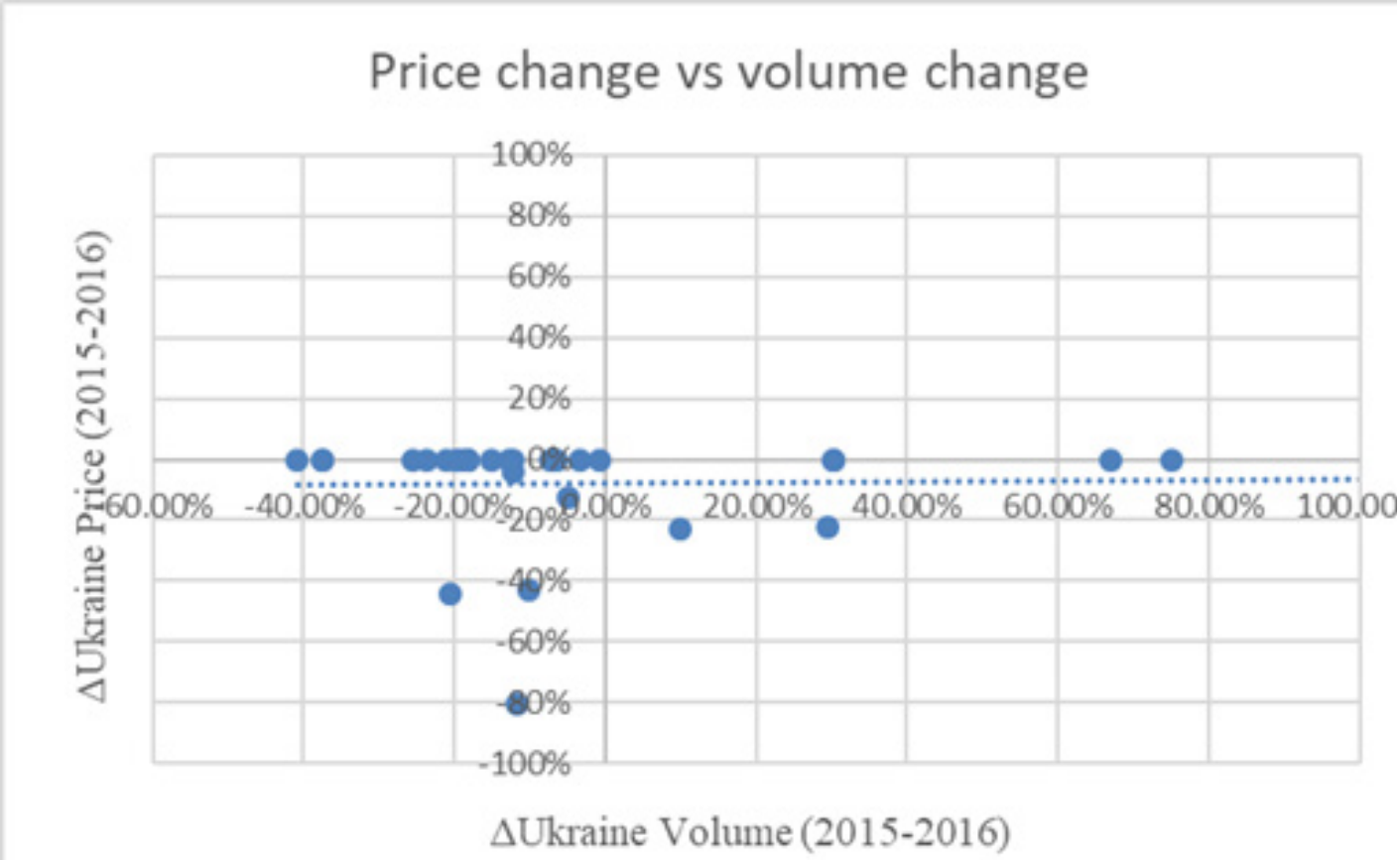

Figure 4 Change in volume vs change in price between 2015 and 2016 in Ukraine

Note: Depicted without Ribavirin outlier

Exchange rate effects

The comparisons above are undertaken in USD, consequently the USD: UAH exchange rate does not directly impact the price analysis. However, the exchange rate does indirectly influence the amount of goods which can be purchased under individual programmes.

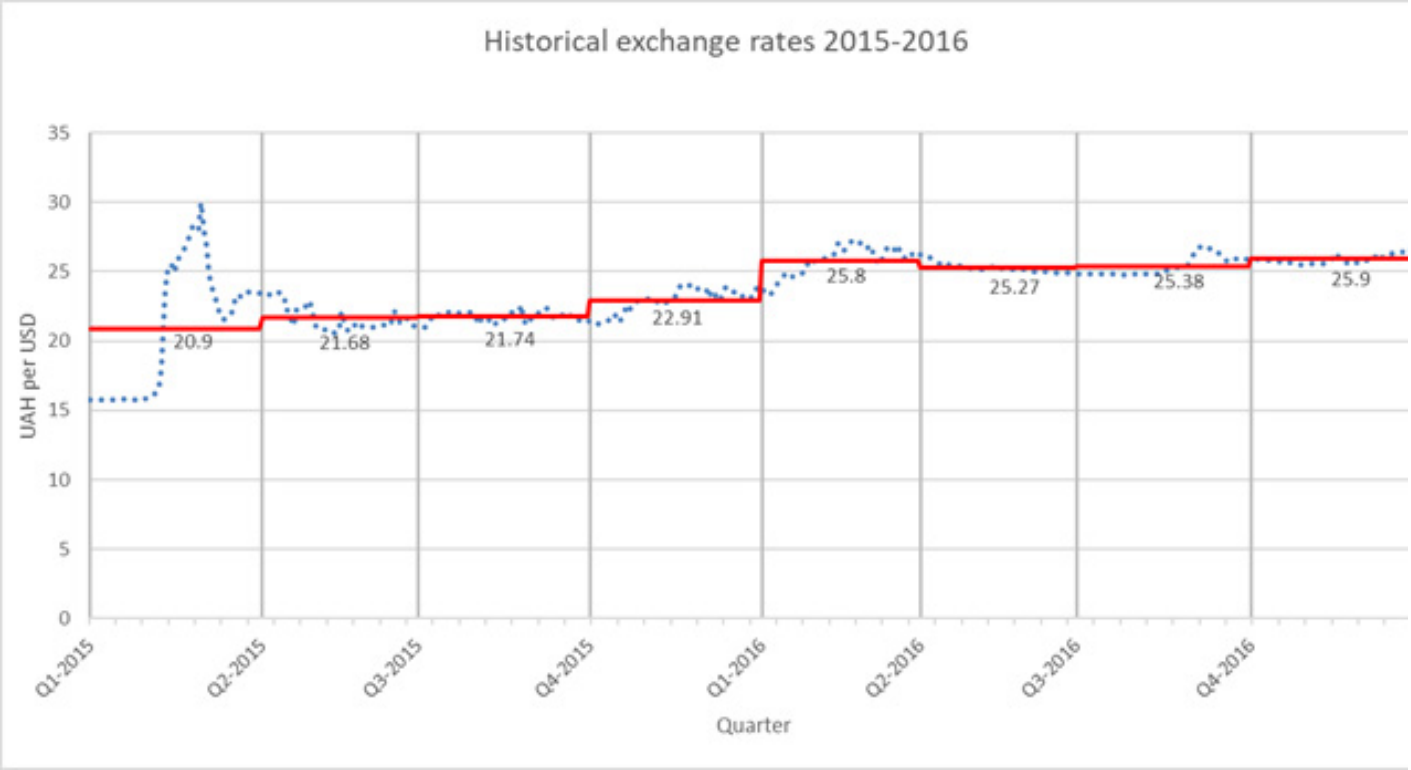

Figure 5 Historical exchanges rates UAH:USD 2015 to 2016

Notes: Qn (Quarter n) denotes start of the quarter. Labels denote average exchange rate over the quarter.

Specifically, the period of time between allocation of funds to procurement programmes and final payment of contracts can influence the purchasing power of the overall budget for international procurement. As Figure 5 shows, average exchange rates between UAH and USD have on average increased steadily by quarter in 2015 (20.90 to 22.91), meaning that funds allocated early in the year in UAH could lose up to approx. 9% of value in USD terms, depending on time scales. A similar but less pronounced trend is observed for 2016 exchange rates.

Overall, the period average exchange rate of UAH to USD has increased from 21.8 UAH per USD in 2015 to 25.6 UAH per USD in 2016. This movement of +17.4% in nominal terms could increase the final price to the Ministry of Health of products from international manufacturers paid in USD, as well as domestic manufacturers paid in UAH who rely on importation of active pharmaceutical ingredients.

Active Pharmaceutical Ingredient price effects

For this analysis, API price could not be determined for Fondaparinux, Iloprost and Pegylated Interferon alpha.

Additionally, Sofosbuvir, Ledipasvir, Tenofovir and Ticagrelor API's were traded internationally using a tiered pricing structure to different categories of countries, with prices varying up to several thousand percent. Consequently, these were excluded from analysis. It should be noted that the price of the finished hepatitis medicines using these API's are more likely to be driven by commercial considerations than API cost. API costs were available for comparison for 31 medicines, of which Ukrainian price data for both years was available for 19.

A plot of changes in API prices versus changes in procurement prices in Ukraine from 2015 to 2016 is shown in Figure 6. There is no correlation between the two variables (R2=0.0044, p=0.78), and this did not change when removing the outlier Ribavirin. Consequently, the cost of API is not considered to contribute to the observed overall price reductions.

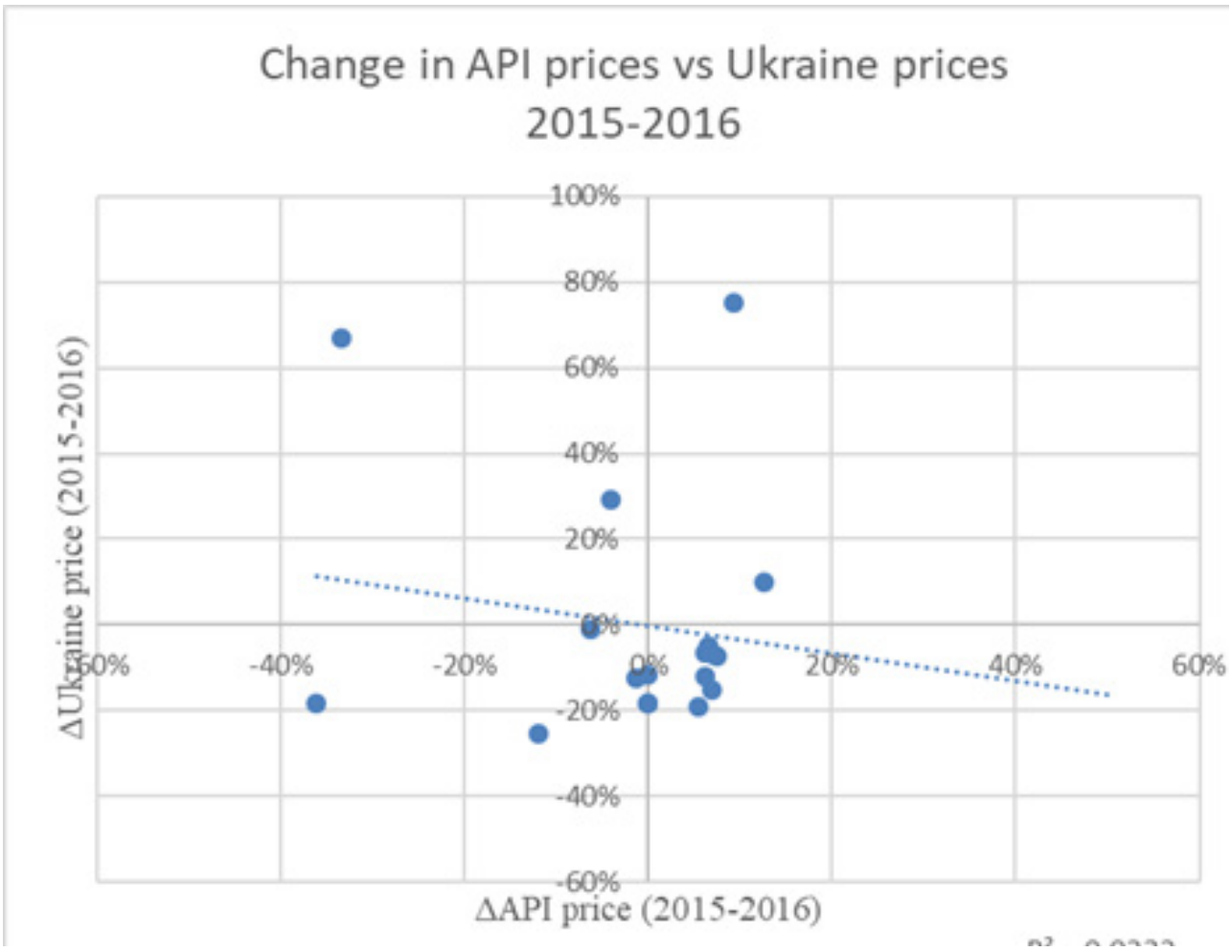

Figure 6 Change in Active Pharmaceutical Ingredient prices relative to procurement price changes in Ukraine

Note:Graph is shown without the Ribavirin outlier

Multivariate model

Due to missing data in several variables, only 19 observations were available for a multivariate model. In this analysis, price change in Ukraine from 2015 to 2016 was modelled as a function of changes in API cost and procurement volume. None of the covariates were significant in the resulting model (p=0.68 for volume and p=0.76 for API) and the fit was poor (R2=0.015), as expected from the univariate model results.

Regional comparison

The regional comparison included a mix of list and procurement prices from Moldovia, Slovenia, Kazakhstan, Armenia and Romania. The regional prices were expressed as a percentage of the 2016 Ukraine price, with 100% indicating the prices were identical. For programme 19 (cardiovascular and cerebrovascular disease, Figure 7) prices in Ukraine compare favourably with other countries in the region. Substantially higher prices are observed in at least one other regional country for all items except Levosimendan and Metoprolol. Levosimendan prices are observed around a narrow interval across the region, while the Ukrainian price of Metoprolol is high compared to other countries.

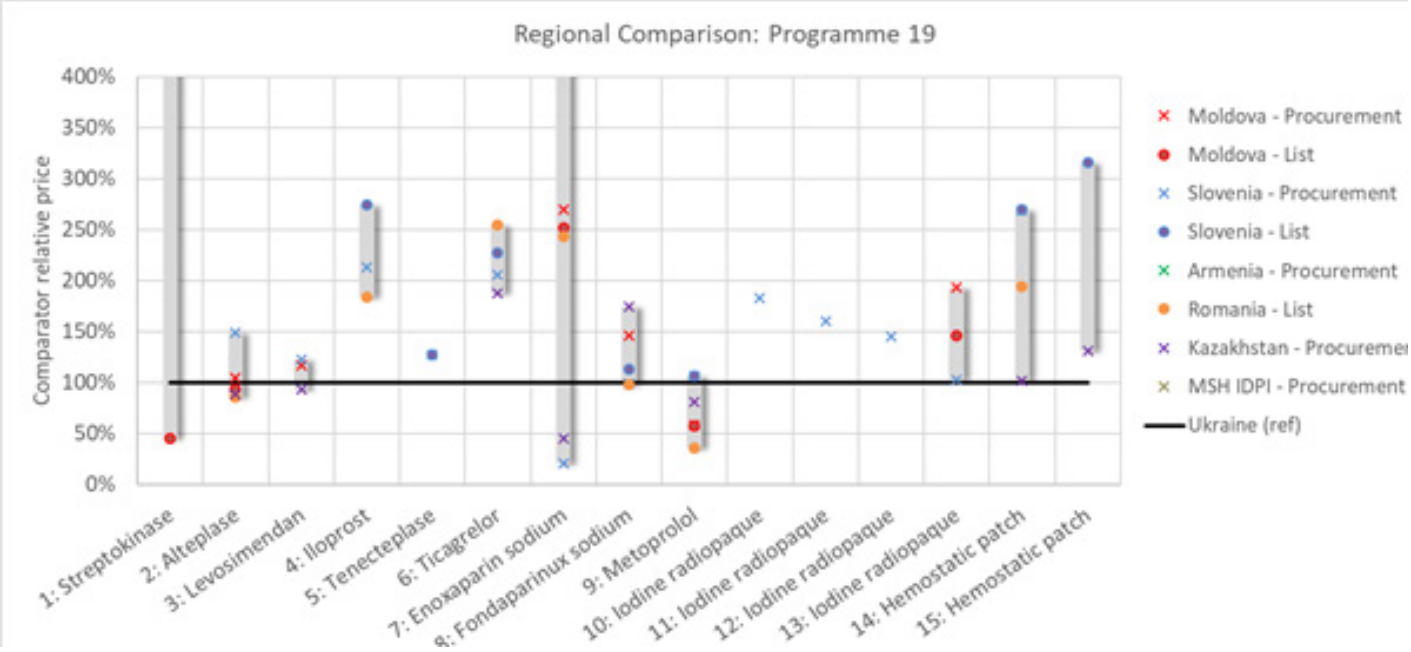

Figure 7 Regional comparison of prices for programme 19

Note: Vertical axis truncated at 400%. Values beyond this are: Streptokinase (856% Slovenia list price); Enoxaparin sodium (472% Slovenia list price, 905% MSH procurement price).

For programme 24 (hepatitis B and C, Figure 8), prices obtained in Ukraine also compared favourably with regional prices for most items. Price in at least one other country was substantially higher for all medicines except Lamivudine, where Ukraine is paying a relatively high price except compared with the Slovenian list price. For most other medicines, the majority of comparator prices are higher than the price in Ukraine.

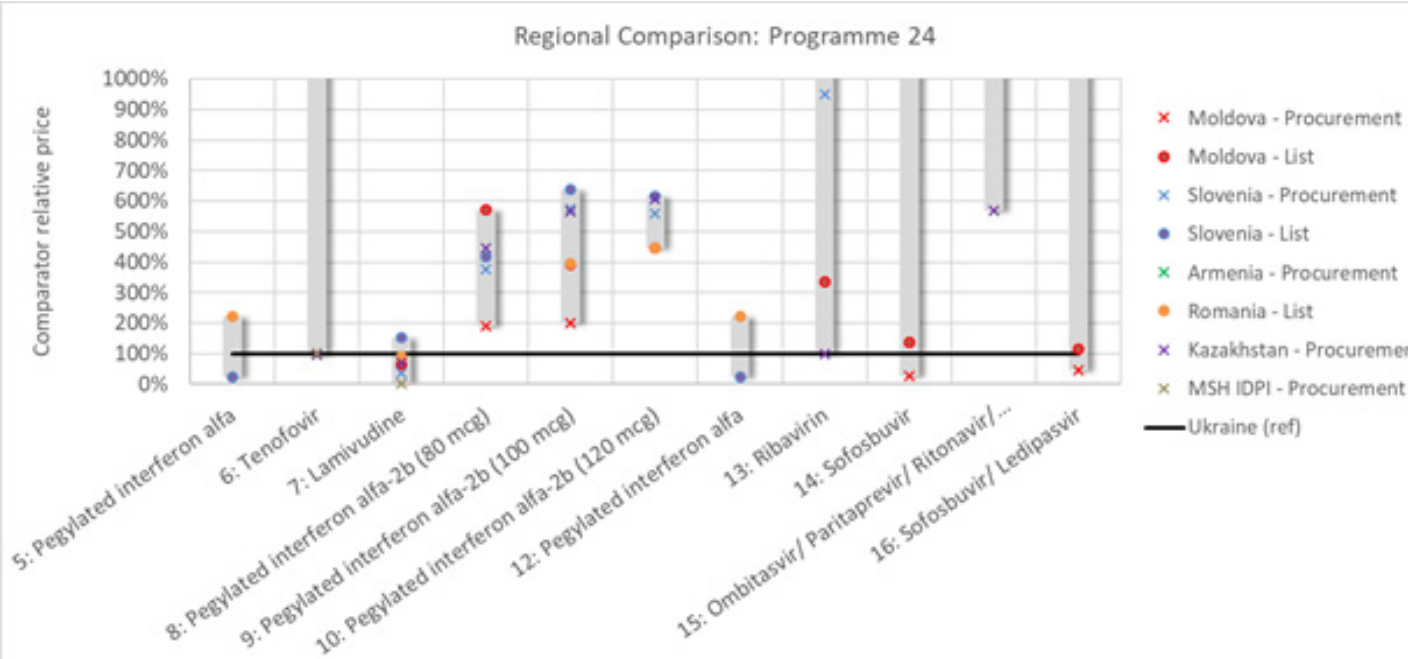

Figure 8 Regional comparison of prices for programme 24

Note: Vertical axis truncated at 1000%. Values beyond this are: Tenofovir (4090% Moldova procurement, 8213% Slovenia procurement, 5477% Romania list price), Ribavirin (1672% Slovenia list price, 1801% Romania list price), Sofosbuvir (5738% Slovenia list price, 5222% Slovenia procurement, 6297% Romania list price), O/P/R/D (1827% Moldova list price, 1486% Slovenia list price), Sofosbuvir/Ledipasvir (5364% Slovenia list price, 4879% Slovenia procurement)

Programmes 27, 28, 29 and 37 are illustrated in Figure 9.

For programme 27 (contraceptives), the price for combined oral contraceptives was at the lower end of the range of other countries in the region.

For programme 28 (emergency medical care for bleeding episodes), however, prices were overall higher in Ukraine for all three items compared.

In programme 29 (neonatal respiratory distress), prices in Ukraine were comparable to other countries in the region.

Finally, for programme 37, methadone was only found for comparison in the Romanian list prices, and the price in Ukraine was substantially lower. Similarly, for Buprenorphine, a comparator was only found in the Slovenian list prices, and the Ukrainian price again was substantially lower.

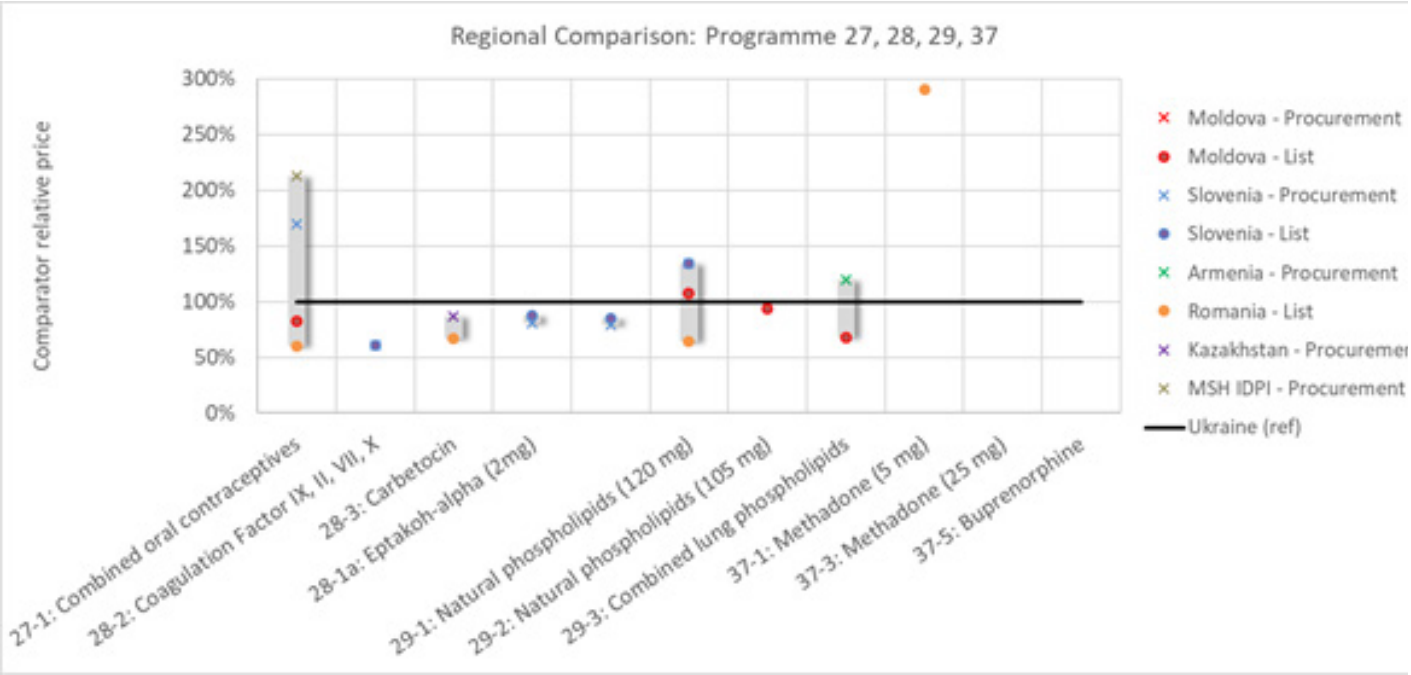

Figure 9 Regional price comparison for programmes, 27, 28, 29, 37

Note: Vertical axis truncated at 300%. Values beyond this are recorded for: Methadone 25mg (816% Romania list price), Buprenorphine (548% Slovenia procurement)

When considering each comparator country separately, prices in Ukraine were lower in the majority of cases (Table 4). For example, compared with procurement in Moldova, prices are lower in Ukraine for 8 out of 11 products which could be compared (73%), and compared with procurement in Slovenia, lower in Ukraine in 21 out of 27 products (78%).

Table 4 Prices in Ukraine versus comparators in the region

	Moldova - Proc.	Moldova - List	Armenia -Proc.	Slovenia - List	Slovenia - Proc.	Romania - List	Kazakh-stan - Proc.
Common sample (n)	11	17	1	23	27	20	16
Price lower in Ukraine	8	10	1	18	21	13	8
(% of products)	73%	59%	100%	78%	78%	65%	50%
Price higher in Ukraine	3	7	0	5	6	7	8
(% of products)	27%	41%	0%	22%	22%	35%	50%

Note: Common sample (n) is the number of products for which price data is available both for Ukraine and the comparator country. "Proc." denotes procurement prices, "List" denotes public list prices.

Conclusions on procurement of pharmaceuticals

Based on the univariate models, in which all available data points were used, and the multivariate model, in which all procurement items with valid observations for all variables were used, neither changes in volume or in cost of API seem to explain the changes observed in procurement price. Analysis of finished product quality did not suggest any effect in price changes.

Depreciation of the Ukrainian Hryvna against the US dollar on average over the period 2015 to 2016 should ceteris paribus cause prices of both imported and domestically produced pharmaceuticals to rise (assuming domestic manufacturers import API's in local currency terms, however as the present analysis is conducted in USD the depreciation does not have a direct impact.

Greater median price increases observed in the tier 2 quality group, which are all domestically sourced, however suggest the currency depreciation may be impacting pharmaceutical prices in local currency. Furthermore, continuous depreciation of the UAH against the USD over the course of a budgeting and procurement cycle may have negative implications for the purchasing power of the overall budget.

In conclusion, median unit prices of pharmaceuticals procured in Ukraine have decreased from 2015 to 2016 in all procurement programmes except one, where the median price remained stable. The reduction in unit prices of pharmaceuticals observed from 2015 to 2016 cannot readily be attributed to changes in order volume or external factors (cost of API or exchange rate fluctuations) and are likely due to improvements in procurement efficiency.

At the same time, a small subsample of medicines (Streptokinase, Lamivudine and Ribavirin) were subject to a disproportionate price increase, warranting specific attention to the causes of this.

Procurement of devices

The programmes 24, 27, 28 and 29 did not encompass medical devices and are not discussed in this section. In the following, price changes observed from 2015 to 2016 are described by programme area, and the effect of volume changes on unit price of medical devices is assessed.

Year-on-year unit price changes

Overall, the distribution of price changes observed for medical devices is shown in Figure 10, for all devices where 2015 and 2016 data is available (n=233). Prices were mostly reduced in the range -100 to 0% (n=194, 83%), with a small number or products (n=39, 17%) increasing in price between 2015 and 2016.

Figure 10 Changes in unit prices for medical devices from 2015 to 2016

Changes in unit prices by programme are presented in Table 5 . Across the whole sample of 233 procurement items, the median price from 2015 to 2016 decreased by -18%. Examination of the programmes reveals the greatest decrease in programme 4 (blood donation, median -30%) and programme 23 (glucose levels, median -26%). In contrast, unit prices increased substantially in programme 21 (endoprostheses, median +61%), although this programme contains only two observations. Under programme 26 (HIV diagnostics), a marginal increase of +7% was also observed for reagents for HIV-1 viral load detection with AmpliPrep/Cobas.

The dispersion of price changes across programmes is illustrated in Figure 11, which shows a relatively narrow distribution for most price changes. The broadest dispersion measured by inter-quartile range (IQR) was observed for cardiovascular devices (programme 19, IQR [-33% to -10%]), endoprostheses (programme 21, IQR [33% to 89%]) and HIV diagnostics (programme 26, IQR [-39% to 0%]). A small number of outliers with high (over 100%) price increases were observed in programme 4 (item 37: 2nd generation hepatitis C test, 929%), programme 19 (item 55: Atraumatic suture material suture, 118%), programme 21 (item 5: Distal femur modular prosthesis, 117%) and programme 33 (items 2, 3, 4: Paediatric haemodialysis kit components, 280% to 322%).

In summary, the majority (83%) of medical device unit prices have decreased from 2015 to 2016, and overall median prices have been reduced by -18%. Median unit prices increased only for a few groups of products, notably programme 21 (endoprostheses, two items) and reagents for determining HIV-1 viral load (six items in programme 26).

[3]Note: Prices for year 2015 and/or 2016 were not available for the following parts/subsections: Cemented hip joint endoprostheses (XXI); Determination of CD4: in HIV-positive pregnant women; for ART follow-up; for dispensary patients (XXVI); Determination of CD4: p.2.10 in HIV-positive pregnant women; p.3.5 for ART follow-up; p.3.5 for dispensary patients; Reagents and consumables compatible with the flow cytofluorimeter "Beckman Coulter" (XXVI); Determination of CD4: p.2.10 in HIV-positive pregnant women; p.3.5 for ART follow-up; p.3.5 for dispensary patients; Reagents and consumables compatible with the flow cytofluorimeter " Becton Dickinson " (XXVI); Determination of viral load: in HIV-positive pregnant women; for ART follow-up; for dispensary patients (XXVI); Reagents and consumables for determining the level of HIV-1 viral load compatible with Abbott m2000sp and amplifier Abbott Real-time m2000rt (XXVI); Set of reagents and consumables for determining the level of viral load of HIV-1, compatible with amplifier "iQ5" with detection of fluorescent signal in "real-time" format (format "Fluorescence Detection in Real-Time" -"FRT") (XXVI); Measures for prevention of mother-to-child transmission of HIV (test-systems for newborns born to HIV-positive women) (XXVI); Reagents and consumables compatible with amplifier "Rotor-Gene 6000TM" or "iQ5" with detection of fluorescent signal in "real-time" format (format "Fluorescence Detection in Real-Time" - "FRT") (XXVI); Reagents and consumables compatible with Abbott m2000sp and amplifier Abbott Real-time m2000rt (XXVI); Laboratory monitoring of HIV resistance to ART (XXVI); Measures to assure external and internal quality control of HIV/AIDS laboratory testing (XXVI); Closed blood sampling systems: p.2.10 for blood collection from newborns of HIV positive women; for pregnant women (immunological and virological studies); p.3.5 for dispensary patients (immunological and biochemical studies) (XXVI)

Table 5 Year on year price changes by procurement programme and part/subsection between 2015 and 2016

Part/subsection	Items (n)	Mean price change (%)	Median price change (%)	
Programme IV - Centralized procurement of medications and medical products for the development of blood donation and its components				
		52	-5%	-30%
Programme XIX - Centralized procurement of medicines and medical products for healthcare institutions for treatment of patients with cardiovascular and cerebrovascular diseases				
All parts/subsections		106	-21%	-18%
Part 2 - Medical device for electrophysiology and cardiac stimulation		18	-11%	-11%
Part 3 - Oxygenators and heart valves		26	-9%	-12%
Part 4 - Medical devices for the surgical treatment of cerebrovascular diseases		16	-29%	-30%
Part 5 - Medical devices for coronary stenting		24	-46%	-44%
Part 6 - Other supplies		22	-11%	-10%
Programme XX - Centralized procurement of consumables for peritoneal dialysis				
		10	-15%	-6%

Programme XXI - Centralized procurement of endoprostheses and sets of implantation instruments			
Endoprostheses for oncology patients	2	61%	61%
Programme XXIII - Centralized procurement of consumables to determine the glucose level in the blood, glycosylated hemoglobin			
		1	-26%
Programme XXV - Centralized procurement of test-systems for HIV diagnostics, ART follow-up and monitoring patients for HIV infection progression, determination of HIV resistance to antiviral drugs, conducting reference studies			
All parts/subsections	39	-19%	-19%
Donation safety measures	1	-9%	-9%
Measures for prevention of mother-to-child transmission of HIV	2	-16%	-16%
Reagents and consumables compatible with Architect i1000sr	11	7%	-5%
Reagents and consumables compatible with Cobas 14	12	-45%	-41%

Measures for conducting confirmatory tests in case antibodies to HIV are detected	5	-48%	-38%
Reagents and consumables for determining the level of HIV-1 viral load compatible with AmpliPrep/Cobas	6	6%	7%
The system of external quality control of HIV diagnostics and quality assessment of test-systems for HIV diagnostics	2	-20%	-20%
Programme III - Centralized procurement of medicines and medical devices for paediatric dialysis			
	23	34%	-4%
Total sample	**233**	**-11%**	**-18%**

[4] Moldova National Catalogue, and procurement order LP 16-02760 (2016)

[5] Moldova, procurement order LP 16-02760 (2016)

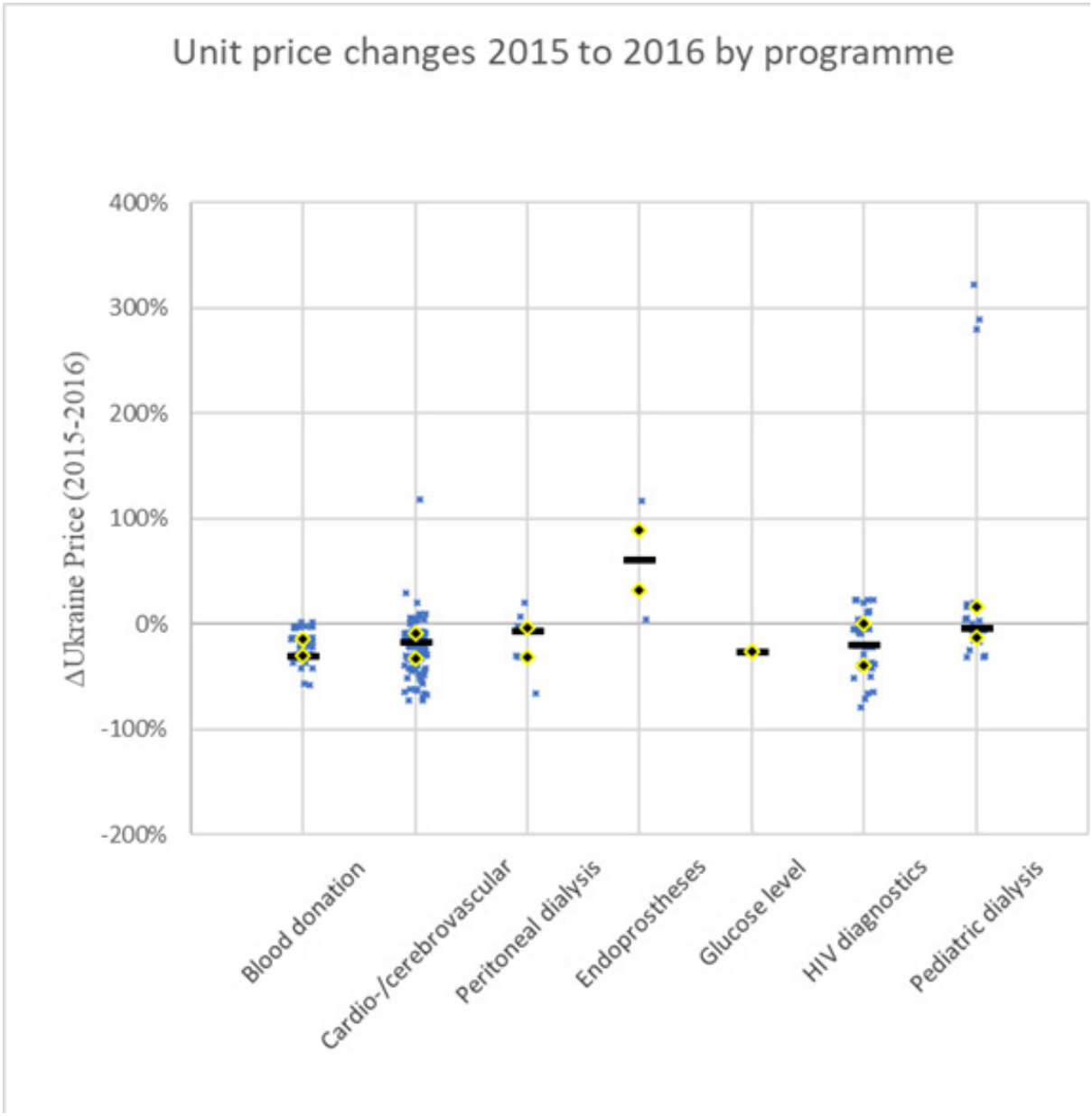

Figure 11 Price changes from 2015 to 2016 for medical devices

Note: Median (black horizontal bar) and 25th/75th percentiles (black/yellow diamonds) are displayed by programme. Vertical axis truncated at 400%, one value exists above the cut-off (Programme 4,item 37: 929%)

Volume effects

The relationship between price and volume changes between 2015-2016 is illustrated in Figure 12. There is no observed relationship between the two variables (R2=4.2*10-5, p=0.92), consequently changes in volumes procured are not considered to impact price changes between 2015-2016.

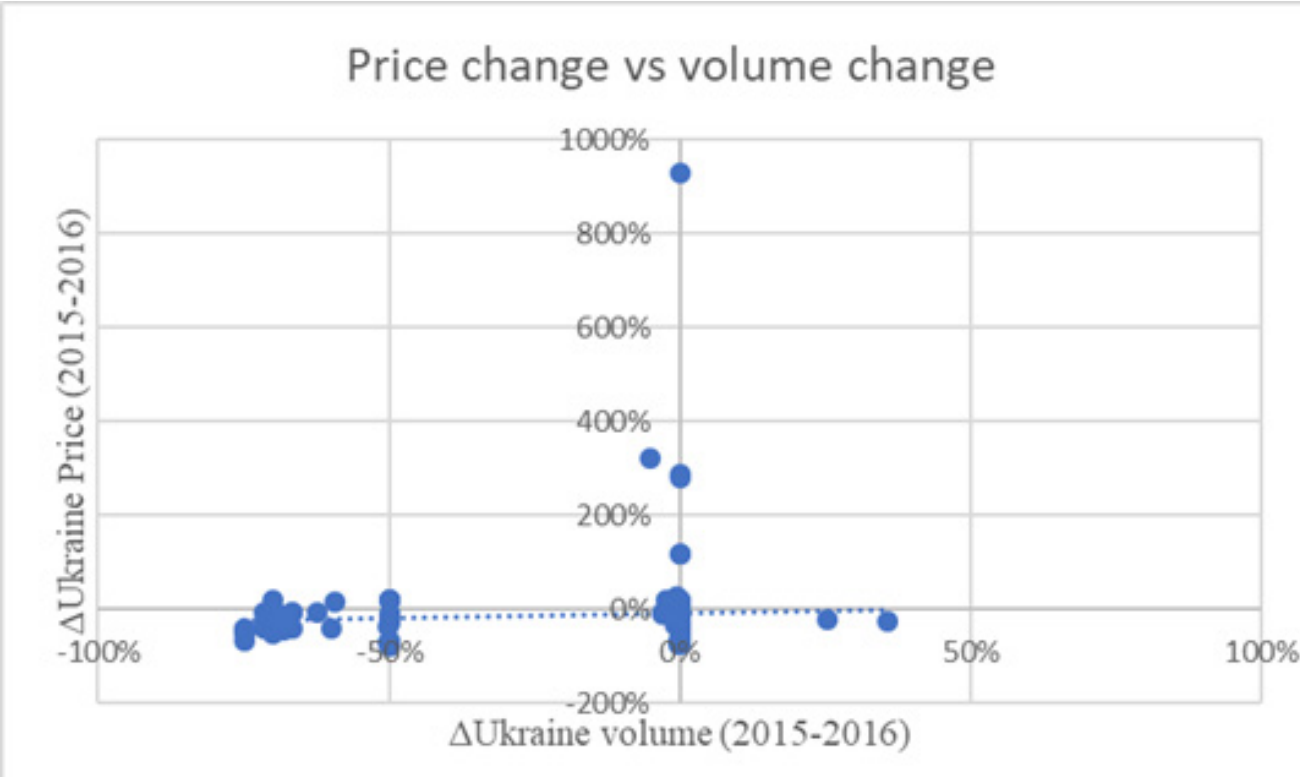

Figure 12 Volume and price change between 2015-2016 in Ukraine

Discussion and conclusions

The present report examines prices paid in Ukraine for pharmaceuticals and medical devices across 12 procurement programmes in 2015 and 2016. Changes in unit prices are examined over time, and analysed to disentangle effects of volume, cost of API, quality and exchange rates.

Pharmaceuticals

Overall, pharmaceuticals are subject to a median unit price decrease of -8%, with the greatest median reduction in programme 19 of -17% (medicines for cardiovascular and cerebrovascular disease). Median prices were reduced in all programmes except 28 (emergency medical care for bleeding), where the median change was 0%. The changes in unit price do not correlate significantly with changes in volume or cost of API, and the majority

of products procured are considered to be of high quality. Consequently, price reductions from 2015 to 2016 are considered to be largely due to procurement efficiency.

A few items were subject to relatively high price increases in Ukraine, warranting further investigation. These were Streptokinase (programme 19), Lamivudine and Ribavirin (programme 24). Despite the increase, the price of Streptokinase was still between list prices observed in Slovenia and Moldova. Similarly, the price of Ribavirin was substantially lower than all regional comparators except Kazakhstan. However, the 2016 price of Lamivudine in Ukraine is among the highest observed regionally.

Medicines for viral hepatitis are known to vary substantially across countries due to the commercial licensing and tiered pricing strategies of Gilead (Iyengar et al. 2016). In the present analysis, Tenofovir (Viread) varied approx. 10-fold in price per pill among most Eastern European countries examined, and was additionally purchased at a fraction of the Ukrainian cost in Kazakhstan (approx. 3%) from an Indian generic company.

Accordingly, Gilead has launched Viread in Kazakhstan as part of its access programme (Gilead 2013), and the price in Kazakhstan should be expected to differ materially from most Eastern European countries.

For high-value products such as Sofosbuvir there is an incentive for manufacturers to hold list prices high for external reference pricing purposes, while giving discounts to different countries according to ability to pay. In Moldova, the procurement price of Sofosbuvir 400mg was approx. 25% of the National Catalogue price, and Sofosbuvir/Ledipasvir 400mg/90mg was under 50% of the National Catalogue price[4]. This makes it particularly challenging to compare prices of novel hepatitis medicines internationally.

Ribavirin is a small molecule generic, and has been observed in the present analysis to be supplied at a nominal cost along with procurement of more expensive medicines. In procurement data from Moldova, more than 4 million Ribavirin 200mg tablets were procured at a total price of approx. US$ 2. In this transaction, Ribavirin tablets were probably provided at a nominal price to incentivise the purchase of Daclatasvir, Sofosbuvir and pegylated interferon from the same manufacturer.

[4] Moldova National Catalogue, and procurement order LP 16-02760 (2016)

[5] Moldova, procurement order LP 16-02760 (2016)

At the same time, Ribavirin is subject to an extremely high price change in Ukraine of 865%, which should be viewed in the context of the Moldova example.

The data from Ukraine highlights an example of the potential impact of market conditions. Natural phospholipids were procured in two content sizes, at a lower price for the lower content product in 2015 (US$ 434 for 105mg, US$ 445 for 120mg).

In 2016 the items were supplied by two different manufacturers, at a higher price for the lower content item (US$ 437 for Infasurf 105mg, US$ 391 for CuroSurf 120mg). Such changes can be due to multiple factors, such as suppliers entering/exiting the market or changing available formulations. In this case, CuroSurf is available in 120mg and 240mg preparations[6], while Infasurf is a 105mg preparation[7]. If these preparations are clinically interchangeable, but procured as different items in which each supplier effectively has a preparation monopoly, there is scope for manufacturers to arbitrarily raise (or lower) prices. In this case, no material price increase was observed for the 105mg preparation, while the 120mg preparation actually decreased in price between 2015-2016.

Market conditions are also an important factor for the substantial discount on Enoxaparin observed in Slovenia, where there is intense competition between suppliers of low molecular weight heparin preparations for the hospital market. The price in Ukraine is also among the lowest observed, and has been reduced by 75% since 2015, suggesting similar dynamics are at play here.

Medical devices

Overall, unit prices for medical devices decreased by a median of -18%. The greatest decreases were observed in programme 4 (blood donation) and 23 (glucose level monitoring), while a median increase in unit prices was observed in programme 21 (endoprostheses). No effect of volume was observed on unit prices. While quality of pharmaceutical products can be approximated by considering the SRA approval and/or GMP status of suppliers, assessing quality of medical devices is not straightforward, and consequently the impact of any changes in quality of devices (which includes diverse items like blood bags, pacemakers, suture, stents, clamps, machines etc) cannot be determined. This analysis did not include data on changes in suppliers, which could explain some of the variation observed.

Conclusions

In summary, prices of the majority (77%) of pharmaceuticals procured via Crown Agents in Ukraine in 2016 were lower than the preceding year, with price reductions mostly in the range of up to -30%. Median prices decreased across all programmes, except programme 28 (emergency medical care for bleeding), where the median change was zero. Similarly, prices of the majority (83%) of medical devices were lower in 2016 than the preceding year, with median prices increasing only in programme 21 (endoprostheses, 2 items) and for a specific set of HIV-1 diagnostic reagents under programme 26.

Across the board, prices achieved in Ukraine in 2016 compared favourably with prices in other Eastern European/Central Asian countries. Price confidentiality for medical products is a common feature of pricing systems in developed countries, and international comparison should be interpreted with caution when undiscounted list prices are used.

Key points

- From 2015 to 2016, prices of pharmaceuticals procured via Crown Agents have mostly decreased by up to -30%, with a median decrease across all procurement programmes of -8%
- Pharmaceutical procurement prices can be affected by order volume, API cost and product quality, however in the present analysis, none of these factors were found to contribute significantly to the price reductions achieved, suggesting the price reductions are due to procurement efficiency
- Compared with other countries in the region, pharmaceutical prices were lower in Ukraine than in comparator countries for the majority of products
- Price changes for medical devices were in the range of -100% to 0% for the majority of products. The median price change across all programmes was -18%.
- The changes in unit prices for medical devices were not found to be related to procurement order volume

[6] www.curosurf.com/wp-content/uploads/2015/03/CurosurfUsersGuide.pdf
[7] www.infasurf.com/infasurfApp/info.asp.html
[8] www.infasurf.com/infasurfApp/info.asp.html

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Appendix A: Country sources contacted for procurement data

List of country contacts from which procurement data and source guidance was requested.

Slovenia

- Institute for Economic Research, Ljubljana, Slovenia
- National Health Insurance Institute
- Public agency for medicines and medicine devices
- Ministry of Public Administration, Public Procurement Directorate
- Procurement portal www.enarocanje.si
- WHO country office Slovenia

The system of determining medicines prices in Slovenia starts with external reference pricing (JAMP) and continues with internal reference pricing (generic and therapeutic). These prices are published and publicly available from HIIS. Specific confidential price reduction agreements are always concluded between HIIS and authorisation holders, these prices are not publicly available.

For prescription drugs, the national database (www.cbz.si) lists pre-discount prices. For generics these are realistic, and the lowest price is reimbursed by the NHI. Patented and expensive medicines are subject to discounts to the NHI, on average 20% lower than database prices. Prices for pharmaceuticals were extracted manually from www.cbz.si using ATC codes.

Central procurement is a relatively new phenomenon in Slovenia. Pooled hospital procurement of high cost medicines was put in place in 2013 by the Ministry of Health, including 95 active substances at level 5 ATC. This system worked well until 2015, at which time the intention was to extend the system to all medicines in hospitals, but due to a number of issues, the system has not yet been implemented. The central government has attempted to collect data on the best prices achieved in hospital procurement, this should be successfully anticipated later in 2017. Currently hospitals are undertaking procurement individually. Pooled procurement of medical equipment (e.g. gloves, needles, some surgical materials, etc.) is being gradually expanded (EC 2016; WHO 2016).

The authors have requested procurement data from hospitals directly. Additionally, the central government has attempted to collect data on the best prices achieved in hospital procurement, but this has not yet been successful, consequently this line of enquiry was not pursued.

Poland

- Jagiellonian University, Krakow, Poland
- WHO country office Poland

Hungary

- WHO country office Hungary
- Pharmaceutical policy expert

In Hungary, public procurement data is confidential to avoid the country's prices being used in international reference pricing.

Moldova

- AGENȚIA MEDICAMENTULUI ŞI DISPOZITIVELOR MEDICALE (Medicines and Medical Device Agency Moldova)

In Moldova, prices are available through two sources. Public tenders are carried out by Centrul pentru Achiziții Publice Centralizate în Sănătate (Center for Centralised Public Procurement in Health, capcs.md/licitatii-desfasurate), these are for medicines for public health programmes. Data from this agency includes both tenders which have been successfully awarded, and tenders for medicines which were not filled.

For 2016 the data was a mix of Excel and PDF files, some with ATC codes but the majority without. Data was extracted manually from these Excel and PDF files, and stored in the master data file under "Moldova Procurement Orders" with references to the appropriate procurement orders by identification number.

Ex-factory prices approved by the regulator are also available. These are subject to mark-ups through the supply chain, so the regulated ex-factory price should be considered a base price, and a mark-up of 15% was added. If more than two products were registered in Moldova, the cheapest was used. If the exact presentation was not found, an approximated price was calculated using existing data if possible (for example: Enoxaparin was available in Moldova in 8,000 IU vial size. In Ukraine, the desired vial size was 10,000 IU. In this case, the Moldova price was adjusted by dividing by 8,000 and multiplying by 10,000 to arrive at an approximate price for 10,000 IU). Approximations were only used if the correct formulation was not found – in cases were several formulations were present in the Ukraine data (for example 5mg, 10mg and 25mg Methadone) and only one was present in the comparator data, approximations were not calculated for the remaining formulations.

Belarus

- WHO country office

To obtain data on medicines procured by the public sector in Belarus, an official letter to the Ministry of Health of the Republic of Belarus must be sent addressed to the Minister of Health. The Minister can authorize relevant specialists/organizations to provide such data, but without approval, data cannot be accessed.

Bulgaria

- WHO country office
- Multiple pharmaceutical policy experts

Procurement data is limited both in quality and quantity in Bulgaria. The only available data is from the National Health Insurance Fund (www.nhif.bg/web/guest/218), which publishes monthly reports on volumes of outpatient medicines only, as well as total expenditure by medical condition. The granularity of this data is not sufficient for the present evaluation.

Romania

- WHO country office Romania
- Pharmaceutical policy expert

List prices of prescription medicines in Romania are available from the National Health Insurance House (preturi.ms.ro/interogare.php) and public procurement data is available from the Ministry of Health (www.ms.ro/centralizatorul-achizitiilor-publice) , however the latter only includes headline product (e.g. "Supply of paediatric hepatitis B vaccine"), contract value and the name of the successful bidder (no volume or detailed data). Consequently, only list prices are used for comparison.

Slovak Republic

- WHO country office Slovakia
- Multiple pharmaceutical policy experts

No data could be obtained for the Slovak Republic.

Czech Republic

- WHO country office Czech Republic
- Pharmaceutical policy specialist

No data could be obtained for the Czech Republic

Latvia

- WHO country office Latvia
- State Agency of Medicines Latvia

The WHO country office in Latvia was contacted, who referred to the State Agency of Medicines of Latvia [Zāļu valsts aģentūra [ZVA], www.zva.gov.lv/]. ZVA provided volumes of vaccines, immunoglobulins and sera procured centrally, but was unable to provide prices according to national legislation. No further products are centrally procured in Latvia, and consequently the country is not considered further for analysis.

Armenia

- WHO country office Armenia
- Arax Hovhannesyan, World Vision
- Ministry of Health, Armenia

Data on medicines procured by all public departments in Armenia [Ministry of Health, National Security Service, Ministry of Defence, etc.] are available publicly at the Ministry of Finance website [www. armeps.am/ppcm/public/procurements]. Apart from centrally procured medicines, individual health facilities can announce tenders which are published on the procurement website [www.gnumner.am/am/home.html], however the results of these tenders are not published and cannot be accessed.

Procurement data from Armenia does not have strength of formulation or quantities listed, so matching could only be done on ATC and product name.

Kyrgyzstan

- WHO country office Kyrgyzstan

No data could be obtained from Kyrgyzstan.

Kazakhstan

- Supplied by Crown Agents

International agencies and organisations

- WHO Regional Office for Europe
- WHO European Observatory on Health Systems and Policies
- UNDP
- WHO Collaborating Centre for Pricing and Reimbursement (Gesundheit Österreich)
- World Bank

Contacts across organisations were approached for additional assistance, however no additional data could be obtained.

[9] The Romanian website was not fully functional for the duration of data collection. The link to download the list price database did not work, however an alternative link to the resource on the official website was identified by web search. It cannot be determined whether this is the latest version of the website, and the contact details given on the website do not work. In addition, the database fields are not adequately described, it is assumed the lowest price represents list price without VAT or mark-ups.

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