

# ZIDOVUDINE/LAMIVUDINE/NEVIRAPINE (AZT/3TC/NVP)

## GENERAL INFORMATION

- Therapeutic class: Two NRTI + one NNRTI in a triple fixed-dose combination.
- WHO guidelines: Indicated for first-line for adults, adolescents and children.<sup>6,22</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): 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 zidovudine (AZT), lamivudine (3TC), AZT/3TC or to nevirapine (NVP) 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	Aurobindo (CF)	Cipla (CF)	Hetero (CF)	Matrix (CF)	Ranbaxy (CF)	Strides
Who can access this price?		See annex 2					
AZT/3TC/NVP 60/30/50mg tablet	4				<b>101 (0.069)</b>	183 (0.125)	
AZT/3TC/NVP 300/150/200mg tablet	2	<b>144 (0.197)</b>	<b>137 (0.188)</b>	<b>143 (0.196)</b>	<b>134 (0.183)</b>	<b>140 (0.192)</b>	<b>141 (0.193)</b>

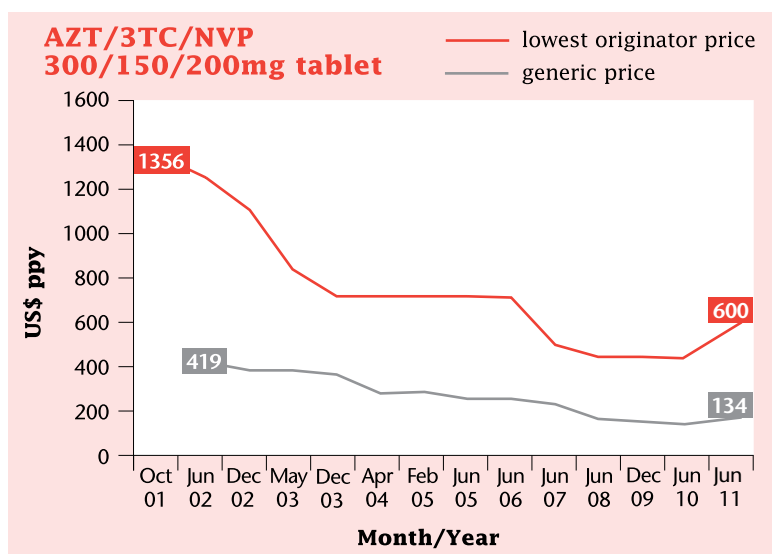
(CF) The Clinton Foundation has negotiated with this manufacturer for reduced prices on some formulations for countries in their consortium. See annex 13 for details.

### Evolution of the lowest price quoted for developing countries since 2001:

As of May 2011, six generic sources of AZT/3TC/NVP 300/150/200mg 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 three individual originator products.

Since 2002, the sum of the originator price has decreased by 56%, while generic prices have dropped by 68%.



## 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 has 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.

### Patents

The Canadian generic company Apotex manufactures an AZT/3TC/NVP fixed-dose combination for export to developing countries under the 30 August 2003 World Trade Organization decision. The purpose of the August 30 Decision is to find an 'expeditious solution' to the problems of developing countries with no or insufficient manufacturing capacity and who therefore would rely on importing medicines produced in and exported from other countries, under compulsory licence.<sup>275</sup>

In early 2004, MSF made the original request for the development of this FDC to Apotex, as no generic versions of the FDC were available at the time.<sup>296</sup>

MSF, however, ultimately ended up procuring the FDC from manufacturers in India, which reached the market earlier because the Indian manufacturers were not hampered by the excessively bureaucratic procedural requirements of the new WTO rules on CL for export.

### 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.<sup>22</sup>

Together with d4T/3TC/NVP, AZT/3TC/NVP is one of the two most commonly used first-line regimens for children today. 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, and therefore the AZT/3TC double fixed-dose combinations is 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.<sup>22</sup> 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.

HIV/TB co-infected young children cannot be given NVP because of interactions between NVP and TB drugs. As there is still no established dosing of EFV, the standard alternative to NVP, for children less than three years of age, there is an urgent need to establish the dosing of EFV for this age group.

As of May 2011, there was only one generic paediatric fixed-dose combination quality-assured by US FDA or WHO prequalification.