

The pricing and procurement of antiretroviral drugs: an observational study of data from the Global Fund

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Abstract The *Purchase price report* released in August 2004 by the Global Fund to Fight AIDS, Tuberculosis, and Malaria (Global Fund) was the first publication of a significant amount of real transaction purchase data for antiretrovirals (ARVs). We did an observational study of the ARV transaction data in the *Purchase price report* to examine the procurement behaviour of principal recipients of Global Fund grants in developing countries. We found that, with a few exceptions for specific products (e.g. lamivudine) and regions (e.g. eastern Europe), prices in low-income countries were broadly consistent or lower than the lowest differential prices quoted by the research and development sector of the pharmaceutical industry. In lower middle-income countries, prices were more varied and in several instances (lopinavir/ritonavir, didanosine, and zidovudine/lamivudine) were very high compared with the per capita income of the country. In all low- and lower middle-income countries, ARV prices were still significantly high given limited local purchasing power and economic strength, thus reaffirming the need for donor support to achieve rapid scale-up of antiretroviral therapy. However, the price of ARVs will have to decrease to render scale-up financially sustainable for donors and eventually for governments themselves. An important first step in reducing prices will be to make available in the public domain as much ARV transaction data as possible to provide a factual basis for discussions on pricing. The price of ARVs has considerable implications for the sustainability of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) treatment in the developing world.

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Voir page 396 le résumé en français. En la página 397 figura un resumen en español.

يمكن الاطلاع على الملخص بالعربية في صفحة 397.

Introduction

Since the launch of the “3 by 5” initiative by the WHO and the Joint United Nations Programme on HIV/AIDS (UNAIDS), the number of people receiving antiretroviral (ARV) therapy has grown from about 300 000 at the end of 2002 to almost 1 000 000 halfway through 2005.¹ One of the key determinants of this growth has been increased funding from the Global Fund to Fight AIDS, Tuberculosis, and Malaria (Global Fund); the World Bank; the US Government; and other donors. However, despite increasing experience with bulk procurement, ARVs remain expensive. At the 2005 World Health Assembly in Geneva, multiple delegations from developing countries raised the issue of high ARV prices as an ongoing barrier to treatment access. Since affordable ARVs are critical to continuing the scaling up of treatment programmes it is important to monitor their prices.

In the past two years, very little actual ARV tender data have been published.^{2,3} Most information has been in

the form of indicative price quotes from the pharmaceutical industry published yearly by the *Sources and Prices* project⁴ and the Médecins sans Frontières Campaign for Access to Essential Medicines.⁵ A recent report on ARV pricing from the US Government also relied mainly on such quotes.⁶ The *Purchase price report*⁷ released in August 2004 by the Global Fund was the first publication of a significant body of real transaction pricing data. The report lists the prices and quantities of ARVs purchased by principal recipient organizations — the organizations that are legally responsible for distributing Global Fund grant money or using it to directly implement programmes intended to tackle national burdens of HIV, malaria, or tuberculosis.

We have done an observational study of the ARV transaction data in the *Purchase price report* to examine the procurement behaviour of principal recipients. In addition, we investigated whether principal recipients were able to purchase ARVs at the widely advertised

differential price quotes from research and development (R&D) firms (who usually hold the relevant patent rights on the product) or generic originator firms, in the case of fixed-dose combinations available only from these companies.⁵ We selected 10 of the most commonly used adult formulation ARVs in treatment programmes in developing countries for which there were sufficient data. We did not consider paediatric formulations because the data were extremely scarce.

Analysis of the Purchase price report

At April 2005, the report included 355 transactions for ARVs, worth approximately US\$ 14 million. This amount is less than half the total reported ARV procurement with Global Fund disbursements, which at the end of 2004 was estimated to be greater than US\$ 30 million (personal communication: Global Fund to Fight AIDS, Tuberculosis, and Malaria; 17 February 2005).

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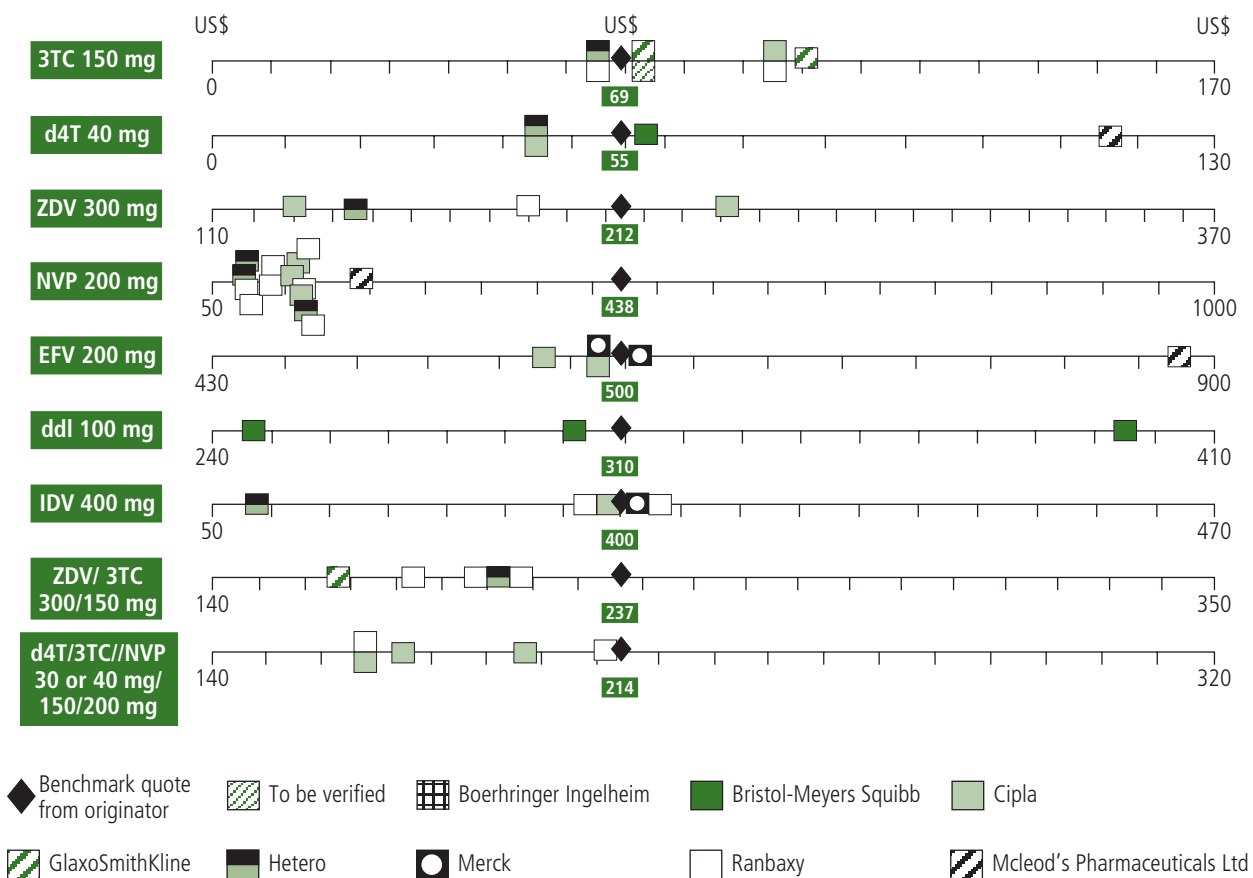
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Fig. 1. Price per patient-year in US\$ for selected antiretrovirals purchased with GFATM^a funds: low-income countries



EFV = efavirenz; ZDV = zidovudine; IDV = indinavir; NVP = nevirapine; ddl = didanosine; 3TC = lamivudine; d4T = stavudine.

^aGFATM = Global Fund to Fight AIDS, TB and Malaria.

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The drugs were purchased for use in 21 countries, 15 of which are classified as low-income by the World Bank, and six as lower middle-income. The quantity of drugs corresponds to 29 269 patient-years of antiretroviral therapy (excluding paediatric formulations). Currently, the report includes only data received from principal recipients who have chosen to upload information via the Global Fund's *Price reporting mechanism*,⁸ and the data are not independently verified by the Global Fund secretariat. The data are limited to source prices paid by bulk purchasers of ARVs, and do not represent end-user prices for patients.⁹ Terms of trade and shipping costs for transactions were not consistently reported, so we did not include them in our study. Shipping and importation tariffs have previously been found to increase the price of medicines by no more than 15% over the factory price, which should not compromise the comparability of prices in this analysis.^{2,6,10} In addition,

while principal recipients must report additional transaction details — e.g. which procurement agent was used, if any, and whether the transaction price was part of a pre-negotiated agreement by another agency, like those arranged by the Clinton Foundation^{11–13} — this information is not included in the public report. These data would probably help to gain a better understanding of why prices fall where they do.

Results of the analysis

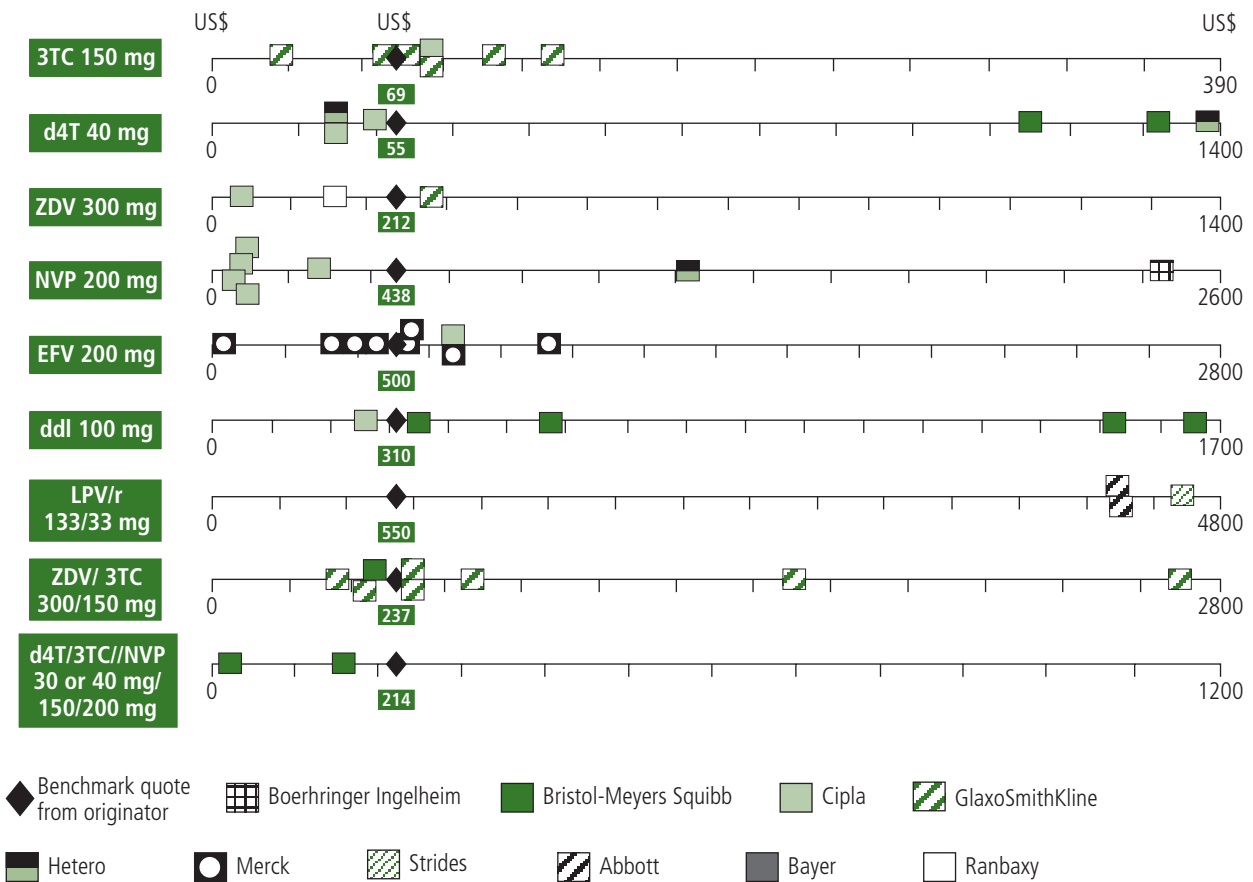
Current prices quoted by R&D or generic originator firms reflect reductions in price quotes during the past 5 years subsequent to the introduction of generic ARVs on the open market.^{5,14} Every pharmaceutical company has its own criteria for countries to be eligible for the lowest differential price of ARVs; in most cases these are country income level and geographic location (e.g. whether the country is in sub-Saharan

Africa). GlaxoSmithKline has a policy of offering its lowest differential price to Global Fund grant recipients, and Merck and Roche even have a separate pricing level for middle-income countries.⁵ For consistency, for every ARV studied we have selected the lowest quoted differential price level from the R&D or generic originator firm as the benchmark price. Fig. 1 and Fig. 2 map the prices and suppliers for all transactions of the ARV products we selected. Each box represents one price at which there was at least one transaction, but for which there may have been multiple transactions at various quantities and for different principal recipients located in different countries.

Low-income countries

Prices for low-income countries (Fig. 1) were generally in line with or lower than the benchmark; most of these transactions involved generic pharmaceutical

Fig. 2. Price per patient-year in US\$ for selected antiretrovirals purchased with GFATM^a funds: lower middle-income countries



EFV = efavirenz; ZDV = zidovudine; IDV = indinavir; NVP = nevirapine; ddl = didanosine; 3TC = lamivudine; d4T = stavudine; LPV/r = lopinavir/ritonavir.

^a GFATM = Global Fund to Fight AIDS, TB and Malaria.

companies. Therefore, in the poorest settings, generic competition seems effective in reducing ARV prices — with notable exceptions such as lamivudine (3TC), for which both R&D and generic suppliers in several transactions priced their product well beyond the benchmark price. All transactions priced at least 10% higher than the benchmark took place in four countries, three of which (Georgia, Kyrgyzstan, and the Republic of Moldova) are members of the Commonwealth of Independent States (CIS). This finding suggests that pharmaceutical companies are strategically pricing their products in this region at levels more suitable for western Europe and, to a lesser extent, the Russian Federation. These data also affirm findings that high prices for ARVs are slowing access to antiretroviral therapy in the CIS countries.¹⁵ Also of note is that the prices paid for nevirapine in low-income countries supplied by generic manufacturers were approximately three times (200%) lower

than the benchmark from Boehringer Ingelheim, the originator, and thus we note that in this dataset there were no purchases of nevirapine from Boehringer Ingelheim made by principal recipients in low-income countries.

Lower middle-income countries

Prices in lower middle-income countries (Fig. 2) varied more than those for the same product in low-income countries, and there were several instances where significantly high prices were paid.

- Abbott Laboratories, whose lowest differential price for lopinavir/ritonavir (Kaletra) is published as US\$ 550, charged El Salvador and Peru between US\$ 4468 and US\$ 4511, respectively — over eight times (712–720%) more expensive than the benchmark, and over double the gross domestic product (GDP) per capita in each of these countries.¹⁶

- Bristol-Meyers Squibb priced didanosine (Videx) more than five times (432%) higher than the benchmark in El Salvador, and priced stavudine (Zerit) nearly 22 times (2063%) over their own benchmark in Honduras.
- GlaxoSmithKline priced zidovudine/lamivudine (Combivir) as high as 11 times (1030%) the benchmark of US\$ 237 per patient-year in one transaction in Honduras.

Only two of the 11 transactions in lower middle-income countries that were priced at least three times (400%) higher than the benchmark were sourced from generic producers. Hetero priced stavudine at US\$ 1351 per patient-year in Honduras, nearly 25 times (2356%) the benchmark price, but for a total volume of only 60 units. Another firm, Strides, priced lopinavir/ritonavir at US\$ 4687 per patient-year for Cuba — 8.5 times (752%) the reference price. However, this price might reflect a supplier

vacuum, and hence monopoly pricing, due to the market restriction created by US trade sanctions on Cuba.

Further analyses

Though limited, these data show that several R&D companies are pricing ARVs higher for lower middle-income regions where they face little or no competition from the generic industry. Possible explanations for these uncompetitive markets include strong patent protection in countries that are members of the World Trade Organization, and issues of registration and marketing of generic drugs. Lower middle-income nations are often as financially constrained as their low-income counterparts. For example, the GDP per capita for Ukraine (US\$ 851), officially a lower middle-income economy, approximates that of Angola (US\$ 857) and the Congo (US\$ 825) — both low-income nations.¹⁶ Economic indicators for some better performing lower middle-income nations can be deceptive because of high levels of income inequality. For instance, Namibia has a per capita GDP of US\$ 1463, but the wealthiest 20% of the population represent nearly 80% of total national income.¹⁶ Continued exploitation of these markets and their exclusion from differential pricing schemes could have serious ramifications on access to antiretroviral therapy in these countries — in the short term as coverage expands and in the long term as the number of patients in need of treatment increases.

Some transactions, seemingly outliers, took place at extremely low prices in both low- and lower middle-income

countries. These prices were often one-time, small purchases intended to help establish a relationship between a principal recipient organization and a particular supplier of ARVs. These transactions can also reveal bottlenecks in the procurement and importation end of the pharmaceutical supply chain. For example, GlaxoSmithKline's price of US\$ 29 per patient-year for lamivudine to Honduras was approximately 58% lower than their benchmark of US\$ 69. However, only 3000 total units were purchased at this price; the price was higher in subsequent transactions between GlaxoSmithKline and Honduras of larger quantities. Similar examples include pricing for the fixed-dose combination of stavudine/lamivudine/nevirapine (d4T/3TC/NVP) from Cipla and efavirenz from Merck. These prices should not be considered typical.

While low-income countries procured more nevirapine than efavirenz — both commonly used drugs in the same class (non-nucleoside reverse transcriptase inhibitors, NNRTIs) — lower middle-income countries purchased more efavirenz than nevirapine. Including fixed-dose combinations, low-income countries procured nearly eight times the amount of nevirapine versus efavirenz (2 784 900 versus 352 800 units) while lower middle-income countries bought almost 2.5 times the amount of efavirenz versus nevirapine (3 459 600 versus 1 467 840 units). This difference might be explained by the price difference between efavirenz and nevirapine (Fig. 1 and Fig. 2), in addition to the lack of fixed-dose combinations containing

efavirenz. Another reason for the difference could be concerns about the use of efavirenz in populations of women who do not have access to reliable contraception, since it has been linked to birth defects if used in early pregnancy.¹⁷

Conclusions

Our analysis highlights issues that will grow in importance with the continued scaling up of ARV therapy. ARV prices must be reduced further to reach the goal of the intermediate framework of 3 million people on treatment, and ultimately to ensure universal access to ARV therapy. Persistently high prices for ARVs continue to slow the scaling up of treatment for HIV/AIDS in the developing world. Our identification of significant problems and inconsistencies in ARV procurement and pricing from this small and incomplete dataset illustrates the importance of ensuring that ARV procurement data are in the public domain and reinforces the need for timely reporting of these transactions. A solid evidence base on pricing could empower the developing world to make cost-effective procurement choices, a critical factor in the long-term sustainability of treatment for HIV/AIDS within these countries. ■

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Résumé

Politiques de fixation des prix et d'achat pour les antirétroviraux : étude d'observation sur des données provenant du Fonds mondial

Le *Purchase price report*, publié en août 2004 par le Fonds mondial de lutte contre le SIDA, la tuberculose et le paludisme (Fonds mondial), a été la première publication à contenir une quantité importante de données de transaction réelles concernant les antirétroviraux (ARV). Une étude d'observation a été réalisée sur les données de ce rapport en vue d'analyser les comportements d'achat des principaux bénéficiaires des subventions du Fonds mondial parmi les pays en développement. D'après les résultats de cette étude, mises à part quelques exceptions concernant des produits (lamivudine, par exemple) ou des régions spécifiques (Europe de l'Est, par exemple), les prix payés par les pays à faible revenu étaient à peu près du même ordre, voire plus faibles, que les prix différentiels les plus bas cités par le secteur recherche et développement de l'industrie pharmaceutique. Dans les pays à revenu faible à modéré, les prix présentaient de plus fortes variations et, dans certains cas (lopinavir/ritonavir, didanosine et

zidovudine/lamivudine) étaient même très hauts en comparaison du revenu par habitant national. Pour l'ensemble de ces pays, les prix des ARV restaient considérablement élevés en regard du pouvoir d'achat et de la puissance économique limités de ces pays, ce qui conduit à réaffirmer la nécessité d'un soutien sous forme de dons pour obtenir un élargissement rapide de l'accès au traitement antirétroviral. Il faudra toutefois que les prix de revient des ARV baissent pour rendre cet élargissement supportable sur le plan financier pour les donateurs et ultérieurement pour les gouvernements eux-mêmes. Une étape importante dans la réduction des prix consistera à rendre publiques, dans la mesure du possible, les données de transaction relatives aux ARV, en vue de fournir une base factuelle aux négociations concernant les prix de ces médicaments. Ces prix ont des conséquences majeures sur les possibilités de maintenir l'accès au traitement du VIH/SIDA dans le monde en développement.

Resumen

Fijación de precios y adquisición de medicamentos antirretrovirales: estudio observacional de datos del Fondo Mundial

El *Informe sobre precios de adquisición* publicado en agosto de 2004 por el Fondo Mundial de Lucha contra el SIDA, la Tuberculosis y la Malaria (Fondo Mundial) fue la primera publicación en la que se presentó un conjunto relevante de datos de compras de antirretrovirales (ARV) correspondientes a transacciones reales. Llevamos a cabo un estudio observacional de los datos de transacción de ARV que figuran en el *Informe sobre precios de adquisición* a fin de examinar el comportamiento de adquisición de los principales beneficiarios de las subvenciones del Fondo Mundial en los países en desarrollo. Descubrimos que, exceptuando sólo algunos productos (como la lamivudina) y regiones (por ejemplo Europa oriental), los precios en los países de bajos ingresos eran en general similares o inferiores a los precios diferenciales más bajos citados por el sector de investigación y desarrollo de la industria farmacéutica. En los países de ingresos medianos bajos, los precios eran más variados y en algunos casos (lopinavir/ritonavir, didanosina y zidovudina/lamivudina) eran muy altos en

comparación con los ingresos por habitante del país. En todos los países de ingresos bajos o medianos bajos, los precios de los ARV eran todavía significativamente altos, considerando el nivel económico y el limitado poder adquisitivo local, lo que confirma la necesidad de conseguir apoyo de donantes para expandir rápidamente el tratamiento antirretroviral. Sin embargo, el precio de los ARV tendrá que disminuir si se quiere que la expansión sea económicamente sostenible para los donantes y, en definitiva, para los propios gobiernos. Un primer e importante paso para reducir los precios consistirá en hacer de dominio público todos los datos posibles sobre transacciones de ARV, proporcionando así una base objetiva para las discusiones sobre la fijación de precios. Del precio de los ARV depende en gran medida la sostenibilidad de la terapia contra el virus de la inmunodeficiencia humana/síndrome de inmunodeficiencia adquirida (VIH/SIDA) en el mundo en desarrollo.

ملخص

تسعير وشراء الأدوية المضادة للفيروسات القهقرية:**دراسة وصفية لمعطيات الصندوق العالمي لمكافحة الإيدز والسل والملاريا**

واللاميفودين) كانت مرتفعة جداً بالمقارنة مع دخل الفرد في تلك البلدان. وفي جميع البلدان المنخفضة الدخل والبلدان ذات الدخل المتوسط الأقرب للمنخفض، كانت أسعار الأدوية المضادة للفيروسات القهقرية أعلى بكثير رغم ضعف القوة الشرائية والاقتصادية مما يؤكد الحاجة إلى دعم المانحين للنهوض بالمعالجة بالأدوية المضادة للفيروسات القهقرية. وينبغي أن تنخفض أسعار الأدوية المضادة للفيروسات القهقرية ليصبح بالإمكان ضمان استمرار النهوض الاقتصادي بالعروض التي يقدم الدعم لها المانحون والحكومات. ولعل الخطوة الهامة الأولى في خفض أسعار تلك الأدوية ستتيح للقطاع العام الحصول على معطيات حول شراء الأدوية المضادة للفيروسات القهقرية وتوطيد قاعدة صلبة وحقيقية لمناقشة تسعيرها. إن لأسعار الأدوية المضادة للفيروسات القهقرية آثاراً هامة على ضمان استمرار معالجة الإيدز في العالم النامي.

لقد كان التقرير حول أسعار الشراء الذي أصدره الصندوق العالمي لمكافحة الإيدز والسل والملاريا في شهر آب/أغسطس 2004 أول إعلان عن معطيات هامة حول كمية التعامل والشراء للأدوية المضادة للفيروسات القهقرية. وقد أجرينا دراسة توصيفية لتلك المعطيات في هذا التقرير للتعرف على السلوك الخاص بالشراء لدى أهم المتلقين للمنع من الصندوق العالمي لمكافحة الإيدز والسل والملاريا في البلدان النامية، وقد وجدنا أنه باستثناء بعض المنتجات النوعية مثل اللاميفودين وباستثناء بعض الأقاليم مثل شرق أوروبا، فإن الأسعار في البلدان المنخفضة الدخل متماثلة مع بعضها إلى حد بعيد، أو أنها أخفض من أدنى الأسعار التفضيلية التي أشير إليها في قطاع البحوث والتطوير في شركات الصناعة الدوائية. أما في البلدان ذات الدخل المتوسط الأقرب للمنخفض فإن الأسعار كانت أكثر اختلافاً، بل إنها في بعض الأمثلة (مثل اللوبينافير والريتونافير، والديداونين، والزيدوفودين

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