

# TENOFOVIR DISOPROXIL FUMARATE/LAMIVUDINE (TDF/3TC)

## GENERAL INFORMATION

- Therapeutic class: One NtRTI and one NRTI in a double fixed-dose combination.
- WHO guidelines: Indicated for first- and second-line for adults and adolescents.<sup>6</sup>
- Originator company and product brand name: No originator product exists.
- First approval by U.S. Food and Drug Administration (FDA): Not applicable.
- WHO Model List of Essential Medicines (EML): Individual medicines included in the 17th edition. 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.<sup>24</sup>
- Patents: Most patents related to tenofovir (TDF) or to lamivudine (3TC) also affect this combination. In addition, other patents may have been applied for, more specifically related to the use of these medicines in combination, or to this specific FDC, such as by Cipla.<sup>312</sup>

## PRICE INFORMATION

### Developing country prices in US\$ per patient per year, as quoted by companies.

The price in brackets corresponds to the price of one tablet. Products quality-assured by US FDA or WHO prequalification (as of May 2011) are in **bold**.

|                            | Daily dose | Aurobindo (CF)     | Cipla (CF)         | Hetero (CF)        | Matrix (CF)       |
|----------------------------|------------|--------------------|--------------------|--------------------|-------------------|
| Who can access this price? |            | See annex 2        |                    |                    |                   |
| TDF/3TC 300/300mg tablet   | 1          | <b>116 (0.317)</b> | <b>103 (0.283)</b> | <b>116 (0.317)</b> | <b>91 (0.250)</b> |

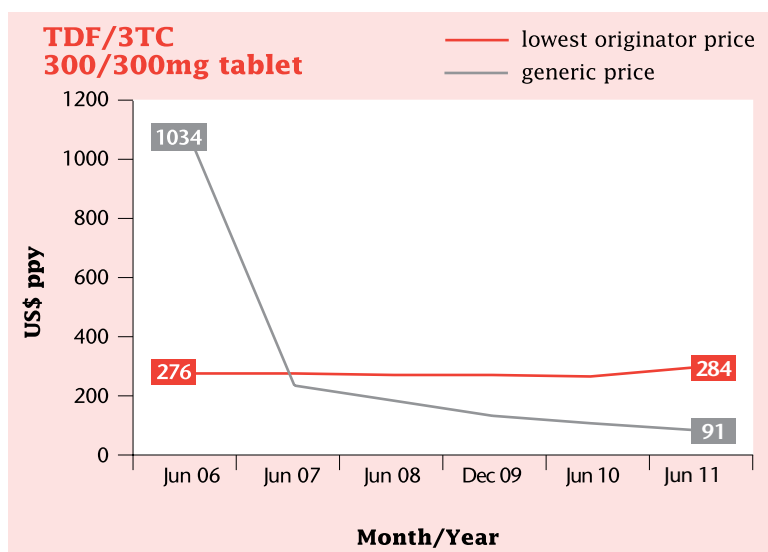
(CF) The Clinton Foundation has negotiated with this manufacturer for reduced prices on some formulations for countries in their consortium. See annex 13 for details.

### Evolution of the lowest quoted price for developing countries since 2006:

As of May 2011, four generic sources of TDF/3TC 300/300mg tablet were quality-assured by US FDA or WHO prequalification. The one with the lowest price is shown here.

As there is no originator fixed-dose combination or co-pack, the price shown for the originator product is the sum of the two individual originator products.

Since 2006, the sum of the originator prices has increased by 3%, while generic prices have dropped by 91%. The most affordable generic product is 68% less expensive than the sum of the originator products.



Continued overleaf ❖

## SPOTLIGHT ON ACCESS ISSUES

This combination is likely to be widely used in developing countries as a backbone in first- and second-line regimens.

In 2010, WHO released new recommendations for antiretroviral therapy for HIV in adults and adolescents. These new recommendations advise countries to phase out stavudine- (d4T) based regimens because of their long-term irreversible side effects and to move towards zidovudine- (AZT) or tenofovir- (TDF) based first-line regimens.

For many years, the regimen containing d4T played a crucial role in ART scale-up in resource-limited settings, due to its availability in a fixed-dose combination and most importantly its low cost. d4T remains a widely used ARV in first-line regimens.

It is time for countries to invest in a more robust, TDF-containing first-line regimen, such as TDF/3TC/EFV or TDF/FTC/EFV, which are both one pill, once a day or TDF/3TC + NVP (available in co-pack). While the price today is still higher than a d4T-based regimen, there is a need to generate greater demand which will, in turn, increase the competition and the economies of scale needed to further decrease prices.<sup>7</sup>

TDF is also recommended for second-line treatment if d4T or AZT have been used in first-line.

TDF should then be used as the NRTI backbone, in combination with either lamivudine (3TC) or emtricitabine (FTC), to which a boosted protease inhibitor (PI) should be added.

TDF is also active against hepatitis B Virus (HBV) and therefore plays an important role in co-infected patients. The latest WHO 2010 guidelines recommend using TDF with either FTC- or 3TC-containing antiretroviral regimens in all HIV/HBV co-infected individuals needing treatment.<sup>22</sup>

### Patents

This combination is produced by Indian generic companies because neither of the individual components is patented in India today. However, Gilead has applied for patents related to TDF, which if granted will affect the production of not only TDF but also of this combination.

For further details on the patent status of TDF in India and Brazil, the voluntary licences agreements signed by Gilead and generic companies, and the Brazilian initiative for local production, please refer to the tenofovir drug profile.

### Paediatrics

TDF is approved for adolescents from 12 years old and 3TC is approved for use in children. Both medicines have the advantage of once-daily dosing.

Gilead's Phase II trial involving children (aged between two and 12 years), using an oral powder formulation is still on-going. Such data, provided appropriate formulations are developed, will be crucial to address the urgent needs of this paediatric population. Having safety and efficacy data in paediatric populations would enable children to stay longer on the same treatment regimen, and would facilitate harmonisation with adult regimens, as TDF-based first-line regimens are also the preferred option for adults.

However, no paediatric fixed-dose combination has been developed with TDF and 3TC.

There is an urgent need to have this combination developed for HIV and hepatitis B co-infected paediatric patients, for whom no treatment options currently exist.

The Paediatric Antiretroviral Working Group of WHO considers the development of a fixed-dose combination of TDF/3TC 75/75mg tablet and a scored 300/300mg tablet to be a high priority.<sup>22</sup>