IMS INSTITUTE FOR HEALTHCARE INFORMATICS

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Understanding the pharmaceutical value chain

Introduction

The role of medicines in healthcare systems globally is becoming more important as innovative treatments become available to address unmet clinical needs at the same time that economic development and the imperative of universal health coverage become drivers of expanded access. In 2014 it is estimated that $1 trillion will be spent on medicines of all types globally.[1]

Understanding the full set of activities that occur prior to a patient receiving a medicine provides useful perspective on the pharmaceutical value chain, including the specific elements of that chain, the value that is provided at each step and the cost components that are incurred. These can differ both between and within markets depending on the type of medicine, channel of distribution, reimbursement regulation, or geographic region. Country comparisons underscore the extent to which health systems differ in a multitude of ways and for many reasons.

The purpose of this report is to advance the understanding of the pharmaceutical value chain and specifically to:

1. Describe the elements of the medicine value chain and outline factors and costs that contribute to the difference between the net price a pharmaceutical manufacturer receives for a drug and the final amount paid for the drug by the end user.

2. Quantify the price build-up for specific therapy areas and countries.

3. Illustrate the diversity of approaches and costs associated with the value chain through case studies.

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Elements of the medicine value chain

Ensuring that patients receive the correct medicine, at the appropriate time and from a convenient location, requires a complex value chain involving three major components:

1. **Manufacturing of the medicine:** In order in produce a medicine, a number of steps are involved, from the initial research and development phase, to gaining regulatory approval which allows a medicine to be sold in a market to the final commercialization phase. The specific steps and requirements will differ between types of medicine, manufacturers and countries.

2. **Distribution to the dispensing point:** This step includes the transportation and handling of the medicine from the manufacturer to the end user, whether this is a retail pharmacy (retailer), hospital or dispensing doctor. The complexity of this journey will differ depending on manufacturer location, the need for importation of the medicine, the nature of special handling requirements, and the geographic location of the end user which will vary between large urban centres and remote rural villages.

3. **Dispensing to the end user:** Providing the correct medicine dosage and form, to the right patient, in a convenient and timely manner is the final step in the value chain. This step can also involve a number of additional activities, including checking for potential interactions, providing advice, and processing reimbursement claims, each of which is intended to ensure the patient receives the full benefit and value from the medicines they receive.

In defining and measuring the elements of the value chain, an initiative between the World Health Organization (WHO) and Health Action International (HAI) has established a useful methodology to classify the level of medicine price build-up at each step.[2] According to the WHO/HAI there are six key components which contribute to the price build-up of medicines (see Exhibit 1). These are as follows:

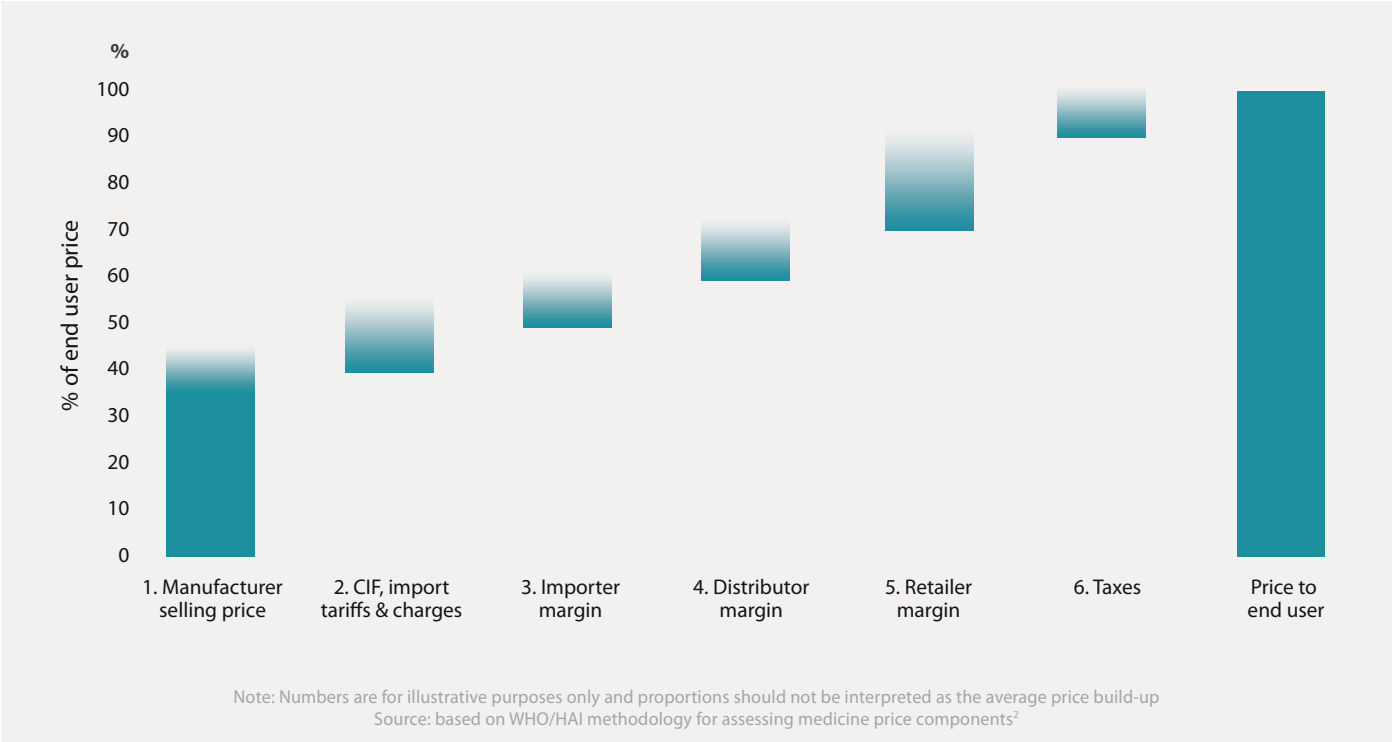
1. **Manufacturer selling price:** the net acquisition cost of the medicine from the manufacturer, reflecting all discounts, rebates or other reductions in price.

2. **Cost, insurance, freight charges (CIF), import tariffs and charges:** the cost of importing a finished pharmaceutical product (FPP) or active pharmaceutical ingredient (API) into a country.

3. **Importer margin:** applied by the importer who is tasked with procuring and receiving delivery of imported goods.

4. **Distributor margin:** applied by wholesalers and sub-wholesalers to perform the logistical role of storing and subsequently transporting medicine to point of sale.
5. **Retailer margin:** applied by retailers in the final step of the distribution chain, the point at which medicines are dispensed to patients.
6. **Taxes:** the final component of the price build-up which can include both national and regional taxes.

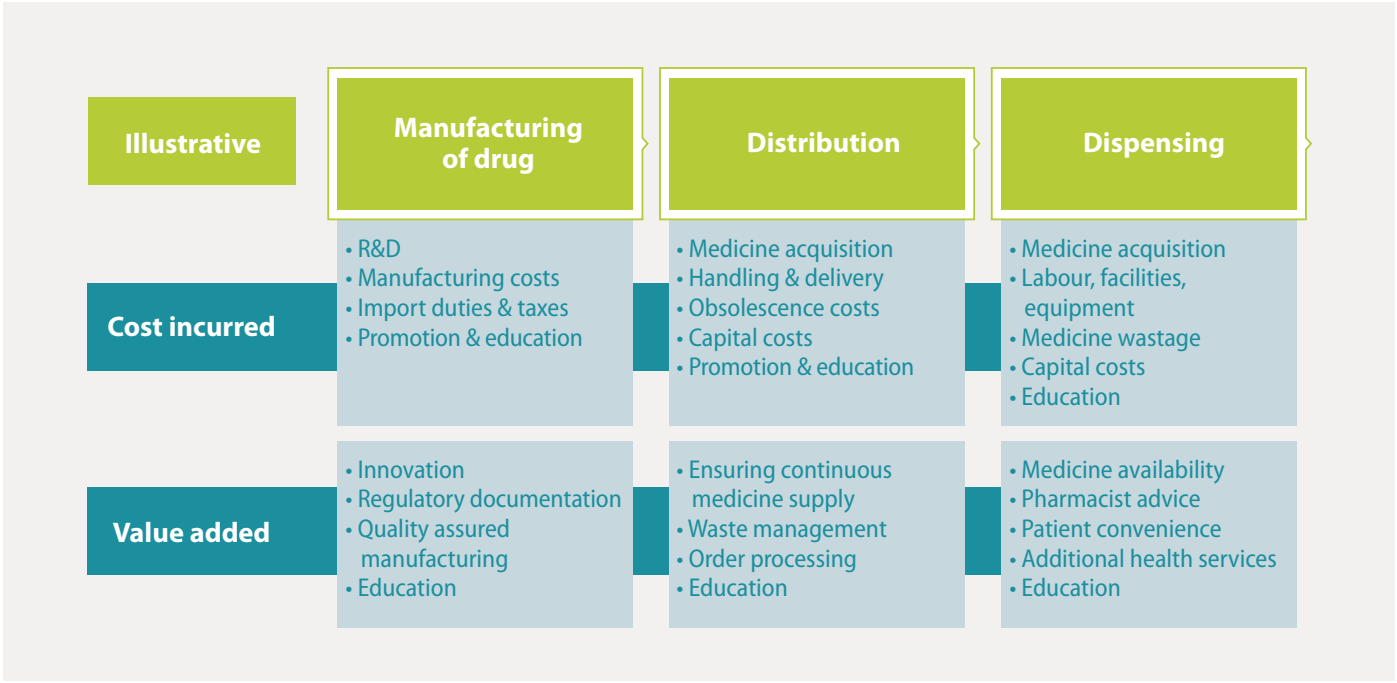
Exhibit 1: Illustration of the WHO/HAI pharmaceutical price build-up



Note: Numbers are for illustrative purposes only and proportions should not be interpreted as the average price build-up
Source: based on WHO/HAI methodology for assessing medicine price components[2]

The combination of the value added at each stage as well as the costs incurred provides the basis for understanding the pharmaceutical value chain. Exhibit 2 summarizes the potential costs incurred and value added; however, the degree to which these occur in specific markets will differ depending on the sophistication and efficiency of the supply chain and common commercial practices.

Exhibit 2: Breakdown of the medicine value chain by stakeholder



Methodology, approaches and sources

This study has been designed to focus on a set of seven countries representing diversity in their regional location and health systems: Brazil, India, Indonesia, Kenya, the Netherlands, Russia and South Africa. The Netherlands was selected as an efficient, high income market that can provide a useful reference point for the remaining countries.

Five therapeutic areas that are important in all health systems were selected for detailed analysis: antibiotics, anti-diabetics, anti-epileptics, anti-hypertensives and respiratory agents. Medicines in these therapy areas are typically dispensed through retail pharmacies, which are the focus of this study in terms of dispensing location. Those medicines used in hospital settings are often regarded as a fixed cost and not allocated by product, making it impossible to assign a full end user price for the medicine. Furthermore, these medicines are normally subject to business to business price negotiations, resulting in a more unpredictable and higher variation of non-transparent discounts between products which cannot be accurately estimated for in pricing analysis.

In each country and for each therapy area, a detailed analysis of the different types of medicine used was undertaken, based on IMS Health sales audits. These audits measure the volume of monthly sales of medicine into and/or out of retail and hospital pharmacies based primarily on information gathered from retailers, hospitals, distributors and manufacturers. In most cases a sample of all transactions is captured and projected to a national total.

The IMS Health country sales audits were used to determine the mix of different types of medicines that may be the basis for different pricing or margins in each step of the value chain. For example, in some countries protected brands, no longer protected brands and generics may each have a different margin applied as part of the price build-up. Similarly, imported and domestically manufactured goods are often subject to different levels of tariffs or taxes. Since the IMS Health audits capture data at the most granular level, this enables appropriate application of different pricing and margin at the pack level, based on the actual mix of product flow during the 12 months ending December 31, 2013.

To determine pricing levels for each product type, a range of sources were used. These included IMS Health sales audit data which is typically based on official or list price. Adjustments to these values were made to account for discounts and rebates which were assessed based on local market knowledge by IMS Health and interviews with local stakeholders participating in the pharmaceutical value chain. In those cases where a range of values was captured for specific data points, the mid-point was selected for inclusion in the analysis. For other price levels, publically available information, official margins/mark-ups, or best estimates of industry margins/mark-ups were applied on a pack by pack basis and bridged to the IMS Health data.

In order to accurately assess end user price in an un-regulated market such as the Kenyan private retail market, a different approach was required. IMS Health Kenya surveyed 60 private retail pharmacies in the greater Nairobi area to calculate the median end user price for 30 packs in 3 therapy areas (antibiotics, anti-epileptics and anti-hypertensives). This information was then bridged to the volume and trade price data available from the IMS Health Kenya National Indicator Report and information gathered through interviews with market stakeholders provided the means to create business rules to model margins and additional price levels.

In reporting the results of this analysis, an index value of 100 was assigned to the end user price. Prices for each component of the value chain – manufacturer price, import tariffs and charges, distribution margin, retailer margin and taxes – were calculated relative to the end user price of 100. In addition, an aggregate value for each country was calculated by weighting each individual therapy class average based on the total cost of each therapy class in that country.

The approach taken in this study enables a clear understanding of the value chain price levels and margins relative to the end user price. It does not, however, reflect differences in absolute price level or absolute amounts received by each stakeholder in the value chain.

Manufacturing of the drug

Broadly speaking, there are two categories of manufacturing required for drug production: API manufacturers which produce the raw ingredients used in medicine; and finished form manufacturers which produce the final product to be sold to market and consumed by the patient. Finished form manufacturers can also be categorized as innovators or generic companies.

Innovator companies invest in research and development in order to discover and bring new medicines to market. Due to the large financial investment involved, these medicines receive a period of market exclusivity. At the point this expires, generic manufacturers are able to manufacture and bring to market generic versions of the original brand molecule which contain the same active substance, produce the same therapeutic effect and are manufactured to the same quality as the original product.[3]

Determinants of manufacturer price

Unlike prices for other products, medicine prices are set by pricing policies which are unique to each country. For example, in Russia the maximum ex-manufacturer price for drugs on the essential drugs list is based on product type and whether the product is manufactured in Russia. In contrast, in Brazil, trade and end user prices are regulated and the price at which the pharmacy purchases medicine (plus VAT) must not exceed this regulated trade price, leaving wholesalers to negotiate their discounts with the manufacturers.

The official (regulated) or negotiated price however, is not always the price that the manufacturer receives. There are a number of factors which impact the level of a manufacturer's net price. One of the largest is trade discounts which are offered by manufacturers to wholesalers or pharmacies and are negotiated in business to business transactions. These discounts vary in size depending on the purchasing power of the buyer and level of competition, but as a general rule of thumb generic manufacturers often offer much larger discounts in order to secure volume share. For example in Brazil generic manufacturers may offer discounts of over 50% from list prices, while originators may offer discounts in the range of 10-15%.

Costs incurred by manufacturers

For originators, the first and most expensive step of bringing a new medicine to market is the drug discovery phase, which identifies new chemical or biologic entities that have the potential to advance the current standard of disease treatment.

Following the discovery phase, potential candidates are subject to rigorous testing through clinical trials, which many will fail to complete. Those that achieve their desired endpoints are then subject to a regulatory phase, whereby clinical trial results and details of the manufacturing process are submitted to regulatory agencies to evaluate the safety and effectiveness of medicines, before they receive approval to be launched on the market. In total, this development phase can last up to 13 years and is becoming more difficult as the diseases that are being targeted are becoming increasingly complex and therefore require even greater investments. It is difficult to put an exact figure on the cost involved in bringing a medicine to market, as this will differ between the type of drug, level of innovation and magnitude of risk involved.[4]

Once a new medicine is available on the market there is then a cost involved in order to promote and educate key stakeholders about the product and the benefits it can bring to patients.

In contrast, generic manufacturers normally have relatively low development and manufacturing costs. Their main means of promotion is through trade incentives, offering larger discounts to secure volume sales.

Value added by manufacturers

The value added from the generation of new medicine is first and foremost that which directly relates to patient treatment. Such advances may tackle a new disease or indication, improve health outcomes, treatment safety, tolerability and/or side effects and the ability to better treat specific patient sub-populations. In addition, there are wider benefits to the health system such as decreasing the burden on other health resources and overall societal benefits such as enabling people to return to work.

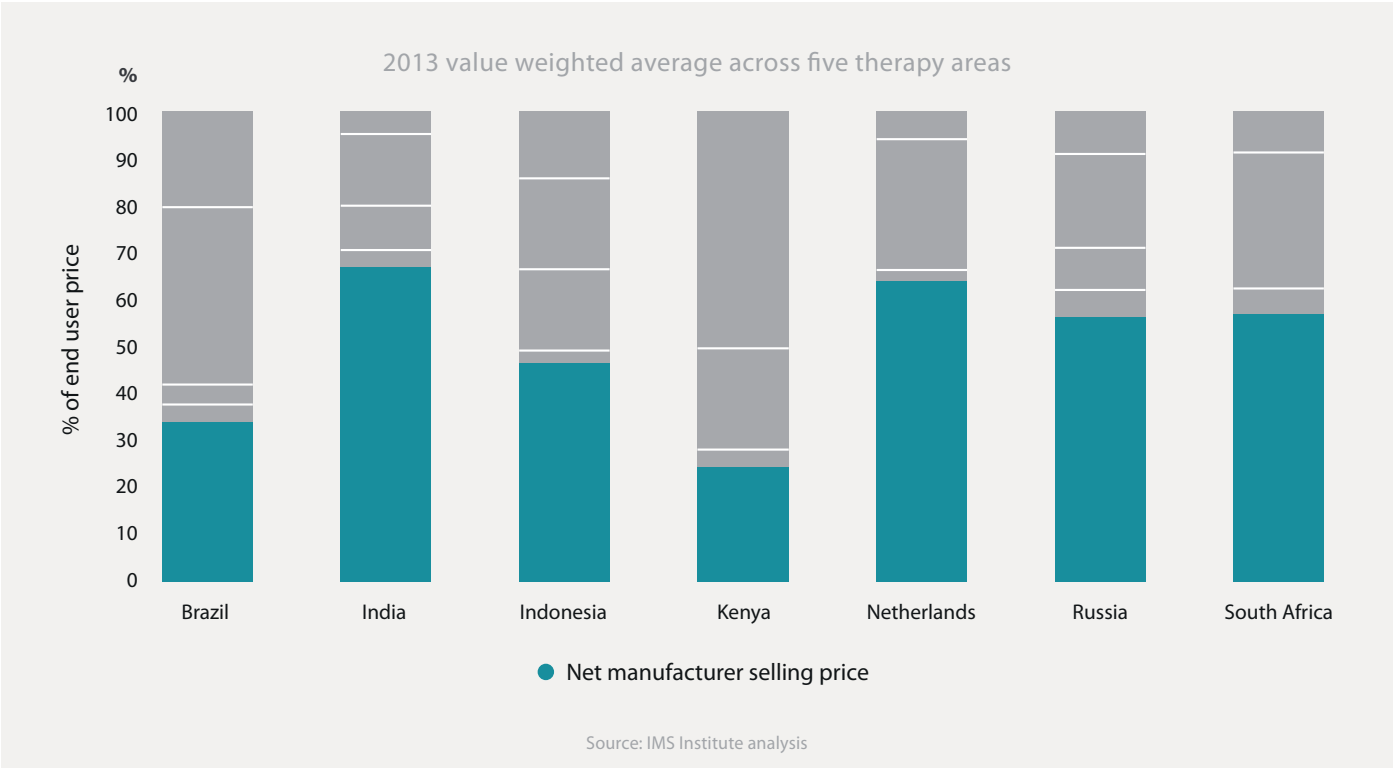
Although the main cost involved in drug discovery is R&D, the value added is not only the medicine produced. On top of this, there is scientific knowledge and technological advancements which have the potential to diffuse to and advance other areas of industry. In addition, the promotional and educational efforts made on the ground can help those working directly with patients to ensure the most appropriate, effective and highest quality standard of care is offered.

The value added from generic manufacturers is that of introducing competition into the market, which in an efficient market can help payers achieve savings on older treatments in order to invest in new ones or offer lower cost alternatives to patients in out-of-pocket markets.

Levels of manufacturer cost

Manufacturer costs relative to end user price vary widely across the countries studied, and range from 24% in Kenya, to over 64% in the Netherlands (see Exhibit 3). At an individual therapy class level, the range was also significant in certain countries. For example, in Brazil the average for antibiotics was 31% of end user price, but 42% for respiratory drugs, while the Netherlands saw the widest variation with 38% for antibiotics and 78% for respiratory. There can also be differences in total therapy drug costs based on the mix of different types of drugs which have different costs relative to end user price. For example, in South Africa manufacturer selling price for generics typically average 52%, versus 63% for protected branded products and 57% for un-protected branded products.

Exhibit 3: Net manufacturer selling price



Source: IMS Institute analysis

Distribution

The distribution of medicines in most markets is carried out by importers and wholesalers, which act as a link between manufacturers and retailers to ensure the continuous supply of medicine, regardless of the geographical location and portfolio of medicine required.[5] For those medicines which are imported, there is often an additional step from the importer who organises the logistics of bringing the medicine into the country which are then transferred to the wholesaler for domestic distribution. In some cases the two entities are vertically integrated, decreasing the number of steps in the distribution stage of the value chain. In others scenarios, particularly when supplying to rural regions, wholesalers may engage sub-wholesalers, thereby increasing the distribution complexity.

Determinants of distributor margin

Distributors are traditionally paid on a regulated margin basis set as a fixed percentage of the price. In some countries, this has become a regressive margin with a lower percentage applied for more expensive packs. In markets with regulated margins, discounts from the manufacturer might also exist; in other countries and for some categories of products, discounts may not be allowed. Generally, discounts are given when the wholesalers can influence which manufacturer's product is sold, meaning that they are more common on products without patent protection (no longer protected originals or generics). Some countries have moved to a "fee-for-service model" in which the margin for the wholesaler is negotiated between the distributor and the manufacturer.

Costs incurred by distributors

Pharmaceutical distribution needs to meet the logistical challenge of serving a large number of pharmacies with products sourced from many manufacturers and often in a short period of time. At the same time regulation may require a certain level of distribution standards to ensure that medicines are handled according to Good Distribution Practice.

The distributor invests in inventory to be able to service its customers. The distributor might typically be holding one to two months' worth of inventory and the cost to carry inventory includes warehousing cost, capital cost, and obsolescence. The working capital, both for the inventory held and supply stock to pharmacies is done on a credit cycle which can range from 28 days in the Netherlands to 120-150 days in Kenya (90 days to get paid by the retailer and two months of stock holding). For the wholesaler this results in additional costs from interest and the risk that pharmacy repayment may be delayed or in a worst case scenario, default on their obligations. Furthermore, in countries such as Kenya, the importer is unlikely to pay for goods with domestic currency and will be impacted by the financial cost of acquiring foreign currency and any fluctuations in exchange rate when purchasing medicines from manufacturers.

Depending on what scripts pharmacies receive, they can place orders with wholesalers up to three times a day. Ordering can be done over the phone or electronically depending on the sophistication of the infrastructure within the country. Selecting the products under order can be manual or highly automated and may also require a quality assurance step. The cost of delivery is highly dependent on the frequency and volume of medicine delivered. The more often a wholesaler is required to make trips to a retailer, the higher the cost for the wholesaler.

Value added by distributors

The key function of wholesaler is to resolve the challenge of being able to meet varied and un-predictable patient needs, by supplying medicines from manufacturers, without requiring the retailer to hold large inventories on-site. A second major function (and cost) is to provide the necessary working capital for pharmacies to allow them to purchase the required drugs, before receiving end user payment. Finally, in some markets wholesalers provide a broad set of commercial support to independent pharmacies to improve the operation of the business, such as category management (retail initiatives to help grow the pharmacies business), sales training, accounting and continuing education for pharmacies.

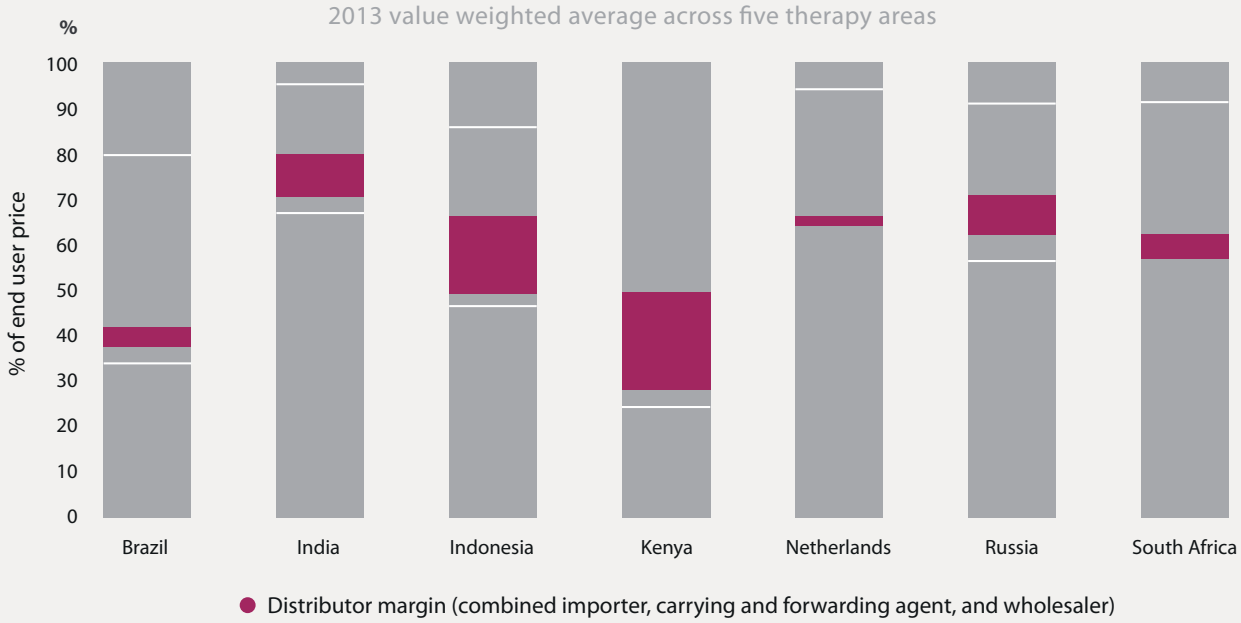
Levels of distribution margin

Across countries the total distribution margin can vary from 2% of the end user price in the Netherlands to 22% in Kenya. There may however, be a need for these types of differences. For example longer payment cycles for pharmacies in Kenya and a greater reliance on labor force versus wholesalers in the Netherlands means that operating and labor costs are likely to be substantially higher. For example, Kenyan wholesalers will run call centers to deal with pharmacy orders, while in the Netherlands much of this is automated.

In India, under the Drugs Price Control Order 2013, both the wholesaler and retailer margins are differentially regulated based on essential drug classification, with maximum margin for distributors at 8% for scheduled drugs and 10% for non-scheduled drugs.

In Russia, distributor margins are regulated for products on the essential medicine list and differ according to the geographic location in which the medicine is purchased, as regional authorities are required to calculate maximum mark-up for both wholesalers (and retailers) for products on the essential drugs list (see Exhibit 5).

Exhibit 4: Distributor margin



Source: IMS Institute analysis

Exhibit 5: Regulated margins for products on the essential drugs list in Russia

Ex-manufacturer price	<50 RUR		<50-500 RUR		>500 RUR	
Region	**1. Urban**	**2. Rural**	**1. Urban**	**2. Rural**	**1. Urban**	**2. Rural**
Stockists or distributors	20%	18%	15%	14.5%	10%	11%
Retailers	32%	70%	28%	61%	15%	55%

Source: http://www.mosgorzdrav.ru/mgz/komzdravsite.nsf/va_WebPages/page_npa (Moscow); http://kraszdrav.ru/assets/documents/2014_09_30_bf08.10.2014%2009:04.rar (Krasnoyar Krai)

Dispensing to the patient

Determinants of retailer remuneration

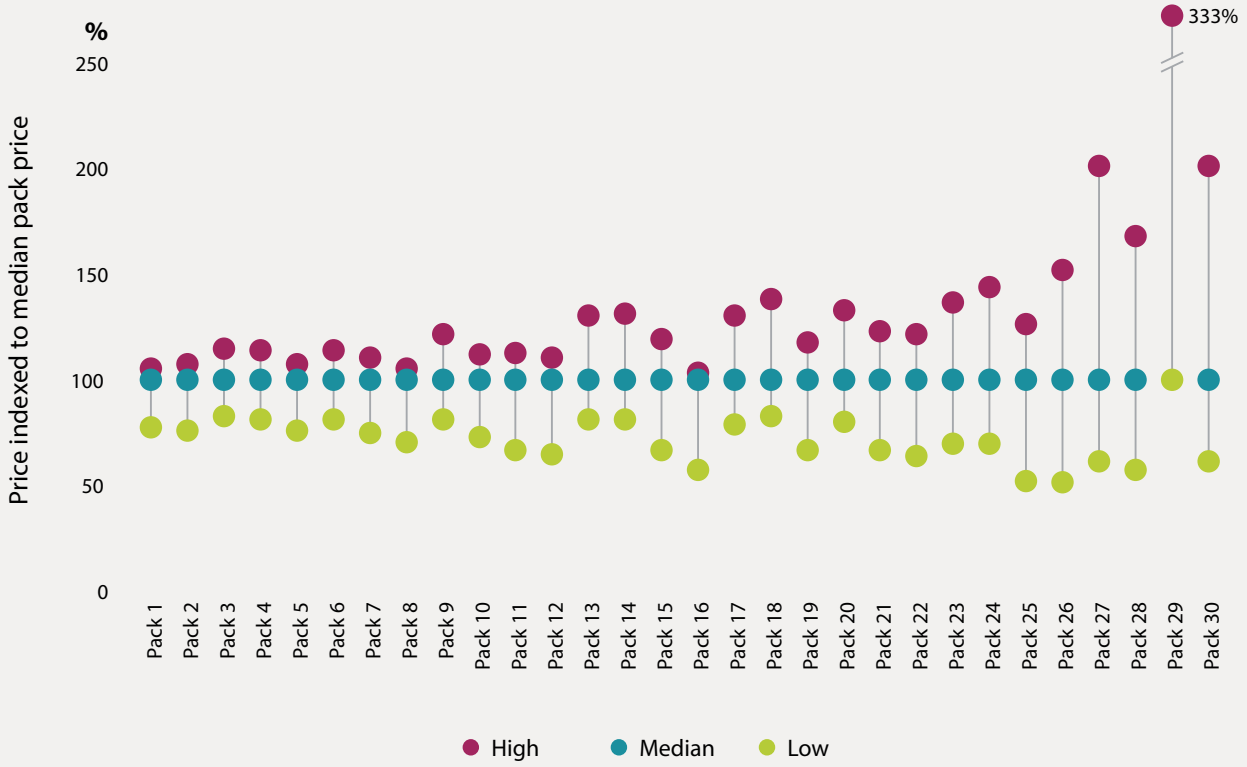
Retailer remuneration is determined by two key factors. Firstly the level of discounts negotiated from the wholesaler, which determines the acquisition cost of the medicine. Secondly, the margin made on the acquisition cost of the medicine paid by the end user.

Mark-up/margin can be set by free pricing, a regulated fixed percentage of the acquisition cost and/or a regulated fixed dispensing fee. The most common method of regulation used in the markets studied was the percentage mark-up/margin model. South Africa uses a mixture of a fixed and percentage variable component, while the Netherlands is the only country where remuneration is a fixed fee per prescription (regardless of the number of packs dispensed).

Competition and purchasing power

Retail dispensing fees in many of the markets analysed - Brazil, India, Russia and South Africa - are capped to help regulate the end-consumer price. However, to differentiate themselves from competition, pharmacies may charge below this maximum either by foregoing or reducing the dispensing fee (South Africa) or passing on discounts acquired from the wholesaler to the patient (Brazil). This means that the prices of drugs are often well below the official regulated end user price. However, the ability to discount varies between types of pharmacies. Those which are able to negotiate high discounts from wholesalers – normally the large chains- are subsequently able to offer cheaper prices to patients than smaller independent pharmacies which are unable to run on smaller margins. This means that there is potential for variations in the end user price as demonstrated in the Kenyan market, see exhibit 6.

Exhibit 6: Range of prices to end consumer in Kenya's private retail market



Source: IMS Health Kenya – retail pharmacy survey

In some markets, retailers make a loss from selling prescription medicine, profit is instead generated from additional over-the-counter and health and beauty sales. An alternative business model finds other retailers which are very much focused on prescription drug dispensing to drive their business profitability.

Costs incurred by retailers

Retailer costs can be split into those which are fixed and those which vary depending on the level of business.[6] Fixed costs include the cost of labour (pharmacist, etc), facilities, equipment (including information technology), utilities and insurance. Variable costs include product acquisition cost and the volume being purchased; medicine wastage resulting from expiry or damage; and the capital cost of inventory.

The costs of running a retailer in a rural location compared to an urban area can be quite different. The size of a retailer in a rural location is often much smaller, clientele is scarcer and often poorer, both of which reduce the opportunity to recover fixed costs.[6]

Value added by retailers

One fundamental role of a retail pharmacist is that of logistics: being able to dispense the right drug, to the right time at the correct dosage. This in itself is an over-simplification as this task also entails correcting prescribing errors, processing the prescription, labelling etc. and advising and educating patients on the safe use of prescribed drug, contraindications, interactions and side effects. For example, some pharmacists in the Netherlands suggest that 15% of prescriptions require an intervention from the pharmacist, e.g. adjusting dose to patient weight, change of label due to preference etc.[7]

In recent years, medicine shortages have become a global issue.[8,9] Even in a market known to be one of the most efficient in Europe, reports from the Netherlands indicate that 3-5% of drugs are un-available at the time they are ordered.[10] The impact of medicine shortages can range from patient inconvenience to adverse health outcomes and generally requires patients to switch medication. To mitigate the impact of medicine shortages on patients, pharmacists dedicate a substantial amount of time either sourcing drugs or finding alternatives.[11]

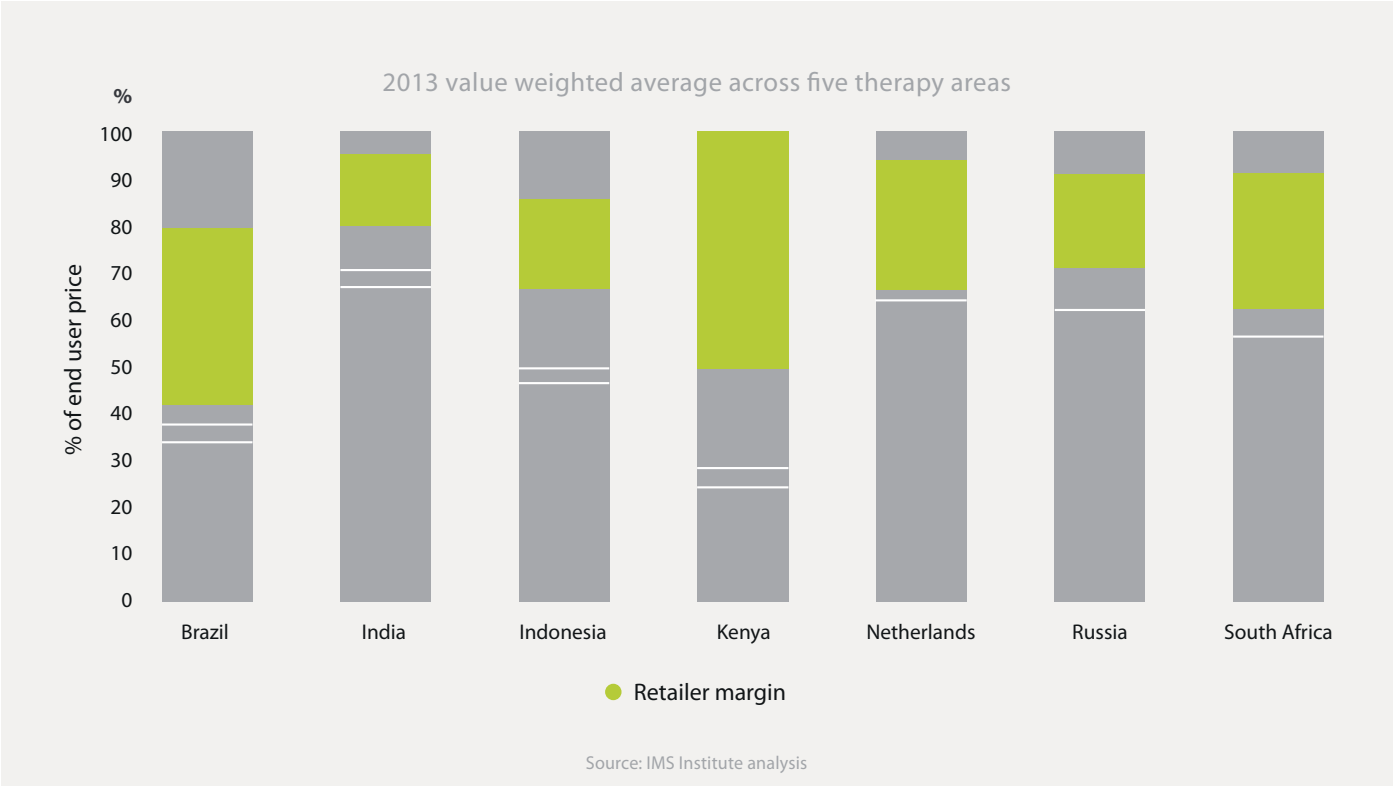
As retailer business models evolve, additional services are becoming more common and the role of a pharmacist is no longer just about medicine provision, but the provision of services which help maintain patient health.[12] These can include training on the administration of medications including inhalation and injectables, blood pressure testing and measurement of blood glucose and triglyceride levels, education on disease management through non-medical means such as nutrition and other lifestyle factors, and improving patient adherence through education and patient monitoring.[13]

Such initiatives have the potential to improve patient health outcomes and reduce health service utilization, which can ultimately reduce the burden on the overall health system.[12]

Levels of retailer margin

The average level of retailer margin ranges from 15% of end user price in India and 50% in Kenya (see Exhibit 7). The magnitude of retailer margin can also differ between therapy area and product types depending in part on the level of regulation or negotiation that retailers have with wholesalers and manufacturers.

Exhibit 7: Retailer margin

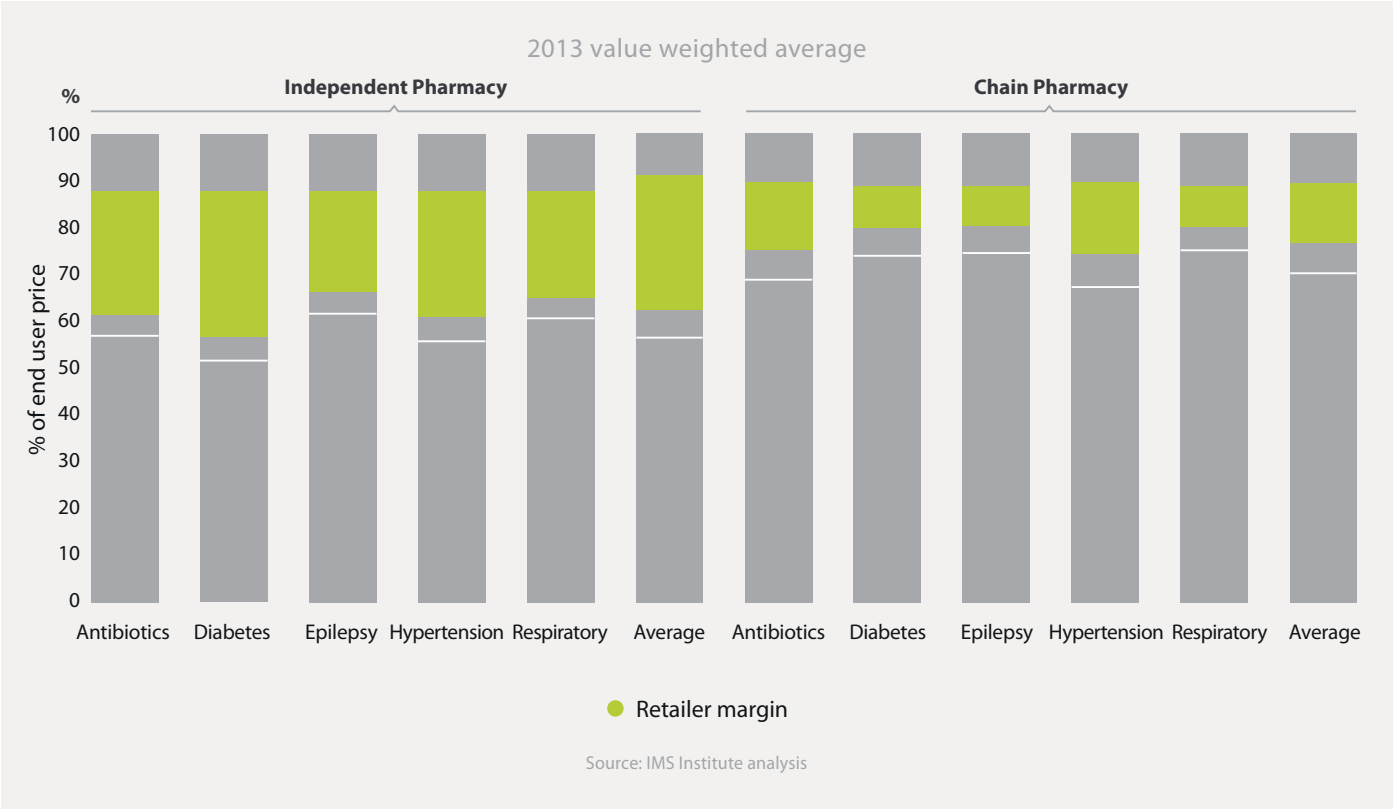


Source: IMS Institute analysis

For example, in Brazil in 2012, wholesalers on average provide discounts to pharmacies of approximately 60.4% of the regulated trade price for generics, 30.3% for branded originals, and 16.2% for off-patent branded originals.[14] Similarly in the Netherlands, the implementation of a fixed dispensing fee means that in areas where there are largely patented protected brands, these more expensive medicines make up a smaller proportion of the total price build-up, compared to their lower cost generic counterparts.

In South Africa, where there is a combination of chain and independent pharmacies, differences in the price build–up can vary drastically(see exhibit 8). While there is a maximum margin in place, for larger chains a lower price can be offered to patients without negatively impacting business viability.[15] Furthermore, while trade discounts are prohibited in South Africa, logistics providers pay fees to the pharmacy under the guise of 'marketing fees' and 'data fees' which act as incentives to purchase from certain logistics providers, or to stock certain manufacturers' products as priority. The Department of Health is currently proposing to ban such practices, as well as reviewing retailer dispensing fees to help adjust for the loss retailers receive from such practices.

Exhibit 8: Retailer margin South Africa



Source: IMS Institute analysis

Government tariffs, taxes and charges

Taxes have been shown to be one of the larger components contributing to the price build-up of medicines.[16,17] The most prominent of these in certain markets is the import tariff, which is a customs duty imposed by importing countries on the value of goods brought in from other countries".[17] Import duties are used to raise government revenues and help domestic producers by providing a price advantage versus international competitors.[16] Another form of taxation is medicine sales tax, commonly in the form of value-added tax (VAT). Similarly to import tariffs, VAT is applied in different magnitudes between countries and can be applied at both a national and state level. Exhibit 9 summarizes the import tariffs and national sales taxes applied in each market.

In addition there are many examples of country specific taxes charged. For example in India under the Customs Act 1962, a 3% Education Cess is applied on the aggregate of customs duties.

Exhibit 9: Summary of medicine import tariffs and national sales taxes[i]

Country	Customs duty (MFN duty rate[ii])[18] (unless otherwise indicated)		National sales tax
	Finished form products	API's	
Brazil	9.8%	9.5%	Average 18%
India	10%	10%	Average 5%
Kenya[19]	10%	0%	0%
Indonesia	4.3%	4.2%	10%
Netherlands	0%	0%	6%
Russia	10.2%	0%	10%
South Africa	0%	0%	14%

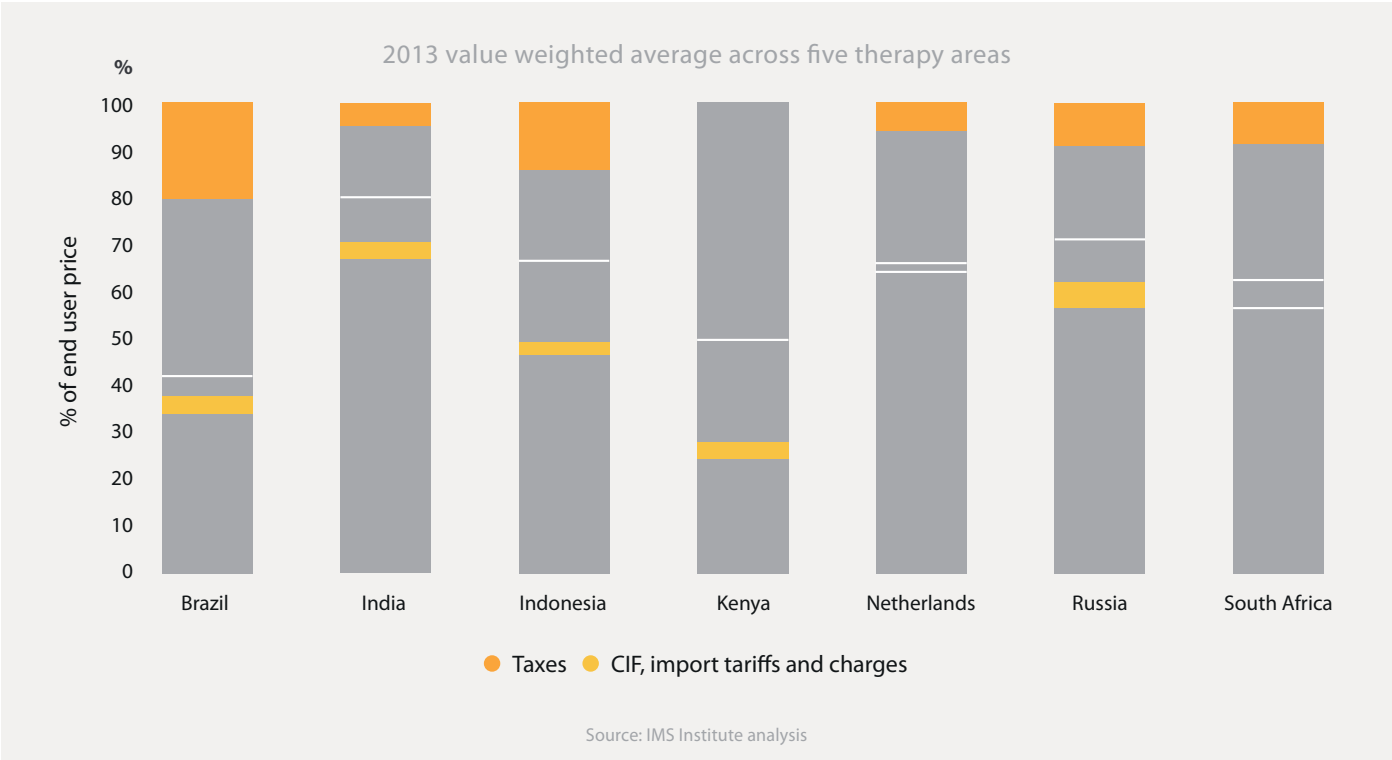
[i] Latest data available

[ii] Most favoured nation (MFN) duty rate is that which each country has agreed to offer all countries which are member of the World Trade Organization. Countries with other trade agreements in place may have rates in place that are lower than the MFN. The rates stated in this table are an average of all Ad valorem duties under the HS code 3004 for finished form pharmaceuticals and 3003 for API's. Any conclusions based on this data are the responsibility of the authors and do not necessarily represent the opinion of the WTO.

Levels of government tariffs, taxes and charges

Across countries the level of total government tariffs, taxes and charges can vary from 6% of end user price in Kenya to 24% in Brazil. Aside from Kenya, where sales tax in general does not apply to medicine (there are some exceptions to this rule), tax is the larger of the two components, (see Exhibit 10).

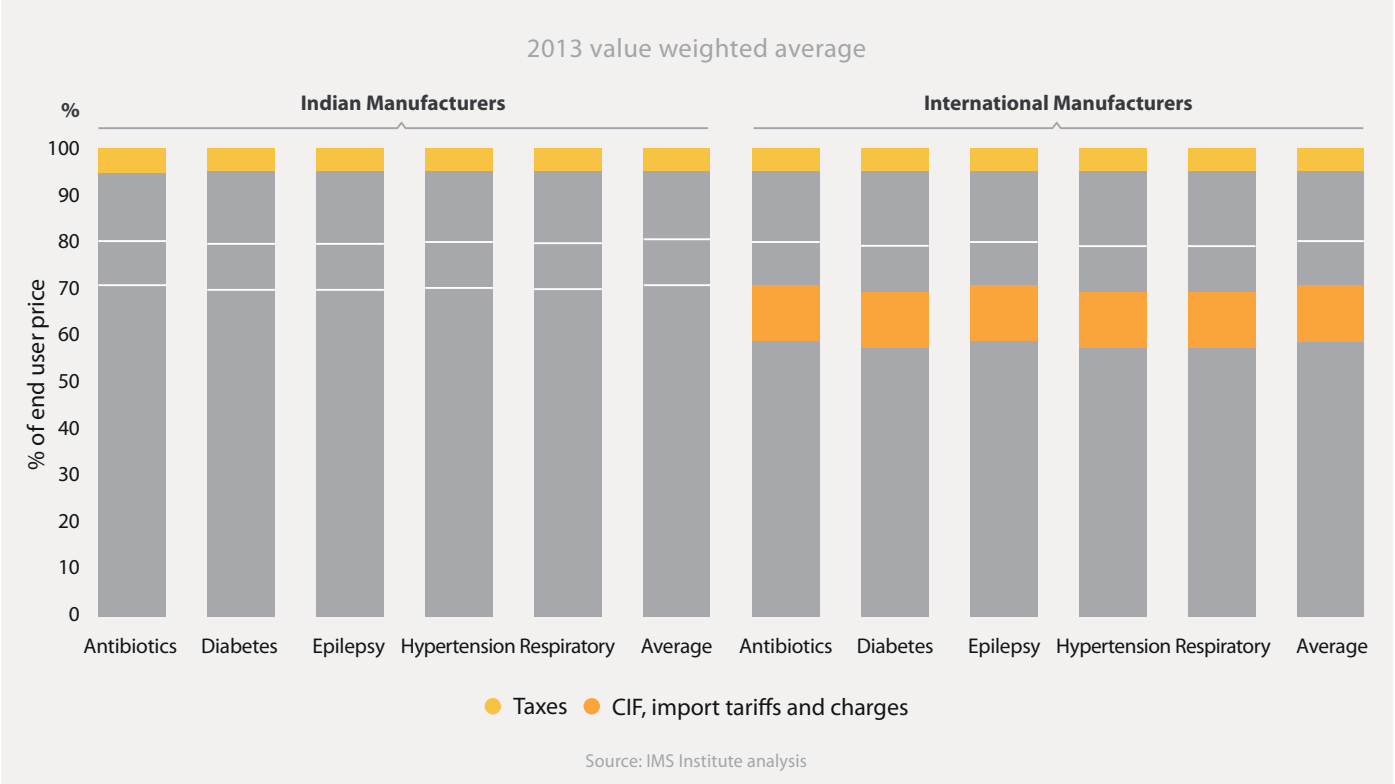
Exhibit 10: Government, taxes, tariffs and charges



Source: IMS Institute analysis

Variation in the impact of taxes and tariffs between countries occur because of different approaches taken by governments to raising revenue and different mixes of business that attract these costs. For example, tariffs applied to imported goods but not to domestically manufactured goods can have a large impact on the overall cost structure in a country. In India, import tariffs contribute about 11% of the end user price for international manufacturers' products (see Exhibit 11) but do not impact products sourced from the domestic production of API's and finished form products.

Exhibit 11: Government, taxes, tariffs and charges in India



Source: IMS Institute analysis

By contrast, in Kenya, where the majority of medicine is imported from India the impact on end user price at the aggregate level is much larger.

For sales tax, differences of the impact on price build-up most commonly relates to whether a drug is deemed essential for public health and therefore on the national essential drugs list and/or the tax level applied regionally. In Brazil, for example, both are factors. For products on the negative list (non-essential) an 18% average state sales tax (Impostos Sobre Circulação de Mercadorias e Prestação de Serviços, ICMS) and two federal sales taxes (9.9% social security tax and 2.1% integration tax) are applied, while for drugs on the positive list (essential) only the state tax is charged. Variation also occurs regionally, as the level of ICMS varies between states from 7-25%. Both of these factors will influence the contribution of sales tax to the price build-up in Brazil.

Limitations

A number of factors provide limitations to the analysis and results of this research, at a country and cross-country level. While every attempt has been made to apply a uniform approach to each market, differences in data availability or transparency of rules means that each market is subject to its own caveats and limitations. These are described in detail in Appendix 3.

Efforts to capture the impact of confidential rebates and discounts have been made in the course of this study and are based on local IMS Health industry knowledge and expert interviews. This approach improves upon standard IMS Health prices or other sources of official list prices but may not fully capture the extent and nature of these important factors in determining net manufacturer selling price. In addition, estimates of the level of rebates and discounts have been sought separately for generics and brands and for the mix of products included in the therapy areas studied. However, it was not feasible to capture this information at an individual product and manufacturer level.

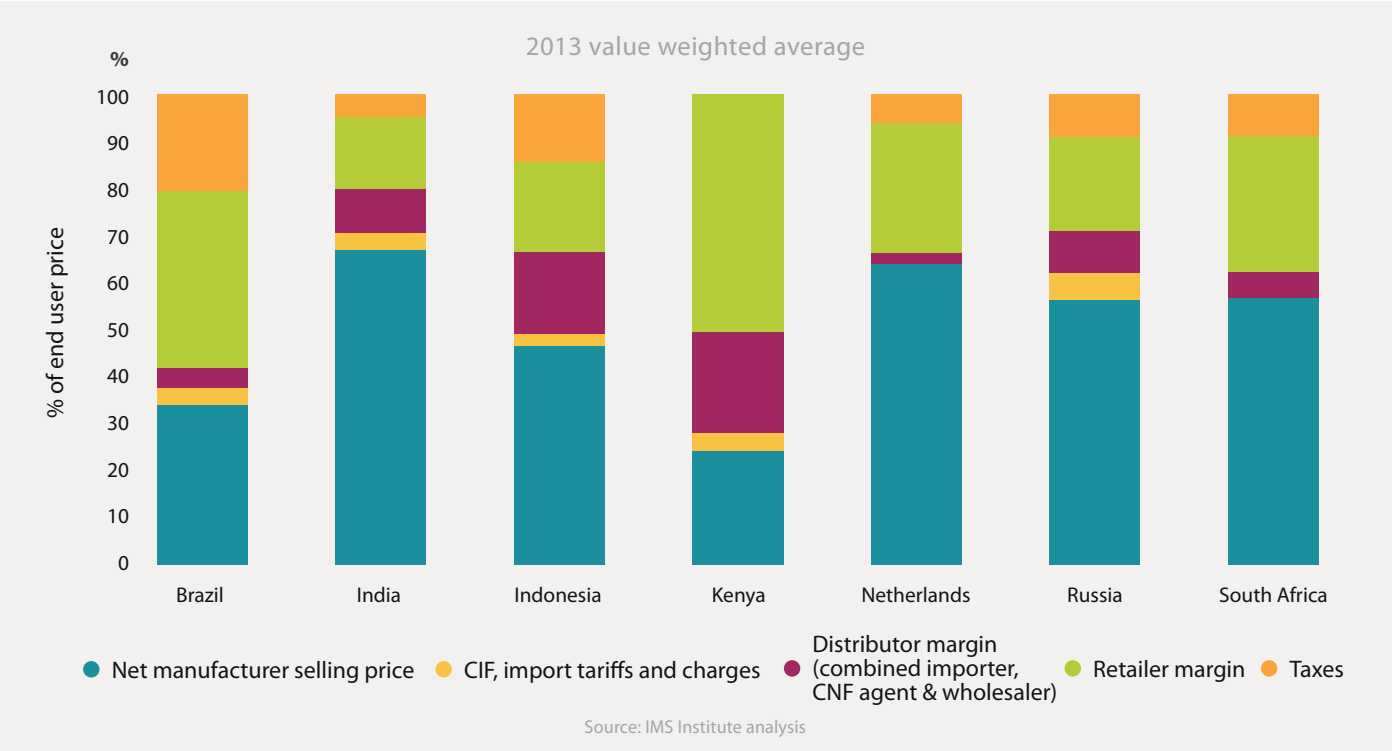
For countries where there are rules which set maximum margins, it is possible to reflect the maximum end user price. However, competitive forces may force pharmacies and wholesalers to price below this limit.[2] Where possible best industry estimates have been developed and applied; however, for some countries the large range of differences would leave any average estimates un-reliable. Under these circumstances, the maximum margin has been used as the default.

Discussion

The relative magnitude of price components along the pharmaceutical value chain is often analyzed in light of affordability and access to medicine issues. This study has set about analyzing these trends in the context of supply chain sustainability which is vital for continuity of access.

Across the seven markets there is a wide diversity of price build-up at the aggregate level (see Exhibit 12). However, as many of the regulations which are currently in place are triggered by specific factors such as presence of an essential drugs list, geographical regional policy variation, or product type distinctions, there are also differences between product categories within a given country.

Exhibit 12: Price build-up across five therapy areas



Source: IMS Institute analysis

There are three key common triggers which appear to influence the impact of the average price build-up:

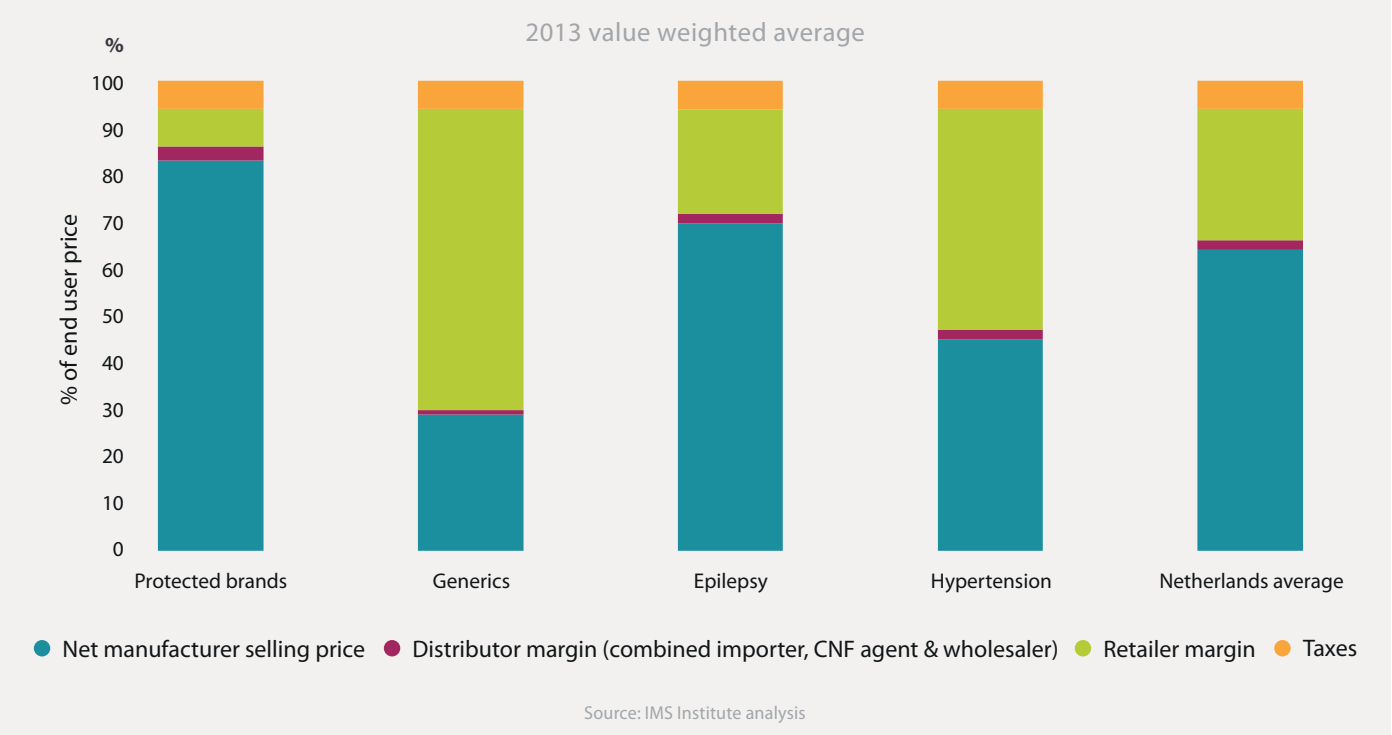
1. Essential drugs list: Since 1977 the WHO has compiled an "essential drugs list" which lists the medicines which at a minimum patients should have access to. The list targets the "most efficacious, safe and cost-effective medicine for priority conditions".[20] In markets where funding for medicine is limited or to help patients afford essential medicine, certain countries will compile a national essential medicines list and the selected products are often subjected to tighter pricing and margin regulations.

2. Regional differences: Even within a country, regional differences can occur in the value chain evolution. For example, this can relate to the sales tax applied or the regulated margin applied at the level of the distribution chain or retail outlets.

3. Product type: In many markets, product type is not a factor in drug pricing, and the regulated margin in percentage terms is equivalent for both generics and original brands. However, the difference comes from the absolute size of discounts offered for each product type.

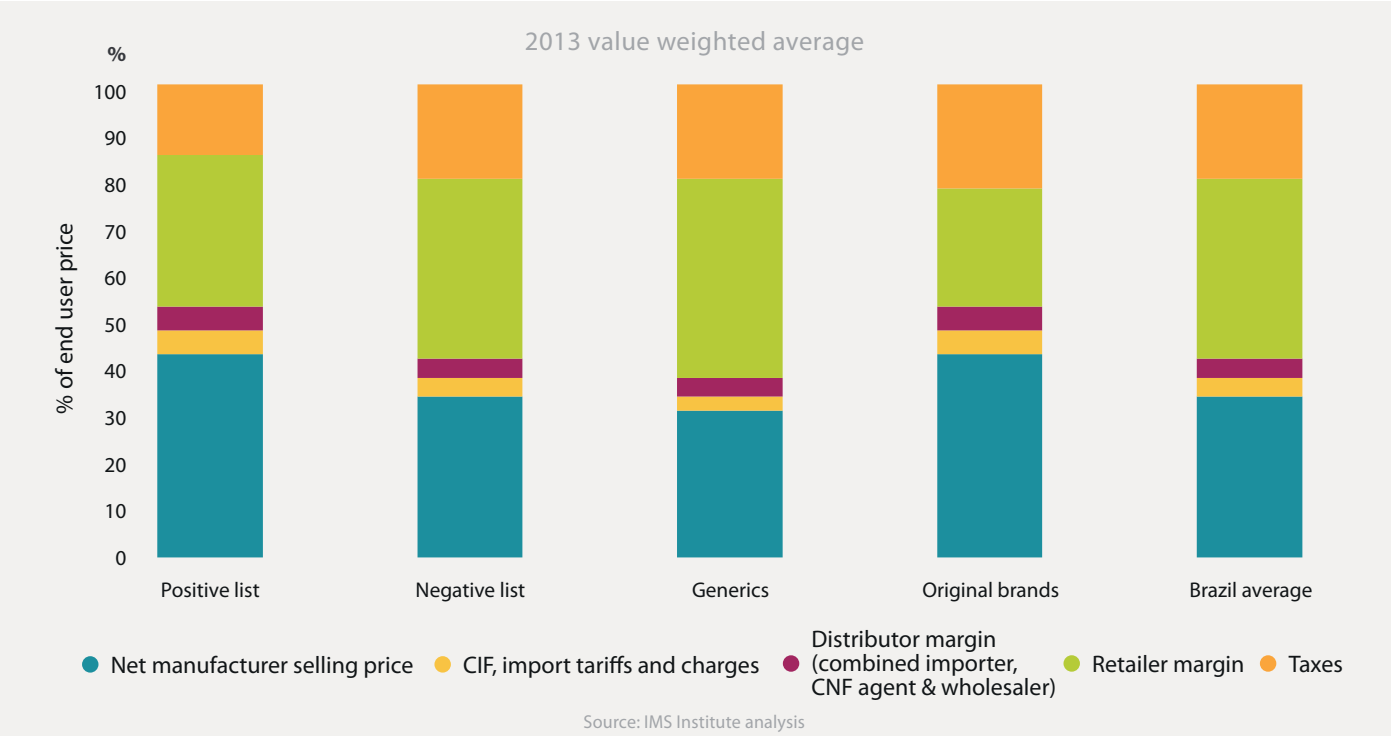
The combined impact of each of these three factors, where applicable, dictate the impact at a therapy area level. For example, in the Netherlands the product mix in a therapy area is the main determinant of the magnitude of components in the medicine value chain. A highly genericised therapy area such as hypertension will show a different profile to a more brand dominated therapy area such an anti-epileptics in a market (see exhibit 13). The difference between product type is also seen in Brazil, where products can be separated by those included in the positive list (essential medicines) and negative list (non-essential medicines), where the difference in the treatment of tax alters the relative magnitude of each component (see exhibit 14). More commonly in developed markets, regulation can foster the situation where the supply chain makes more money (proportionally) on lower cost generics than patented products. This tends to encourage the dispensing of generics which lowers the reimbursement price paid by the government. In contrast for low and middle income countries, where regulation is less stringent and there is less incentive to switch patients to generics, differences between product types are simply the result of who can negotiate the highest discounts.

Exhibit 13: Price build-up for selected product categories in the Netherlands



Source: IMS Institute analysis

Exhibit 14: Price build-up for selected product categories in Brazil



Source: IMS Institute analysis

There are two key factors which impact a manufacturer's share of the medicine price build-up: regulation and the level of discounting. In countries such as Kenya where there is little regulation in place, the manufacturer's share of the price build-up is considerably lower than more regulated markets. This is in part due to lack of regulation on the retail mark-up and secondly, the greater reliance of these markets on importing. Under these circumstances, non-domestic manufacturers are required to pay additional tariffs and taxes to ensure patients within the country can access the appropriate treatment. Furthermore, the prices of imported drugs can be impacted by the exchange rate, particularly if regulation does not allow for flexibility to counter these fluctuations.[21]

The level of discounting is a complex, but necessary factor to consider in this type of analysis, especially when it is used to inform policy decisions. While it is not feasible to factor in discounts product by product due to the confidential nature in which they are set, it is possible to use industry insight to estimate the level of discounting that occurs along the medicine value chain. The gross manufacturer price or visible wholesaler/retailer margins are often not reflective of the true price received. A full understanding of the realities of margins and prices is necessary to ensure policy-making that aims to adjust margins and prices does not inadvertently reduce or eliminate the viability of a particular stakeholder continuing to do business in that market. This may particularly be the case when local environmental factors are considered, such as the additional costs required to provide specific types of medicine or to provide reliable supply to rural areas.

Ultimately, policies need to strike a balance between making medicine affordable to patients and ensuring the viability of the supply chain.[6] Furthermore, there is scope in many countries to capitalise on the value that each stakeholder is already bringing to the healthcare system, and exploring how efficiencies can be gained in the overall system rather than a pursuing a narrow focus on the cost of medicine or one particular element of the value chain.

Appendix 1: Country and therapy area selection

Seven markets have been chosen for this study, which represent a range of income levels, health system development and geographic regions.

1. **Netherlands:** High income country with a rationale approach to pricing and margins. Useful as "anchor" country for comparison purposes.
2. **Brazil:** Upper-middle income country, large retail out-of-pocket market and a major market in the region.
3. **India:** Lower-middle income country, again with a large out-of-pocket market but under-going change and implementing mechanisms to control the build-up of medicine prices.
4. **Indonesia:** Lower-middle income country with little price regulation and relatively large out-of-pocket spend
5. **Kenya:** Low income country with high levels of inefficiencies in the medicine supply chain
6. **Russia:** High income market with a high level of out-of-pocket, mix of regulated and un-regulated market
7. **South Africa:** Upper-middle income country with a large proportion of the medicine market funded privately, but a highly transparent pricing system in place

Therapy area selection

Five therapy classes have been selected which represent a mixture of chronic and acute disease areas

1. **Antibiotics:** high importance across all countries
2. **Diabetes:** chronic disease relevant to all health systems and of growing importance/ visibility
3. **Epilepsy:** chronic disease, small, but high profile therapy area, with a high sensitivity to getting patients the right medicine
4. **Hypertension:** highly genericised therapy area, relevant to all health systems
5. **Respiratory:** chronic disease area, with growing importance globally

Appendix 2: Results Tables

Table 1: Brazil

All Product types	Antibiotics	Diabetes	Epilepsy	Hypertension	Respiratory	Average
Net ex-mnf price	31%	39%	37%	33%	42%	34%
Import tariff & charges	3%	4%	4%	4%	5%	4%
Distribution margin	4%	5%	5%	4%	5%	4%
Retailer margin	42%	31%	34%	40%	27%	38%
Taxes	20%	21%	21%	20%	22%	20%
End user price	100%	100%	100%	100%	100%	100%
Volume weighting	47%	14%	3%	29%	7%	100%

Table 2: India

All Product types	Antibiotics	Diabetes	Epilepsy	Hypertension	Respiratory	Average
Net ex-mnf price	67%	65%	66%	68%	69%	67%
Import tariff & charges	4%	5%	5%	2%	1%	4%
Distribution margin	9%	10%	9%	9%	10%	9%
Retailer margin	15%	16%	15%	15%	16%	15%
Taxes	5%	5%	5%	5%	5%	5%
End user price	100%	100%	100%	100%	100%	100%
Volume weighting	39%	18%	7%	24%	12%	100%

Table 3: Indonesia

All Product types	Antibiotics	Diabetes	Epilepsy	Hypertension	Respiratory	Average
Net ex-mnf price	47%	46%	46%	46%	46%	46%
Import tariff & charges	3%	3%	3%	3%	3%	3%
Distribution margin	19%	16%	17%	17%	16%	17%
Retailer margin	16%	21%	19%	20%	21%	19%
Taxes	14%	14%	14%	14%	14%	14%
End user price	100%	100%	100%	100%	100%	100%
Volume weighting	47%	14%	3%	29%	7%	100%

Table 4: Netherlands

All Product types	Antibiotics	Diabetes	Epilepsy	Hypertension	Respiratory	Average
Net ex-mnf price	38%	69%	69%	45%	78%	64%
Import tariff & charges	0%	0%	0%	0%	0%	0%
Distribution margin	2%	2%	2%	2%	3%	2%
Retailer margin	55%	23%	22%	47%	14%	28%
Taxes	6%	6%	6%	6%	6%	6%
End user price	100%	100%	100%	100%	100%	100%
Volume weighting	7%	16%	4%	60%	13%	100%

Table 5: Russia

All Product types	Antibiotics	Diabetes	Epilepsy	Hypertension	Respiratory	Average
Net ex-mnf price	57%	57%	58%	56%	57%	56%
Import tariff & charges	5%	6%	6%	6%	6%	6%
Distribution margin	9%	8%	8%	9%	8%	9%
Retailer margin	20%	20%	19%	20%	20%	20%
Taxes	9%	9%	9%	9%	9%	9%
End user price	100%	100%	100%	100%	100%	100%
Volume weighting	34%	4%	2%	53%	7%	100%

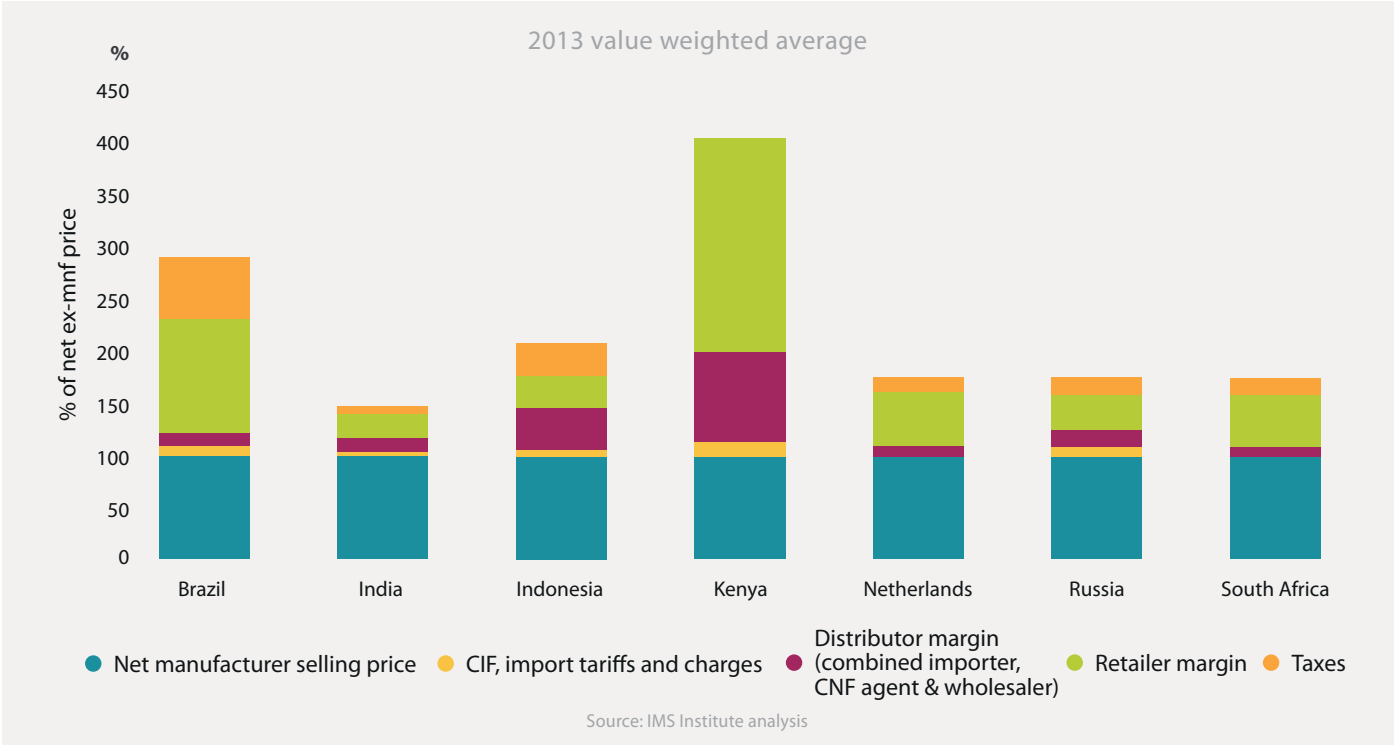
Table 6: South Africa

All Product types	Antibiotics	Diabetes	Epilepsy	Hypertension	Respiratory	Average
Net ex-mnf price	56%	53%	62%	56%	61%	57%
Import tariff & charges	0%	0%	0%	0%	0%	0%
Distribution margin	6%	6%	5%	6%	5%	6%
Retailer margin	29%	34%	23%	30%	25%	29%
Taxes	9%	8%	9%	9%	9%	9%
End user price	100%	100%	100%	100%	100%	100%
Volume weighting	31%	10%	4%	50%	5%	100%

Table 7: Kenya

Pack	Net-ex mnf price	Import duties	Distributor margin	Retail margin	End user price
Value weighted Average	24%	4%	22%	50%	100%
Un-weighted Average	27%	4%	24%	45%	100%
Un-weighted Median	29%	4%	26%	41%	100%
Pack 1	20%	3%	17%	60%	100%
Pack 2	15%	2%	13%	69%	100%
Pack 3	25%	4%	22%	50%	100%
Pack 4	17%	3%	15%	66%	100%
Pack 5	10%	2%	9%	79%	100%
Pack 6	34%	5%	30%	31%	100%
Pack 7	20%	3%	17%	60%	100%
Pack 8	16%	2%	14%	68%	100%
Pack 9	33%	5%	29%	34%	100%
Pack 10	39%	6%	35%	21%	100%
Pack 11	36%	5%	31%	28%	100%
Pack 12	43%	6%	38%	12%	100%
Pack 13	31%	5%	27%	38%	100%
Pack 14	37%	6%	33%	25%	100%
Pack 15	36%	5%	32%	26%	100%
Pack 16	36%	5%	32%	26%	100%
Pack 17	33%	5%	29%	34%	100%
Pack 18	37%	6%	33%	25%	100%
Pack 19	28%	4%	24%	44%	100%
Pack 20	28%	4%	25%	43%	100%
Pack 21	28%	4%	24%	44%	100%
Pack 22	27%	4%	24%	45%	100%
Pack 23	36%	5%	32%	27%	100%
Pack 24	6%	1%	6%	87%	100%
Pack 25	34%	5%	30%	31%	100%
Pack 26	8%	1%	7%	83%	100%
Pack 27	13%	2%	11%	74%	100%
Pack 28	32%	5%	29%	34%	100%
Pack 29	24%	4%	21%	51%	100%
Pack 30	34%	5%	30%	31%	100%

Exhibit 15: Average price build-up across five therapy areas, indexed to net ex-mnf price



Source: IMS Institute analysis

Appendix 3: Country specific methodology, approach and sources

The following sources were used in the modeling process to quantify the price build-up across countries. Some sources provided data which has been bridged to IMS Health data at the pack level, while others have been used to build the business rules applied.

Brazil

Analysis was performed on the Brazilian private retail market. The pivotal "data fact" used was the official published trade price. Products were separated at pack level based on whether they were present on the positive and negative list and by product type. Retailer acquisition price is collected as a data fact from the IMS Health audit, while distributor acquisition price was modeled using best industry estimates. Average tax rates were applied to each pack, with state tax only applicable to those on the negative list.

Sample size: 3,387 different packs
Volume consumption: IMS Brazil Mercado Farmacêutico Brasileiro
Initial price source: List price - Câmara de Regulação do Mercado de Medicamentos (CMED)

India

Analysis was performed on the Indian private retail market. The pivotal "data fact" used was the official published trade price. Products were separated based on whether they were present in the national essential drugs list and regulated maximum distribution and pharmacy margins were applied respectively to the estimated acquisition price for each stakeholder. Trade discounts were modeled based on best industry estimates.

Sample size: 15,465 different packs
Volume consumption: IMS Secondary Stockist Audit
Initial price source: Manufacturer published price list

Indonesia

Analysis was performed on the Indonesian private retail market. The pivotal "data fact" used was the official published trade price. Products were separated based on product type and best industry estimates used to model the acquisition price for each stakeholder. As all medicines must be manufactured in Indonesia, only tariffs for API's were included. In addition to 10% VAT, manufacturers are required to pay 10% income tax which has been applied to the estimated net manufacturer price for each pack.

Sample size: 5,017 packs
Volume consumption: IMS Indonesia drugstore audit and pharmacy audit
Initial price source: Official published list price

Kenya

Analysis was performed on the Kenyan private retail market. The pivotal "data facts" used were average trade price from the IMS Kenya market audit and the median public price based on results from a survey of 60 pharmacies in the Greater Nairobi area. Product unavailability was common and so for packs to be included in the analysis there needed to be a minimum of 10 observations.

Sample size: 30 packs
Volume consumption: IMS Kenya National Indicator Report
Initial price source: Average price over a six month period of transactions from the seller (importer / distributor) and results of IMS Kenya retail survey

Netherlands

Analysis was performed on the Netherlands retail market. The pivotal "data fact" used was the official published trade price. Products were separated based on product type and trade acquisition costs were modeled based on benchmarks of discount received from distributors and level of rebate paid to the insurance fund provided by a retailer. Pharmacy dispensing fee was calculated based on a 90 days dispensing fee of €5.2, which was then adjusted by for each pack depending on pack size. E.g. a pack of 90 would receive €5.2, while a pack of 30 would receive €5.2/3.

Sample size: 47,083 packs
Volume consumption: IMS Netherlands - National Prescription Audit
Initial price source: List price

Russia

Analysis was performed on the Russian private retail market. The pivotal "data fact" used was the average invoiced trade price. As regulation generally occurs regionally, Moscow was used as the case study. Products were separated based on product type and whether they were on the essential drugs list. Companies were separated by nationality and the assumption made that most international manufacturers still import drugs into Russia rather than manufacturer domestically. Retailer acquisition price is collected as a data fact from the IMS Health audit, while distributor acquisition price was modeled using best industry estimates

Sample size: 3,305 packs
Volume consumption: IMS Russian Federation Pharmaceutical Index
Initial price source: average invoiced pack price

South Africa

Analysis was performed on the South African private retail market. The pivotal "data fact" used was the official published trade price. This data was bridged at pack level to the manufacturer selling price and logistics fee published in the *"Database of medicine prices 20th Dec 2013*. To estimate the price build up-for an independent pharmacy, maximum regulated margins were applied, as an example of a chain Retailer the 26/26 rule was applied, the greater of R26 or 26% of the regulated single exit price. As discounting is prohibited in South Africa, no estimation was required. However, it is noted that 'marketing fees' and 'data fees' as well as other mechanisms of influencing costs are common but cannot be quantified within this analysis".

Sample size: 1,616 different packs
Volume consumption: IMS MIDAS Pharmaceutical Market South Africa
Initial price source: List price - MEDprax, Blue Book|
Manufacturer selling price and logistics fee: *Database of medicine prices 20th Dec 2013*: available at http://www.mpr.gov.za/PublishedDocuments.aspx#DocCatId=21

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Murray Aitken is executive director, IMS Institute for Healthcare Informatics, which provides policy setters and decision makers in the global health sector with objective insights into healthcare dynamics. He assumed this role in January 2011. Murray previously was senior vice president, Healthcare Insight, leading IMS Health's thought leadership initiatives worldwide. Before that, he served as senior vice president, Corporate Strategy, from 2004 to 2007. Murray joined IMS Health in 2001 with responsibility for developing the company's consulting and services businesses. Prior to IMS Health, Murray had a 14-year career with McKinsey & Company, where he was a leader in the Pharmaceutical and Medical Products practice from 1997 to 2001. Murray writes and speaks regularly on the challenges facing the healthcare industry. He is editor of HealthIQ, a publication focused on the value of information in advancing evidence-based healthcare, and also serves on the editorial advisory board of Pharmaceutical Executive. Murray holds a Master of Commerce degree from the University of Auckland in New Zealand, and received an M.B.A. degree with distinction from Harvard University.

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Claire has worked at IMS Health for 4 years and is working with European industry associations, policymakers and academic institutions, providing analytical capabilities and industry expertise on European pharmaceutical policy and supply chain issues. Prior to this Claire was part of the IMS Thought Leadership team, which focused on developing compelling and original perspectives on the key issues that affect pharmaceutical companies, globally and locally, now and in the future. Claire holds a BA in Physiological Sciences from the University of Oxford and an Msc in Health Economics, Policy and Management from London School of Economics.

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Per Troein has been with IMS Health for 18 years and is responsible for supplier and associations government relationships. The dispensing and distribution environment is very dynamic. Pricing of pharmaceutical is as complicated. One of IMS Health's priorities is to have the best understanding of those dynamics to secure the most appropriate data, to be the best partner with the different data partners, and to be able to support the industry and also when appropriate governments. He is a well known speaker in the field of distribution trends and pricing and is very active in consulting projects in the area. Prior to joining IMS Health, Per worked for Pharmacia. His last 6 years were spent in strategic development including several major mergers and acquisitions. He holds an MSc in engineering from Lund's Institute of Technology and an MBA from INSEAD.

About the Institute

The IMS Institute for Healthcare Informatics leverages collaborative relationships in the public and private sectors to strengthen the vital role of information in advancing healthcare globally. Its mission is to provide key policy setters and decision makers in the global health sector with unique and transformational insights into healthcare dynamics derived from granular analysis of information.

Fulfilling an essential need within healthcare, the Institute delivers objective, relevant insights and research that accelerate understanding and innovation critical to sound decision making and improved patient care. With access to IMS Health's extensive global data assets and analytics, the Institute works in tandem with a broad set of healthcare stakeholders, including government agencies, academic institutions, the life sciences industry and payers, to drive a research agenda dedicated to addressing today's healthcare challenges.

By collaborating on research of common interest, it builds on a long-standing and extensive tradition of using IMS Health information and expertise to support the advancement of evidence-based healthcare around the world.

Research Agenda

The research agenda for the Institute centers on five areas considered vital to the advancement of healthcare globally:

The effective use of information by healthcare stakeholders globally to improve health outcomes, reduce costs and increase access to available treatments.

Optimizing the performance of medical care through better understanding of disease causes, treatment consequences and measures to improve quality and cost of healthcare delivered to patients.

Understanding the future global role for biopharmaceuticals, the dynamics that shape the market and implications for manufacturers, public and private payers, providers, patients, pharmacists and distributors.

Researching the role of innovation in health system products, processes and delivery systems, and the business and policy systems that drive innovation.

Informing and advancing the healthcare agendas in developing nations through information and analysis.

Guiding Principles

The Institute operates from a set of Guiding Principles:

The advancement of healthcare globally is a vital, continuous process.

Timely, high-quality and relevant information is critical to sound healthcare decision making.

Insights gained from information and analysis should be made widely available to healthcare stakeholders.

Effective use of information is often complex, requiring unique knowledge and expertise.

The ongoing innovation and reform in all aspects of healthcare require a dynamic approach to understanding the entire healthcare system.

Personal health information is confidential and patient privacy must be protected.

The private sector has a valuable role to play in collaborating with the public sector related to the use of healthcare data.

IMS INSTITUTE FOR HEALTHCARE INFORMATICS

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