Untangling the web of price reductions:

a pricing guide for the purchase of ARVs for developing countries

9th Edition

July 2006 (Revised)

CAMPAIGN FOR ACCESS TO ESSENTIAL MEDICINES

MEDECINS SANS FRONTIERES

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BACKGROUND

This is the ninth edition of *Untangling the web of price reductions: a pricing guide for the purchase of ARVs for developing countries*. The report was first published by Médecins Sans Frontières (MSF) in October 2001[1] in response to the lack of transparent and reliable information about prices of pharmaceutical products on the international market – a factor which significantly hampers access to essential medicines in developing countries.

The purpose of this document is to provide information on prices and suppliers that will help purchasers make informed decisions when buying antiretrovirals (ARVs). This report is a pricing guide and does not include detailed information about the quality of the products listed. For further information on quality, please see box 1.

Since the first edition of "*Untangling*", prices of some first-line ARVs have fallen significantly due to competition between multiple producers. However, MSF finds that there are still common problems affecting the availability of the most needed essential medicines: (1) that in the absence of competition from multiple producers, companies may charge prohibitive prices (this is particularly the case for the most recent ARVs, including those recommended in the 2006 WHO treatment guidelines[2] for both first- and second-line), (2) that most originator companies establish a country premium, thereby excluding patients in some developing countries, (3) that even if companies announce discounted prices for their products in some eligible developing countries, the products are in fact not always available or affordable, and (4) that paediatric HIV/AIDS is neglected by most pharmaceutical companies.

Box 1: Quality issues

This report is a pricing guide and does not include detailed information about the quality of the products listed. However, price should not be the only factor determining procurement decisions. Readers and purchasers wishing to obtain more information about drug quality are therefore encouraged to consult "The WHO Prequalification Project: Access to HIV/AIDS Drugs and Diagnostics of Acceptable Quality" (known as the WHO prequalification list), a project initiated by the World Health Organization (WHO) and developed in collaboration with other United Nations organisations. This project evaluates pharmaceutical manufacturers and products according to WHO recommended standards of quality and compliance with Good Manufacturing Practices. It is part of an ongoing process that will expand as the participation of suppliers increases. Not all the products listed in this report have been prequalified by WHO, and only some of them are used by MSF in its own projects. Products included in the last edition of the WHO prequalification list (38th edition, published on 13th July 2006) appear in bold in the tables. Please consult the WHO website (*http://mednet3.who.int/prequal/*) for the latest information.

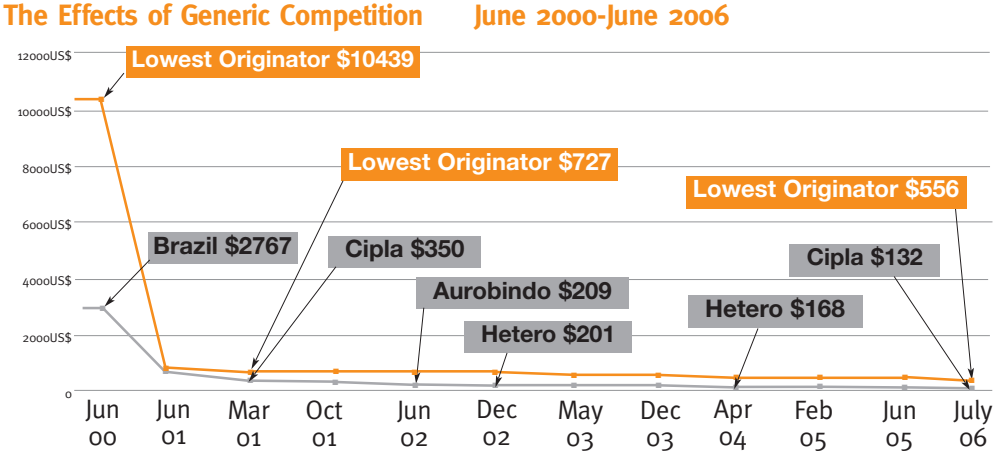
(1) Absence of competition leads to prohibitive prices for ARVs

Competition between multiple manufacturers has had a major impact in driving prices down. Treating an adult patient for one year with a triple antiretroviral first-line regimens may now cost as low as US$ 132.

Graph 1 provides a good illustration of how prices charged by originator manufacturers fall as generic competitors enter the market.

Such reduced prices were a necessary prerequisite for the scaling up of AIDS treatment to the levels we see today. But the picture is about to change radically. Faced with the emergence of resistance and the arrival of improved

Graph 1: *Sample of ARV triple-combination: stavudine (d4T) + lamivudine (3TC) + nevirapine (NVP). Lowest world prices per patient per year.*



Generic competition has shown to be the most effective means of lowering drug prices. During the last five years, originator companies have often responded to generic competition.

products on the market, the new WHO guidelines include second generation ARVs for both first- and second-line treatment. In the absence of competition, the price of treatment based on these second generation ARVs is currently extremely high.

Improved first-line treatment

Whereas most of the regimens previously recommended included stavudine (d4T) or zidovudine (AZT), the 2006 WHO treatment guidelines have added an improved first-line treatment based on combinations including tenofovir disoproxil fumarate (TDF). TDF is to be administered in combination with two drugs – one being either lamivudine (3TC) or emtricitabine (FTC), the other being either efavirenz (EFV) or nevirapine (NVP).

The improved first-line regimen therefore represents only a change in one drug – replacing d4T or AZT with TDF. But using such an improved first-line, based on TDF+3TC+NVP, would increase the annual cost of treating an adult for one year in a developing country from US$ 132 (with the triple fixed-dose combination 3TC/d4T/NVP) to:

- at the very least, US$ 321, which is two and a half times more. This assumes that Gilead's advertised differential prices for TDF can be obtained, and that countries choose to purchase the cheapest WHO prequalified generics for 3TC and NVP.
- up to US$ 708, which is almost five and a half times more. This assumes the originator manufacturers' advertised differential prices can be obtained for all three drugs. If they cannot be obtained, the price would be higher still.
- Scaling up treatment to one million people with this improved regimen would therefore imply an extra financial burden of between US$ 189 million and US$ 576 million.

Second-line treatment

It is estimated that 5-10% of a patient cohort in a given year will need to move from first- to second- line treatment. Data from an MSF project in South Africa shows that 16.7% of patients were on a second-line regimen after 48 months[3].

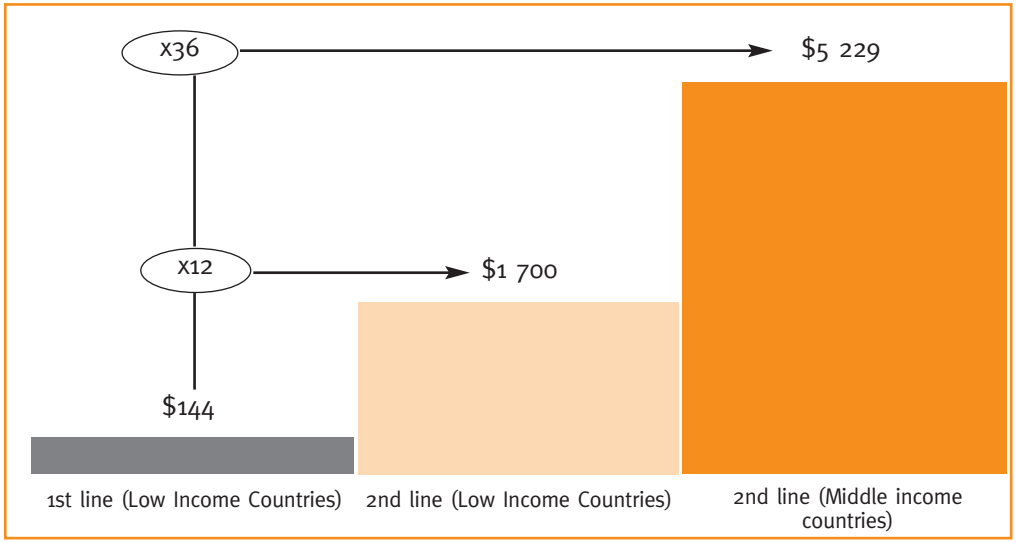
As more and more patients will need to move to second-line regimens, the impact of these prices on the financial sustainability of AIDS programmes is devastating. Switching one-tenth of patients in a given country in Africa to second-line treatment would double the costs of drugs for the national budget.

Graph 2 illustrates this change, by comparing the price paid in low-income countries for the first-line combination (3TC/d4T/NVP) with the price paid in low- and middle-income countries for one of the WHO recommended second-line regimens (ABC+ddI+LPV/r), according to the WHO Global Price Reporting Mechanism (GPRM) database[4].

Patent barriers

Although Least Developed Countries (LDCs) are not obliged under the World Trade Organization (WTO) rules enshrined in the 2001 Doha Declaration to grant or enforce pharmaceutical product patents until at least 2016, other developing countries saw this transition period end in January 2005[5]. This includes countries with significant manufacturing capacity, such as India, a major source of WHO prequalified generic antiretrovirals,

Graph 2: *Average weighted prices paid in 2005, reported to WHO GPRM for second-line ARVs in low- and middle-income countries, compared with first-line regimens*



Note: the price of US$ 132 quoted above is the price advertised by generic companies. In this graph, US$ 144 is the 2005 average weighted price reported to WHO GPRM as actually paid by countries.

which were required to introduce new pharmaceutical patent legislation. It is crucial to note that changes in patent laws in countries with manufacturing capacity also affect other countries that depend on imports from these countries.

India was therefore required to change its patent legislation in 2005. The new 2005 Indian Patents Act does not affect medicines that were invented before 1995. However, patent applications could be filed in India from 1995 onwards. The Indian patent offices have started to examine the thousands of pending patent applications, and patents on key AIDS medicines may subsequently be granted.

If a patent were granted for a medicine for which generic versions were available before January 2005, it would not stop Indian generic manufacturers who already produce from continuing to market the medicine, provided they have made a "significant investment". Indeed, the 2005 India Patents Act stipulates an automatic licensing system which allows for the continued production of the generic version upon payment of a "reasonable" royalty.

If a patent were granted for a medicine, but no generic version was marketed before 2005, only patent holders would have the right to produce this medicine unless India, and other countries where the drug is under patent, make use of the flexibilities enshrined in the Doha Declaration on the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and Public Health. They could, for example, authorise governmental use or issue compulsory licenses, thereby giving a third party the right to produce, market, export and import the patented product.

These TRIPS flexibilities, however, remain underused. Least Developed Countries still continue to purchase unnecessarily expensive originator products, when much cheaper generics of equivalent quality exist, and are accessible to them under the transition period described above. Other developing countries are not making full use of the TRIPS and Doha flexibilities to purchase generics, and are continuing to pay prohibitive prices for originator ARVs or ration access to these drugs, when cheaper WHO prequalified generic versions exist.

Some recent examples include:

- purchases of nevirapine 200 mg illustrated in the WHO Global Price Reporting Mechanism (GPRM) summary report issued in March 2006[4], which shows how "low-income countries paid on average US$ 219 per patient-year (even more than middle-income countries, at US$ 112) as 40.5% of their total transaction volume was with Boehringer Ingelheim (BI), at an average price of US$ 445 per patient-year, the remainder 59.5% being with generic companies, at an average price of US$ 64 per patient-year." In countries such as Kenya, all buyers (including UNICEF, the Global Fund, IDA, MSH) reported having bought BI's product at even US$ 499 per patient per year. Nevirapine is still under patent in Kenya and in other several low-income countries or regions such as Malawi, Uganda, Zambia, Zimbabwe[6] and most francophone African countries[7].
- purchases of older ARVs such as lamivudine/zidovudine, for which GPRM data shows that many countries purchased the originator product at prices ranging from US$ 240 in LDCs such as Zambia, Ethiopia or Rwanda to more than US$ 270 in South Africa or Sudan, despite the existence of WHO prequalified generics available at an average of US$ 131.

Lack of generic competition also impacts the production of fixed-dose combinations (FDCs), which were a key factor for starting ARV treatment in resource-poor settings. FDCs increase adherence, decrease costs, and facilitate supplies. But with generic production under threat, the production of appropriate FDCs for newer ARVs is at risk.

The Doha Declaration was a milestone in its affirmation of the primacy of public health interests in the application of intellectual property rights protection. By confirming the inherent flexibilities within the TRIPS Agreement, it allows governments to take measures to protect public health, and places the responsibility for ensuring that patents do not constitute a barrier to access to medicines firmly in the hands of national authorities.

Member States of the World Trade Organization classified as "Least Developed" are authorised, under paragraph 7 of the Doha Declaration, to not recognise, grant or enforce patents or data exclusivity rights on pharmaceutical products that have already been granted until at least 1st January 2016.

Article 31 of the TRIPS Agreement, confirmed by paragraph 5(b) of the Doha Declaration, authorises WTO Members to produce, purchase, import

and use generic versions of medicines under patent protection through the granting of a compulsory licence or government use.

Countries should proactively make use of these provisions and donor countries and agencies should actively encourage countries to use the TRIPS safeguards to ensure that already scarce resources are not wasted on the purchase of overpriced products.

(2) Most of the originator companies establish a country premium thereby excluding patients in some developing countries

When originator companies apply discounted prices on ARVs, each has different eligibility criteria, which is a considerable source of confusion for purchasers.

Most originator companies offer their most discounted prices only to a certain group of countries, usually Least Developed Countries and sub-Saharan Africa. These prices are referred in this document as first category prices. Other companies do it differently: Merck extends first category prices to countries ranked as 'low' and 'medium' on the Human Development Index with HIV prevalence rates greater than 1%; GlaxoSmithKline offers differential prices for their products to all Global Fund grantees; and Gilead has established its own list of eligible countries with a sort of mixed criteria, including some middle-income countries. This means that if a country qualifies for the discounted prices offered by one company, it may not necessarily be included in the list of eligible countries of another company.

Certain manufacturers (such as Merck and Roche) also offer second category prices for some middle-income countries. These are almost twice as high as the first category prices. Also, Bristol-Myers Squibb (BMS) places all Southern African countries in its second category prices, including countries as poor as Mozambique and others with the highest prevalence rate in all Africa.

Graph 2, and Graph 3 below both show how middle-income countries are paying extremely high prices for ARVs. Without competition, the price of second generation ARVs is prohibitive, and limitations imposed by companies to accessing the lowest price lead to huge discrepancies among developing countries. Middle-income countries are still paying 1.5 times the price paid in low-income countries for first-line ARVs and even up to nine times more, for new ARVs such as LPV/r, according to data published by WHO[9].

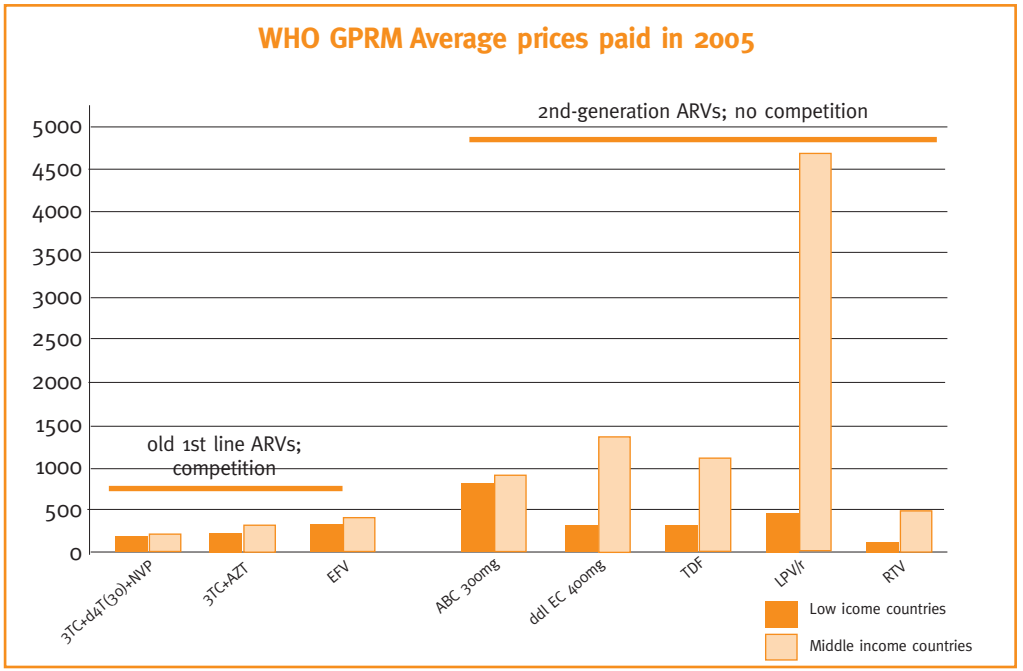
(3) Advertised differential prices are not always available in eligible developing countries

There are two issues here: the marketing and registration of products, and complexity of companies' 'access programmes'.

Box 2: Limiting the scope of patentability

On a more positive note, the 2005 India Patents Act includes key provisions to ensure that patents are not used to extend monopolies on medicines artificially at the expense of the public. Firstly, the law states that patents should not be granted on derivatives of known molecules, such as salts, polymorphs or combinations, unless efficacy is improved. Secondly, third parties can seek to oppose a patent before it is granted, on the basis of such provisions, to make sure that patents are not unduly granted[8].

Graph 3: *Brand and country premium: example of prices **paid** by developing countries for ARVs*



Marketing and registration

Registration of a medicine allows it to be marketed in a country after evaluation of the product dossier by the relevant National Drug Regulatory Authorities (NDRA). In order to purchase or import a drug into a country, it must be registered there. Applications must come from manufacturers or their representatives in each country.

Nevertheless, some companies are neglecting to register their products even in countries for which they have announced a discounted price. Even in countries with the greatest needs, such as Mozambique or Cambodia, some ARVs manufactured by originator companies are neither registered nor marketed, and must be bought in neighbouring countries, with all the additional expenses and investment in human and administrative resources that this implies.

In fact, non-registered drugs become unattainable for all but those who can obtain a special authorisation for import from the Ministry of Health. In several countries, including Uganda, Guatemala, Honduras, Laos or Ethiopia, Médecins Sans Frontières' experience has shown that obtaining such authorisations to import non-registered drugs can be extremely complex and time-consuming.
The consequences of not registering a drug are obvious in terms of access. Gilead's TDF is registered in thirteen of the 97 countries deemed eligible for a discounted price according to Gilead's own policies. The significant time required to overcome the lack of registration makes the use of TDF a practical impossibility for most care-providers. For instance, in South Africa, MSF must apply for special authorisation to use TDF on a patient-by-patient basis. Another example concerns Abbott's new thermostable lopinavir/ritonavir (LPV/r), which is not registered anywhere but in the United States and the European Union. Other countries are therefore forced to use the older version that is ill-suited to storage at high temperatures, and therefore unsuitable for much of developing countries[10].

The problem is compounded by the fact that National Drug Regulatory Authorities' procedures for registering the products are often slow, even if companies do everything necessary to get approval. Fast-track registration procedures should be put in place for new products of relevant interest for public health, based on WHO prequalification or on registration in high-regulated countries.

The pace of registration of ARVs, including generic formulations as they become available, is of critical importance. It is strongly recommended for countries to accelerate registration of needed ARVs, applying fast-track procedures for WHO prequalified products, thus avoiding unnecessary delays.

Complexity of companies' so-called 'access programmes'

The sheer complexity of these schemes also impacts the availability of advertised differential prices in eligible countries. The channel chosen by the companies to distribute the products offered at lower price is still too burdensome.

Roche's products, for example, have to be ordered from Basel, Switzerland, and paid for in Swiss francs, which is difficult for procurement centres in developing countries.

MSF's experience purchasing TDF directly from Gilead for patients in South Africa has revealed how the procedure involves extensive paperwork, including supplying information on the history of the treatment programme, funding sources, catchment areas, the type and number of employees, protocols initiating treatment, the first- and second-line regimens used, laboratory monitoring and other programme details.

(4) Paediatric HIV/AIDS is neglected by most companies:

Today, most small children are treated with liquid formulations. These syrups or oral solutions are ill-adapted for use in remote settings, as they are complex to reconstitute and administer, can taste foul, and are cumbersome to transport and store. They are also expensive. Indeed, treating a child weighing 10 kg for one year with stavudine, nevirapine and lamivudine (d4T, NVP and 3TC) syrups can cost up to US$ 534, while treating an adult with the same drugs costs US$ 132, or five times less. A major difference is also that adult treatment exists in fixed-dose combinations, whereas production of paediatric FDCs is extremely limited. An alternative is to treat children by opening adult capsules or breaking adult tablets. However, such non-standard practice presents significant risks of under- or over-dosing.

Yet most manufacturers still produce paediatric versions of their drugs only in syrups, suspensions or oral solutions. Some companies such as Gilead, Hetero and Strides do not manufacture any paediatric

formulations at all. Pharmaceutical companies are not investing enough resources in the development of appropriate paediatric formulations, since it is a small and risky market without enough importance in wealthier countries, where prevention of mother-to-child transmission is largely successful.

A limited number of generic paediatric triple fixed-dose combinations are currently reaching the market, however, and pressure should be put on these manufacturers to complete their dossiers and submit it to the WHO prequalification as a priority. These are for first-line therapies (such as the d4T/3TC/NVP FDC manufactured by both Cipla and Ranbaxy). But no second-line formulations are in the pipeline for children and more formulations are needed to complete the spectrum of regimens needed in an AIDS programme.

Donors and international organisations need to prioritise paediatric AIDS therapy, and work proactively to encourage much-needed R&D for this neglected group of patients. WHO must give clear recommendations to manufacturers on dosages for children, to avoid the current situation where Cipla and Ranbaxy are developing paediatric formulations for 3TC/d4T/NVP, but at different dosages. The WHO Prequalification project must prioritise these products, by outlining the requirements needed for the qualification of the new formulations. If necessary, support should be organised to help manufacturers speed up the completion of their product dossiers.

FINAL CONSIDERATIONS

According to UNAIDS and WHO, an estimated 250,000 to 350,000 deaths were averted in 2005 because of expanded access to AIDS treatment. This picture must be balanced with the three million people who died of AIDS-related illnesses in 2005. Of these, more than 500,000 were children[11]. Proactive efforts must be taken. These must not only focus on increasing the number of patients on treatment, but also on providing them with the best possible treatment, which includes ensuring that those who begin treatment will receive at affordable prices second- and even third-line treatment, when they eventually need it.

95% of the people living with HIV live in developing countries. Research and development (R&D) for diagnostics, medicines, preventive therapies, and vaccines, for children, mothers, and adults must be conducted to develop products that are affordable and suitable for use in remoter settings. The need for these specific medical tools is clear. This echoes the recent decision by the 2006 World Health Assembly to draw up a strategy and plan of action to secure an enhanced and sustainable basis for needs-driven, essential health R&D.

Patents should no longer be a barrier to accessing affordable medicines, increasing generic competition and assuring that the appropriate FDCs, including those for children, are developed. Flexibilities in both international and national patent rules exist to allow for this and there is no excuse for delaying the use of these safeguards. However, despite the medical urgency, it seems that the political will to do so is often lacking.

METHODOLOGY

As with previous editions, MSF sent questionnaires to both originator and generic companies asking them to provide the following information about ARV prices for developing countries: price per unit (or per daily dose), restrictions that apply to each of the prices quoted (eligibility criteria), and any additional specificity applicable to the quoted prices. The data were collected up to 18th May 2006.

All originator companies marketing ARVs were included in the survey. But the list of generic producers is by no means exhaustive[12]. Indeed, only those generic companies having at least one antiretroviral prequalified by WHO are included in the survey.

Some important preliminary remarks on the data presented in this report:

- The information on prices given in this document only relates to ARVs. It does not include other costs linked to antiretroviral treatment, such as diagnosis, monitoring or treatment of opportunistic infections. For information on the prices of these products, please consult the most recent edition of "Sources and prices of selected drugs and diagnostics for people living with HIV/AIDS", published yearly by UNICEF, UNAIDS, WHO, and MSF[13].

- The prices listed here are those quoted as sale prices by the manufacturers. The prices paid by the consumer might be higher because of add-ons (such as import taxes and distribution mark-ups), or may be lower if subsidised.

- Companies might use different trade terms (known as incoterms[14]). Prices quoted by all generic companies, plus Roche, Abbott and Gilead are "FCA" or "FOB", meaning that transport, international freight and insurance costs are not included. Remaining companies listed in this report do include freight and insurance in their prices. Prices have nevertheless not been adjusted. As recently demonstrated by US General Accountability Office, these differences do not undermine their essential comparability[15].

- Originator companies have different eligibility criteria for countries and entities, as explained in the introductory chapter. The different categories of prices are detailed in the product cards. **Please refer to Table 2 for explanations on different eligibility criteria quoted by companies.**

- Generic companies normally do not impose restrictions on prices, except for Aspen. But occasionally generic companies may negotiate prices different from those quoted here.

- The Clinton HIV/AIDS Initiative[16] for example negotiates prices for ARVs and diagnostic tests with generic companies on behalf of national AIDS programmes included in their consortium. To date the Clinton Foundation has reached agreements with five ARVs manufacturers to lower the prices of 20 ARV formulations. When these prices differ significantly from those quoted in the survey by companies, they are mentioned in the product card.

- Information on patents is only indicative and should be checked with national authorities. It should in no way form the basis of a procurement decision.

- Information on the WHO pre-qualification status must always be checked in the WHO website (*http://mednet3.who.int/prequal/*)

How to read the product cards?

General information:
For each of the ARVs, general information on the history of the product and relevant WHO guidance is provided[2,17].

Table 1: Prices quoted by companies for eligible developing countries
All prices are quoted in US$. Conversions have been made on the day the price information was received using the currency converter site: *www.oanda.com*. Prices are rounded up to the third decimal for unit price and to the nearest whole number for yearly price per patient.

The annual cost of treatment per patient (ppy) has been calculated according to WHO dosing schedules, multiplying the unit price (one tablet or capsule) by the number of units required for the daily dose and by 365. The price of smallest unit is included in brackets.

When no information was provided, we have inserted "n/a" for "not available".

For paediatric treatments, prices are calculated for a 10 kg child using WHO treatment guidelines[2]. This is an estimate since the weight of a child increases during any given year. When it was not possible to calculate the dose for a 10 kg child, only the unit price is indicated.

To know whether a country is eligible for a given price of a given company, please refer to table 2 and the list of countries for each category given in the annexes.

Products included in the most recent edition of the WHO prequalification list (38th edition, published 13th July 2006) **appear in bold in the tables**. Readers and purchasers wishing to obtain more information about the quality of ARVs are encouraged to consult the WHO Prequalification project website (*http://mednet3.who.int/prequal/*) **as this list is updated very frequently**. Initiated by WHO in 2001, and developed in collaboration with other United Nations agencies, this project evaluates pharmaceutical manufacturers and products according to WHO recommended standards of quality and Good Manufacturing Practices.

Chart 1: Evolution of the lowest price quoted by companies for eligible countries since 2001
This chart shows the price evolution over time, for both originator and generic products, as quoted to MSF surveys since 2001. When they exist, only generic products that are WHO prequalified are considered for the graph. If no generic is WHO prequalified yet, the lowest possible price is taken into account.

Chart 2: Transaction prices of ARVs purchased in developing countries as compiled by WHO GPRM 2005-2006
This chart gives examples of transaction prices of ARVs purchased in some developing countries, as compiled by WHO/AMDS Global Price Reporting Mechanism (GPRM)[9,18], based on information from UNICEF, International Dispensary Association, MSH/Deliver, and the Global Fund. This chart does not represent the price paid by consumers, which might be higher (due to taxes, transport, and other add-ons along the distribution chain), or lower if subsidised. Each point in the chart represents one transaction, so one country can be represented by several points.

Spotlight on access issues
In this new edition we have tried to summarise the most salient issues related to access to each product, with the aim of facilitating informed decisions at country level, taking into account the problems and obstacles that may be encountered when trying to gain access to a product, and at the best price.

ABACAVIR (ABC)

General information

- Therapeutic class: HIV-1 and HIV-2 nucleoside reverse transcriptase inhibitor (NRTI)
- Indicated for first- and second-line, for adults, adolescents and children (WHO 2006 guidelines[2])
- Originator company, and product brand name: GlaxoSmithKline (GSK), Ziagen
- First approval by US Food and Drug Administration (FDA): 17th December 1998
- Included in the WHO Model List of Essential Medicines (EML)[17]
- World sales of originator product: US$ 290 million in 2004[19]

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries

	Daily dose	GSK	Aurobindo	Cipla	Hetero	Ranbaxy
Eligibility restrictions		See table 2	none	none	none	none
ABC 300 mg tablets	2	**636 (0.871)**	**564 (0.780)**	456 (0.625)	727 (0.995)	511 (0.700)
ABC 20 mg/ml oral solution	--	**304 (0.104/ml)**		336 (0.115/ml)		

Note: the Clinton Foundation has agreed with Cipla to sell ABC 300 mg at US$ 447 per patient per year in countries included in their consortium[16].

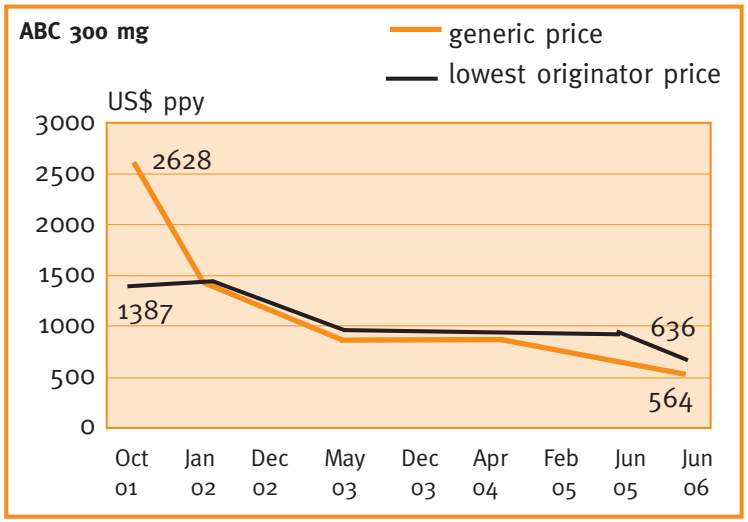


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001

As of June 2006, there was a WHO prequalified generic source of Abacavir, and hence its price is considered here.

Between October 2001 and June 2006, the lowest price of the originator product was divided by 2.2. During same period of time, generic prices have been divided by 4.5.

Spotlight on access issues:

There is a need for greater competition between manufacturers to reduce prices further. The current lowest price for the originator product, at US$ 636, is almost five times the price of the triple FDC used in most first-line regimens today.

In addition, because of GSK's eligibility restrictions, potential non-African buyers of abacavir that are not funded by the Global Fund, have no access to the lowest prices for the GSK product.

Although the abacavir molecule was developed in the 1980's, GSK applied for patents in 1997 on abacavir sulphate. This may hamper generic competition. If the Indian patent office grants a patent, Indian manufacturers may have to withdraw their products from the market, unless they can make use of the automatic licensing provisions of the 2005 India Patents Act (see introduction). Indian NGOs and manufacturers may however seek to oppose the granting of this patent in India.

Although abacavir was included as part of first-line NRTI backbone in most recent WHO recommendations for paediatric treatment, no company has yet developed a child-friendly version.

ATAZANAVIR (ATZ)

General information

- Therapeutic class: HIV-1 protease inhibitor (PI)
- Indicated for second-line, for adults and adolescents (WHO 2006 guidelines[2])
- Originator company, and product brand name: Bristol-Myers Squibb (BMS), Reyataz
- First approval by US Food and Drug Administration (FDA): 20th June 2003
- Not included in the WHO Model List of Essential Medicines (EML)[17]
- World sales of originator product: US$ 81 million in 2003, US$ 369 million in 2004. ATZ represents 19.6% of all PI sales in the US[20].

Spotlight on access issues:

Atazanavir is one of the three protease inhibitors recommended by WHO for second-line treatment, and is the most patient-friendly PI as its administration requires an intake of only two 150mg pills a day. But its price, at more than US$ 6,125 per adult patient per year in rich markets[21], is prohibitive for developing countries. Moreover, it must be combined with ritonavir as a booster, so the final cost when compared with other PI regimens is prohibitive.

Patents on ATZ were applied for in 1997-98 in many countries, including India. Oppositions to the patent application may however be filed in India. Unrestrained generic competition from Indian companies will only be possible if the patent is rejected by the Indian patent office or if the Indian government is willing to grant compulsory licenses to Indian manufacturers or applies for governmental use.

DIDANOSINE (ddI)

General information

- Therapeutic class: HIV-1 and HIV-2 nucleoside reverse transcriptase inhibitor (NRTI)

- Indicated for second-line, for adults, adolescents and children (WHO 2006 guidelines[12])

- Originator company, and product brand name: Bristol-Myers Squibb (BMS), Videx

- First approval by US Food and Drug Administration (FDA): October 1991 for chewable tablets; October 2000 for enteric-coated tablets

- Included in the WHO Model List of Essential Medicines (EML)[17]

- World sales of originator product: US$ 274 million in 2004[22] (in 1999, the figure was already US$ 205 million[23])

- Didanosine was developed by the National Institutes of Health (NIH), a US government research institute, which then licensed the drug to Bristol-Myers Squibb, in exchange for a 5 to 6% royalty on sales[24]. NIH basic patents on didanosine are supposed to expire in the US in 2006-2007, but BMS holds patents on improved formulations, which run until 2012 and 2018.

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	BMS		Aspen VL from BMS	Aurobindo	Cipla	Hetero	Ranbaxy
		1st category	Southern African countries					
Eligibility restrictions		See table 2		See table 2	None	None	None	None
ddI 25 mg tablets	--			(0.191)		(0.063)		
ddI 50 mg tablets	--			(0.192)		(0.075)		
ddI 100 mg tablets	4	**310 (0.212)**	**401 (0.275)**	307 (0.210)	**233 (0.160)**	195 (0.134)	280 (0.192)	321 (0.220)
ddI 200 mg tablets	2					146 (0.200)		
ddI 250 mg enteric-coated capsules	1	**223 (0.611)**	**273 (0.747)**		127 (0.350)	103 (0.283)		146 (0.400)
ddI 400 mg enteric-coated capsules	1	**288 (0.789)**	**352 (0.964)**		208 (0.570)	134 (0.367)		219 (0.600)
ddI 2 g powder for reconstitution	--	**130 (6.295/2g)**	**140 (7.697/2g)**		44 (2.160/2g)			

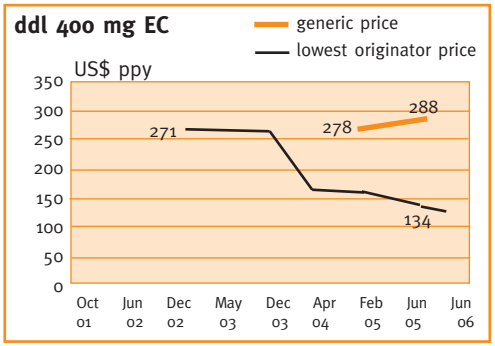


Chart 1: Evolution of the lowest price quoted for developing countries since 2001
As of June 2006, there was no WHO prequalified generic source of didanosine 400mg. The lowest available generic price is therefore given here.

In the absence of strong competition, originator prices have not changed in the last five years.

Spotlight on access issues:

The Bristol-Myers Squibb list of eligible countries is too limited, as it only includes 66 countries, and the product is not always available in the countries defined as eligible. Additionally, BMS has no pricing policy for middle-income countries. For instance, according to the WHO GPRM database in 2005, in El Salvador, where there is no competition, purchasers paid US$ 1,533 per patient per year for the originator 100 mg formulation (five times the price fixed by BMS in eligible countries). But in neighbouring Honduras, where there is competition between the originator and generic alternatives, the same report lists the price charged by BMS at US$ 429 per patient per year.

Similarly, according to a Médecins Sans Frontières (MSF) survey completed in September 2005, MSF paid US$ 3,175 per patient per year for ddI EC 400 in Guatemala (or 1000% more than the lowest BMS price), US$ 1,091 in Thailand (280%), and US$ 975 in Ukraine (238%). The enteric-coated ddI is not yet widely used, but is recommended in the new WHO guidelines for second-line treatment, and therefore all steps should be taken to improve access to this product as scaling up occurs. There is an urgent need to have generic versions prequalified by WHO, and made available in countries. However, it remains to be seen whether BMS will obtain patents in India on the enteric-coated formulation of ddI.

EFAVIRENZ (EFV)

General information

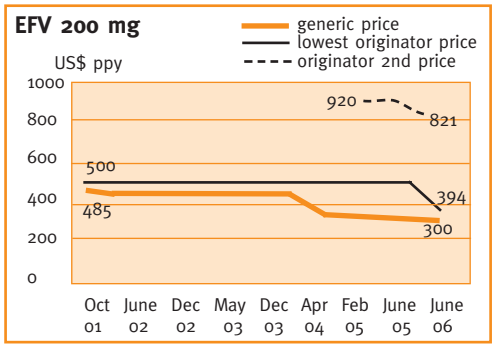
- Therapeutic class: HIV-1 non-nucleoside reverse transcriptase inhibitor (NNRTI)
- Indicated for first- and second-line, for adults, adolescents and children (WHO 2006 guidelines[2])
- Originator companies, and product brand names: Bristol-Myers Squibb (BMS), Sustiva, or Merck, Stocrin
- First approval by US Food and Drug Administration (FDA): 17th September 1998
- Included in the WHO Model List of Essential Medicines (EML) [17]
- World sales of originator product: US$ 621 million in 2004[19]. In 2004, EFV was the most prescribed ARV in the US, representing 65% of all NNRTIs prescriptions
- Efavirenz was developed by Dupont Pharma and is now marketed by BMS. Merck has the marketing license in several countries.

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	Merck		Aurobindo	Cipla	Hetero	Ranbaxy	Strides
		1st category	2nd category					
Eligibility restrictions		See table 2		None	None	None	None	None
EFV 50 mg capsule	--	**(0.116)**	**(0.213)**	(0.110)				
EFV 200 mg capsule	3	**394 (0.360)**	**821 (0.750)**	292 (0.267)	225 (0.206)	292 (0.267)	**300 (0.274)**	
EFV 600 mg tablet	1	**277 (0.760)**	**697 (1.910)**	**299 (0.820)**	**217 (0.597)**	291(0.750)	**292 (0.800)**	240 (0.670)
EFV 30 mg/ml suspension	--	**309 (0.094)**	**496 (0.151)**	227 (0.069)				

Note: the Clinton Foundation has agreed with Aspen, Cipla, Ranbaxy, and Strides to sell EFV 600 mg at the price of US$ 240 per patient per year, and with Ranbaxy and Strides to sell EFV 200 mg at the price of US$ 240 per patient per year, in countries of their consortium[16].



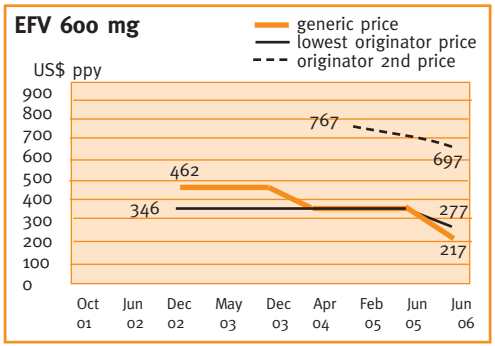


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001

The price of the lowest WHO prequalified generic of EFV is given here.

Spotlight on access issues:

Efavirenz is a key drug for first-line treatment. Although EFV has been marketed for a considerable period already, its price is still very high. Alone, it is priced at more than twice the price of the most widely used triple FDC (stavudine, lamivudine and nevirapine).
The generic products are priced between 2.4 and 3.2 times cheaper than Merck's second category price, but countries are still purchasing the originator product. Even buyers in some countries such as El Salvador, Bolivia or Tajikistan were reported by the WHO GPRM as paying more than US$ 800 and as much as US$ 1,128 in 2005. In Brazil, where this product is under patent, in 2005 EFV alone took up 14% of the National AIDS Programme budget[25].

There is an urgent need to have fixed-dose combinations including efavirenz that could simplify the new WHO recommended treatment.

EMTRICITABINE (FTC)

General information

- Therapeutic class: HIV-1 nucleoside reverse transcriptase inhibitor (NRTI)
- Indicated for first-line, for adults (WHO 2006 guidelines[21])
- Originator company and product brand name: Gilead, Emtriva
- First approval by US Food and Drug Administration (FDA): July 2003
- Not included in the WHO Model List of Essential Medicines (EML) [17]
- World sales of originator product: US$ 10 million in 2003 (in five months)[26], US$ 57.6 million in 2004[27].
- Emtricitabine was developed by Emory University in 1996. The University agreed to waive their right to a royalty on sales within the Gilead Access Program[28].
- Patents on the basic molecule are due to expire in 2010-2011[28].

Spotlight on access issues:

Emtricitabine is neither registered nor marketed in developing countries, but is available co-formulated with TDF. When making the choice, it should be taken into account that there are potential intellectual property issues that could affect this product in countries in need, while its older therapeutic equivalent, lamivudine (which has the same indications and profile), could be free of such restrictions.

LAMIVUDINE (3TC)

General information

- Therapeutic class: HIV-1 and HIV-2 nucleoside reverse transcriptase inhibitor (NRTI)
- Indicated for first- and second-line for adults and adolescents, and for first-line only for children (WHO 2006 guidelines[2])
- Originator company, and product brand name: GlaxoSmithKline (GSK), Epivir
- First approval by US Food and Drug Administration (FDA): November 1995
- Included in the WHO Model List of Essential Medicines (EML)[17]
- World sales of originator product: US$ 549 million in 2004[19] and more than US$ 500 million each year for last nine years[29].
- Patent status: the patent holder is IAF Biochem International SA (Canada). Various litigations have taken place with the rights, as research was undertaken by others including a Yale University scientist. GSK pays a 14 % royalty to the Canadian firm[30].

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	GSK	Aspen under VL from GSK	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
Eligibility restrictions		See table 2	See table 2	None	None	None	None	None
3TC 150 mg tablet	2	**69 (0.095)**	**69 (0.095)**	**54 (0.075)**	**51 (0.070)**	53 (0.073)	**66 (0.090)**	**58 (0.080)**
3TC 300 mg tablet	1	**n/a**		**56 (0.155)**	54 (0.150)		66 (0.18)	
3TC 10 mg/ml oral solution and dry syrup	--	**82 (0.028)**	50 (0.017)	**58 (0.020)**	**52 (0.018)**			

Note: the Clinton Foundation has agreed with Cipla to sell abacavir 50 mg / 5 ml at US$ 0.009 per unit (ml) in countries included in their consortium[16].

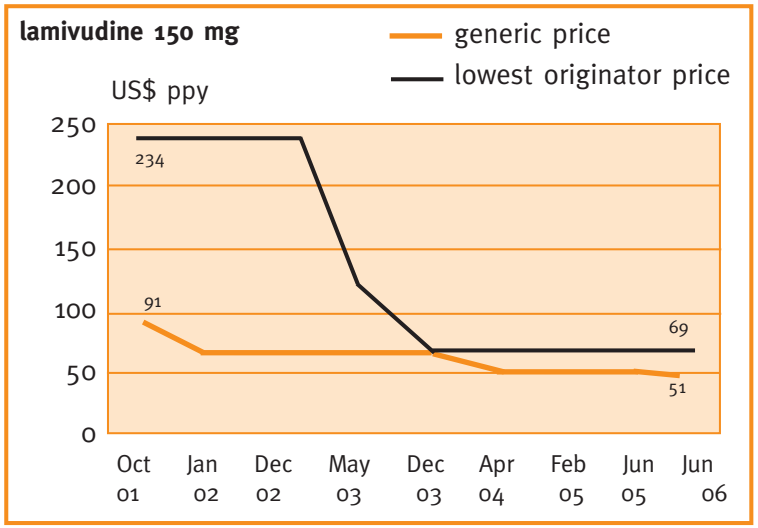


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001
The price of the lowest WHO prequalified generic of 3TC is given here.

Spotlight on access issues:

Lamivudine is a product in high demand, whose price has substantially decreased. There are, as of June 2006, five generic versions prequalified by WHO. In 2005, most countries reported to the WHO GPRM having paid the lowest price, whether for the generic or the originator product.

Some transactions, however, were reported at double the price, or more, for example in Swaziland - with Cipla's product, or in Thailand - with GPO's product.

In China, lamivudine is still unaffordable at US$ 1,977 per patient per year, due to GSK monopoly rights on the drug.

No company produces a child-friendly low dosage pill, and adapted dosages, for example 75 mg tablets, are urgently required. Some fixed-dose combination formulations for children containing 3TC have been developed by generic companies and should reach the market very soon.

NELFINAVIR (NFV)

General information

- Therapeutic class: HIV-1 and HIV-2 protease inhibitor (PI)
- Indicated only for second-line in adults, adolescents and children (WHO 2006 guidelines[2])
- Originator company, and product brand name: Roche, Viracept
- First approval by US Food and Drug Administration (FDA): 14th March 1997
- Included in the WHO Model List of Essential Medicines (EML) [17]
- World sales of originator product: US$ 259 million in 2004[19]
- Nelfinavir was developed by Agouron Pharmaceuticals Inc. in collaboration with the pharmaceutical division of Japan Tobacco Inc. In Europe and a few other countries outside the United States, Agouron/Pfizer has licensed Roche to market nelfinavir[31]. Patents on nelfinavir are due to expire in 2014.

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries

	Daily dose	Roche		Aurobindo	Cipla	Hetero
		1st category	2nd category			
Eligibility restrictions		See table 2		None	None	None
NFV 250 mg tablets	9	**683 (0.208)**	**1,543 (0.470)**	1,379 (0.420)	1,337 (0.407)	986 (0.300)
NFV 625 mg tablets	4	**n/a**	**n/a**			
NFV 50 mg/g oral powder	--	**69 (0.174)**[32]	**82 (0.199)**[32]			

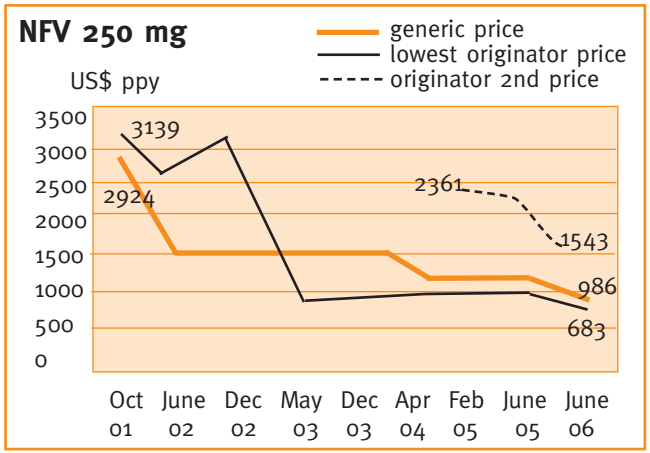


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001

As of June 2006, there was no WHO prequalified generic source of nelfinavir. The lowest available generic price is therefore given here

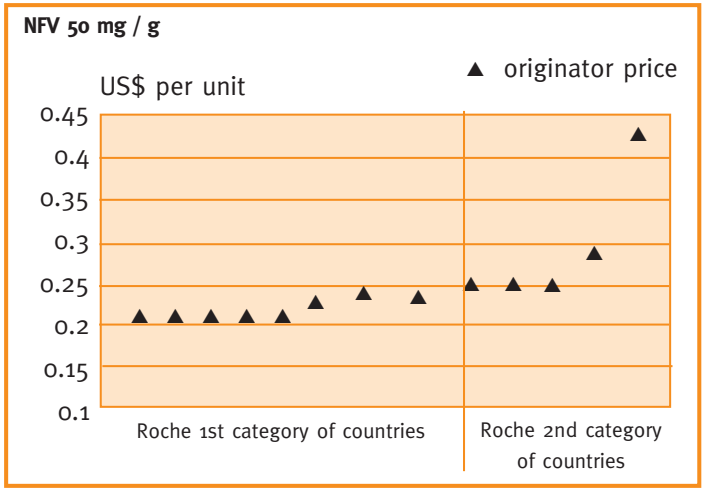


Chart 2: Transaction prices for NFV as compiled by WHO GPRM in 2005-06 (see "how to read the product cards" box)

For the treatment of children, procurement prices reported in 2005 to the WHO GPRM were always higher than the price announced by the company - more than twice in Guatemala, for example.

Spotlight on access issues:

The use of nelfinavir in children is extremely complex, due to the significant amounts of powder that have to be taken on a daily basis (12 grams of powder twice a day for a 10 kg child). Not only is this formulation ill-adapted, but its price remains prohibitive, as is the case with other protease inhibitors. There is no generic production of adapted paediatric formulations.

NEVIRAPINE (NVP)

General information

- Therapeutic class: HIV-1 non-nucleoside reverse transcriptase inhibitor (NNRTI)
- Indicated for first- and second-line, for adults, adolescents and children (WHO 2006 guidelines[2])
- Originator company, and product brand name: Boehringer-Ingelheim (BI), Viramune
- First approval by US Food and Drug Administration (FDA): 21st June 1996
- Included in the WHO Model List of Essential Medicines (EML) [17]
- World sales of originator product in 2004: US$ 282 million[33]
- Patents on the nevirapine molecule are due to expire in 2010 in most countries, but BI also holds patents on the syrup formulation of nevirapine, which could run until 2018.

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	BI	Aspen under VL from BI	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
Eligibility restrictions		See table 2	See table 2	None	None	None	None	None
NVP 200 mg tablets	2	**432 (0.600)**	**97 (0.133)**	**61 (0.083)**	**56 (0.075)**	**73 (0.100)**	**61 (0.083)**	**60 (0.080)**
NVP 10 mg / ml or 50 mg / 5ml suspension	--	**401 (0.073)**	214 (0.039)	**135 (0.025)**	99 (0.018)			

Note: the Clinton Foundation has agreed with Cipla to sell NVP 50 mg / 5 ml at US$ 0.009 per unit (ml) in countries included in their consortium[16].

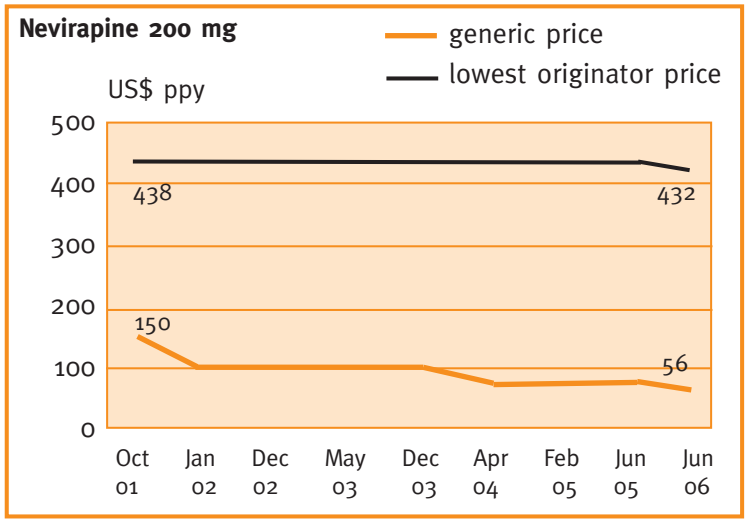


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001

The lowest WHO prequalified generic price for NVP is given here. In five years, the generic price, (which from the outset was already much lower than the originator price) has been halved, while the originator price has remained constant.
As of June 2006, the originator price was eight times more expensive (770%), than the WHO prequalified generics.

Spotlight on access issues:

In many developing countries, Boehringer-Ingelheim's nevirapine is still being bought, although cheaper WHO prequalified generic versions exist.
The brand premium for NVP is prohibitive: in 2005, many buyers reported to the WHO GPRM paying prices five times higher than WHO prequalified generics. Countries such as Bulgaria, Belarus and the Russian Federation are paying between US$ 2,614 and US$ 5,213 per patient per year (or between 500 and 1100% higher than the lowest BI price).
Further, according to WHO GPRM Summary report issued in March 2006, "in the case of nevirapine 200 mg, low-income countries paid on average US$ 219 per patient-year as 40.5% of their total transaction volume was with Boehringer Ingelheim, at an average price of US$ 445 per patient-year, the remainder 59.5% being with generic companies, at an average price of US$ 64 per patient-year."
But these generics need to be registered - this is especially urgent in the case of paediatric formulations, as the originator product is not always available.
Some FDC tablet formulations containing NVP for children have been developed by generic companies and will be soon on the market. BI applied for a patent on the syrup formulation of nevirapine, which, if granted, could hamper such developments. PLWHA groups in India opposed the grant of this patent before the Indian patent office on 9th May 2006. The final decision was still pending at the time of publication.

RITONAVIR (r or RTV)

General information

- Therapeutic class: HIV-1 and HIV-2 protease inhibitor (PI)
- Indicated for second-line as a booster, for adults, adolescents and children (WHO 2006 guidelines[2])
- Originator company, and product brand name: Abbott Laboratories, Norvir
- First approval by US Food and Drug Administration (FDA): March 1996 for the oral solution and 29th June 1999 for capsules
- Included in the WHO Model List of Essential Medicines (EML)[17]
- World sales of originator product: US$ 194 million in 2004, US$ 93 million in 2003, and US$ 122 million in 2002[34].

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose used as booster	Abbott	Aurobindo	Cipla	Hetero	Strides
Eligibility restrictions		See table 2	None	None	None	None
100 mg capsule	2	**83 (0.114)**	336 (0.460)	313 (0.429)	190 (0.260)	438 (0.600)
80 mg/ml oral solution	--	**34 (0.093)**				

Note: the daily dose referred to is 100 mg twice daily, for use as booster medication.

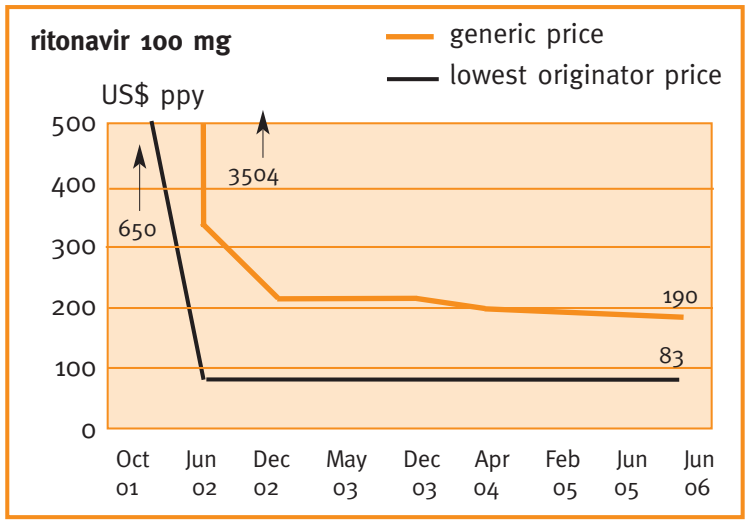


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001

As of June 2006, there was no WHO prequalified generic source of ritonavir. The lowest available generic price is therefore given here.

The price of ritonavir, both originator and generic, fell dramatically in 2001.
Today, the lowest originator price is 2.3 times lower than the generic prices.

Spotlight on access issues:

RTV is of crucial importance for scaling up and management of second-line treatment, as all protease inhibitors must be boosted with this drug.

Abbott has developed a heat-stable fixed-dose combination of ritonavir combined with lopinavir, but the heat-stable ritonavir alone is not commercialised yet. Manufacturing this formulation is crucial, in order to make other PIs, such as atazanavir, free of refrigeration constraints when used together.

Generic firms are working on the development of the ritonavir heat-stable tablets. There is a need for WHO prequalification of generic versions of RTV, in particular for middle-income countries which do not have access to Abbott's lowest price. Abbott has applied for various patents on improved formulations on ritonavir, which renders the extent of generic competition unclear. Oppositions to these derivative patents in India will be needed to ensure prices can decrease further, as demand will increase with scaling up.

SAQUINAVIR (SQV)

General information

- Therapeutic class: HIV-1 and HIV-2 protease inhibitor (PI)
- Indicated for second-line, to be used boosted by ritonavir, for adults, adolescents and children. (WHO 2006 guidelines)
- Originator company, and product brand name: Roche, Invirase
- First approval by US Food and Drug Administration (FDA): December 1995
- Included in the WHO Model List of Essential Medicines (EML) [17]

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	Roche		Cipla	Hetero
		1st category	2nd category		
Eligibility restrictions		See table 2		None	None
SQV 200 mg hard capsules	10 (boosted by ritonavir)	**989 (0.271)**	**2212 (0.606)**	1825 (0.500)	986 (0.270)
SQV 500 mg tablets	4 (boosted by ritonavir)	**n/a**	**n/a**		

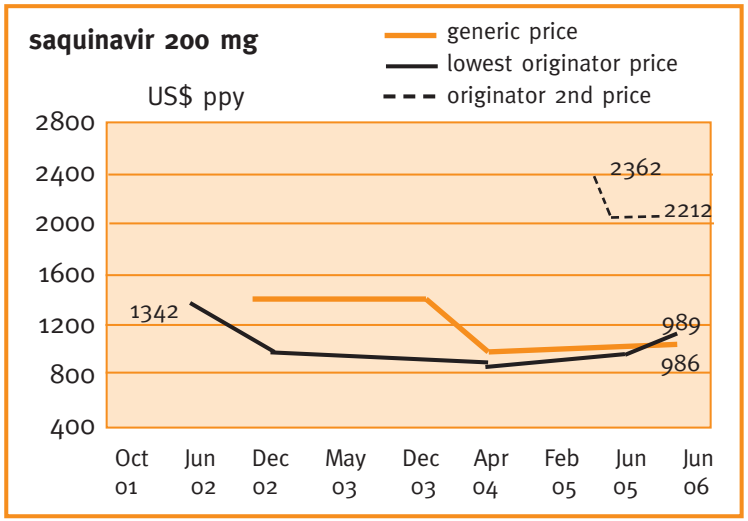


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001

As of June 2006, there was no WHO prequalified generic source of saquinavir. The lowest available generic price is therefore given here.

Spotlight on access issues:

Saquinavir is very difficult to administer, due to a high pill burden (ten capsules a day, to be combined with three other products including the booster). Nevertheless, the product is still recommended by WHO. Very few transactions were reported during last year to the WHO GPRM. As with other protease inhibitors, its high price continues to be a barrier. Solid competition and economies of scale among producers are severely limited, as its use is very reduced.

Since 2004, Roche has been marketing in the US a new version of saquinavir, in a tablet of 500 mg. This formulation reduces the pill burden from ten to four tablets, but is not marketed in developing countries.

STAVUDINE (d4T)

General information

- Therapeutic class: HIV-1 and HIV-2 nucleoside reverse transcriptase inhibitor (NRTI)
- Indicated for first-line, for adults, adolescents and children (WHO 2006 guidelines[21])
- Originator company, and product brand name: Bristol-Myers Squibb (BMS), Zerit
- First approval by US Food and Drug Administration (FDA): December 1994
- Included in the WHO Model List of Essential Medicines (EML)[17]
- World sales of originator product: $272 million in 2004[19], US$354 million in 2003[24]
- Stavudine was the result of US public sector research. It was originally synthesised by the Michigan Cancer Foundation in 1966 on a grant from the National Cancer Institute. Researchers from Yale University first discovered its activity against HIV/AIDS and hold the key use patent filed in the US in December 1986. Yale licensed its marketing and distribution rights to BMS in 1988[24].

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	BMS		Aspen under VL from BMS	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
		1st category	Southern African countries						
Eligibility restrictions		See table 2		See table 2	None	None	None	None	None
15 mg capsule	--	**(0.082)**	---	(0.054)		(0.048)			
20 mg capsule	--	**(0.094)**	**(0.101)**	**(0.056)**		(0.050)			
30 mg capsule	2	**48 (0.066)**	**74 (0.101)**	**41 (0.056)**	**44 (0.060)**	39 (0.053)	20(0.027)	**36 (0.049)**	29 (0.040)
40 mg capsule	2	**55 (0.075)**	**74 (0.101)**	**41 (0.057)**	**42 (0.058)**	41 (0.057)	24 (0.033)	**45 (0.062)**	**36 (0.050)**
1 mg / ml powder for syrup	--	**51 (0.007)**	**66 (0.009)**		**146 (0.020)**	146 (0.020)			

Note: the Clinton Foundation has agreed with Cipla to sell d4T 1 mg / ml at US$ 0.017 per unit (ml) in countries included in their consortium[16].

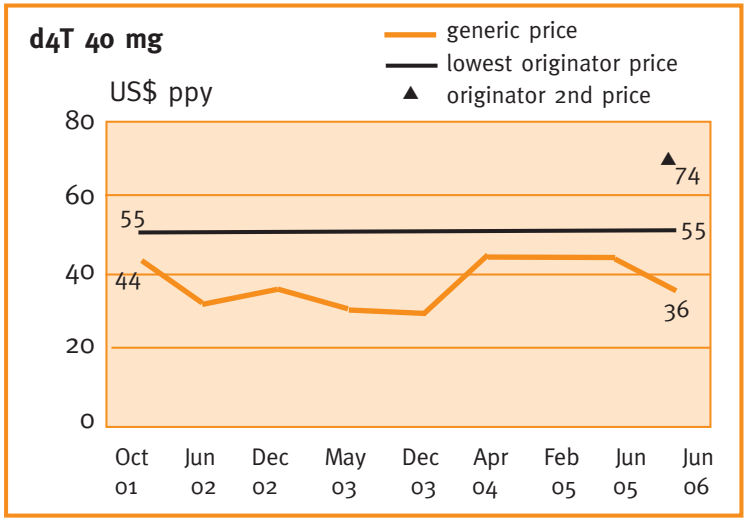


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001:
The lowest WHO prequalified generic price for d4T is given here.

Spotlight on access issues:

Bristol-Myers Squibb has no policy for middle-income countries, and prices are negotiated on a case-by-case basis. The new criteria chosen by BMS to establish eligibility for discounted prices aims to protect certain markets, and imposes a premium (34% more expensive) that applies even to countries as poor as Mozambique.

Nevertheless, many WHO prequalified generics exist as alternatives to this ARV and have already been on the market for a considerable time.

In any case, d4T is mostly used today in double or triple fixed-dose combinations.

The price of BMS's paediatric formulation has decreased significantly since last year (divided by 6.33).

TENOFOVIR DISOPROXIL FUMARATE (TDF)

General information

- Therapeutic class: HIV-1 nucleotide reverse transcriptase inhibitor (NtRTI)
- Indicated for first- and second-line, for adults and adolescents (WHO 2006 guidelines[2])
- Originator company, and product brand name: Gilead, Viread
- First approval by US Food and Drug Administration (FDA): October 2001
- Not included in the WHO Model List of Essential Medicines (EML) [17]
- World sales of originator product: today, TDF is the most commonly prescribed branded ARV in the US, with sales climbing to US$ 783 million in 2004, representing a 38% increase over the previous year[27]
- Although tenofovir was discovered and patented in the USA in 1985, Gilead later applied for additional patents on a new form of the drug, tenofovir disoproxil fumarate. These later patents are due to expire in 2018[26].

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	Gilead	Cipla	Hetero
Eligibility restrictions		See table 2	None	None
TDF 300 mg tablets	1	**207 (0.567)**	973 (2.667)	365 (1.000)

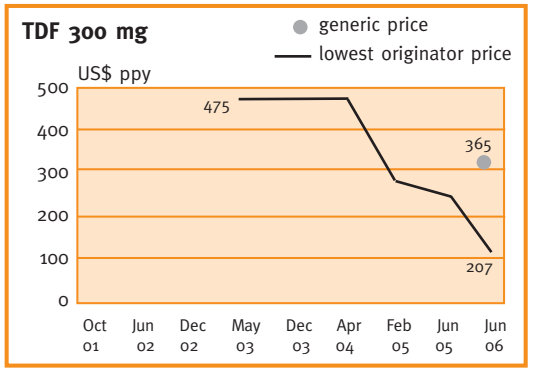


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001
As of June 2006, there was no WHO prequalified generic source of TDF. The lowest available generic price is therefore given here.

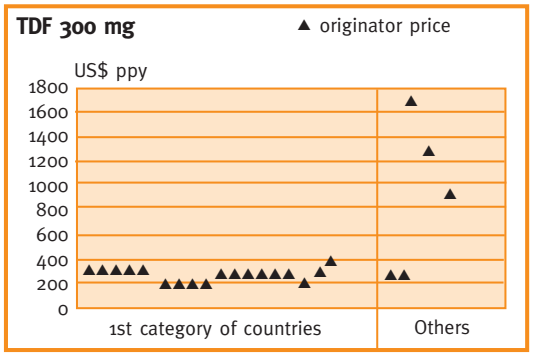


Chart 2: Transaction prices for NFV as compiled by WHO GPRM in 2005-06 (see "how to read the product cards" box)
Countries deemed ineligible by Gilead for the discounted price (see list in annex 8) are paying up to five times the price paid by eligible countries. El Salvador, for example, reported to the WHO GPRM paying US$ 1,700 per patient per year in August 2005.

Spotlight on access issues:

The use of tenofovir disoproxil fumarate is likely to increase, as it is now part of the WHO recommended first-line treatment. The addition of TDF to these regimens will have a substantial impact on the budgets of AIDS programmes. First-line regimens now costs as low as US$ 132 per patient per year (triple FDC 3TC/d4T/NVP), but unless important reductions are seen with the entry of generics in the market in the near future, the use of TDF will raise the cost from a minimum of 2.5 up to 5.5 times more per patient per year in Sub-Saharan African and other countries eligible for lowest prices. The impact will be even more dramatic in countries that are excluded from the lowest prices. Further price reductions can be expected in the near future with the entry of generic versions on the market.

Some middle-income countries, such as Brazil, possess negotiating capacity through the threat of local production or importation through compulsory licenses. As a result, Gilead recently agreed to halve the price from US$ 2,766 to US$ 1,380 per patient per year in Brazil.

Nevertheless, this product is barely available in developing countries. As of June 2006, Gilead's TDF was registered in only 13 of the 97 countries Gilead deems eligible[35]. For instance, TDF is not registered in either Zimbabwe or South Africa, where HIV/AIDS prevalence exceeds 25%, and there are to date no distributors to import the product in these countries.

Competition between generics and originators for TDF is now underway, as generic products have already been marketed in India for several months. But such generic competition will depend on the patent status of TDF in India. Gilead patent applications are currently under examination at the Indian patent office. PLWHA groups opposed the grant of this patent on 9th May 2006[36]. If the Indian patent office grants patents on TDF, generic competition from Indian manufacturers will be very limited and prices of TDF will likely remain high. Fixed-dose combinations are also being developed, but their availability will also necessarily depend on the patent status of TDF in India.

TDF is not included in the 2005 revision of the WHO Model List of Essential Medicines (EML) because Gilead opposed the publication of certain data by WHO[37]. Inclusion of a drug on the EML facilitates fast-track registration approval and encourages countries to ensure that the drug is available.

Crucially, TDF has not yet been tested in children, despite urgent needs.

ZIDOVUDINE (AZT, ZDV)

General information

- Therapeutic class: HIV-1 and HIV-2 nucleoside reverse transcriptase inhibitor (NRTI)
- Indicated for first- and second-line, for adults, adolescents and children (WHO 2006 guidelines[12])
- Originator company, and product brand name: GlaxoSmithKline (GSK), Retrovir
- First approval by US Food and Drug Administration (FDA): March 1987
- Included in the WHO Model List of Essential Medicines (EML)[17]
- World sales of originator product: GB£ 43 million in 2004; down from US$ 476 million in 1997
- Zidovudine was first discovered in 1964 as an anti-cancer medicine. Most of the research that showed the drug's effectiveness as an antiretroviral was done by the US National Institutes of Health. Nevertheless, Glaxo Wellcome, having obtained the patent for zidovudine for the treatment of AIDS, brought the drug onto the market in 1987 as one of the most expensive ever sold[38]. GlaxoSmithKline's patents on AZT expired in September 2005 in the USA and several generic versions of the drug are therefore available on the US market. Patents in other countries are due to expire in 2006.

Price information:

Table 1: Prices in US$ quoted by companies for developing countries:

	Daily dose	GSK	Aspen under VL from GSK	Aurobindo	Cipla	Hetero	Ranbaxy
Eligibility restrictions		See table 2	See table 2	None	None	None	None
AZT 300 mg tabs	2	**212 (0.290)**	**158 (0.216)**	**134 (0.183)**	**103 (0.142)**	133 (0.181)	**139 (0.190)**
AZT 100 mg caps**	--	**(0.158)**	(0.201)		**(0.075)**		
AZT 250 mg caps**	--	**(0.332)**	(0.205)				
AZT 50 mg/5ml oral sol and 10 mg/ml syrop	--	**259 (0.036)**	202 (0.028)	**108 (0.015)**	**101 (0.014)**		

Note: the Clinton Foundation has agreed with Cipla to sell AZT 50 mg / ml at US$ 0.011 per unit (ml) in countries included in their consortium[16].

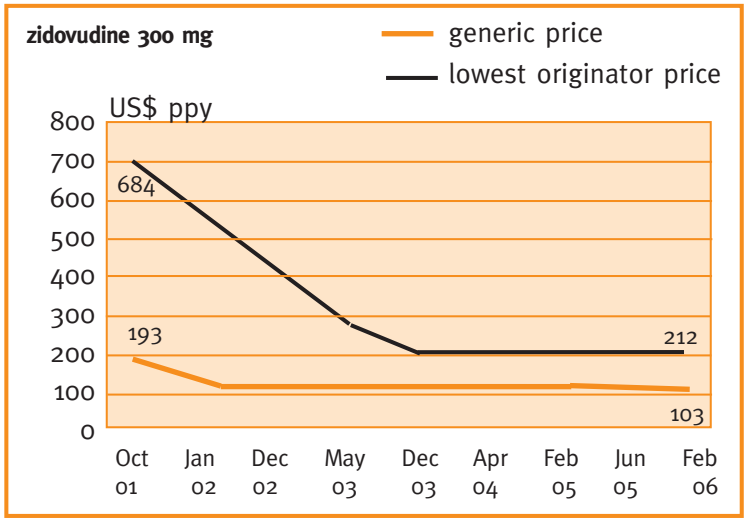


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001

The lowest WHO prequalified generic price for zidovudine is given here.

Spotlight on access issues:

In 2005, despite the existence of generic competition and the availability of WHO prequalified products, many countries, including Least Developed Countries such as Haiti or Ethiopia, were still purchasing the originator version of zidovudine. Countries have reported to the WHO GPRM that they were purchasing GSK products at prices between US$ 212 and US$ 241 (almost double the generic price).

In January 2006, GSK announced a shortage of AZT.

ABACAVIR/LAMIVUDINE (ABC/3TC)

General information

- Therapeutic class: double fixed-dose combination, for HIV-1 and HIV-2 (NRTIs)
- Indicated for first-line, for adults, adolescents and children (WHO 2006 guidelines[21])
- Originator company, and product brand name: GlaxoSmithKline (GSK), Kivexa
- First approval by US Food and Drug Administration (FDA): August 2004
- The WHO Expert Committee on the Selection and Use of Essential Medicines recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations[17]
- World sales of originator product: GSK estimates that sales will reach $490 million in 2009[39].

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	GSK	Cipla
Eligibility restrictions		See table 2	None
ABC 600 / 3TC 300 mg	1	**678 (1.858)**	255 (0.700)

Spotlight on access issues:

To date, no transactions have been reported in the WHO GPRM database. GSK only very recently quoted a specific price for this double fixed-dose combination for developing countries.

Generic production is very recent.

LAMIVUDINE/STAVUDINE (3TC/d4T)

General information

- Therapeutic class: 2 NRTIs in double fixed-dose combination, for HIV-1 and HIV-2
- Indicated for first-line, for adults, adolescents and children (WHO 2006 guidelines[12])
- The WHO Expert Committee on the Selection and Use of Essential Medicines recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations[17]
- The product is developed only by generic manufacturers and is not available in Western countries because of various patents on 3TC and d4T.

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
Eligibility restrictions		None	None	None	None	None
3TC 150 mg / d4T 30 mg tablet	2	80 (0.110)	64 (0.088)	143 (0.195)	**74 (0.101)**	73 (0.100)
3TC 150 mg / d4T 40 mg tablet	2	87 (0.120)	67 (0.092)	146 (0.200)	**80 (0.109)**	**80 (0.110)**

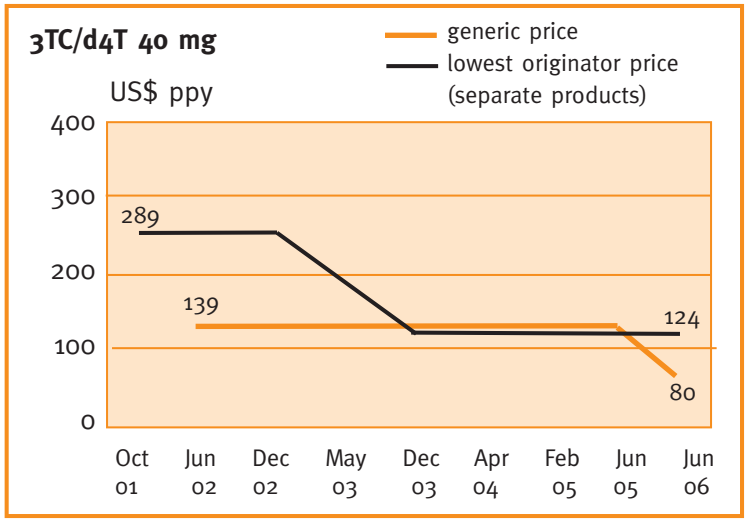


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001

The lowest WHO prequalified generic price for 3TC/d4T is given here.

The first generic to be WHO prequalified was from Strides in February 2005. Prices of generic drugs have been decreasing since that date.

Combined, the lowest price of originator products, only available separately instead of FDCs, reaches US$ 124.

Spotlight on access issues:

Although included in the WHO recommendations for children, to date there are no adapted formulations available.

LOPINAVIR/RITONAVIR (LPV/r)

General information

- Therapeutic class: boosted Protease Inhibitor (PI) in double fixed-dose combination, for HIV-1 and HIV-2
- Indicated for second-line, for adults, adolescents and children (WHO 2006 guidelines[2])
- First approval by US Food and Drug Administration (FDA): soft gel capsules were approved in September 2000. Heat-stable tablets were approved in October 2005.
- Originator company, and product brand name: Abbott Laboratories, Kaletra
- Included in the WHO Model List of Essential Medicines (EML)[17]
- World sales of originator product: LPV/r is the most commonly used PI in the US, representing 34% of total PI prescriptions. In four years, from 2001 to 2004, sales amounted to US$ 2.5 billion (US$ 292 million in 2001, US$ 551 million in 2002, US$ 754 million in 2003 and US$ 897 million in 2004)[34]. Cumulative sales are estimated to reach US$ 7 billion over the years 2001 to 2008[34].
- Abbott patents on soft gel capsules are due to expire in the USA in 2018. Patents were also filed to protect the heat-stable tablets, which are to run until 2024.

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

		Abbott	Cipla	Hetero
Eligibility restrictions	Daily dose	See table 2	None	None
LPV/r 133 / 33 mg Soft gel capsule	6	**500 (0.228)**	1338 (0.611)	1,898 (0.867)
LPV/r 200 / 50 mg Tablet (heat-stable)	4	**n/a**		
LPV/r 80 + 20 mg / ml Oral solution	--	**152 (0.139)**		

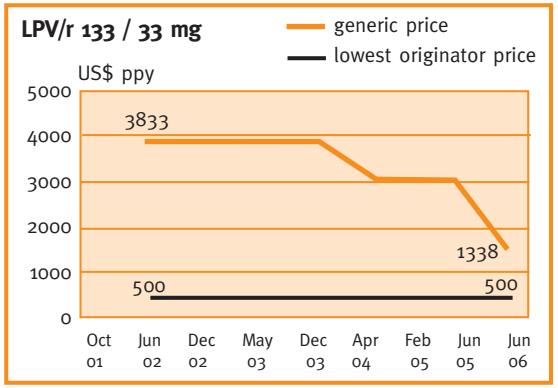


Chart 1: Evolution of the lowest quoted price for eligible developing countries since 2001 As of June 2006, there was no WHO prequalified generic source of lopinavir/ritonavir. The lowest available generic price is therefore considered for the graph.

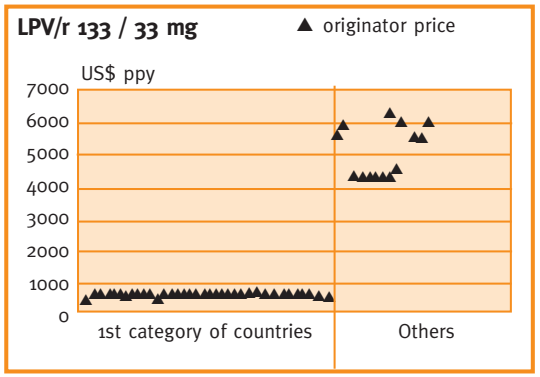


Chart 2: Transaction prices of LPV/r as compiled by WHO GPRM in 2005-06 (see "how to read the product cards" box)

Only originator sales were reported to the WHO GPRM in 2005. In countries excluded from Abbott's list of eligible countries, such as some low-income (Tajikistan), and lower middle-income countries (Jordan, Belarus, Georgia, Guyana, Ukraine), transactions were reported up to US$ 6,300 per patient per year.
Information on add-ons (transportation, taxes, margins of private distributors) in the local market are not included here.

Spotlight on access issues:

Abbott developed a new formulation of the LPV/r FDC, but it is not made available in developing countries. Crucially, the new formulation has great advantages for these resource-poor settings: it has a lower pill count (reducing the burden from six to four pills per day), there is no need for refrigeration, and there are no dietary restrictions. Nevertheless, Abbott has not filed for registration in developing countries, except for South Africa. It is only after Médecins Sans Frontières (MSF) publicly placed an order, supported by a petition letter signed by more than 300 scientists and organisations, that Abbott allowed the drug to be delivered to MSF programmes in African countries where it is not registered. But as of July 2006, the company declined to fill orders placed for Guatemala or Thailand.
Further, there are still problems of availability of the old formulation. In China, for example, negotiations between Abbott and the Chinese authorities have been ongoing for two years. In June 2004, Abbott told MSF that the product would be marketed there by October 2004, but as of June 2006, it was still not available. Moreover, current generic competition, which would be expected to drive prices down as demand increases, is under threat. Abbott has applied for patents on both combinations in India (soft gel capsules and more recent heat-stable tablets). Opposition to the grant of Indian patents on the combination is needed.
In Brazil, where this product is under patent, the cost of it alone used to take up 27% of the National AIDS Programme budget. After strong negotiations with the company, the price was recently further reduced to US$ 1,518 for the heat-stable tablets[25]. Adapted paediatric formulations and FDCs to facilitate the administration of the recommended WHO combination therapy are urgently needed.

TENOFOVIR DISOPROXIL FUMARATE/ EMTRICITABINE (TDF/FTC)

General information

- Therapeutic class: one NtRTI + one NRTI in double fixed-dose combination, for HIV-1
- Indicated for first-line, for adults and adolescents (WHO 2006 guidelines[2])
- Originator company, and product brand name: Gilead, Truvada
- First approval by US Food and Drug Administration (FDA): August 2004
- The WHO Expert Committee on the Selection and Use of Essential Medicines recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations[17]
- World sales of originator product: TDF/FTC was launched in August 2004 and within six months sales already accounted for US$ 70 million[27]. In 2005, sales reached US$ 568 million[26], meaning an increase of sales of 735%.
- Patent holders of both TDF and FTC have agreed to waive their right to the royalties for sales within Gilead's Access Program[28].

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	Gilead
Eligibility restrictions		See table 2
TDF/FTC 300 + 200 mg tablets	1	**319 (0.875)**

Spotlight on access issues:

As of February 2006, this combination was registered in only four developing countries. The publicised offered price is therefore meaningless.

Purchases reported to the WHO GPRM are so far extremely limited, and can be found only among countries eligible for the lowest Gilead price (only three transactions reported).

The final patent status of TDF in India will have implications on the availability of generic versions of this FDC (see TDF product card).

TENOFOVIR DISOPROXIL FUMARATE/ LAMIVUDINE (TDF/3TC)

General information

- Therapeutic class: NtRTI + NRTI in double fixed-dose combination, HIV-1
- Indicated for first-line, for adults and adolescents (2006 WHO guidelines[2])
- The WHO Expert Committee on the Selection and Use of Essential Medicines recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations[17]
- The product is developed only by generic companies but its final availability will depend on the patent status of TDF in India. It is not available in Western countries because of various patents on TDF and 3TC.

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	Cipla
Eligibility restrictions		None
TDF/3TC 300 + 300 mg tablets	1	1,034 (2.833)

ZIDOVUDINE/LAMIVUDINE (AZT/3TC)

General information

- Therapeutic class: 2 NRTI in double fixed-dose combination, for HIV-1 and HIV-2
- Indicated for first- and second-line for adults and adolescents, and only for first-line in children (WHO 2006 guidelines[2])
- Originator company, and product brand name: GlaxoSmithKline (GSK), Combivir
- First approval by US Food and Drug Administration (FDA): September 1997
- The WHO Expert Committee on the Selection and Use of Essential Medicines recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations. [17]
- World sales of originator product: US$ 914 million in 2004[39], US$ 1,045 million in 2005 - of which 89% comes from Europe and the US[40]
- Patent status: GSK holds a patent for this combination in tablet form in most countries of the world, which is due to expire in 2017.

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	GSK	Aspen under VL from BMS	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
Eligibility restrictions		See table 2	See table 2	See table 2	None	None	None	None
AZT 300 / 3TC 150 mg	2	**237 (0.325)**	220 (0.302)	**197 (0.270)**	**134 (0.183)**	**161 (0.220)**	**168 (0.230)**	**182 (0.250)**

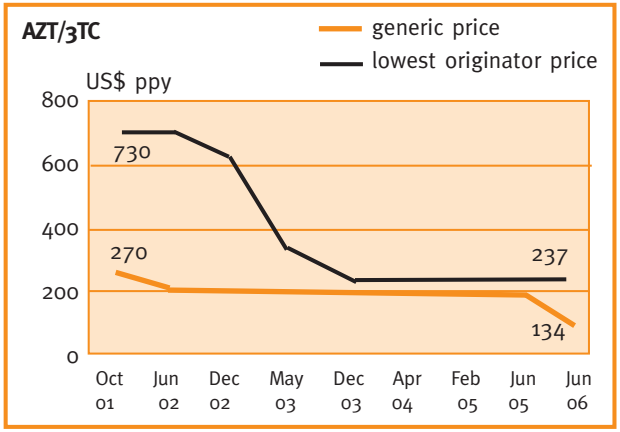


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001
The lowest WHO prequalified generic price for AZT/3TC is given here.
Competition among WHO prequalified sources continues, and has led to a steady decrease in prices.

Spotlight on access issues:

Competition between originator and generics exist for adult formulations but Indian generic versions of the medicine are under threat. GSK applied for a patent on the combination, which is currently under examination by the Indian patent office. PLWHA opposed the grant of this patent in India on 30th March 2006[41]. If the Indian patent office grants the patent, Indian generic manufacturers will only be able to continue producing the medicine under the "automatic licensing" provisions of the 2005 India Patents Act, but will have to pay a "reasonable royalty" to GSK, which may increase the price of the combination (see introduction).

In some countries, generic versions of the FDC are not available because of GSK patent rights. In China, only the originator product is available at US$ 593 because of GSK exclusive rights on 3TC alone.

In Honduras, the government only decided to procure from a generic source after GSK's shortage of AZT in January 2006.

WHO GPRM 2005 data show that many countries, including Least Developed Countries, such as Zambia, Ethiopia, Sudan or Rwanda, purchased the originator product at prices around US$ 250, despite the existence of WHO prequalified generics available at an average of US$ 131.

To date, no formulation adapted for children is marketed and it is urgently needed.

LAMIVUDINE/STAVUDINE/ NEVIRAPINE (3TC/d4T/NVP)

General information

- Therapeutic class: two NRTI + one NNRTI in triple fixed-dose combination, for HIV-1
- Indicated for first-line, for adults, adolescents and children ((WHO 2006 guidelines[12])
- The WHO Expert Committee on the Selection and Use of Essential Medicines recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations. [17]
- The product is developed only by generic companies; it is not available in Western countries because of various patents on 3TC, d4T and NVP. If these medicines had been under patent in India, this important FDC may never have been developed.

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
Eligibility restrictions		None	None	None	None	None
30 / 6 / 50 mg dispersible tablets	--		(0.108)			
60 / 12 / 100 mg dispersible tablets	--		91 (0.125)			
20 / 5 / 35 mg dispersible tablets	--				80 (0.055)	
40 / 10 / 70 mg dispersible tablets	--				79 (0.108)	
150 / 30 / 200 mg tablets	2	138 (0.190)	**132 (0.181)**	**143 (0.195)**	**146 (0.200)**	146 (0.200)
150 / 40 / 200 mg tablets	2	146 (0.200)	**140 (0.192)**	**146 (0.200)**	**153 (0.210)**	153 (0.210)

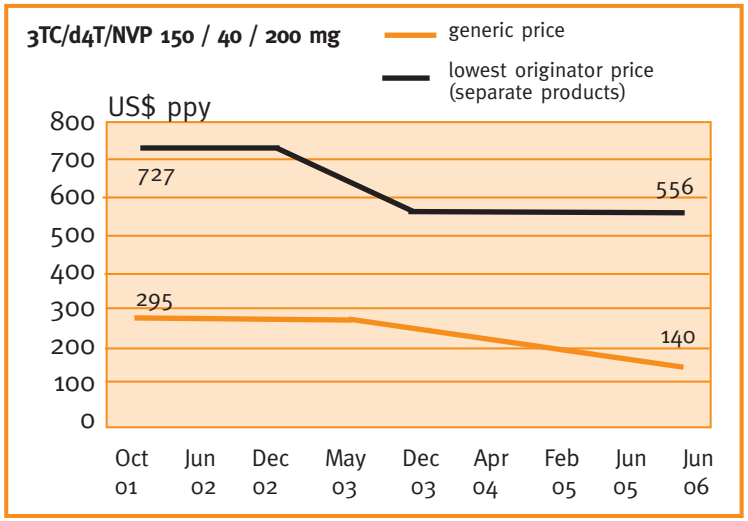


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001

Over the last five years, generic competition has shown to be the most effective means of lowering drug prices. Prices are still decreasing, with a WHO prequalified product being currently available at US$ 132. Combined, the price of originator products marketed separately, and not in FDCs, reaches US$ 556.

Spotlight on access issues:

This is still the most commonly prescribed therapy in resource-limited settings for first-line treatment in adults.

Unfortunately, as equivalent paediatric formulations have not existed until recently, and separate syrups are expensive and ill-adapted to resource-poor settings, care providers have been forced to use adult tablets for children, by breaking or crushing them, which is a sub-optimal practice.

A limited number of generic paediatric triple fixed-dose combinations are currently reaching the market. But WHO must urgently give clear guidance on the best dosages for children. The WHO Prequalification project must also prioritise these products, by outlining the requirements needed for the qualification of the new formulations to be developed, and facilitating the speedy completion of product dossiers.

TENOFOVIR DISOPROXIL FUMARATE/EMTRICITABINE/ EFAVIRENZ (TDF/FTC/EFV)

General information

- Therapeutic class: 1 NtRTI + 1 NRTI + 1 NNRTI in a triple fixed-dose combination, for HIV-1
- Indicated for first-line for adults (WHO 2006 guidelines[2])
- Originator company, and product brand name: Gilead and BMS/Merck, Atripla
- First approval by US Food and Drug Administration (FDA): July 2006
- The WHO Expert Committee on the Selection and Use of Essential Medicines recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations.[17]

Spotlight on access issues:

This is the first one-pill-a-day FDC, which makes it well adapted to resource-poor settings. This combination will probably become one of the most recommended first-line therapies, as it is well tolerated and delays the emergence of resistance, but it cannot be used in women of childbearing age.

To date, there has been no announcement as to what the price for this FDC will be or any indication of a registration timeline.

Generic versions are being developed in India and the approximate market launch could be expected before the end of 2006 in India. However, Gilead patent applications are currently under examination at the Indian patent office, and PLWHA groups opposed the grant of TDF patent in May 2006[36].

If the patent is granted on TDF, any generic production could be blocked, or severely restricted, until the patent expires, which could be as late as 2018.

ZIDOVUDINE/LAMIVUDINE/ ABACAVIR (AZT/3TC/ABC)

General information

- Therapeutic class: three NRTI in triple fixed-dose combination, for HIV-1 and -2
- Indicated for first-line, for adults, adolescents and children (WHO 2006 guidelines[12])
- The WHO Expert Committee on the Selection and Use of Essential Medicines recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations. [17]
- Originator company, and product brand name: GlaxoSmithKline (GSK), Trizivir
- First approval by US Food and Drug Administration (FDA): November 2000
- World sales of originator product: US$ 602 million in 2004[19].

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	GSK	Cipla	Hetero	Ranbaxy
Eligibility restrictions		See table 2	None	None	None
300 /150 /300 mg tablet	2	**852 (1.167)**	548 (0.750)	950 (1.300)	745 (1.020)

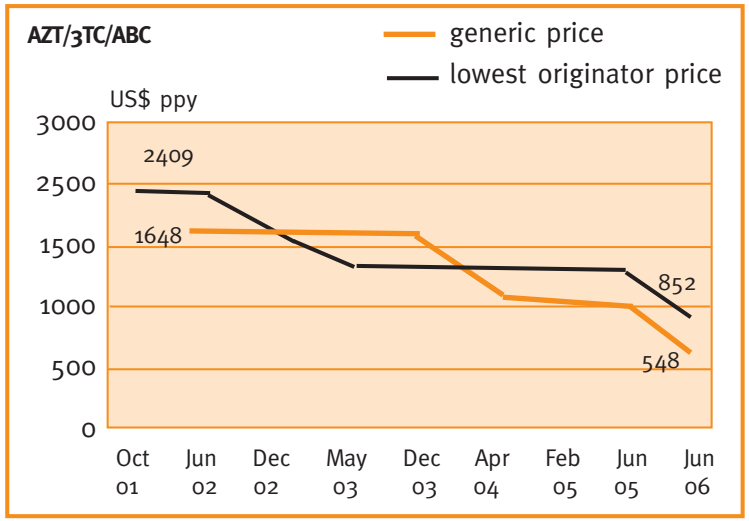


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001

As of June 2006, there was no WHO prequalified generic source of AZT/3TC/ABC. The lowest available generic price is therefore given here.

Spotlight on access issues:

This FDC is the only triple formulation available in Western countries. It is hence one of the most commonly prescribed regimens, but the market is very small in developing countries.

The FDC is still very expensive compared to other triple first-line FDCs, notably because of the high price of abacavir.

ZIDOVUDINE/LAMIVUDINE/ NEVIRAPINE (AZT/3TC/NVP)

General information

- Therapeutic class: two NRTI + one NNRTI in triple fixed-dose combination, for HIV-1
- Indicated for first-line, for adults, adolescents and children (WHO 2006 guidelines[21])
- The WHO Expert Committee on the Selection and Use of Essential Medicines recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations. [17]
- The product is developed only by generic companies; it is not available in Western countries because of various patent rights on AZT, 3TC and NVP.

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	Aspen under VL from GSK and BI	Aurobindo	Cipla	Hetero	Ranbaxy
Eligibility restrictions		See table 2	None	None	None	None
300 / 150 / 200 mg tablet	2	**308 (0.422)** co-blister, not FDC	**257 (0.352)**	231 (0.317)	**263 (0.360)**	255 (0.350)

Note: the Clinton Foundation has agreed with Cipla, Hetero and Ranbaxy for a price of US$ 239 per patient per year, in countries of their consortium.

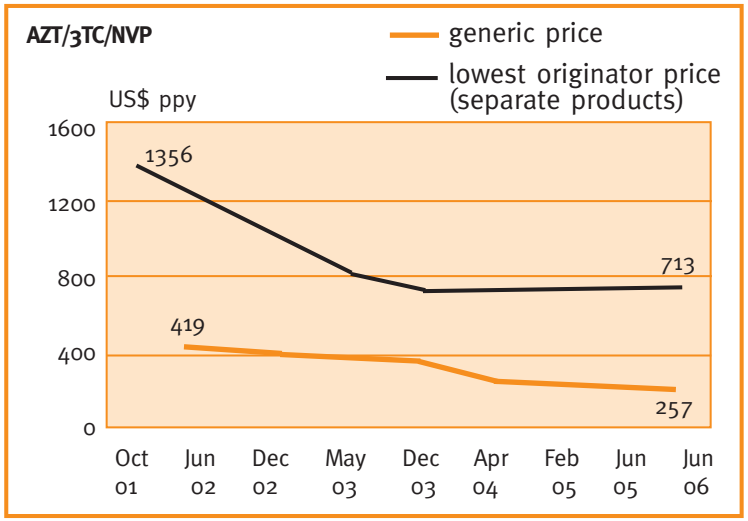


Chart 1: Evolution of the lowest price quoted for eligible developing countries since 2001

The lowest WHO prequalified generic price for AZT/3TC/NVP is considered here. Generic products have led to a decrease in prices, especially when compared with originator products marketed separately and not in FDCs, whose combined price reaches US$ 713

Spotlight on access issues:

The price of this triple FDC is still a barrier for use and for scaling up programmes, especially when compared with other triple first-line FDCs.

Today, there are no paediatric formulations available for this FDC, although it is recommended by WHO for first-line children treatment.

LAMIVUDINE/STAVUDINE + EFAVIRENZ (3TC/d4T+EFV)

General information

- Therapeutic class: two NRTI +one NNRTI in a co-blister, for HIV-1
- Indicated for first-line, for adults, adolescents and children (WHO 2006 guidelines[2])
- The WHO Expert Committee on the Selection and Use of Essential Medicines recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations[17]
- The product is developed only by generic companies; it is not available in Western countries because of various patents rights on 3TC, d4T and EFV.

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	Cipla	Ranbaxy
Eligibility restrictions		None	None
3TC/d4T+EFV 150 / 30 + 600 mg daily co-blister	1 kit (3 tabs)	274 (0.750)	365 (1.000)
3TC/d4T+EFV 150 / 40 + 600 mg daily co-blister	1 kit (3 tabs)	280 (0.767)	372 (1.020)

ZIDOVUDINE/LAMIVUDINE + EFAVIRENZ (AZT/3TC+EFV)

General information

- Therapeutic class: two NRTI +one NNRTI in a co-blister, for HIV-1
- Indicated for first-line, for adults, adolescents and children (WHO 2006 guidelines[2])
- The WHO Expert Committee on the Selection and Use of Essential Medicines recommends and endorses the use of fixed-dose combinations and the development of appropriate new fixed-dose combinations[17]
- This product is developed only by generic companies; it is not available in Western countries because of various patents on AZT, 3TC and EFV.

Price information:

Table 1: Prices in US$ quoted by companies for eligible developing countries:

	Daily dose	Aurobindo	Cipla	Ranbaxy
Eligibility restrictions		None	None	None
AZT/3TC+EFV 150 / 300 + 600 mg daily co-blister	1 kit (3 tabs)	**451 (1.237)**	347 (0.950)	457 (1.250)

Table 2: Conditions of offer by company

Company	Eligibility (countries)	Eligibility (bodies)	Additional comments	Delivery of goods
Abbott	All African countries and LDCs outside of Africa For other developing countries, prices are negotiated on a case-by-case basis	Governments, NGOs, UN organisations and other national and international health institutions		FOB
Aspen	Sub-Sahara Africa including Mauritius, Seychelles, Madagascar	Governments, NGOs and other partners including private and such organisations that are able to run programmes in a responsible, sustainable and medically sound manner	Delivery terms: 90-120 days No minimum order unless any special labelling is required.	Quote ex works. Deliver CIF as per client request - freight charges to consignees account. Payment by telegraphic transfer
Aurobindo	No reported restrictions	NGOs and governmental organisations	Prices available for at least 1,000,000 units for each product per single shipment	Payment by letter of credit FOB Hyderabad (India)
Bristol-Myers Squibb	**First category of countries:** Sub-Saharan African countries (except Southern African countries) plus countries classified as low-income by the World Bank (except Korea, Kyrgyzstan, Moldova and Uzbekistan). **Second category of countries:** Southern African countries See annex 6 for more details. For other developing countries, prices are negotiated on a case-by-case basis with BMS local representatives	Both private and public sector organisations that are able to provide effective, sustainable and medically sound care and treatment of HIV/AIDS	For southern African countries, invoices will be only in South African Rand.	DDU to French-speaking Africa and CIP incoterm for English-speaking Africa (Kenya, Uganda, Tanzania, Ethiopia, Nigeria, Ghana, Eritrea, Zambia)
Boehringer-Ingelheim	All countries classified by the World Bank as low-income, and sub-Saharan Africa Other countries on a case-by-case basis	Governments, NGOs and other partners who can guarantee that the programme is run in a responsible manner		CIF
Cipla	No reported restrictions, but higher prices were negotiated separately for ten Latin American countries	No restrictions	No quantity related conditions Prices for larger quantities are negotiable	FOB Mumbai (India) or CIF - Freight charges separately on actual
Gilead	97 countries including all African states and 44 additional countries classified as low-income by the World Bank. For other developing countries, prices are negotiated on a case by case basis	Organisations that provide HIV treatment in the 97 countries covered by the Gilead Access Program. Application instructions at www.gileadaccess.org	The programme is managed through Gilead Access Program (GAP) In African countries where the drugs are approved, they can be obtained through distributors. In the course of 2006, Gilead's new manufacturing and distribution partner, Aspen Pharmacare, will begin manufacturing Gilead ARVs in South Africa	FOB Origin

Company	Eligibility (countries)	Eligibility (bodies)	Additional comments	Delivery of goods
GlaxoSmithKline	Least Developed Countries (LDCs) plus sub-Saharan Africa All Country Coordination Mechanisms (CCM) projects fully financed by the Global Fund to Fight AIDS, TB and Malaria, as well as projects funded by PEPFAR. For other low and middle-income countries, public sector prices are negotiated on a case-by-case basis, either bilaterally or through GSK's Accelerating Access Initiative	Governments, aid organisations, charities, UN agencies, other not-for-profit organisations and international procurement agencies In sub-Saharan Africa, employers offering HIV/AIDS care and treatment directly to their staff through workplace clinics or similar arrangements	Supply Agreement required (For NGOs requiring fewer than ten patient packs per month, this requirement may be waived) All organisations must supply the preferentially priced products on a not-for-profit basis.	CIP
Hetero Drugs Ltd	No reported restrictions	Private sector, public sector and NGOs	Prices may be negotiated on individual basis according commercial terms	FOB Mumbai (India)
Merck & Co. Inc	**First category of countries:** Low Human Development Index (HDI) countries plus medium HDI countries with adult HIV prevalence of 1% or greater **Second category of countries:** Medium HDI countries with adult HIV prevalence less than 1% Although Romania does not fall under these categories, it also benefits from these prices due to a government commitment to a programme of universal access	Governments, international organisations, NGOs, private sector organisations (e.g. employers, hospitals and insurers)	Merck & Co. Inc does not rule out supplying ARVs to patients through retail pharmacies	CIP
Ranbaxy	No reported restrictions, but higher prices were negotiated separately for ten Latin American countries	NGOs and governments or programmes supported by them	Confirmed letter of credit or advance payment preferred for new customers	FOB Delhi (India)
Roche	**First category of countries:** All countries in sub-Saharan Africa and all countries classified as Least Developed Countries by the United Nations **Second category of countries:** Low-income countries and lower middle-income countries, as classified by the World Bank.	Governments, non-profit institutional providers of HIV care, NGOs	CAD (Cash Against Documents) 30 days at sight. Minimum order and delivery amount per shipment is CHF 10,000 (US$ 8,179)	FCA Basel (Switzerland)
Strides Arcolab Ltd	No reported restrictions	Governments, non-profit institutional providers of HIV treatment, NGOs	Payment by signed letter of credit	FOB Bangalore (India)

Notes: The conditions detailed in the table above were those quoted directly by the companies. Definitions of eligibility vary from company to company. Each originator company establishes different restrictions to their offer of reduced prices, and classifies countries according to different categories. Some companies resort to Least Developed Countries (LDC) criteria developed by the United Nations, others to the UN Development Programme's Human Development Index (UNDP HDI), and others still to World Bank classifications concerning country income.

This lack of uniformity leads to significant differences in the eligibility of a country for different products. For instance, some countries are considered Least Developed Countries by the United Nations, but are classified as having medium development by UNDP. These include Bangladesh, Cambodia, Laos and Sudan. Six other LDCs do not appear in the UNDP HDI rankings at all - these include Liberia and Somalia.

Furthermore, many developing countries are left out of the differential pricing scheme altogether. These include Bolivia, Nicaragua, and Ukraine for the UNDP classification, and China, Honduras and Sri Lanka for the World Bank classification.
For full details please refer to annexes 1-8.

Table 3: Summary of prices in US$ quoted by companies for eligible developing countries

The price for adult formulations is the yearly price per patient. The price for paediatric formulations is the price for the smallest unit available. Products that were WHO prequalified as of July 2006 are listed in bold.

Product	Originator lowest offer / originator second price when specified	Generic offers					
Single formulations							
abacavir	GSK	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
300 mg tablet	**636**		**564**	456	727	511	
20 mg / ml oral solution	**0.104 / ml**			0.115 / ml			
atazanavir	BMS	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
150 mg	n/a						
didanosine	BMS	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
25 mg tablet		0.191 / tab		0.063 / tab			
50 mg tablet		0.192 / tab		0.075 / tab			
100 mg tablet	**310 / 401**	307	**233**	195	280	321	
200 mg tablet				146			
250 mg enteric-coated capsule	**223 / 273**		127	103		146	
400 mg enteric-coated capsule	**288 / 352**		208	134		219	
2 g powder for reconstitution	**6.295 / 7.697 / 2 g**		2.160 / 2 g				
efavirenz	Merck	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
50 mg capsule	**0.116 / 0.213 / cap**		0.110 / cap				
200 mg capsule	**394 / 821**		292	225	292	**300**	
600 mg tablet	**277 / 697**		**299**	**217**	291	**292**	240
30 mg / ml suspension	**0.094 / 0.151 / ml**		0.069 / ml				
emtricitabine	Gilead	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
200 mg capsule	n/a						
lamivudine	GSK	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
150 mg tablet	**69**	**69**	**54**	**51**	53	**66**	**58**
300 mg tablet			**56**	27		66	
10 mg / ml oral solution and syrup and dry syrup	**0.028 / ml**	0.017 / ml	0.020 / ml	0.018 / ml			
nelfinavir	Roche	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
250 mg tablet	**683 / 1.543**		1,379	1,337	986		
50 mg / g oral powder	**0.174 / 0.199 / g**						
nevirapine	Boehringer	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
200 mg tablet	**432**	**97**	**61**	**56**	**73**	**61**	**60**
10 mg / ml or 50 mg / 5 ml suspension	**0.073 / ml**	0.039 / ml	**0.025 / ml**	0.018 / ml			
ritonavir	Abbott	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
100 mg capsule	**83**		336	313	190		438
80 mg / ml oral solution	**0.093 / ml**						
saquinavir	Roche	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
200 mg hard capsule	**989 / 2,212**			1825	986		
stavudine	BMS	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
15 mg capsule	**0.082 / cap**	0.054 / cap		0.048 / cap			
20 mg capsule	**0.094 / 0.101 / cap**	**0.056 / cap**		0.050 / cap			
30 mg capsule	**48 / 74**	**41**	**44**	39	20	**36**	29
40 mg capsule	**55 / 74**	**41**	**42**	41	24	**45**	**36**
1 mg / ml powder for syrup	**0.007 / 0.009 / ml**		**0.020 / ml**	0.020 / ml			

Product	Originator lowest offer / originator second price when specified	Generic offers					
Single formulations							
tenofovir	Gilead	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
300 mg tablet	**207**			973	365		
zidovudine	GSK	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
100 mg capsule	**0.158 / cap**	0,201 / cap		**0,075 / cap**			
250 mg capsule	**0.332 / cap**	0,205 / cap					
300 mg tablet	**212**	**158**	**134**	**103**	139	**139**	
50 mg / 5 ml oral solution and 10 mg/ml syrup	**0.036 / ml**	0,028 / ml	**0.015 / ml**	**0.014 / ml**			
Double fixed-dose combination							
abacavir / lamivudine	GSK	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
600 + 300 mg tablet	**678**			255			
lamivudine / stavudine		Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
150 + 30 mg tablet			80	64	143	**74**	73
150 + 40 mg tablet			87	67	146	**80**	**80**
lopinavir / ritonavir	Abbott	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
133 + 33 mg soft gel capsule	**500**			1,338	1,898		
200 + 50 mg tablet	**n.a.**						
80 + 20 mg / ml oral solution	**0.139 / ml**						
tenofovir / emtricitabine	Gilead	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
300 + 200 mg tablet	**319**						
tenofovir / lamivudine		Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
300 + 300 mg tablet				1,034			
zidovudine / lamivudine	GSK	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
300 + 150 mg tablet	**237**	220	**197**	**134**	**161**	**168**	**182**
Triple fixed-dose combination							
lamivudine / stavudine / nevirapine		Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
30 + 6 + 50 mg tablet				0.108 / tab			
60 + 12 + 100 mg tablet				0.125 / tab			
20 + 5 + 35 mg tablet						0.055 / tab	
40 + 10 + 70 mg tablet						0.108 / tab	
150 + 30 + 200 mg tablet			138	**132**	**143**	**146**	146
150 + 40 + 200 mg tablet			146	**140**	**146**	**153**	153
lamivudine / zidovudine / nevirapine		Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
150 + 300 + 200 mg tablet		**308 co-blister**	**257**	231	**263**	255	
zidovudine / lamivudine / abacavir	GSK	Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
300 + 150 + 300 mg tablet	**852**			548	950	745	
tenofovir / emtricitabine / efavirenz	Gilead / BMS / Merck						
300 + 200 + 600 mg tablet	n/a						
Double fixed-dose combination in co-blister							
lamivudine / stavudine + efavirenz		Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
150 / 30 + 600 mg co-blister (daily kit), tablet				274		365	
150 / 40 + 600 mg co-blister (daily kit) tablet				280		372	
zidovudine / lamivudine + efavirenz		Aspen	Aurobindo	Cipla	Hetero	Ranbaxy	Strides
300 / 150 + 600 mg co-blister (daily kit) tablet			**451**	347		457	

Annexes

Annex 1: Least Developed Countries (LDCs)

Source: United Nations
http://www.un.org/specialrep/ohrlls/ldc/list.htm

Fifty countries are currently designated by the United Nations as least developed countries (LDCs). The list is scheduled for review in 2006.

Afghanistan; Angola; Bangladesh; Benin; Bhutan; Burkina Faso; Burundi; Cambodia; Cape Verde; Central African Republic; Chad; Comoros; Congo (Democratic Republic); Djibouti; Equatorial Guinea; Eritrea; Ethiopia; Gambia; Guinea; Guinea-Bissau; Haiti; Kiribati; Lao PDR; Lesotho; Liberia; Madagascar; Malawi; Maldives; Mali; Mauritania; Mozambique; Myanmar; Nepal; Niger; Rwanda; Samoa; São Tomé and Principe; Senegal; Sierra Leone; Solomon Islands; Somalia; Sudan; Timor-Leste; Togo; Tuvalu; Uganda; Tanzania; Vanuatu; Yemen; Zambia.

Annex 2: Human Development Index (HDI)

Source: United Nations Development Programme (UNDP)
http://hdr.undp.org/reports/global/2005/pdf/HDR05_HDI.pdf

The Human Development Index is published annually as a part of UNDP's annual Human Development Report.

Low human development:
Angola; Benin; Burkina Faso; Burundi; Cameroon, Central African Republic; Chad; Congo (Democratic Republic); Côte d'Ivoire; Djibouti; Eritrea; Ethiopia; Gambia; Guinea; Guinea-Bissau; Haiti; Kenya; Lesotho; Madagascar; Malawi; Mali; Mauritania; Mozambique; Niger; Nigeria; Rwanda; Senegal; Sierra Leone; Swaziland, Tanzania; Yemen; Zambia.

Medium human development:
Albania; Algeria; Antigua and Barbuda, Armenia; Azerbaijan; Bangladesh; Belarus; Belize; Bhutan; Bolivia; Bosnia and Herzegovina; Botswana; Brazil; Cambodia; Cape Verde; China; Colombia; Comoros; Congo; Dominica; Dominican Republic; Ecuador; Egypt; El Salvador; Equatorial Guinea; Fiji; Gabon; Georgia; Ghana; Grenada; Guatemala; Guyana; Honduras; India; Indonesia; Iran; Jamaica; Jordan; Kazakhstan; Kyrgyzstan; Lao PDR; Lebanon; Libya; Macedonia; Malaysia; Maldives; Mauritius; Moldova; Mongolia; Morocco; Myanmar; Namibia; Nepal; Nicaragua; Oman; Pakistan; Palestinian Territories; Papua New Guinea; Paraguay; Peru; Philippines; Romania; Russian Federation; St. Lucia; St. Vincent and the Grenadines; Samoa; São Tomé and Principe; Saudi Arabia; Solomon Islands; South Africa; Sri Lanka; Sudan; Suriname; Syrian Arab Republic; Tajikistan; Thailand; Timor-Leste; Togo; Tunisia; Turkey; Turkmenistan; Uganda; Ukraine; Uzbekistan; Vanuatu; Venezuela; Viet Nam; Zimbabwe.

Annex 3: Sub-Saharan countries

Source: United Nations Secretariat, Department of Economic and Social Affairs
http://esa.un.org/unpp/index.asp?panel=5

Angola; Benin; Botswana; Burkina Faso; Burundi; Cameroon; Cape Verde; Central African Republic; Chad; Comoros; Congo; Congo (Democratic Republic); Côte d'Ivoire; Djibouti; Equatorial Guinea; Eritrea; Ethiopia; Gabon; Gambia; Ghana; Guinea; Guinea-Bissau; Kenya; Lesotho; Liberia; Madagascar; Malawi; Mali; Mauritania; Mauritius; Mozambique; Namibia; Niger; Nigeria; Rwanda; São Tomé and Principe; Senegal;

Seychelles; Sierra Leone; Somalia; South Africa; Sudan; Swaziland; Tanzania; Togo; Uganda; Zambia; Zimbabwe.

Annex 4: World Bank classification of economies

Source: World Bank
http://web.worldbank.org/WBSITE/EXTERNAL/DATASTATISTICS/0,,contentMDK:20421402~pagePK:64133150~piPK:64133175~theSitePK:239419,00.html

The list is updated every year on 1st July. This version is from 2006.

Low-income economies:
Afghanistan; Bangladesh; Benin; Bhutan; Burkina Faso; Burundi; Cambodia; Central African Republic; Chad; Comoros; Congo (Democratic Republic); Côte d'Ivoire; Eritrea; Ethiopia; Gambia; Ghana; Guinea; Guinea-Bissau; Haiti; India; Kenya; Korea (Democratic Republic); Kyrgyzstan; Lao PDR; Liberia; Madagascar; Malawi; Mali; Mauritania; Mongolia; Mozambique; Myanmar; Nepal; Niger; Nigeria; Pakistan; Papua New Guinea; Rwanda; São Tomé and Principe; Senegal; Sierra Leone; Solomon Islands; Somalia; Sudan; Tajikistan; Tanzania; Timor-Leste; Togo; Uganda; Uzbekistan; Viet Nam; Yemen; Zambia; Zimbabwe.

Lower middle-income economies: Albania; Algeria; Angola; Armenia; Azerbaijan; Belarus; Bolivia; Bosnia and Herzegovina; Brazil; Bulgaria; Cameroon; Cape Verde; China; Colombia; Congo; Cuba; Djibouti; Dominican Republic; Ecuador; Egypt; El Salvador; Fiji; Georgia; Guatemala; Guyana; Honduras; Indonesia; Iran; Iraq; Jamaica; Jordan; Kazakhstan; Kiribati; Lesotho; Macedonia; Maldives; Marshall Islands; Micronesia; Moldova; Morocco; Namibia; Nicaragua; Palestinian Territories; Paraguay; Peru; Philippines; Samoa; Serbia and Montenegro; Sri Lanka; Suriname; Swaziland; Syria; Thailand; Tonga; Tunisia; Turkmenistan; Ukraine; Vanuatu.

Upper middle-income economies:
American Samoa; Argentina; Barbados; Belize; Botswana; Chile; Costa Rica; Croatia; Czech Republic; Dominica; Equatorial Guinea; Estonia; Gabon; Grenada; Hungary; Latvia; Lebanon; Libya; Lithuania; Malaysia; Mauritius; Mayotte; Mexico; Northern Mariana Islands; Oman; Palau; Panama; Poland; Romania; Russian Federation; Seychelles; Slovakia; South Africa; St. Kitts and Nevis; St. Lucia; St. Vincent and the Grenadines; Trinidad and Tobago; Turkey; Uruguay; Venezuela.

Annex 5: Global Fund recipient countries

Source: The Global Fund to Fight Aids, Tuberculosis and Malaria
http://www.theglobalfund.org

Albania; Algeria; Angola; Argentina; Armenia; Azerbaijan; Bangladesh; Belarus; Belize; Benin; Bolivia; Bosnia and Herzegovina; Botswana; Brazil; Bulgaria; Burkina Faso; Burundi; Cambodia; Cameroon; Central African Republic; Chad; Chile; China; Colombia; Comoros; Congo; Congo (Democratic Republic); Costa Rica; Côte d'Ivoire; Croatia; Cuba; Djibouti; Dominican Republic; Ecuador; El Salvador; Equatorial Guinea; Eritrea; Estonia; Ethiopia; Gabon; Gambia; Georgia; Ghana; Guatemala; Guinea; Guinea-Bissau; Guyana; Haiti; Honduras; India; Indonesia; Iran; Jamaica; Jordan; Kazakhstan; Kenya; Kyrgyzstan; Lao PDR; Lesotho; Liberia; Macedonia; Madagascar; Malawi; Mali; Mauritania; Mongolia; Morocco; Mozambique; Myanmar; Namibia; Nepal; Nicaragua; Niger; Nigeria; Pakistan; Papua New Guinea; Peru; Philippines; Romania; Russian Federation; Rwanda; São Tomé and Principe; Senegal; Serbia and Montenegro; Sierra Leone; Somalia; South Africa; Sudan; Suriname; Swaziland; Tajikistan; Tanzania; Thailand; Timor-Leste; Togo; Turkey; Uganda; Uzbekistan; Viet Nam; Yemen; Zambia; Zimbabwe.

Annex 6: Bristol-Myers Squibb eligible countries

Countries eligible for 1st price category:
Afghanistan; Angola; Bangladesh; Benin; Bhutan; Burkina Faso; Burundi; Cambodia; Cameroon; Cape Verde; Central African Republic; Chad; Comoros; Congo; Congo (Democratic Republic); Côte d'Ivoire; Djibouti; Equatorial Guinea; Eritrea; Ethiopia; Gabon; Gambia; Ghana; Guinea; Guinea-Bissau; Haiti; India; Kenya; Lao PDR; Liberia; Madagascar; Mali; Mauritania; Mauritius; Mongolia; Myanmar; Nepal; Nicaragua; Niger; Nigeria; Pakistan; Papua New Guinea; Rwanda; São Tomé and Principe; Senegal; Seychelles; Sierra Leone; Solomon Islands; Somalia; Sudan; Tanzania; Timor-Leste; Togo; Tuvalu; Uganda; Viet Nam; Yemen.

Countries eligible for Southern African prices:
Botswana; Lesotho; Malawi; Mozambique; Namibia; South Africa; Swaziland; Zambia; Zimbabwe.

Annex 7: Abbott eligible countries

Source: Abbott's Access to HIV Care Program
http://www.accesstohivcare.org/en/partners/countries.aspx

Afghanistan; Algeria; Angola; Bangladesh; Benin; Bhutan; Botswana; Burkina Faso; Burundi; Cambodia; Cameroon; Cape Verde; Central African Republic; Chad; Comoros; Congo; Congo (Democratic Republic); Côte d'Ivoire; Djibouti; Egypt; Equatorial Guinea; Eritrea; Ethiopia; Gabon; Gambia; Ghana; Guinea; Guinea-Bissau; Haiti; Kiribati; Kenya; Laos; Lesotho; Liberia; Libya; Madagascar; Malawi; Maldives; Mali; Mauritania; Mauritius; Morocco; Mozambique; Myanmar; Namibia; Nepal; Niger; Nigeria; Rwanda; Samoa; São Tomé and Principe; Senegal; Seychelles; Sierra Leone; Solomon Islands; Somalia; South Africa; Sudan; Swaziland; Tanzania; Timor-Leste; Togo; Tunisia; Tuvalu; Uganda; Vanuatu; Yemen; Zambia; Zimbabwe.

Annex 8: Gilead eligible countries

Source: Gilead Access Program
http://www.gileadaccess.org

Afghanistan; Algeria; Angola; Antigua and Barbuda; Bahamas; Bangladesh; Barbados; Belize; Benin; Bhutan; Bolivia; Botswana; Burkina Faso; Burundi; Cambodia; Cameroon; Cape Verde; Central African Republic; Chad; Comoros; Congo; Congo (Democratic Republic); Côte d'Ivoire; Djibouti; Dominica; Dominican Republic; Egypt; Equatorial Guinea; Eritrea; Ethiopia; Gabon; Gambia; Ghana; Grenada; Guatemala; Guinea; Guinea-Bissau; Guyana; Haiti; Honduras; Indonesia; Jamaica; Kenya; Kiribati; Kyrgyzstan; Lesotho; Liberia; Libya; Madagascar; Malawi; Maldives; Mali; Mauritania; Mauritius; Moldova; Mongolia; Morocco; Mozambique; Myanmar; Namibia; Nepal; Nicaragua; Niger; Nigeria; Pakistan; Papua; New Guinea; Rwanda; St. Kitts and Nevis; St. Lucia; St. Vincent and the Grenadines; Samoa; São Tomé and Principe; Senegal; Seychelles; Sierra Leone; Solomon Islands; Somalia; South Africa; Sudan; Suriname; Swaziland; Syria; Tajikistan; Tanzania; Timor-Leste; Togo; Trinidad and Tobago; Tunisia; Tuvalu; Uganda; Uzbekistan; Vanuatu; Viet Nam; Yemen; Zambia; Zimbabwe.

Annex 9: Suggested resources for further information:

For documentation on prices quoted by companies:

- Untangling the web of price reductions: a pricing guide for the purchase of ARVs for developing countries, 8th edition, June 2005, Médecins Sans Frontières *http://www.accessmed-msf.org/documents/untanglingtheweb%208.pdf*
- Sources and prices of selected medicines and diagnostics for people living with HIV/AIDS (June 2005) *http://mednet2.who.int/sourcesprices/sources.pdf*
- Global HIV/Aids Epidemic Selection of Antiretroviral Medications Provided under U.S. Emergency Plan Is Limited, January 2005: *http://pdf.dec.org/pdf_docs/Pcaab266.pdf*

For documentation on prices reported by countries:

- WHO, AMDS, Global Price Reporting Mechanism for ARVs in Developing Countries *http://www.who.int/3by5/amds/price/hdd/*
- The Global Fund Price Reporting Mechanism *http://www.theglobalfund.org/en/funds_raised/price_reporting/default.asp* and *http://web.theglobalfund.org/prm/rc?sessionid=1126169666669_1&command[PrincipleRecipients_report]=show*
- Management Sciences for Health (MSH) International Drug Price Indicator Guide *http://erc.msh.org/mainpage.cfm?file=1.0.htm&id=1&temptitle=Introduction&module=DMP&language=English#top*
- WHO AFRO region Essential Medicines Price Indicator *http://www.who.int/medicines/areas/access/ecofin/en/index.html* or *http://www.who.int/medicines/publications/afroessential_med_price_indicator_nocover.pdf*

For documentation on patents:

- "Determining the patent status of essential medicines in developing countries", Health Economies and Drugs, EDM Series No. 17, UNAIDS/WHO/MSF, 2004
- HIV/AIDS medicines and related supplies: Contemporary context and procurement. Technical guide. Chapter 2 and Annex B. World Bank, Washington, DC, 2004 *http://siteresources.worldbank.org/INTPROCUREMENT/Resources/Technical-Guide-HIV-AIDS.pdf*

"Drug patents under the spotlight. Sharing practical knowledge about pharmaceutical patents" MSF, June 2004

For documentation on quality:

- Prequalification project managed by the World Health Organization (WHO) *http://mednet3.who.int/prequal/*
- US Food and Drug Administration (FDA) tentative approval *http://www.fda.gov/cder/ogd/approvals/*

Other useful websites referenced in this document:

- White List for ARV Procurement, 5th June 2005, Clinton Foundation *http://www.clintonfoundation.org/pdf/060505-white-list-for-arv-procurement.pdf*
- WHO AFRO region Essential Medicines Price Indicator *http://www.who.int/medicines/publications/afroessential_med_price_indicator_nocover.pdf*
- International Dispensary Association (IDA) price indicator *http://www.idafoundation.org*
- US Food and Drug Administration orange book *http://www.fda.gov/cder/ob/*
- Catalogue of US Food and Drug Administration approved products, products documentation *http://www.accessdata.fda.gov/scripts/cder/drugsatfda/*
- WHO registration *http://ftp.who.int/htm/AMDS/drugsdatabase.pdf*
- WHO HIV treatment guidelines for adults and adolescents
WHO Antiretroviral Therapy for HIV Infection in Adults and Adolescents in Resource-Limited Settings: Towards Universal Access: Recommendations for a public health approach 2006 version (in press). WHO Geneva 2006.
- WHO HIV treatment guidelines for Children
Antiretroviral therapy of HIV infection in infants and children in resource-limited settings: towards universal access: Recommendations for a public health approach 2006 (in press) WHO Geneva 2006.
- Biotechnology/Pharmaceuticals HIV/AIDS Industry Report - April 2005 *http://www.aethlonmedical.com/pdfs/IndustryReport.pdf*
- Clinton Foundation *http://www.clintonfoundation.org/*
- Access Campaign web site *http://www.accessmed-msf.org/*

Annex 10: Company contacts

Abbott:
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AXIOS International manages the request process:
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Glossary

3TC lamivudine; nucleoside analogue reverse transcriptase inhibitor

ABC abacavir; nucleoside analogue reverse transcriptase inhibitor

AIDS Acquired Immune Deficiency Syndrome

ARV Antiretroviral drug

ATZ atazanavir; protease inhibitor

BI Boehringer-Ingelheim

BMS Bristol-Myers Squibb

CIF "Cost Insurance and Freight". A commercial term (incoterm) meaning that the seller delivers once the goods pass the ship's rail in the port of shipment. The seller must pay the costs and freight necessary to bring the goods to the named port of destination BUT the risk of loss or damage to the goods, as well as any additional costs due to events occurring after the time of delivery, are transferred from the seller to the buyer.

CIP "Carriage and Insurance paid to...". A commercial term (incoterm) meaning that the seller delivers the goods to the carrier nominated by him, but the seller must in addition pay the cost of carriage necessary to bring the goods to the named destination. This means that the buyer bears all the risks and any additional costs occurring after the goods have been delivered. However, in CIP the seller also has to procure insurance against the buyer's risk of loss of or damage to the goods during carriage. Consequently, the seller contracts for insurance and pays the insurance premium.

d4T stavudine; nucleoside analogue reverse transcriptase inhibitor

ddI didanosine; nucleoside analogue reverse transcriptase inhibitor

DDU "Delivered duty unpaid". A commercial term (incoterm) meaning that the seller delivers the goods to the buyer, not cleared for import, and not unloaded from any arriving means of transport at the named place of destination. The seller has to bear the costs and risks involved in shipping the goods, other than, where applicable, any 'duty' (which includes the responsibility for the risks of the carrying out of the customs formalities, and the payment of formalities, customs duties, taxes and other charges) for import in the country of destination. Such 'duty' has to be borne by the buyer as well as any costs and risks caused by his failure to clear the goods for the import time.

EC enteric-coated

EML Essential Medicines List. First published by WHO in 1977, it serves to identify a list of medicines, which provide safe and effective treatment for infectious and chronic diseases affecting the vast majority of the world's population. The 12th Updated List was published in April 2002 and includes twelve antiretrovirals.

EFV or **EFZ** efavirenz; non-nucleoside analogue reverse transcriptase inhibitor

EXW "Ex-works". A commercial term (incoterm) meaning that the seller delivers when he places the goods at the disposal of the buyer at the seller's premises or another named place (i.e. works, factory, warehouse etc.) not cleared for export and not loaded on any collecting vehicle.

FOB "Free on board". A commercial (incoterm) term meaning that the seller delivers when the goods pass the ship's rail at the named port of shipment. This means that the buyer has to bear all costs and risks of loss or damage to the goods from that point. The FOB term requires the seller to clear the goods for export.

FDC fixed-dose combination - several drugs combined in a single pill

FTC emtricitabine; nucleoside analogue reverse transcriptase inhibitor

Generic drug According to WHO, a pharmaceutical product usually intended to be interchangeable with the originator product, which is usually manufactured without a license from the originator company.

GPRM WHO Global Price Reporting Mechanism is a database containing prices paid by UNICEF, the International Dispensary Association (IDA), Management Sciences for Health (MSH)/Deliver, and the Global Fund to Fight AIDS, Tuberculosis and Malaria.

GSK GlaxoSmithKline

HDI Human Development Index. A summary composite index, compile by UNDP, that measures a country's average achievements in three basic aspects of human development: longevity (or life expectancy at birth), knowledge (or adult literacy rate and enrolment in education), and a decent standard of living (gross domestic product per capita).

HIV Human Immunodeficiency Virus

LDCs Least Developed Countries, according to United Nations classification

LPV/r Lopinavir/ritonavir; boosted protease inhibitor

MSD Merck Sharp & Dome (Merck & Co., Inc.)

MSF Médecins Sans Frontières

NDRA National Drug Regulatory Authority

NGO Non-Governmental Organisation

NFV nelfinavir; protease inhibitor

NNRTI Non-Nucleoside Reverse Transcriptase Inhibitor

NRTI Nucleoside Analogue Reverse Transcriptase Inhibitor

NtRTI Nucleotide Reverse Transcriptase Inhibitor

NVP nevirapine; non-nucleoside analogue reverse transcriptase inhibitor

OAPI Organisation Africaine de la Propriété Intellectuelle, African Intellectual Property Organisation, whose member states are Benin, Burkina Faso, Cameroon, Central African Republic, Chad, Congo, Côte d'Ivoire, Gabon, Guinea, Guinea-Bissau, Equatorial Guinea, Mali, Mauritania, Niger, Senegal, Togo.

PEPFAR President's Emergency Plan for AIDS Relief, a United States programme to fight HIV/AIDS in developing countries

PI protease inhibitor

PLWHA People Living With HIV/AIDS

PMTCT Prevention of Mother-to-Child Transmission

ppy per patient per year

R&D Research and Development

RTV ritonavir, protease inhibitor

r low-dose ritonavir, used as a booster

SQV saquinavir; protease inhibitor

TDF tenofovir disoproxil fumarate; nucleotide reverse transcriptase inhibitor

TRIPS Trade-Related aspects of Intellectual Property Rights

UNAIDS United Nations Joint Cosponsored Programme on HIV/AIDS, created in 1996, to lead, strengthen and support an expanded response to the HIV/AIDS epidemic. The six original cosponsors are UNICEF, UNDP, UNFPA, UNESCO, WHO and the World Bank. UNDCP joined in April 1999.

UNDP United Nations Development Programme

US FDA United States Food and Drug Administration

VL Voluntary license

WHO World Health Organization

WHO GPRM WHO Global Price Reporting Mechanism

WTO World Trade Organization

ZDV zidovudine; nucleoside analogue reverse transcriptase inhibitor

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