TAC Electronic Newsletter

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Contents

Campaign for tenofovir to be registered

TAC is campaigning for the Medicines Control Council (MCC) to register tenofovir, a drug that has been available to people with HIV in the United States since 2001, as well as many other countries. On 22 February we will hold protests at the offices of the MCC and Aspen Pharmacare, who together with Gilead, the patent-holder of tenofovir, we hold responsible for the tardy registration of this essential medicine.

Tenofovir Fact Sheet

Introduction

Tenofovir disoproxil fumerate (tenofovir) is an antiretroviral that we need to have registered in South Africa, so it can become part of first-line antiretroviral therapy (ART) as an option to stavudine (d4T). Studies have shown tenofovir has a good side effect and resistance profile. Additionally, it has an easy, once a day dosage.

Several leading HIV clinicians have called for the South African antiretroviral treatment guidelines to be updated to include tenofovir, so that public sector patients can access it, but this can only happen once tenofovir is registered. Also, various combination pills that include tenofovir must also be registered because patients taking them will have to swallow fewer pills, which is the most important factor for good adherence.

What is tenofovir?

There are three classes of antiretrovirals available in South Africa: nucleoside reverse transcriptase inhibitors (e.g. AZT, d4T), non-nucleoside reverse transcriptase inhibitors (e.g. nevirapine) and protease inhibitors (e.g. lopinavir/ritonavir - better known by the brand-name Kaletra).

Tenofovir is a nucleotide analogue, which is a type of nucleotide reverse transcriptase inhibitor (NRTI). NRTIs help prevent HIV from reproducing inside CD4 cells by stopping or "inhibiting" reverse transcriptase, a protein used in the process of HIV replication. In 2006 tenofovir was recommended by the World Health Organization (WHO) as a possible replacement for d4T in first-line ART, because of its "excellent safety profile and ease of use." This went a step beyond a 2003 recommendation by the WHO for tenofovir only to be used in second-line ART because of its high cost and limited availability, issues that still remain.

Why is tenofovir advantageous over d4T?

Results from various sites around South Africa demonstrate that ART is saving many lives. See for example the Western Cape Government's report Western Cape Antiretroviral Treatment Programme: Monitoring Report June 2006. It found that "by four years duration on ART, 7 out of 10 treatment-naÃ¯ve adult patients are still in care. Without treatment almost all of these patients would have died in this time period."

Nevertheless one of the drugs in the standard first-line regimen, d4T, is associated with serious side-effects for some people that in rare cases can be life-threatening. For example, d4T can cause lactic acidosis, a sometimes fatal condition, particularly for overweight women. It is also associated with neuropathy and lipoatrophy. Compared with d4T, tenofovir has a reduced risk of the mitochondrial toxicity that results in these serious side-effects. tenofovir also has activity against Hepatitis B.

However, studies have shown that tenofovir has a low risk of renal toxiticy (kidney damage), which can be monitored by checking creatine levels. Tenofovir can have a small effect on bone toxicity in the first year, but five year follow up shows no accumulation over time. There is also, as yet, no paediatric formulation for tenofovir.

How often is tenofovir taken?

Tenofovir comes in 300 mg doses and should be taken once a day, with or without food. Tenofovir must be taken in combination with other antiretrovirals. Combination drugs that include tenofovir Tenofovir is also manufactured in a co-formulation with another antiretroviral known as FTC (branded as Truvada).

Critically, tenofovir is one of the three drugs comprising the world's first one-pill-a-day antiretroviral regimen. This all-in-one pill consists of tenofovir, FTC and efavirenz (branded as Atripla in the United States). Reducing the number of pills patients need to take has been shown in a South African study to be the best way to improve patient adherence.

These formulations are not licensed or registered in South Africa. TAC will campaign to change this in 2007.

Along with treating HIV, tenofovir is being tested for preventing mother to child transmission (PMTCT), as a

microbicide and as chemoprophylaxis, i.e. using antiretrovirals to prevent the sexual transmission of HIV. However, it has not yet been shown to be effective for these purposes.

Interactions between tenofovir and other drugs

Like many medications, tenofovir can interact with other drugs. Taking tenofovir with didanosine (ddI), another antiretroviral, increases ddI levels and therefore ddI associated side effects, so tenofovir and ddI should not be taken together. If you take tenofovir with the antiretroviral protease inhibitor atazanavir, then you must also take an antiretroviral called ritonavir, else the levels of atazanavir will be decreased below their correct amount.

Is tenofovir available in South Africa?

Currently tenofovir is only available under what is known as a Section 21 authorisation from the Medicines Control Council on a patient-name basis. This administratively time-consuming mechanism is impractical for public sector patients, as well as many private sector ones. Furthermore, the South African antiretroviral treatment guidelines cannot include tenofovir until it is registered. Only by registering the drug can it become generally available.

Is tenofovir too expensive?

Yes. Tenofovir's manufacturer, Gilead Sciences, has a manufacturing agreement with South Africa's largest drug manufacturer, Aspen Pharmacare, to produce and distribute tenofovir, making it easier to distribute in many countries, including South Africa. However, the price at which Gilead has set it is $17/month (about R120). This is more than the price at which the state buys the entire current standard first-line regimen from Aspen. TAC will campaign for the price to be brought down, but only competition from generic suppliers will keep the price sustainably low and reduce the possibility of stock-outs.

JOIN TAC'S MARCHES IN GAUTENG AND KWAZULU-NATAL ON 22 FEBRUARY!

DEMAND TENOFOVIR REGISTRATION NOW!

DEMAND INCLUSION OF TENOFOVIR IN THE NATIONAL TREATMENT GUIDELINES NOW !

[END OF FACT SHEET]

ALP Letter on Behalf of TAC to the Medicines Control Council

[We have not received a response to this letter even though the deadline has passed - Ed.]

23 January 2007

Ms Mandisa Hela
Registrar of Medicines
Medicines Control Council
Private Bag X828
Pretoria 0001

Per fax: (012) 312-3105

Dear Ms Hela

URGENT: REGISTRATION OF TENOFOVIR IN SOUTH AFRICA

- We act on behalf of the Treatment Action Campaign (TAC).

- On 27 January 2006, the TAC wrote to the then Acting Registrar of Medicines - Dr J. Gouws - informing her of the urgent need for the Medicines Control Council (MCC) to expedite the registration of tenofovir disoproxil fumarate (TDF), an essential antiretroviral (ARV) medicine widely used in the treatment of HIV infection abroad. For your ease of reference, a copy of that letter is attached hereto marked "TDF1".

- Almost a year later, with TDF and all other medicines containing tenofovir remaining unregistered, the need is now even more urgent. While private sector use remains limited to section 21 authorisations, the National ARV Treatment Guideline cannot be amended to include the use of TDF in the public sector for as long as it remains unregistered. Thus the broad recognition of the need for an amendment to the guideline has been accompanied by calls from ARV treatment providers, the Southern African HIV Clinicians' Society and the Joint Civil Society Monitoring Forum for the expedited registration of TDF.

- The need is further exacerbated by the US and European drug regulatory authorities' registration of the fixed-dose combination of TDF, emtricitabine (FTC) and efavirenz. That product - which is marketed as Atripla - simplifies ARV treatment to a single pill taken once daily. This has significant implications for adherence to treatment regimens and therefore improved public health outcomes. Importantly, Atripla's registration in South Africa appears dependant on the registration of TDF and/or Truvada (the fixed-dose combination of TDF and FTC).

- In its letter dated 27 January 2006, the TAC requested the following information regarding the registration process in respect of TDF:

    - The original application for registration by Gilead Sciences, Inc. (Gilead):

        - The date on which Gilead submitted its original application for the registration of TDF; and

        - A summary of the process leading to the return of the original dossier and the MCC's request that it be resubmitted in another form; and

    - The application for registration by Aspen Pharmacare (Aspen):

        - The date on which Aspen submitted the revised application for the registration of TDF;

- If, at the time of application, Aspen requested fast track review status;
- If fast track review status was requested, when it was granted;
- If fast track review status was not granted immediately, the reason for the delay;
- If fast track review status was not granted at all, the reason for the refusal to grant such status;
- Given that the Medicines Act now requires fast track procedures to be completed within nine months, the date by which TDF is expected to be registered; and
- Any other information that, in your opinion, is necessary to explain why this essential medicine has not yet been registered by the MCC."

- In her brief response (incorrectly dated 2 January 2005), Dr Gouws informed the TAC that "the matter ... [had] been forwarded to the Legal Office of the Cluster: Medicines Regulatory Affairs, Mr Thomani Mulaudzi to assist with ... [the TAC's] request." To date, the TAC has not received a response from Mr Mulaudzi or anyone else in the Cluster: Medicines Regulatory Affairs.

- In her response, Dr Gouws also drew the TAC's attention "to the provisions of Section 34 of the Medicines and Related Substances Act, 1965 (Act 101 of 1965) 'Presentation of Secrecy'", without explaining anything more. Section 34 provides as follows:

  - "No person shall, except for the purpose of the exercise of his powers or the performance of his functions under this Act, or for the purpose of legal proceedings under this Act, or when required to do so by any competent court or under any law, or with the written authority of the Director-General, disclose to any other person any information acquired by him in the exercise of his powers or the performance of his functions under this Act and relating to the business or affairs of any person, or use such information for self-gain or for the benefit of his employer."

- We are unclear about the exact purpose of Dr Gouws' reference to section 34, which we surmise may have been meant to inform our client that the relevant section prohibits the disclosure of the requisite information. Had Mr Mulaudzi or anyone else in the Cluster: Medicines Regulatory Affairs responded to the TAC's letter of 27 January 2006, this may indeed have been clarified.

- In our view, however, section 34 does not appear as a bar to a full and proper response by the MCC. This is because:
    - We do not believe that either Gilead or Aspen would object to the MCC answering the questions posed in our client's letter dated 27 January 2006; and
    - There appears to be no lawful basis upon which the Director-General (DG) may refuse to authorise the required disclosure, given the public interest in understanding the reasons why an essential medicine such as TDF remains unregistered.
- Further, to the extent that section 34 may be understood to prevent the disclosure of the requested information in the absence of Gilead's and/or Aspen's consent or the DG's written authorisation, it is particularly vulnerable to constitutional challenge.
- During 2006, we were informed by Aspen that the company had complied timeously with the MCC's requests for it to submit additional information. We were also advised that Aspen's dossier was under clinical review in or about June 2006 and that the application had indeed been granted fast-track approval status. Thus, while restating what our client wrote almost a year ago - "that it is in the public interest to release this information as a matter of urgency" - we would like to reformulate the original questions as follows:
    - The original application for registration by Gilead:
        - The date on which Gilead submitted its original application for the registration of TDF; and
        - A summary of the process leading to the return of the original dossier and the MCC's request that it be resubmitted in another form; and
    - The application for registration by Aspen:
        - The date on which Aspen submitted the revised application for the registration of TDF;
        - Confirmation that Aspen requested fast track review status, and if so, the date upon which this was requested;

- The date upon which fast track review status was granted, if indeed requested;
- If fast track review status was not granted immediately, the reason for the delay, if indeed granted sometime later;
- Given that the Medicines Act now requires fast track procedures to be completed within nine months, the date by which TDF is expected to be registered; and f.Any other information that, in your opinion, is necessary to explain why this essential medicine has not yet been registered by the MCC.

12.In respect of Truvada and Atripla, kindly answer the following similar questions:

1.The date on which applications for the registration of Truvada and/or Atripla were submitted, if at all;

If submitted:

- If, at the time of application, the relevant company requested fast track review status;
- If fast track review status was requested for a product, when it was granted;
- If fast track review status - if requested - was not granted immediately, the reason for the delay;
- If fast track review status - if requested - was not granted at all, the reason for the refusal to grant such status;
- Given that the Medicines Act now requires fast track procedures to be completed within nine months, the date by which the relevant product is expected to be registered; and
- Any other information that, in your opinion, is necessary to explain why these essential medicines have not yet been registered by the MCC.

- We look forward to hearing from your offices by not later than Friday, 2 February 2007. We sincerely hope that we will not have to resort to a court of law to resolve this matter.

Yours sincerely

Jonathan Berger

CC: Mr Stephen Saad: Group Chief Executive, Aspen Pharmacare
(Per fax: 031 580 8647)
Mr Joseph Steele: Vice-President, Commercial Development, Gilead Sciences, Inc.
(Per fax: +1 650 522 5870)

ALP Letter on Behalf of TAC to Aspen Pharmacare

[Aspen has responded to this letter. - Ed.]

23 January 2007

Mr Stephen Saad
Group Chief Executive
Aspen Pharmacare
Aspen Park
98 Armstrong Avenue
La Lucia Ridge Durban 4019

Per fax: 031 580 8647

Dear Mr Saad

URGENT: REGISTRATION OF TENOFOVIR IN SOUTH AFRICA

- We act on behalf of the Treatment Action Campaign (TAC).

- As you are well aware, tenofovir disoproxil fumarate (TDF) - or any other essential antiretroviral (ARV) medicine containing tenofovir - has yet to be registered by the Medicines Control Council of South Africa (MCC). By now, you should have received a copy of a letter we sent to the MCC this morning, in which we detail our concerns.

- When I last met with Aspen Pharmacare's Stavros Nicolaou and Kai Crooks-Chissano on 10 July 2006, I was advised that:

    - The application for the registration of TDF had already been with the MCC for nine months; and

- The application for the registration of Truvada - the fixed-dose combination of TDF and emtricitabine (FTC) - had been filed some three months before our meeting.

- It is now six months later and neither drug has been registered. This is unacceptable, particularly given the fact that TDF has been available in other countries for more than five years.

- The U.S. Food and Drug Administration, for example, registered -

  - TDF more than five years ago on 26 October 2001;

  - Truvada almost 2Â½ years ago on 2 August 2004; and

  - Atripla - the fixed-dose combination of Truvada and efavirenz - more than six months ago on 12 July 2006.

- For some time, Aspen officials have repeatedly assured my colleague Fatima Hassan and me that TDF's registration is on track. This does not appear to be the case.

- We trust that Aspen shares our view that the public interest requires the expedited registration of TDF and all other essential ARV medicines containing tenofovir. If this is indeed the case, kindly inform us what steps - if any - Aspen is taking to ensure that these essential medicines - and TDF in particular - are available for general use in South Africa in the near future.

- We trust that you will respond to us urgently.

Yours sincerely

Jonathan Berger

CC: Mr Joseph Steele: Vice-President, Commercial Development, Gilead Sciences, Inc.
(Per fax: +1 650 522 5870)

[END OF LETTERS]

TB and social grants: A series of interviews by Sylvia Flynn

Sylvia Flynn is a TAC trainee journalist. She interviewed three people about the importance of social grants for people with TB. In South Africa, the government provides a disability grant of R820 (approx. US$115 per month). People who have progressed to AIDS can apply for this means-tested grant, but if they take antiretrovirals and recover, the grant is taken away. Therefore poor people with HIV face a troubling dilemma: when they are sick, they receive a grant which gives them the means to eat, but when they recover because they take antiretroviral treatment, they lose the grant and a source of essential income. Determining a social grant policy that resolves this problem is difficult and will be one of the research questions that TAC examines in more detail in 2007.

Marianhill is a predominantly African settlement near Durban. It is mostly poor and overcrowded. Many people are unemployed and HIV prevalence is high. Consequently there is a large TB epidemic. I received many complaints from people who had TB and applied for social grants, so I decided to interview some people of them and a nurse who works with TB patients.

Sister Pillay of the Mosque Clinic says she cannot describe the sadness of seeing people suffer from TB when the problem can be eradicated. She says there are cases that make her want to pack her bags and leave. Sometimes she sees people in their 30s with weights less than 40kg. I asked her about the problem of people not adhering to their TB medications so that their social grant could be prolonged. Sister Pillay said that it would help if government worked with communities to develop the hand crafts industry and vegetable growing gardening. She would also like to see the grant replaced with vouchers to use at specific shops so that people don't misuse their grants ***[This is not a view supported by TAC. - Ed].***

FM says she struggled with TB when it attacked her in 2003. Her father had been sick with the disease in the same year. She found the side-effects of the TB medicines unbearable and eventually defaulted. She believes the reason for this was because she could not access the disability grant nor healthy food. Consequently she was re-infected with TB in 2006. This time she got a grant. Usually TB treatment is six months, but because she got re-infected she had to have streptomycin injections and took treatment for eight months. Despite this, her grant ended two months before her treatment stopped. The disability grant is provided for only six months, irrespective of the treatment time of an individual patient.

TG got TB in 1999. He recalls a lot of difficulties with his treatment as he received no grant. His grant applications were denied and he was constantly told to re-apply.

Many people suffer from TB in the overcrowded slums of Marianhill. How do we ensure that people with TB have enough money to live on when they are being treated? How do we get government to show the necessary political will to deal with the TB crisis?

[END OF TB STORY]

- Antiretrovirals
- Tuberculosis

- Antiretrovirals
- Tuberculosis
