



ZIDOVUDINE/LAMIVUDINE + EFAVIRENZ (AZT/3TC + EFV)

GENERAL INFORMATION

- Therapeutic class: Two NRTI (in a fixed-dose combination) + one NNRTI in a co-pack.
- WHO guidelines: Indicated for first-line for adults, adolescents and children.^{6,22}
- 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 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: Most patents related to zidovudine (AZT), lamivudine (3TC), AZT/3TC or to efavirenz (EFV) also affect this combination. In addition, Cipla applied for patents specifically related to the use of AZT, 3TC and EFV in combination.³¹⁹

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 kit of three tablets. Products quality-assured by US FDA or WHO prequalification (as of May 2011) are in **bold**.

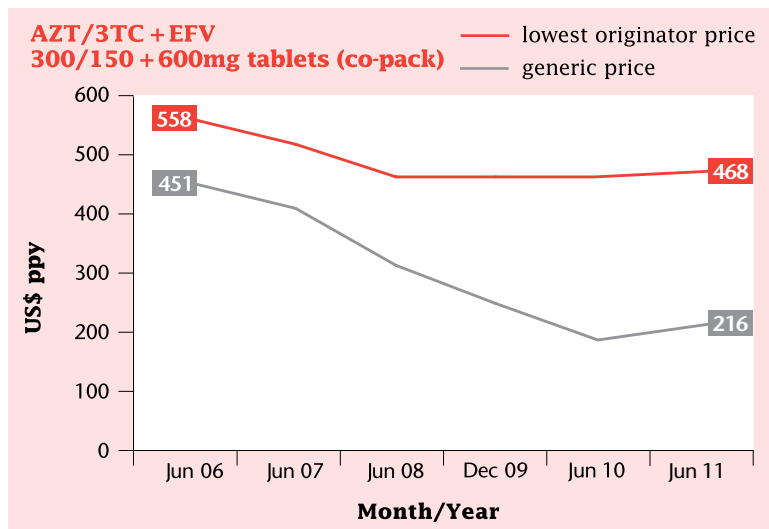
	Daily dose	Aurobindo	Ranbaxy	Strides
Who can access this price?		See annex 2		
AZT/3TC + EFV 300/150 + 600mg tablets (co-pack)	1 kit (3 tablets)	216 (0.593)	292 (0.800)	225 (0.617)

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

As of May 2011, three generic sources of AZT/3TC + EFV 300/150 + 600mg tablets (co-pack) were quality-assured by US FDA or WHO prequalification. The one with the lowest price is shown here.

As there is no originator 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 decreased by 16%, while the generic prices have dropped by 52%.



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 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.

AZT is also recommended for second-line treatment if tenofovir has been used in first-line. AZT 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.

In addition, efavirenz (EFV) is the preferred NNRTI for use in patients starting ART while on TB treatment.⁷

Patents

Basic patents related to AZT, 3TC or EFV could not be obtained in some developing countries such as India, which did not grant product patents on pharmaceuticals at the time. This allowed Indian drug companies to manufacture generic versions of the medicines and to develop this product.

However, GlaxoSmithKline and Merck may hold patents in other developing countries, which could prevent the importation and use of this co-pack combination.

Paediatrics

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

Currently a co-pack of AZT/3TC + EFV for children does not exist.

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 there is still no established dosing of EFV for children less than three years of age, there is an urgent need to establish the dosing of EFV for this age group for children with HIV/TB co-infection.

In the absence of such data, treatment options for children remain limited, particularly for HIV/TB co-infected young children who cannot be given NVP because of interactions between NVP and TB drugs.