



Surmounting Challenges : Procurement of Antiretroviral Medicines in Low- and Middle-Income Countries

The Experience of Médecins Sans Frontières

Executive Summary

Background

As the price of antiretrovirals (ARVs) in low- and middle-income countries has fallen in recent years, governments, international agencies and non-governmental organizations (NGOs) have been able to start developing treatment programmes for people living with HIV/AIDS (PLWHA). Procurement strategies are a key element in this global scaling-up process. As Médecins Sans Frontières (MSF) was one of the first international NGOs providing ARV therapy, the World Health Organization (WHO) requested that MSF document its procurement experiences in 10 countries where it has ARV treatment programmes, so that others could benefit from what has been learnt.

The importance of assisting ARV treatment programmes to procure low-cost, quality ARVs cannot be underestimated. In sub-Saharan Africa, the region hardest-hit by the HIV virus, only one percent of the four million people in need currently receives ARV therapy. While other medicines can cure the opportunistic infections caused by HIV or provide relief from symptoms, these are ultimately only temporary measures. Conversely, ARVs decrease the level of the virus in the body, reduce morbidity, prolong and improve quality of life, and prevent most opportunistic infections.

MSF's experience shows that for numerous reasons ARV procurement is often more challenging than that of other types of essential medicines. Products are expensive and stock management is crucial to avoid disruption of treatment. Treatment protocols are diverse, and procurement systems have to respond quickly to evolving treatment regimens. Also, the limited amount of publicly available information, including the lack of quality reference standards, makes assessing the quality of generic ARVs more difficult than that of most other essential medicines - even though quality generic ARVs are being produced.

Method

Data collection for this report is based on MSF's purchasing experience over the past two years in 10 countries. Potential ARV sources, patent and registration status, prices, and distribution options have been analysed and systematically documented in each of the 10 countries - Cambodia, Cameroon, Guatemala, Honduras, Kenya, Malawi, Mozambique, South Africa, Thailand and Ukraine.

Before presenting the detailed country case studies, the report looks in some detail at ARV selection, pricing and procurement issues in general, as part of the medicines management cycle. Five issues of particular importance are highlighted: sources (quality); registration; prices; patents; and continuous availability of medicines.

Main findings

An important finding from the country case studies is that procurement works best when there is a national HIV/AIDS strategy that includes ARV treatment, and that is supported by government commitment and political will. Sufficient funding is crucial to implement national action plans.

Another major finding is that there is no single or ideal approach to ARV procurement. There are several effective strategies that can result in the supply of affordable, quality ARVs. Often a combination of these procurement strategies worked well for MSF country programmes. From MSF's perspective, the most effective and easiest systems are either one or a combination of: strong public procurement agency (Cameroon); local drug production (Thailand); and/or dynamic private sector distributors (Malawi).

It was also found that the following factors affected efficient procurement systems at country level: limited numbers of registered ARV products (generic and originator); unclear patent status of ARV medicines; lack of generic policies; limited information available about internationally publicized prices; and countries' eligibility for differential prices offered by pharmaceutical companies. The ability to use generics has been one critical factor for procurement success, to allow competition and guarantee a continuous supply of ARVs.

Although MSF was relatively successful in procuring ARVs in the countries described in this report, it is important to note that drug procurement continues to be a complicated and labour-intensive process, both in terms of ensuring the continuous supply of drugs in countries where projects have been begun and in starting up procurement in countries where MSF is opening new projects.

Main recommendations

The report's main recommendations on ARV procurement highlight that for

Ministries of health/national AIDS programme/policy-makers – it is important to have national HIV/AIDS treatment guidelines and ARVs included in the national list of essential medicines. Taxes, duties and mark-ups on ARVs should be lowered or abolished by governments to avoid significant price increases that make products unaffordable. Systematically collected information on patents, and international and local prices of medicines will increase price transparency and will facilitate price negotiations and improve procurement.

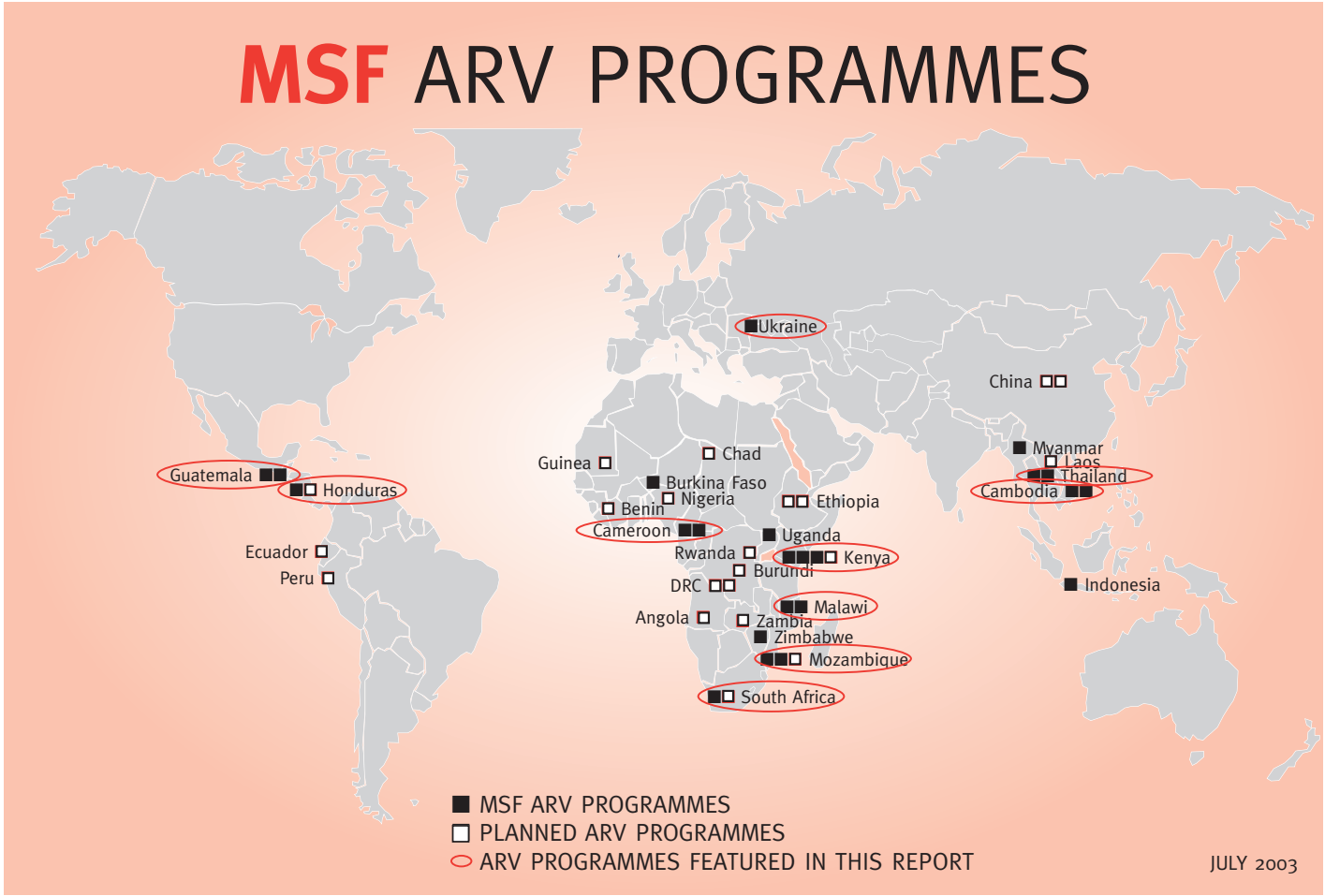
Governments of Least Developed Countries (LDCs) – have no need to grant and enforce patents on pharmaceuticals until 2016, as stipulated in the Doha Declaration on TRIPS and Public Health, 2001. Also they can exercise their right to access low-cost medicines (compulsory licences or parallel importation), as provided for in the World Trade Organization (WTO) Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement.

ARV procurers – the most important task is to obtain appropriate ARV products and formulations of assured quality at the lowest price possible. Some of the key issues for successful procurement are: forecasting ARV needs accurately, having up-to-date price information and quality assessment (WHO's pre-qualification project) obtaining ARVs that are registered by the national drug regulatory authority (NDRA), introducing generic competition, knowing of reliable suppliers and distributors (international and national) and having guaranteed funding (e.g. from the Global Fund to Fight AIDS, Tuberculosis and Malaria).

Manufacturers – manufacturers worldwide should develop fixed-dose combinations (FDCs) and paediatric formulations, as well as more user-friendly and affordable diagnostics. They should also be committed to developing and participating in a differential pricing mechanism, in WHO's pre-qualification project and in maintaining stocks at country level.

United Nations and international agencies – a differential pricing system for newer medicines should be further explored at international level. Regional, as well as national, ARV procurement initiatives should be supported. If requested, UN and international agencies should stock ARV supplies on a country's behalf.

MSF ARV PROGRAMMES



Main findings and recommendations

The following section draws together the common themes and findings from the 10 country cases. No ideal ARV procurement model was identified but analysis of the cases illustrated which factors had the most significant impact on availability and affordability of ARVs.

Government HIV/AIDS strategy:
The most critical factor affecting ARV procurement is a clear government commitment and policy to include treatment in a national HIV/AIDS strategy and securing the funding for this. Next come the registration status of medicines; the patent situation and the government's approach to overcoming patent barriers; accessibility to best prices by ensuring competition including originator and generic companies; and setting up an effective mix of public/private and NGO procurement and service delivery systems that best serve treatment programmes nationwide.

Political will:
Whether it led to the decision to produce locally (Thailand) or to a system whereby imported drugs are made available at competitive prices (Cameroon and Malawi), national political will was a critical factor in ensuring the availability and affordability of quality selected drugs. MSF's procurement experience was profoundly influenced by governments' policies, whether written or implied. In some countries (Kenya and South Africa), the lack of political will led MSF to identify and apply "exceptional" strategies. Such strategies need case-by-case government approval, and therefore have only demonstrative potential but do not significantly improve access across-the-board to patients in need.

Drug registration:
Having a limited number of registered generics and originator products created a serious barrier to ARV affordability and availability, this was the case in Cambodia, Guatemala, Kenya, Mozambique, South Africa and the Ukraine. Government policy regarding registration and other factors, such as the size of the market or a country's wealth, played critical roles in which drugs were registered.

Manufacturers are not always keen to register their products in Low- and Middle-Income countries where the market remains small; for instance, in Cambodia and Mozambique few originator drugs are registered. This is true even in countries included in international offers. Therefore price offers remain "virtual" unless temporary authorization for import and use can be attained.

Governments were often ready to give MSF special authorization when drugs were not registered, which has helped to foster competition between producers. This happened in Cambodia, Guatemala, Mozambique and South Africa.

Patents:
In most of the 10 countries MSF had difficulty finding reliable information on the patent status of particular drugs, although some patents existed. MSF spent considerable time and resources hiring lawyers in various countries to analyse the national patent system and to ascertain the patent status of needed ARVs.

But it is clear that some countries are using the maximum flexibility allowed under TRIPS and strengthened in the Doha Declaration by ensuring accessibility of generic ARVs when patents were granted. Also, whether there was a government policy or not, MSF and its suppliers have had no legal problems (have never been sued or received legal threats) when using generic drugs.

Generic competition:
The most significant factor in lowering prices was the introduction of generic sources in a country. Prices for first-line therapy in the 10 countries ranged from US$277 ppy in Cameroon to US$867 in Guatemala.

Generally prices are significantly lower for generics than then they are for even differentially priced originator products. South Africa provides a good example. The differential price offered by originator companies for ZDV/3TC* and NVP in May 2003 was US$767 ppy, while MSF was paying US$400 for generic drugs from Brazil.

In some LDCs or sub-Saharan countries generic prices have dropped to less than US$300 ppy. But countries that are not LDCs or not in sub-Saharan Africa are only getting significantly reduced prices when they have access to generics. Country cases show that generic producers are willing to charge their lowest prices in some mid-level countries, for example, Honduras, where the first-line treatment costs US$288 ppy.

However, generic companies did not always make their internationally publicized prices available at country level. This was the case in Cambodia for most Cipla drugs, which forced the MSF team to import the drugs from the manufacturer.

ARVs are still unaffordable for people living in developing countries. Large scale-up will depend on further price reductions. MSF estimates that with a combination of large production volumes and generic competition, a price of US$50-100 ppy for triple therapy is achievable.

Differential prices:
In general, MSF found that it took extraordinary measures to get the published differential prices at country level. The drugs were often unregistered, unavailable or available from local agents that were adding surcharges. But with a lot of

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Summary of MSF's procurement experience in ten countries (information as of March 2003)

	Level of Development	Availability	Registration Situation	Patent Situation	Generics Purchased?	MSF 1st line and price (per patient/year)	MSF 2nd line and Price (per patient/year)	International Price Offers Available?	National Production?	Government Commitment?	Main Characteristics of Procurement
Cambodia	Medium HDI[1], LDC[2]	Generics and originators imported, not locally available.	Few ARVs registered; special govt authorization obtained.	No patent barriers. As LDC, not obliged to enforce patents before 2016.	Yes.	D4T/3TC/NVP US$ 350	ZDV+ddI+LPV/r US$ 1215	Differential prices sometimes not available locally; needed to contact companies' headquarters.	No (but announced).	No.	Procurement is resource-intensive and complex.
Cameroon	Medium HDI	Local purchase through national government procurement centre.	All govt purchased drugs registered, or in process.	Several key ARVs patented, but govt authorizes purchase of generics.	Yes.	D4T/3TC/NVP US$ 277	ZDV+ddI+NFV US$ 4763	Yes. Access to some of the best prices internationally.	No.	Yes.	Centralized procurement strategy. Procurement is simple, efficient, and reliable.
Guatemala	Medium HDI	Generics imported; originators bought locally or regionally.	Few ARVs registered; special govt authorization obtained. Data exclusivity limits access to generics.	No patent barriers.	Yes.	ZDV/3TC+EFV or ZDV/3TC+NVP US$ 867 or US$ 520	D4T+ddI+NFV US$ 1161	Guatemala eligible for few originator differential prices; prices often very high.	No.	No. Import fees add to costs; data exclusivity provision hampers access.	Time-consuming negotiations with originator firms required.
Honduras	Medium HDI	Generics bought locally; originators bought regionally.	Govt information unclear; most generics registered.	Govt information unclear.	Yes.	D4T/3TC/NVP US$ 426	ZDV+ddI+NFV, or D4T+ddI+NFV US$ 3796 for NFV only	Yes.	No.	No.	Local generic agents facilitate procurement.
Kenya	Medium HDI	Generics imported; originators bought locally.	Originators registered; generics not, but some generic applications pending.	Most ARVs on patent; exceptions made for NGO/mission sector.	Yes.	D4T/3TC/NVP US$ 292	ZDV+ddI+NFV US$ 1594	Yes.	No (but announced).	No. Lack of national AIDS plan hampers access; generics only available as special case.	Cumbersome; special authorizations for generics required.
Malawi	Low HDI, LDC	Generics and originators bought locally.	Generics and originators widely registered.	Little patent information available. As LDC, not obliged to enforce patents before 2016.	Yes.	D4T/3TC/NVP US$ 288	ZDV+ddI+NFV US$ 1875	Yes.	No.	Yes. By registering both generics and originators.	Dynamic private sector distributors; but no central procurement agency.
Mozambique	Low HDI, LDC	Generics and originators bought locally through private distributors.	No registration system yet; special govt authorization obtained.	No patent barriers. As LDC, not obliged to enforce patents before 2016.	Yes.	D4T/3TC/NVP or D4T/3TC+EFV US$ 389 or US$ 463	ZDV+ddI+NFV Not yet purchased.	Differential prices sometimes not available locally; needed to contact companies' headquarters.	No.	Yes. By quickly authorizing imports of generics.	Not overly cumbersome; central procurement agency planned.
South Africa	Medium HDI	Generics not available; originators bought locally.	Most originators and a few generics registered; special govt authorization obtained.	Most ARVs on patent.	Yes, by MSF under special authorization.	ZDV/3TC+EFV or ZDV/3TC+NVP US$ 1000 or US$ 400	ddI+d4T+LPV/r US$ 1203	Yes.	Yes (under voluntary license).	No.	Cumbersome; special authorizations for generics required.
Thailand	Medium HDI	Locally produced generics (GPO[3]) available; originators bought locally.	All originator and GPO generics registered.	Some ARVs on patent.	Yes.	D4T/3TC/NVP US$ 352	ZDV+ddI+SQV/r US$ 3500	Thailand eligible for few originator differential prices.	Yes (GPO).	Yes.	Easy for locally-produced drugs; complex for originators.
Ukraine	Medium HDI	A few generics imported; originators usually bought locally.	Most originator and some generics registered.	Some ARVs on patent.	Yes.	ZDV/3TC+NVP US$ 500	ddI+d4T+LPV/r Not yet purchased.	Ukraine eligible for few originator differential prices.	No.	No. Govt only negotiates with originators.	Somewhat difficult; no local distributors for generics, and small stock for originators.

Key: [1]HDI: Human Development Index [2]LDC: Least Developed Country [3]GPO: Government Pharmaceutical Organization (public-sector drug manufacturer)

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persistence, some of these problems were resolved for LDCs and sub-Saharan African countries although this is a continuous challenge. It should be noted that a number of originator companies are offering some of the best prices available internationally in LDCs and sub-Saharan Africa, as some BMS and Merck & Co products show.

MSF's experiences in Guatemala, Honduras, Thailand and Ukraine show that in UNDP-classified Medium Human Development Countries not in sub-Saharan Africa, differential prices are not usually available. Merck & Co's products are the exception as the company has publicized differential prices for Medium Human Development countries. Roche now has a policy of differential prices for World Bank-classified Lower-Middle Income Countries, but only accepts orders in Basle, Switzerland, and charges transport, insurance and freight costs to the customer (up to 20% surcharge).

Procurement system:
Procurement systems are partly driven by a country's political will to tackle the HIV/AIDS epidemic. From MSF's perspective, the most effective and easiest procurement systems are:

1) a strong public procurement agency: For instance, the Cameroon government takes full responsibility for authorizing the use of drugs of assured quality, purchasing through competitive bidding (tenders) and managing stock to avoid supply interruption.

2) private sector distributors: Another more complicated but equally effective system is purchase through dynamic private sector distributors. Malawi's first-line ARV combination price is one of the lowest in the world (US$288/ppy) because of local distributors' ability to act as agents of originator and generic manufacturers. This spares MSF or other buyers the administrative burden of importing, which is handled by the distributor. The low prices have partly been achieved by demanding that local distributors charge prices that have been publicized by the manufacturers. When surcharges were added, MSF complained to the manufacturer as well as the local distributor.

3a) direct from manufacturers: In some cases, because ARVs were unavailable or were over-priced, MSF imported needed ARVs directly from manufacturers (Cambodia and Guatemala). This is the most difficult means of procurement, as the full burden of registration (provisional) and importation falls on the organization. Also this supply line is more vulnerable because of long-delivery times and the lack of a local buffer stock.

3b) local manufacturers: Like Brazil, Thailand is an example of a country that produces ARVs locally. Local production has led to affordable, straightforward procurement of some drugs but for those that need to be imported, difficult price negotiations have been necessary.

In some countries, such as Kenya and Ukraine, MSF used a dual approach, buying from both private sector distributors and importing directly from manufacturers. This approach imposes a heavy administrative burden but does bring down medicine prices. (Note: importation is only just beginning in Ukraine).

Recommendations for ministries of health/ national AIDS programmes/policy-makers:
In countries where national HIV/AIDS guidelines are not yet developed, ARVs should be added to a country's EML and should include specific formulations, such as double and triple FDCs and paediatric formulations. WHO treatment guidelines are good references. When drugs are in the national EML, it simplifies procurers' work in purchasing ARVs.

National governments should consider fast-track registration of originator and generic ARVS, especially when drug/suppliers have been pre-qualified by WHO.

Governments should lower or abolish taxes, duties and wholesaler and dispenser mark-ups on ARVs, to ensure that the prices obtained through competition or differential pricing mechanisms are not being increased prohibitively.

Governments should work more effectively with national and regional patent offices to increase information on the patent status of ARVs.
LDCs should take advantage of the fact that under the terms of the Doha Declaration they do not need to grant or enforce patents on pharmaceuticals until 2016.

Subject to certain safeguards and limitations, governments can exercise their right to issue compulsory licences on patents on public health grounds. This provision is made under the WTO TRIPS Agreement.

Recommendations for ARV procurers:
The procurement agent should endeavour to make the best clinical choice of ARVs of assured quality at the lowest available price.

The lesson learned on registration is that buyers should advocate full registration rather than rely on special authorizations wherever possible. Pressure may have to be applied on both manufacturers or their representatives and NDRAs to achieve this.

Procurers need not assume that patents are barriers if generic products are available in-country. In actual practice it may be possible to purchase generic versions of drugs which are theoretically patented.

If publicized originator or generic prices are unavailable from local or regional subsidiaries or agents, it is advisable to contact the company headquarters, which will often provide information about prices and conditions. Procurers should insist that the company's global offers are respected by local agents.

To access the best possible prices and avoid shortages, it is important to plan drug requirements as far in advance as possible. Suppliers should also receive this information in advance, even if actual orders are placed at a later date, as quantities can always be adjusted if necessary.

If the government procurement agency in the country does not supply ARVs, it might be possible to get local importers or agents to stock them locally, rather than being forced to buy ARVs direct from each supplier. Manufacturers sometimes ask local buyers to recommend agents to represent their products if they do not yet have distributors.

When national procurement agencies are supplying ARVs, customers can demand that they use generic competition rather than negotiation. Customers can help by supplying these agencies with information on sources and prices.

The Global Fund will cover medicines approved by local regulatory authorities even if they are not yet pre-qualified by WHO and therefore countries need not limit their use of generics to pre-qualified drugs. Currently the Global Fund's intention is to continue this policy until the end of 2004[26].

Recommendations for manufacturers:
As part of the global commitment to scaling up access to treatment, manufacturers should support the development of FDCs, paediatric formulations and user-friendly, affordable diagnostics that will enable simplification of treatment.

Manufacturers should participate in the development of differential pricing and join WHO's pre-qualification project through expressions of interest.

Recommendations for UN and other international agencies:
A differential pricing system for new drugs that are not available in generic forms should be explored internationally. This is particularly important for "mid-level" countries that are still often faced with prices that put needed drugs out of reach. International agencies should also support regional ARV procurement initiatives.

Since national procurement agencies can work effectively, the international community should support countries' efforts to expand national procurement agencies' capacity to procure, distribute and manage stocks of ARVs.

On behalf of countries, international procurement agencies (UN and non-profit) should consider stocking a full range of generic and originator ARVs, in countries that cannot build procurement capacity easily. Pooled procurement would also increase volumes, and so decrease prices.

Recommendations for NGOs:
NGOs should work together to avoid duplication of effort and maximize their contribution to global scaling up of ARV treatment. Collaboration with governments is particularly important when encountering problems.

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