

LAMIVUDINE/ STAVUDINE (3TC/d4T)

GENERAL INFORMATION

- Therapeutic class: Two NRTI in a double fixed-dose combination.
- WHO guidelines: Indicated for first-line in children WHO 2009 guidelines also recommended to move away from d4T first-line in adults and adolescents.^{6,22} WHO updated the 2006 guidelines to recommend a reduction in dose of d4T 40mg to d4T 30mg for all weight categories of patients.²²
- 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.²⁴
- Patents: Individual patents on lamivudine (3TC) or stavudine (d4T) also affect this combination.

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 | Cipla (CF) | Hetero (CF) | Matrix | Ranbaxy (CF) | Strides |
|------------------------------------|------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| Who can access this price? | | See annex 2 | | | | |
| 3TC/d4T 30/6mg dispersible tablet | 4 | 47 (0.032) | | | | |
| 3TC/d4T 60/12mg dispersible tablet | 2 | 40 (0.055) | | | | |
| 3TC/d4T 150/30mg tablet | 2 | 42 (0.058) | 46 (0.063) | 39 (0.054) | 42 (0.058) | 41 (0.056) |

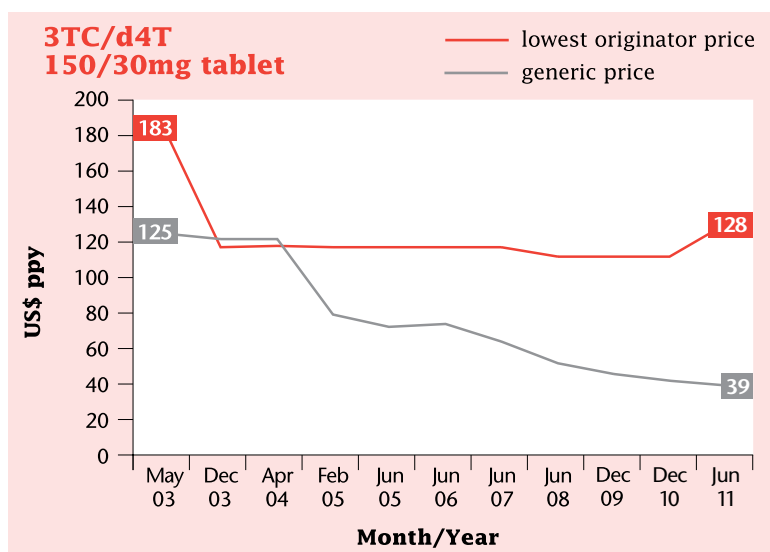
(CF) The Clinton Foundation has negotiated with this manufacturer for reduced prices on some formulations for countries in their consortium. See annex 13 for details.

Evolution of the lowest price quoted for developing countries since 2003:

As of May 2011, seven generic sources of 3TC/d4T 150/30mg 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 2003, the sum of the originator prices has decreased by 30%, while generic prices have dropped by 69%.



Continued overleaf ❖

SPOTLIGHT ON ACCESS ISSUES

In 2010, WHO released new recommendations for antiretroviral therapy for HIV in adults and adolescents. These new recommendations advise countries to phase out d4T-based regimens because of their long-term irreversible side effects and to move towards zidovudine- (AZT) or tenofovir-based (TDF) first-line regimens.⁷

For many years, the stavudine- (d4T) containing regimen 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.

During the review of the marketing authorisation of this medicine in February 2011, the European Medicines Agency (EMA) decided to severely restrict its use in both adults and children, recommending that in view of its long-term toxicities, d4T be used for as short a time as possible and only when no appropriate alternatives⁸ exist.

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.⁷

We can therefore expect to see a decrease in the use of this formulation in the future.

Patents

Generic companies in certain developing countries were able to develop these fixed-dose combinations because patents on the individual products did not exist.

The fixed-dose combination is not available in developed countries or in countries such as China, however, where one or both medicines are under patent.

Paediatrics

In its 2010 guidelines for antiretroviral therapy for HIV in infants and children, WHO recommends 3TC/d4T as one of the possible combinations to be given with either an NNRTI or a PI in the first-line.²²

3TC/d4T, when used with NVP, is part of one of the two most commonly used first-line regimens for children today (the other being

AZT/3TC/NVP). With both of these regimens, there is a need to start NVP at a lower dose for the first two weeks to minimise the side effects. Quality-assured double fixed-dose combinations are therefore of great value in allowing children to be safely and accurately dosed while starting treatment. In their absence, the alternative is to use two different syrups, which can be difficult to administer.

Because of the long-term risks of toxicity, particularly lipoatrophy in children treated with d4T-containing regimens, the use of AZT is preferred. Toxicity risks are also associated with AZT, with possible anaemia developing over the first few months of therapy, but the drug remains much better tolerated than d4T.²² WHO guidelines recommend a preferential order of NRTIs to be used in first-line regimens, with AZT preferred over ABC, and ABC preferred over d4T.

As of May 2011, two generic dispersible formulations were quality-assured by either US FDA or WHO prequalification.