

Affordability and Accessibility to Medicines in EMs: Differential pricing is the solution

Differential pricing by pharmaceutical companies whereby prices charged in each country are commensurate with either its ability to pay or with its average per capita income, could be a solution to improving affordability and accessibility to medicines in emerging markets such as India where most patients pay out-of-pocket. Price discrimination offers more affordable prices to customers with lower ability/willingness to pay, thereby increasing their access and revenues for companies.

India's generics industry is a huge success story, generating major revenues in global markets and providing India's population with inexpensive medicines. Its business model has thrived on the small molecule (chemical) drugs for mass diseases that were developed by multinational companies (MNCs) in the 1980s and 1990s. As these drugs lost patent protection over the last few decades, billions of dollars of sales were genericised, particularly in the US, where regulatory and reimbursement regimes are favorable to generics and over 80% of all prescriptions are now generically dispensed.

At the same time, innovative R&D has shifted towards large molecule biologics, which have more complex and costly manufacturing processes and delivery mechanisms, with a focus on smaller, speciality diseases classes, including orphan drugs that now account for one-third of new drugs approved by the US FDA. These new drug cohorts have the potential to address unmet medical needs, including some cancers, but they also bring challenges. These drugs are often priced much higher than conventional small molecule drugs, putting pressure on health budgets of payers and patients. For generic producers, bringing biosimilars (follow-on biologics) to market entails new skill sets in R&D, manufacturing and marketing, and significantly greater scientific, regulatory and market risk, compared to traditional chemical generics. This paper discusses these related challenges of high-priced originator drugs, low cost generics and complex biosimilars in the Indian context.

The High Price Originator Challenge

In the US, from 1995 to 2013, the launch prices of new cancer drugs rose 10% a year, after adjusting for inflation and expected survival benefits. New cancer drugs are routinely priced above \$100,000 per patient/treatment in the US, and up to \$400,000 for some orphan drugs. Post-launch price increases for on-patent drugs average 5% to 10% a year. These trends are the result of an environment in which patients with comprehensive insurance are price-insensitive and payers exert no control over prices, although some negotiate rebates when feasible. These high and rising US prices create challenges for other countries, where payers seek to manage health expenditures within annual budgets. For example, the UK National Institute for Health and Care Excellence (NICE) evaluates the cost-effectiveness of new drugs and considers drugs that cost more than roughly \$50,000 per quality-adjusted life year (QALY) to be low value-for-money, compared to other potential uses of health resources. By contrast, some of the high-

priced new drugs offer only moderate benefits, implying a cost-per-QALY of \$300,000 or more, unless significant discounts are given.

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One obvious solution to this dilemma is for pharmaceutical companies to practice differential pricing, that is, to adapt the price charged in each country commensurate with either its ability to pay or with its average per capita income. Basic economic theory shows that price discrimination (varying price across market segments based on inverse price elasticity) can increase profits for companies and improve access for customers, compared to charging a single price across all markets. The intuition is obvious: price discrimination offers more affordable prices to customers with lower ability/willingness to pay, thereby increasing their access and revenues for companies.

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In practice, pharmaceutical prices vary only weakly with average per capita income across middle and lower income countries (MLICs). This invariance of drug prices with average per capita income across countries may partly be a corporate response to policies by some governments to adopt external referencing (regulating domestic drug prices based on foreign prices) and parallel trade (permitting wholesalers to arbitrage international price differences). Both policies undermine MNCs' willingness to sell at lower prices in lower-income countries, even if this might undermine potentially higher prices in high-income countries. But, although external referencing and parallel trade are common within the EU, such policies rarely extend, from developed to EM countries.

A more likely explanation for relatively high drug prices across EMs is the nature of competition in differentiated product markets with wide income-dispersion. In such contexts, originator manufacturers rationally target the affluent segment, while lower-priced branded generics compete for the more price-sensitive consumers. But for some patent-protected originator drugs there may be no good, cheaper alternative treatments available to lower income consumers. In such contexts, both the originator firm and patients overall could benefit from within-country differential pricing by the originator, through such tactics as setting relatively high prices to private markets that target affluent customers, with discounts to public hospitals and other outlets that serve primarily lower-income patients; dual branding, possibly by licensing a generic producer to produce a second, cheaper brand; and dual formulations/packaging, offering smaller packs etc. to lower income segments. Some companies already use these and other strategies in attempts to differentiate price by ability to pay, but such segmentation is often undermined by price arbitragers and other policies. For example, differential pricing within India is likely hampered by resale price maintenance (RPM) on drugs, which maintains a uniform price for a

given product across all distributors. Manufacturers have no incentive to sell at a lower price to distributors that supply low-income areas, because this differential would simply be captured by the distributors if the RPM price is stamped on the box. Manufacturers that have attempted to bypass this distribution system, using direct distribution to patients that would ensure safe supply – and enable differential pricing by customer have been boycotted by distributors. Thus although RPM may have other benefits, it may also limit access-improving differential pricing of drugs in India.

Countries like India with high dispersion of personal income might choose to set a relatively high maximum cost per unit health gain, to assure prompt access to new drugs for high income groups with high willingness-to-pay for health, and then negotiate discounts for public sector providers and others that serve lower income groups.

Another potentially important policy for assuring appropriate access and affordability of drugs is the use of health technology assessment, in particular, tools for evaluating cost-effectiveness that are widely used in Europe and are increasingly being adopted in EMs. Specifically, payers evaluate the value of new and existing technologies in terms of the cost per unit of health gain, where health gain may be measured as life years saved, quality-adjusted life-years saved or other measures. By setting a maximum cost per unit health gain and paying only for technologies that meet this value-for-money threshold, a government or payer can assure that it is getting the maximum possible health gain from its budget. Countries like India with high dispersion of personal income might choose to set a relatively high maximum cost per unit health gain, to assure prompt access to new drugs for high income groups with high willingness-to-pay for health, and then negotiate discounts for public sector providers and others that serve lower income groups. Brazil, for example, used such a two-tier pricing strategy, with higher prices in the private sector and discounted prices in the public sector. Note that this approach, of evaluating the health benefit offered by a new technology and allowing a price premium based on the incremental benefits (health gain plus any other cost savings) relative to current treatment, rewards and preserves incentives for innovative R&D while assuring that health budgets are efficiently spent. Applying cost-effectiveness and other evaluative tools will become more important as India expands its health insurance coverage. Insurance is designed to protect consumers from health costs, but this inevitably undermines patient cost-sensitivity, leading to increased utilisation and higher producer prices unless payers counteract this effect through such tools as cost-effectiveness limits on price.

Generic Markets: Are Price Controls Useful or Counterproductive?

Generics account for the great majority of drug use in all countries, particularly in EMs including India, hence maximising value for money in such markets is important. In the US and most other developed countries, generic versions of a chemical originator drug can be approved by showing bioequivalence to the originator and meeting current good manufacturing practices (cGMP), referencing the originator's clinical trials ("data") for evidence of safety and efficacy. Bioequivalence is inexpensive to demonstrate and provides assurance of clinical equivalence. It is the foundation that enables physicians, patients and payers to accept pharmacy substitution of bioequivalent generics for originator drugs, except where the physician expressly requires that the originator brand be dispensed. In markets that require bioequivalence, generic companies

forgo investment in brand and promotion to doctors as a waste of money. Competition focuses on price because quality can be assumed equal. US regulatory and reimbursement policies have emphasised this approach and have resulted in the US having among the cheapest generic prices and largest generic market shares among developed countries, in contrast to the US' relatively high originator prices. For off-patent drugs in the US, over 90% of scripts are filled generically and post-patent sales of off-patent originators are minimal, because physicians and consumers have confidence that the cheaper generics are bioequivalent.

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By contrast, in most emerging markets including India, generics are not required to meet bioequivalence and equivalent manufacturing standards in order to be approved, hence consumers cannot assume that all generics are of equal safety, effectiveness and quality to the originator brand. Generic firms in EMs invest in branding and other strategies to attempt to differentiate their products, because consumers perceive brand and price as proxies for quality. In markets where generic quality is uncertain, originator products retain a significant market share after patent expiry, despite their relatively high prices, because many consumers are willing to pay a premium for assurance of quality. Because India has so many generic manufacturers, generic prices on average are cheap, but MNC brands and large domestic generic firms that sell in international markets still command premium prices on off-patent products, because such firms are known to have met international standards for quality, in the major regulated markets (US, EU) or WHO for international tenders. Several EM countries have enacted but delayed implementation of generic bioequivalence requirements, for fear of harming local firms that might not meet the standards or would incur costs to comply. However, the evidence suggests that consumers are more willing to buy from local generic suppliers that have met international standards for quality. Thus consumers and local firms would ultimately likely benefit from bioequivalence and cGMP requirements, with any modest increment in cost of compliance offset by lower investment in branding and promotion.

India has attempted to deal with dispersion of generic prices by the 2013 adoption of price controls for certain “essential medicines,” setting the ceiling price for all forms of a molecule at the simple average market price of products with at least 1% market share. Since this price cap mechanism is only binding on products whose free market price was above average, it penalises those firms that invested in quality and reduces the ability of consumers to identify higher quality firms, assuming that prices are positively correlated with quality in the absence of price controls, as theory and evidence suggest. Yet these price controls fail to increase affordability for those consumers who were buying below-average priced products before the controls, since their prices are unaffected by the cap. There is no evidence that access to these drugs by lower income subgroups increased after the price controls, in fact the growth of price-controlled medicines slowed relative to growth of non-controlled alternatives. This outcome is consistent with incentives of companies and pharmacies, to promote those drugs on which they receive higher margins, which presumably means other drugs that are not subject to price-controls. More generally, the rationale for price controls on generic drugs is questionable. With over 30 producers per molecule for the price-controlled substances in India, price competition would

surely suffice to achieve the lowest possible prices consistent with quality, once quality is assured by bioequivalence and cGMP requirements for market entry. Consistent with this, the evidence from the US and some EU markets shows that four or more generic producers is sufficient to bid generic prices down to the floor, once bioequivalence requirements eliminate quality uncertainty.

The Biosimilar Challenge

Some leading Indian generic firms have responded to the shift in innovative R&D away from chemical drugs and towards biologics by investing in expertise to develop biosimilars for the older biologics that have or soon will lose patent protection. Most countries have adopted a regulatory pathway for approval of biosimilars that is significantly more complex and costly than the relatively simple requirement of bioequivalence for generic versions of chemical drugs. This is particularly true in the US, where biosimilars must do substantial de novo clinical trials, with different requirements depending on compound complexity as defined by the FDA. Further, most biosimilars will not be deemed interchangeable by pharmacists, hence biosimilars will likely need to invest significantly in branding and promotion to persuade doctors/patients/payers to accept their brand. Moreover, originator biologics in the US receive 12 years of data exclusivity before their clinical trial data can be referenced by a would-be biosimilar, compared to five years for small molecule drugs. (Also, a biosimilar producer that successfully challenges an originator biologic's patents will not receive six months market exclusivity as does a first-to-file generic.) Whereas the US has led in the uptake of chemical generics, Europe is ahead of the US in defining a regulatory pathway for biologics and in the launch and market uptake of biosimilars. Given the delays, high cost and regulatory hurdles for approval of biosimilars, which cannot qualify for patent protection or data exclusivity, some companies perceive a higher expected net gain from developing "follow-on biologics" that do not claim similarity to a reference originator. Such products seek to be sufficiently differentiated from the originator to qualify for their own new patent protection and data exclusivity, seeking regulatory approval without waiting for originator patents to expire. Of course, this approach will entail higher clinical trial and promotion costs than the biosimilar route. The follow-on biologic or "bio-better" approach will likely yield higher returns only if the new product is either significantly better and/or cheaper than the original biologic.

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Those Indian companies with the necessary R&D expertise and financing have a great opportunity in this developing biosimilar space. The high price of most originator biologics that do not adopt significant differential pricing puts these originator drugs beyond the reach of even middle income patients in MLICs, leaving a potentially large market to be served by firms that can supply biosimilars of proven quality at prices that are affordable to middle income patients, while still providing high margins over cost, compared to chemical generics. Although most biosimilars will still be unaffordable for the poorest patients if they must pay out-of-pocket, such

drugs might be considered cost-effective for coverage under public health insurance schemes for low income segments, such as RSBY in India. This space is likely to become increasingly competitive, including not only several leading Indian companies like Biocon, Dr. Reddy's and Lupin with products approved and/or under development, but also such multinationals as Sandoz (generic division of Novartis), Hospira (recently acquired by Pfizer), Celltrion (a recent Korean entrant) and originator firms such as Amgen.

Conclusion

As India's health care system evolves to meet the rising incomes and expectations of consumers, its generic industry is poised to play a potentially significant role in the important new field of biosimilars, both at home and globally. At the same time, access and affordability of drugs could be improved by fairly modest policy changes, to encourage value-for-money and differential pricing of originator drugs and assure quality of generics.

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