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Pricing of drugs and donations: options for sustainable equity pricing

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Summary Effective medicines exist to treat or alleviate many diseases which predominate in the developing world and cause high mortality and morbidity rates. Price should not be an obstacle preventing access to these medicines. Increasingly, drug donations have been established by drug companies, but these are often limited in time, place or use. Measures exist which are more sustainable and will have a greater positive impact on people's health. Principally, these are encouraging generic competition; adopting into national legislation and implementing TRIPS safeguards to gain access to cheaper sources of drugs; differential pricing; creating high volume or high demand through global and regional procurement; and supporting the production of quality generic drugs by developing countries through voluntary licenses if needed, and facilitating technology transfer.

keywords pricing, donation, generic drug, compulsory licensing, parallel import, leishmaniasis, trachoma, azithromycin, cryptococcal meningitis, fluconazole, antiretrovirals

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Introduction

Two billion people do not have regular access to life-saving drugs or to those drugs which could vastly improve their living conditions. For diseases affecting the rich and the poor alike, prevalent in both developing and developed countries, there is ongoing research, development and production of effective drugs by the research-based pharmaceutical industry. Frequently, however, the market price of these drugs is so high that they are not affordable, and therefore non-existent, for the great majority of people in need. Drug price is not the only obstacle to access to treatment, but it is clearly a major one.

The final price of a drug for the end user is composed of various factors, a significant part originating from local influences such as import duties and tariffs; local taxes; absence of national price control policy; and mark-ups for wholesaling, distribution and dispensing. But the price set by industry (manufacturing selling price) for new drugs is a major part of the final user price, especially for the public health sector. It is the duty of states to implement health systems to protect the health of their populations. Even the poorest nations could better allocate their resources by giving priority to the basic needs of their citizens. But countries are as powerless as patients are when national drug costs become the greatest fraction of their budget. For some countries drugs can account for over half of the total health budget.

The pricing policy of pharmaceutical companies is not set according to the purchasing power of the different countries, but follows a general strategy of maximizing profit. Originator's drug prices are often equal, or more expensive, in developing countries than in rich countries. Such a profit-driven pricing policy further widens the health gap between the rich and the poor. In many cases, more affordable drugs are produced by the generic industry, even for the most recent drugs. However, decision-makers often do not have the information they need to identify manufacturers who can supply these drugs. They require easier access to comparative, updated prices.

This article summarizes recent price studies for drugs used in the therapy of four diseases that predominate in the developing world, and examines the possibilites available to achieve greater drug access. The price differences among the various manufacturers, the effect a price reduction would have on countries with low health budgetary lines and, in some cases, the effect drug donations have or could have on these populations is presented.

Leishmaniasis

Leishmaniasis currently threatens 350 million people in 88 countries; 12 million people worldwide are believed to be affected by the disease [World Health Organization (WHO) 2000]. Visceral leishmaniasis (kala azar) is the most severe form of the disease and, if left untreated, the fatality rate is as high as 100%. Treatment for leishmaniasis consists of pentavalent antimonial drugs administered through daily intramuscular injections for a period of 30 days. Sodium stibogluconate (SSG), marketed as Pentostam® by Wellcome, is an old drug, off-patent, but still expensive ($US 185 per patient treated). An alternative generic drug, sodium antimony gluconate (SAG) (generic sodium stibogluconate) is manufactured by Albert David Ltd in Calcutta. It is widely used in India and Bangladesh with reported cure rates of 95% (Chowdhury *et al.* 1991). At $US 13 per patient SAG is 14 times cheaper than SSG. For some time, these products were thought to be different but a recent analysis has shown that SSG and SAG are chemically identical (Veeken & Pécoul 2000). Using Indian SAG instead of SSG by Wellcome would allow any country in need to treat 14 times more patients for the same cost. All that is required is approval of SAG by the national drug regulatory authority.

Trachoma

Trachoma is caused by the microorganism *Chlamydia trachomatis* which provokes an inflammatory reaction in the eye with formation of follicles in the conjunctiva. After years of repeated infections, the inside of the eyelids may be scarred so severely that the eyelid turns inwards with eyelashes rubbing on the eyeball. If untreated, this condition leads to blindness. The disease is responsible for at least 15% of the world's blindness; about 6 million people are blinded by trachoma worldwide, most of these irreversibly. If blindness is to be prevented, 146 million active trachoma cases are estimated to be in need of treatment (WHO 2000).

Tetracycline ointment is the basic treatment for trachoma. Used since the 1950s, it is an effective drug that is available at low cost. However, the treatment course, lasting 6 weeks, is difficult to follow. A shorter treatment is possible using the drug azithromycin, a macrolide with a long average lifespan, administrated orally. According to Tabbara *et al.* (1996) a single dose of azithromycin is as effective as the 6-week daily course of tetracycline ointment. The simpler treatment course makes oral azithromycin much more effective for controlling trachoma in communities (Schechter *et al.* 1999). However, azithromycin has an enormous disadvantage compared with tetracycline ointment: its cost. Although it was first developed in 1981 by a Croatian pharmaceutical company, Pliva, exclusive sales rights were granted to Pfizer for the USA and Western Europe. In 1988 Pliva launched Summamed® in central and eastern Europe, and in 1991 Pfizer launched Zithromax® elsewhere. The patent will not expire until 2005 in the USA and 2008 in other countries.

The price fixed by Pfizer is too high for those countries where trachoma is endemic. One 250 mg capsule of Zithromax® costs around $US 4 in the USA, $US 2.17 in Spain. There are, nonetheless, generic manufacturers in countries without patent protection according to the national patent law in force at the time the product was first patented elsewhere. For instance, in India Cipla, an internationally reputed company, sells its generic product at one-sixth of the cost of the Pfizer price ($US 0.37 per 250 mg capsule).

Pfizer has participated in a programme to fight against trachoma, including the donation of Zithromax® for a period of 2 years, within the International Trachoma Initiative, as a part of the current comprehensive strategy to eradicate trachoma, called SAFE. Five pilot countries (Morocco, Vietnam, Ghana, Tanzania and Mali) have been selected for this donation programme out of 16 priority countries identified by the WHO in Africa and Asia where trachoma remains a major cause of blindness. Thanks to this programme, the product has already reached some populations in need. But who will provide treatment for 140 million active cases in dire need of this more effective treatment? Which country, among the most affected by trachoma, can afford Pfizer's current price? Clearly it would be better for countries to make tenders to all producers to introduce market competition so that countries could buy the quantities needed, eliminating their dependence on gifts.

Cryptococcal meningitis

Cryptococcal meningitis, caused by *Cryptococcus neoformans*, is the most frequent systemic fungal infection among HIV-infected people. Without treatment life expectancy is less than a month (UNAIDS 1998). On average this opportunistic infection affects 9% of people living with AIDS. In some countries the prevalence is much higher (19% in Zaire, 20–25% in Thailand). Cryptococcosis is relatively easy to diagnose. However, treatment and secondary chemoprophylaxis are often impossible in developing countries because of the high cost and limited availability of the drugs required.

Fluconazole, recently included in the WHO Model List for Essential Drugs, is one of the drugs recommended by the WHO (WHO 1999) for treatment (induction phase and

secondary prophylaxis for life), but the originator's brand product, Pfizer's Diflucan®, remains expensive with prices from private wholesalers ranging between $US 6.30 and 27.60 in different countries (Pérez-Casas *et al.* 2000a,b). Fluconazole was patented in 1982 by Pfizer and the patent will not expire before January 2004 in the US. In some countries the patent is not recognized, because pharmaceutical products were not patentable according to their national laws when Pfizer was granted the patent. Cheaper sources of fluconazole exist in Colombia, Spain, India and Thailand. Generic fluconazole of equivalent quality is produced, for instance, by a Thai company, Biolab, and available at $US 0.29 per 200 mg capsule (Pérez-Casas *et al.* 2000b).

If South Africa, where fluconazole is under patent, could import generic fluconazole from Thailand, the national cost of treating 10 000 patients suffering from cryptococcal meningitis would decrease from $US 29.70 million to $US 1.04 million per year for maintenance treatment (Pérez-Casas *et al.* 2000a,b). In other words, each year, with a given budget of $US 1.04 million, South Africa would be able to treat 352 patients with Pfizer's fluconazole and as many as 10 000 patients with generic fluconazole. This means 9648 additional lives saved each year for the same budget. In March 2000, the Treatment Action Campaign, a South African NGO, requested Pfizer to lower the price of fluconazole in South Africa or to grant voluntary licences. This request was supported internationally by Médecins sans Frontières (MSF). Pfizer answered by announcing a donation that only began to reach patients a year later.

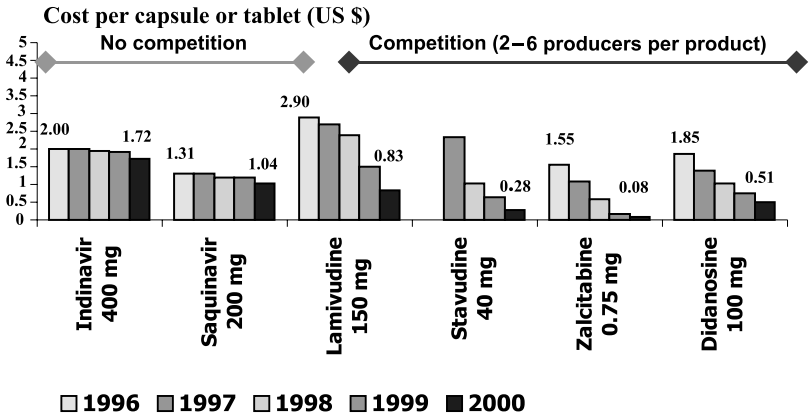
HIV/AIDS

An estimated 36 million people are currently infected with HIV worldwide, over 90% of whom live in the developing world (UNAIDS 2000). The disease is now the single leading cause of death in Africa. Antiretroviral (ARV) drugs have decreased the AIDS-related mortality rate in the USA by 75%, but the cost of these drugs is too high for the majority of infected people. The most effective way to stop the virus from advancing and to prevent resistances is a combination of three drugs. However, the current cost for this triple therapy is $US 10 000–15 000 per year per patient if the originator's brand products are used.

Without patent protection, ARVs are much cheaper. In Brazil pharmaceutical products were not patented until 1997 and most ARVs are produced locally. The average price reduction thanks to the competition posed by generic products, has been 79% up to last year (Figure 1), and the prices continue to drop. This has enabled the Brazilian government to give ARVs free of charge to all patients and more than 90 000 people currently receive treatment. In 1999 this cost only 3% of the Ministry of Health's budget and 0.06% of the country's GMP. In 2 years the Brazilian government was able to save $US 472 million in treatment of opportunistic diseases and hospital-related expenses. Between 1996 and 1999 the mortality rate from AIDS decreased by over 50% (Ministry of Health, Brazil, 2000).

Brazil is a middle-income country with a social security system in place. In less developed countries external funding would be needed to support the purchase of drugs and the national AIDS programme. It is however, clear that a similar or greater decrease in drug prices would increase access to treatment and enable resources to be better used.

There are other examples showing that generic competition leads to price reductions. A comparative study of prices of AIDS drugs (Pérez-Casas *et al.* 2000a) showed that in the range of ARV prices under scrutiny, the lowest price in developing countries is on average 85% less than in the US because of the availability of generic products. If



Source: Ministry of Health, Brazil, 2000

Figure 1 Competition is highly effective in reducing prices.

efavirenz is excluded from this estimate, for which no generic product was included in the study, the average price reduction is 90%. Prices were further reduced in February 2001 by generic companies in India, and the price of ARVs has been falling continuously (Figure 2). In May 2000, the biggest five pharmaceutical companies offered price reductions resulting in triple therapy costing around $US 1000. These reductions, however, have so far benefited only a very small number of those affected by HIV/AIDS, and even the discounted costs are higher than for some generic drugs, with Indian generics companies offering around $ US 250 per patient per year. Some pharmaceutical laboratories donate ARVs to developing countries, but these donations are limited in time and are only addressed to certain population groups. Boehringer Ingelheim, for instance, donates neviparine, but only to prevent vertical transmission.

Discussion: increasing access

Concerted international procurement efforts for vaccines and contraceptives have been able to significantly reduce prices for these products, through a combination of strategies. Prices of 1–5% of western market prices have been achieved, with millions gaining access to these products while pharmaceutical companies increased their sales and re-importation to wealthier markets was prevented. AIDS and other life-threatening diseases require similar longer-lasting, more engaging solutions than the current trend of discounts and drug donations with their associated problems of sustainability, geographical and quantitative restrictions, indication restrictions, time restrictions and delays in implementation (Guilloux & Moon 2000). No single strategy will be sufficient to achieve and sustain a real impact on access to vital drugs in developing countries. Rather, a comprehensive system of mutually supportive strategies is required.

Generic competition is one of the most powerful tools that policy makers have to lower the price of drugs sustainably. So far, it is the only proven way to bring drug prices down. Information on drug prices worldwide is scarce and should be gathered and made available to developing countries. An inter-agency project (UNICEF *et al.* 2001) has been established to improve information about sources and prices of selected drugs and diagnostics for HIV/AIDS. Similar comparative studies are needed for other health areas.

Encouraging generic competition requires a pro public-health interpretation of the World Trade Organization's (WTO) agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and active efforts by countries to produce or import generics. Applying compulsory licensing to import or locally produce generic versions of the products needed, for instance, would guarantee a sustainable way to get cheaper drugs. Through parallel importing, governments can also decrease the price of the patented drugs needed by obtaining them at the lowest price offered on the world market by the patent holder. Both safeguards, as well as others included in the TRIPS agreement, should be adopted into the national legislation (WHO 1997; Correa 2000). Those countries where the TRIPS agreement is not yet in force can benefit from more affordable generic drugs available in the world market as soon as these drugs are approved by national pharmaceutical authorities.

Voluntary lowering of prices by the pharmaceutical companies for low-income countries is a promising strategy. Some aspects and regulations, such as preventing lower-priced drugs from flowing back into high-income markets, the scope of these reductions in terms of populations covered, diseases, and rate of discount applied, require further elaboration. But thus far voluntary price reductions for HIV/AIDS drugs have not been systematic; rather, they appear to have largely been a public relations response to political and international public pressure.

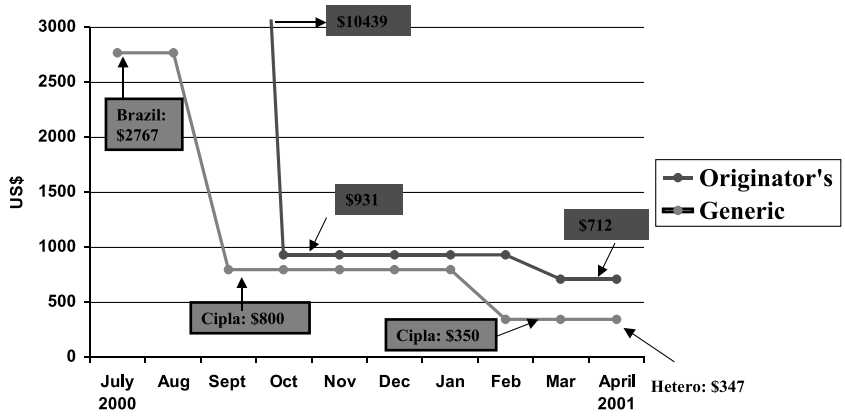


Figure 2 Impact of generic competition. Sample AIDS triple-combination: lowest world prices per patient per year (stavudine + lamivudine + nevirapine).

Centralized purchases, ensuring quality of the products by the WHO and other UN agencies with experience in bulk purchase, would enable prices to be better negotiated among all potential sources. This strategy has been enormously successful for vaccines.

Technology transfer should be supported as well by international organizations and national governments as a way to guarantee the sustainable production of affordable medicines.

Conclusions: towards equity pricing

Quality drugs for the treatment of diseases that are highly prevalent and cause high mortality and morbidity in developing countries are manufactured by different producers. Choosing quality products that are sold at the best prices would enable governments to protect their populations, reduce health-related expenses and, consequently, help a larger number within their countries. Governments of developed and developing countries, as the constituents of intergovernmental bodies such as the WHO and the WTO, are responsible for urging these agencies to look for long-term solutions. Any new pricing policy for essential medicines for developing countries must aim to achieve equity pricing if it is to have real impact on the lives of patients. Equity pricing is based on the principle that the poor should pay less for, and have access to, life-saving, essential medicines. The final aim is to make essential drugs available at a price that is fair, equitable and affordable for all in need. Access to essential drugs should not be a luxury of the privileged few. It is a matter of social equity and justice.

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