

Understanding the pharmaceutical value chain

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Understanding the pharmaceutical value chain requires the identification of each component from manufacturer to end consumer of medicines – and to understand their interaction. In most cases, the manufacturer's selling price represents only a fraction of the retail price of a drug. More than half of the end user price results from insurance, freight charges (CIF), import tariffs and charges, importer margin, distributor margin, retailer margin and taxes.

The article describes the elements of the medicine value chain, outlines 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. It quantifies the price build-up for specific therapy areas and countries and illustrates the diversity of approaches and costs associated with the value chain through case studies.

Keywords: Pharmaceutical value chain, pharmaceutical distribution and retail margins, pharmaceutical cost analysis

1. Introduction

The growing role and use of medicines in healthcare systems globally, driven both by innovative medicines emerging from research and development investments and the expansion of access to meet the imperative of universal health coverage, brings greater importance to understanding the pharmaceutical value chain. This includes the full set of activities that occurs between the point when a medicine is manufactured and shipped from a production or import facility until the time it is received by a patient in the course of their medical care and treatment.

At each step, understanding the specific elements of the value chain, the contribution to the health system that is provided, and the cost components that are incurred provides important context and perspective to the full value that medicines can and do play in advancing population health around the world. However, components of the value chain can and do 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.

Recent research on this topic focused on seven markets, representing a range of income levels, health system development and geographic regions, and comprised the Netherlands (a high income country with a rational approach to pricing and margins

that is useful as an “anchor” country for comparison purposes), Brazil, India, Indonesia, Kenya, Russia and South Africa [1]. The researchers also selected five therapy classes representing a mix of chronic and acute disease areas, and comprised antibiotics, diabetes, epilepsy, hypertension and respiratory. For each therapy area and in each country, analysis of costs, margins and mark-ups was undertaken, indexed to 100 and represented in a way that enables comparison.

2. Major components of the pharmaceutical value chain

In advancing the understanding of the pharmaceutical value chain, it is useful to look at three major components:

1. **Manufacturing of the medicine:** In order to 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 centers 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 each of these components of the value chain, a range of costs are incurred and value added, as summarized in Fig. 1.

3. Activities, costs and value added in manufacturing medicines

Broadly speaking, there are two categories of manufacturing required for drug production: active pharmaceutical ingredient (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

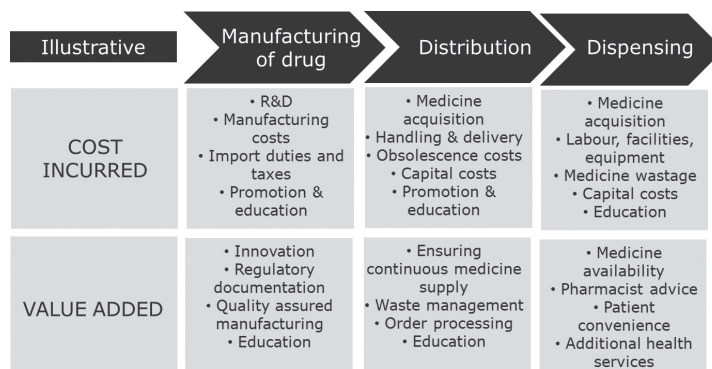


Fig. 1. Costs incurred and value added in components of the pharmaceutical value chain.

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.

For originators, the largest costs are associated with drug discovery, which identifies new chemical or biologic entities that have the potential to advance the current standard of disease treatment, and the costs of subjecting potential drug candidates to rigorous testing through clinical trials, which many will fail to complete. Additional costs are incurred in the submission of applications to regulatory agencies, and once approved, costs are incurred by manufacturers to promote and educate key stakeholders about the product and the benefits it can bring to patients. 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 [2]. 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.

The value added from the generation of a 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.

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.

2013 value weighted average across five therapy areas

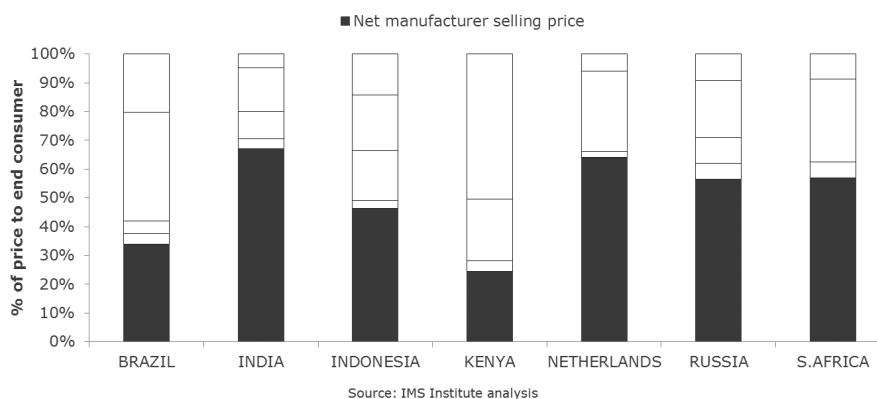


Fig. 2. Net manufacturer selling price compared to end consumer price.

Unlike prices for other products, medicine prices are determined 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% [3].

4. Manufacturer costs relative to end user price

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, as shown in Fig. 2. 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.

5. Activities, costs and value added in distribution of medicines

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. For those medicines which are imported, there is often an additional step in handling the logistics of bringing the medicine into the country. The exact number of steps, participants and complexity in the distribution component differs based on the nature of the products, markets and distribution profile.

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) [3]. 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.

The key function of a 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.

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.

2013 value weighted average across five therapy areas

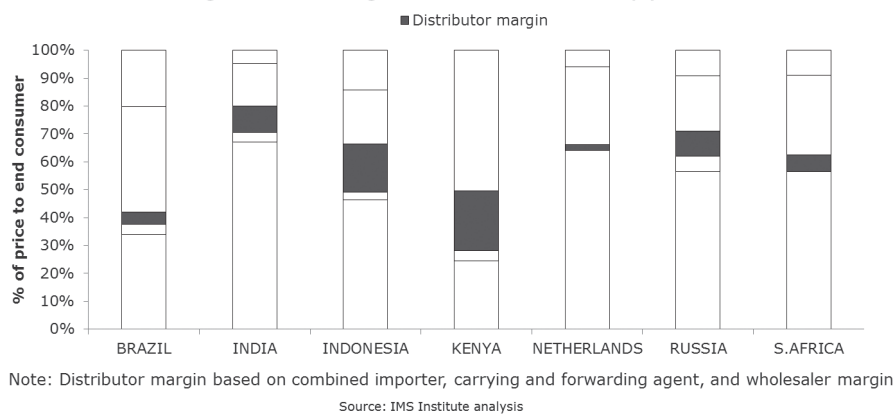


Fig. 3. Distributor margin compared to end consumer price.

6. Distribution costs relative to end user price

Across countries the total distribution margin can vary from 2% of the end user price in the Netherlands to 22% in Kenya (see Fig. 3). 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. Some 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.

7. Activities, costs and value added in dispensing to the patient

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) [4].

Retailer costs can be split into those which are fixed and those which vary depending on the level of business. Fixed costs include the cost of labor (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 [5].

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 oversimplification 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. [6]. Pharmacists can also spend a substantial amount of time mitigating the impact of drug shortages by finding either new sources or alternative medicines.

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 [7]. 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 [8]. 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.

Retail dispensing fees in many of the markets analyzed – 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) [3]. 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.

In some markets where retailers make a loss from selling prescription medicine, profit is instead generated from additional over-the-counter and health and beauty

2013 value weighted average across five therapy areas

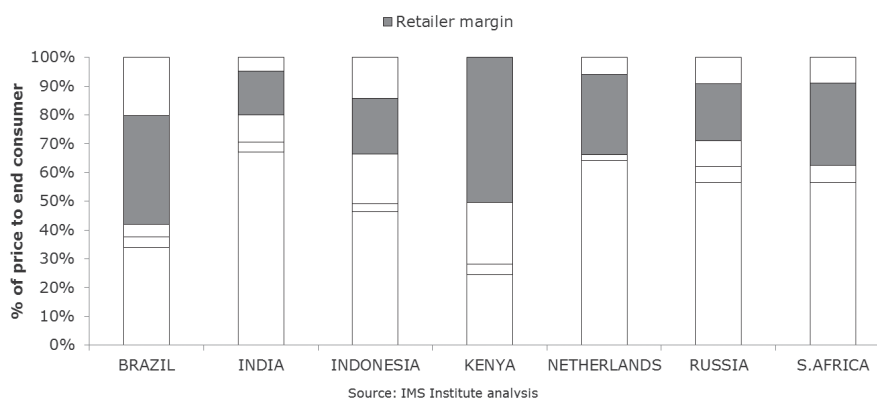


Fig. 4. Retailer margin compared to end consumer price.

sales. An alternative business model finds other retailers which are very much focused on prescription drug dispensing to drive their business profitability.

8. Retailer costs relative to end user price

The average level of retailer margin ranges from 15% of end user price in India to 50% in Kenya (see Fig. 4). 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.

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 [9]. 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. While there is a maximum margin in place, for larger chains a lower price can be offered to patients without negatively impacting business viability [10]. 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.

Country ⁽ⁱ⁾	Customs duty rate ⁽ⁱⁱ⁾		National sales tax
	Finished form products	Active pharmaceutical ingredients	
Brazil	9.8%	9.5%	Average 18%
India	10%	10%	Average 5%
Kenya	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 for each country

(ii) Most favoured nation (MFN) duty rate is that which each country has agreed to offer all countries which are members of the World Trade Organization (WTO). 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 APIs. Any conclusions based on this data are the responsibility of the authors and do not necessarily represent the opinion of the WTO.

Source: World Trade Organisation, September 2014. [Online]. Available: <http://tariffdata.wto.org>

Fig. 5. Medicine import tariffs and national sales taxes.

9. Government tariffs, taxes and charges relative to end user price

Taxes have been shown to be one of the larger components contributing to the price build-up of medicines [11,12]. 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. Import duties are used to raise government revenues and help domestic producers by providing a price advantage versus international competitors. 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. Figure 5 summarizes the import tariffs and national sales taxes applied in each market. In addition there are many examples of country specific taxes charged.

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 Fig. 6). 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 but do not impact products sourced from the domestic production of API's and finished form products.

2013 value weighted average across five therapy areas

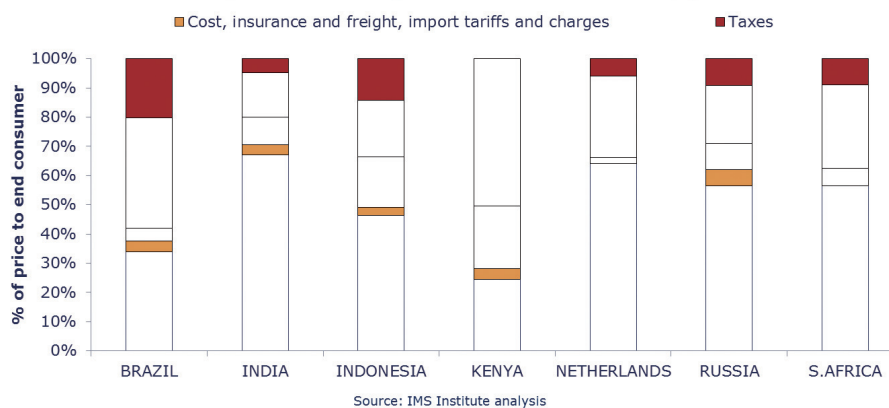


Fig. 6. Government taxes, tariffs and charges compared to end consumer price.

10. Discussion

Understanding the relative magnitude of price components along the pharmaceutical value chain is essential to inform the discussion of affordability and access to medicine issues. By analyzing the components of the pharmaceutical value chain in specific countries and for specific therapy areas stakeholders can better establish a basis of common understanding and evidence.

The analysis presented here illustrates vividly the wide variation by country of the average contributions of manufacturer costs, distributor margins, retail margins and government tariffs, taxes and charges relative to the final end user price (see Fig. 7). These averages are weighted by product type and therapy area based on actual use mix, and therefore also reflect the weighted impact of diverse policies and practices across the value chain in these countries. They are not intended to represent all medicines in each country, but are based on analyzing the best available objective and quantified information for a defined set of therapy areas, supplemented with local market expertise and engagement with each of the major stakeholders.

Across the value chain, 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 that policy-making aimed at adjusting 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

2013 value weighted average

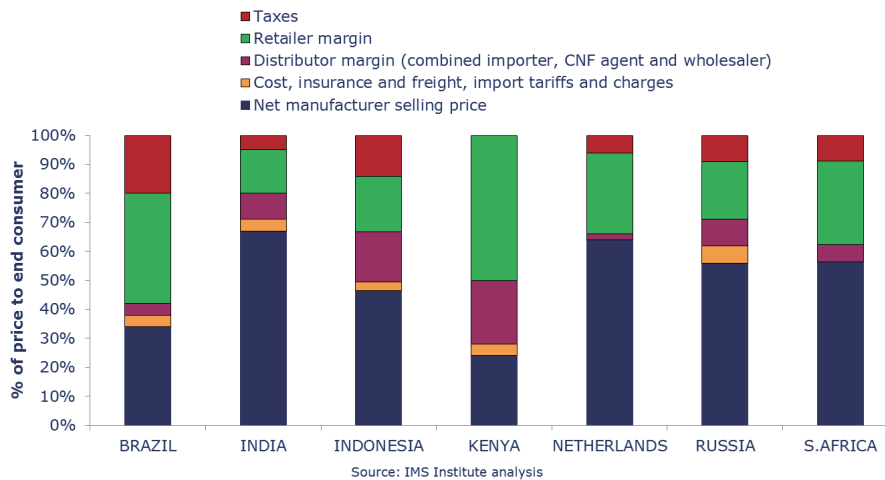


Fig. 7. Price build-up across five therapy areas.

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 maintaining the long-term vitality of each component of the value chain, and making medicines available and affordable to patients. Furthermore, there is scope in many countries to capitalize 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 pursuing a narrow focus on the cost of medicine or one particular element of the value chain.

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