UPDATED FACT SHEET: *TAC v MSD AND MERCK* – COMPLAINT TO THE COMPETITION COMMISSION REGARDING ACCESS TO EFAVIRENZ

Acting on behalf of the Treatment Action Campaign (TAC), the AIDS Law Project (ALP) lodged a complaint with the Competition Commission of South Africa in late 2007 alleging that MSD (Pty) Ltd – the South African subsidiary of multinational drug company Merck – was unlawfully refusing to license the antiretroviral (ARV) medicine efavirenz (EFV) on reasonable terms.[1] On Friday, 30 May 2008, TAC announced that MSD was no longer acting in an anticompetitive way, paving the way for the market entry of a wide range of affordable EFV products.

According to the ALP's records and recent correspondence from the Commission, MSD has –

- Licensed four generic drug companies – two local producers and two locally-based importers – to bring stand-alone EFV products to market;
- Agreed that all four licensees are entitled to bring co-packaged products containing EFV to market;
- Agreed that all four licensees will not unreasonably be refused consent to bring co-formulated products containing EFV to market;
- Agreed that all licensed products can be sold to both public and private sectors in South Africa and 10 other southern African countries (Angola, Botswana, DRC, Lesotho, Madagascar, Mauritius, Namibia, Seychelles, Swaziland and Zimbabwe); and
- Waived any right to a royalty.

On the basis of these significant developments, the Commission believed that there was no reason to refer the complaint to the Competition Tribunal for adjudication. TAC agreed. Because MSD had agreed to grant multiple licences on reasonable terms, which was always the central demand, TAC decided that it too would not refer the matter to the Tribunal. It was – and remains – of the view that there is no compelling purpose served by referring what is now largely a historical complaint. Instead, TAC will focus on ensuring that the reasonable terms of the licensing agreements are appropriately implemented.

Background to the complaint

Over 450,000 people with HIV in South Africa are on life saving highly active ARV therapy (HAART) in the public and private sectors. HAART means having to take at least three ARV medicines daily. Two thirds of people initiating HAART take EFV as one of their three drugs. Yet the state pays far more for EFV than the combined price of the other two drugs.[2] Even though several companies across the world manufacture cheaper and a wider range

[1] See "TAC complains to the Competition Commission about the anti-competitive conduct of the world's largest pharmaceutical company", at http://www.tac.org.za/community/node/2127

[2] In terms of the current tender, the state is still bound to purchase MSD's EFV.

of EFV products than are produced by Merck (the world's largest pharmaceutical manufacturer), almost all of these were not until relatively recently even permitted to be sold in South Africa. Furthermore, there have been at least three stockouts of EFV in southern Africa.

The main reason for these three problems is that Merck, as a result of patent protection, effectively had a monopoly on the sale of EFV in South Africa. Merck and its South African subsidiary, MSD, had refused licences to at least two generic manufacturers. While licences had been given to two local companies, their terms were unreasonable. Further, neither company was able to bring generic EFV products to market until quite recently. The two companies who had been refused licences had registered generic EFV with the Medicines Control Council (MCC) and could have brought their medicines to market immediately if licensed.

Acting in response, the ALP filed its complaint alleging that MSD and Merck were violating the Competition Act 89 of 1998. The complaint argued that their refusal to license EFV to a sufficient number of generic companies on reasonable terms threatened access to comprehensive treatment for HIV/AIDS by –

- Preventing cheaper generic EFV products from being brought to market;
- Preventing co-formulated and co-packaged ARV products containing EFV and at least one other ARV medicine from being brought to market; and
- Placing the sustainability of supply of EFV products in South Africa under threat because of the risk of stockouts.

TAC's complaint was aimed at helping to implement the national *HIV & AIDS and STI Strategic Plan for South Africa 2007-2011* (NSP), which states:

> "The cost implications of the NSP are large, in some options exceeding 20% of the health budget without considering the costs arising from the effect of the epidemic on hospital and primary care services. In attempting to increase the feasibility of this plan … [a]ttention should be placed on increasing the affordability of medicines."

Previous TAC complaints before the Commission

This is the not the first time that the TAC has approached the Commission. In addition to a July 2000 submission regarding the proposed merger between pharmaceutical companies Glaxo Wellcome and SmithKline Beecham – which subsequently formed the company GlaxoSmithKline (GSK) – the TAC has submitted two complaints: the first in 2002 regarding allegations of excessively priced ARV medicines marketed and sold by GSK and Boehringer Ingelheim (BI); and the second in 2004 primarily regarding allegations of price-fixing by members of the National Pathology Group (NPG). On both occasions, TAC was represented by the ALP.

The latter complaint resulted in significant changes in the way the NPG's members conduct their businesses, as well as a further complaint instituted by the Commissioner into various practices in the pathology sector. The Commission's investigation into the pricing of key ARV medicines (zidovudine (AZT), lamivudine (3TC) and nevirapine) sold by GSK and BI revealed that the two companies had indeed abused their dominant positions in the relevant markets. The matter was settled between the parties, thus obviating any need for a Tribunal hearing.[3]

Did TAC try to negotiate with MSD before lodging the complaint?

Prior to filing the complaint, the ALP – on behalf of TAC – engaged with MSD for almost six years regarding the need for it to grant multiple licences on reasonable terms for the local production and/or importation of a range of generic EFV products. Progress over the years was agonizingly slow:

- MSD first licensed Thembalami Pharmaceuticals to produce stand-alone EFV products in April 2004. Thembalami, a joint venture between South Africa's Adcock Ingram and the South African subsidiary of India's Ranbaxy Laboratories, did not survive long enough to bring any EFV products to market.
- Some time after Thembalami's collapse, MSD licensed Aspen Pharmacare – in July 2005 – on substantially similar terms. Only in February 2008 did Aspen manage to get an EFV product registered by the MCC.
- In late August 2007, three months after the ALP sent a final letter of demand to MSD (dated 21 May 2007), a second generic company – Adcock Ingram – was licensed. While TAC welcomed this move, it recognised that this did not address all of its concerns, necessitating the filing of the complaint.

Throughout the course of the Commission's investigation, TAC remained open to further discussions with MSD. It publicly stated that it had no interest in protracted litigation, preferring instead for the parties to negotiate a settlement in the public interest. TAC made it clear that if such a settlement could be reached, as was the case in 2003 with GSK and BI, it would be prepared to withdraw its complaint.

Could government not have taken action against MSD?

According to section 4 of the Patents Act 57 of 1978, a Minister of State (in this case the Minister of Health or the Minister of Trade and Industry) may –
"use an invention for public purposes on such conditions as may be agreed upon with the patentee, or in default of agreement on such conditions as are determined by the commissioner [of patents] on application by or on behalf of such Minister and after hearing the patentee."

In a constitutional democracy that recognises a right to have access to

[3] See "Competition Commission Settlement Agreements Secure Access to Affordable Life-Saving Antiretroviral Medicines", at http://www.tac.org.za/newsletter/2003/ns10_12_2003.htm

medicines (an integral part of the right to have access to health care services), the concept of a "public purpose" clearly includes ensuring access to a sustainable supply of a range of affordable EFV products, particularly when such products are necessary for implementing existing government policy regarding the treatment of HIV infection.

Unfortunately, neither Minister has seen fit to use this crucial public power, despite being urged to do so. In the result, an organisation such as TAC had to assume the responsibility itself. To its credit, government did provide TAC with the legal space within which to operate, primarily by enacting the Competition Act and establishing and resourcing the Competition Commission.

What is EFV?

Like nevirapine, EFV belongs to the class of ARV medicines known as non-nucleoside reverse transcriptase inhibitors (NNRTIs). All ARV medicines target either a particular step in the life cycle of HIV or its interaction with host cells. As NNRTIs, both nevirapine and EFV inhibit a key viral enzyme – reverse transcriptase – required for the completion of the early stages of HIV replication.

Reverse transcription is a process whereby single strands of viral RNA are converted into double-stranded DNA by the reverse transcriptase enzyme. This enables HIV genetic material to combine with the host cell's DNA, a process central to the replication of HIV. NNRTIs work by binding directly to the reverse transcriptase enzyme thereby interfering with its ability to function.

What are stand-alone, co-packaged and co-formulated products?

Stand-alone products include various dosages of EFV tablets sold separately. Co-packaged products include EFV sold in the same single pack – often in the form of a blister – with other ARV medicines that are ordinarily prescribed with EFV. Co-formulated products include EFV sold as part of a fixed-dose combination (FDC) product, which may combine two or more different ARV medicines in a single tablet. FDCs (and co-packaged products to a lesser extent) are widely recognised to improve adherence to ARV and other chronic treatments.

Why is access to EFV important?

EFV is one of a limited number of ARV medicines that are currently provided as part of HAART in the public sector. All adults initiating HAART in the public sector are prescribed a treatment regimen containing stavudine (d4T), 3TC and either EFV or nevirapine (depending on a number of medical and other factors). A majority of people on ARV treatment are using EFV instead of nevirapine. All children on treatment will need to have access to EFV or nevirapine, either as part of an initial (first-line) or a second-line regimen.

EFV is also one of the most widely prescribed ARV medicines in the private

sector, accounting (for the six month period of January to June 2007) for over 80% of all NNRTI sales (in terms of volume). In the US, for example, the most widely prescribed standard treatment regimen for the initiation of HAART – and recommended by the relevant ARV treatment guidelines – is Atripla, a combination of the ARV medicines tenofovir disoproxil fumarate (TDF), emtricitabine (better known as FTC) and EFV. Patients taking Atripla only have to swallow a single pill once a day. While Atripla is not yet registered for use in South Africa, the combination of TDF and FTC (known as Truvada) is available, as is EFV.

What are the implications of the recent developments?

In practical terms, this means that there are now a sufficient number of competitors to ensure that EFV prices are kept as low as is reasonably possible. It also means that the public sector, which until relatively recently was paying 64 cents in every rand spent on first-line ARV treatments for EFV alone, can now choose to procure from up to five suppliers. This fact also means that we no longer have concerns regarding the sustainability of ex-manufacturer supply.

Importantly, the generic licensees are now in a position to sell the following forms of EFV if and when they are registered:

- Stand-alone products:
  - 30mg/ml paediatric suspension;
  - 50mg, 100mg and 200mg capsules; and
  - 600mg tablets;
- Co-packaged products (EFV with either two separate ARV products or a double FDC):
  - EFV + AZT + 3TC;
  - EFV + d4T + 3TC;
  - EFV + TDF + 3TC;
  - EFV + TDF + FTC;
  - EFV + didanosine + 3TC;
  - EFV + AZT/3TC;
  - EFV + d4T/3TC;
  - EFV + TDF/3TC; and
  - EFV + TDF/FTC; and
- Co-formulated products:
  - TDF/3TC/EFV; and
  - TDF/FTC/EFV.

To date, MCC has registered a number of stand-alone generic EFV products. The ALP has been advised, however, that a number of co-packaged products containing EFV are already in the registration queue, and that generic FDC products are likely to be brought to market in the foreseeable future.

Why are licences needed to bring (almost all) combinations to market?

With the single exception of MSD's TDF/FTC/EFV combination (Atripla), none of the co-packaged and co-formulated products would have been able to be placed on the South African market. This is for the following three reasons:

- In the absence of licensing agreements, the EFV patent does not allow any company other than MSD to bring EFV products to market;
- MSD's agreement with Gilead, which holds the rights globally to TDF and FTC, is limited to a single FDC (Atripla); and
- MSD does not have the right, nor has it indicated the intention, to bring 3TC products to the South African market.

In contrast, three of the four licensees have secured licensing agreements to bring generic 3TC products to market. AZT is no longer under patent protection in South Africa, whereas TDF was never patented in this country. In addition, the patents on d4T, ddI, and FTC are not enforced in the country. In short, EFV was the only ARV amongst those already discussed in respect of which a patent barrier prevented much-needed combination products from being sold in South Africa.

What price reductions have we already seen?

When TAC and the ALP first started to engage MSD on this issue as far back as May 2002, the company sold a year's supply of EFV for one adult for US$500. That price has dropped significantly. Today, MSD's best international price for a year's supply is US$237.25. In contrast, the best international price for a generic equivalent of proven quality, safety and efficacy is US$150. In the South African private sector, MSD's EFV sells for R166.90 (VAT inclusive) for a 30 days' supply. In contrast, the cheapest registered generic equivalent sells for R136.80. These prices are expected to drop even further.

Price differentials in respect of FDCs are even greater. MSD has committed to sell Atripla at US$613.20 per patient per year. In contrast, the Clinton Foundation HIV/AIDS Initiative (CHAI) has managed to secure a commitment from a reputable Indian company to bring generic TDF/FTC/EFV to market for only US$349 per patient per year. The same company has also committed to bringing generic TDF/3TC/EFV – which is considered as therapeutically equivalent to the FTC version of the FDC – for US$299 per patient per year. South Africa is entitled to purchase drugs through CHAI.

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