



NEVIRAPINE (NVP)

GENERAL INFORMATION

- Therapeutic class: Non-nucleoside reverse transcriptase inhibitor (NNRTI).
- WHO guidelines: Indicated for first- and second-line for adults, adolescents and children.^{6,22}
- Originator company and product brand name: Boehringer Ingelheim (BI), Viramune and Viramune XR.
- First approval by U.S. Food and Drug Administration (FDA): June 1996.²³
- WHO Model List of Essential Medicines (EML): Included in the 17th edition.²⁴
- World sales of originator product: 2007: US\$ 412 million; 2006: \$370 million; 2005: \$386 million; 2004: \$378 million.^{211, 212, 213, 214} After 2007, there are no sales figures quoted in the company's annual report.
- Patents: The basic patents on NVP were applied for by BI in November 1990, and expired in November 2010.²¹⁵ BI also holds patents on the hemihydrate form of NVP, used in the suspension in 1998, which are due to expire 2018.²¹⁶ Additionally, BI applied for a patent on the extended release formulation of nevirapine in 2008, which is due to expire in 2028.²¹⁷

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/ml of suspension. Products quality-assured by US FDA or WHO prequalification (as of May 2011) are in **bold**.

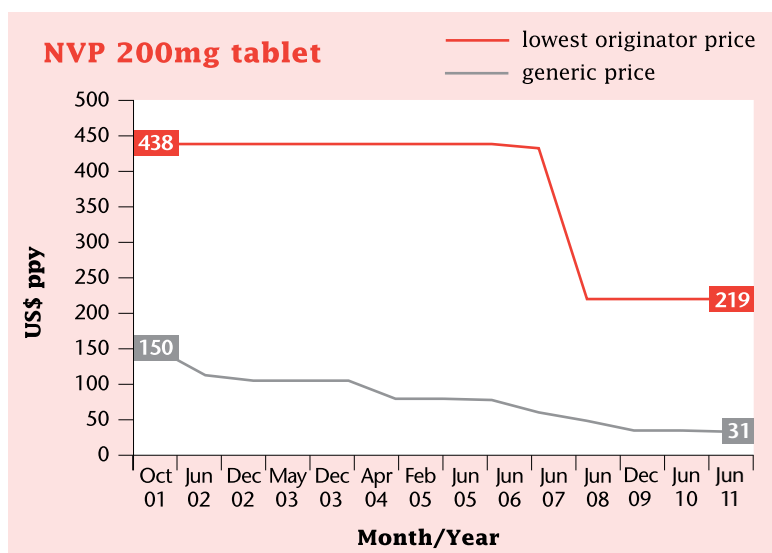
	Daily dose	Boehringer Ingelheim		Aspen	Aurobindo (CF)	Cipla (CF)	Hetero (CF)	Matrix (CF)	Ranbaxy	Strides
		Category 1 countries	Category 2 countries							
Who can access this price?		See annex 2								
NVP 10mg/ml suspension	20 ml	380 (0.052/ml)	533 (0.073/ml)		58 (0.008/ml)	110 (0.015/ml)				
NVP 200 mg tablet	2	219 (0.300)	438 (0.600)	37 (0.051)	37 (0.050)	39 (0.054)	37 (0.050)	31 (0.043)	37 (0.050)	32 (0.044)

(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, 10 generic sources of NVP 200mg tablet were quality-assured by US FDA or WHO prequalification. The one with the lowest price is shown here.

Although the originator price dropped by 50% in 2007, the generic price has decreased by almost 80% since 2001, and today is approximately 14% of the originator price.



SPOTLIGHT ON ACCESS ISSUES

Nevirapine (NVP) is a widely-used ARV, predominately in first-line regimens. It has been an important component of the fixed-dose combinations that have fostered treatment scale-up in resource-limited settings.

However NVP interacts with one of the most commonly used TB drugs, rifampicin, requiring a patient to switch to EFV during the course of TB treatment.

The price of NVP has decreased dramatically over the past years as a result of generic competition.

An extended release formulation of NVP was approved by the US FDA in March 2011, shortly after the patent expiry of NVP worldwide.²¹⁸ While it offers once a day dosing, a lead in dose of 200mg once daily is still required for the first 14 days for patients newly started on NVP. It will remain as a stand-alone tablet due to the specific slow release property in this formulation.

Patents

Boehringer Ingelheim obtained the basic patent on NVP in several developing countries, but no patent could be obtained in countries such as India, Brazil, China or Thailand, which were not granting patents on medicines at the time. Many developing countries, where NVP is under patent, import generic versions of NVP by making use of TRIPS flexibilities. The basic patent expired in many countries in 2010.

However, after India introduced patent protection for pharmaceutical products in 2005, BI applied for a patent on the hemihydrate form of NVP, which relates to the paediatric

suspension. Civil society groups filed a pre-grant opposition to BI's application in May 2006. In June 2008, the application was rejected by the Indian patent office, allowing for unrestricted competition on the paediatric formulation. This constituted an important victory for Indian civil society, as this was the first patent application related to a HIV medicine to have been rejected as a result of a pre-grant opposition process, in accordance with the 2005 Indian Patents Act.²¹⁹

In 2008, BI filed a PCT application²²⁰ for an extended release formulation of NVP – in India the same application was published in 2010.²²¹ This application relates to the once a day dosing of NVP.

In African countries, low-income countries and least-developed countries BI has a non-assert policy for its patents, which overcomes some of the barriers to generic competition, but only for the countries concerned. Many developing countries in Asia, Latin America and the Caribbean are excluded from the policy.

Paediatrics

NVP is approved for use and is widely used in children. In 2010, WHO issued updated guidelines for antiretroviral use in paediatric HIV infection. These guidelines recommend that children under three be given two NRTIs plus nevirapine (to be replaced with lopinavir/ritonavir in case of peripartum nevirapin exposure); for children > 3 years the recommended regime is two NRTIs plus efavirenz (or lopinavir/ritonavir).

NVP is part of both of the most commonly used first-line regimens for children today (3TC/d4T/NVP and 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. This can be done by giving one tablet of a double FDC and one tablet of a triple FDC once a day.

With the increased prevalence of TB/HIV co-infection, there is a need for further studies into the interactions between NVP and the TB drugs rifampicin and rifabutin in children.¹⁹⁹ For this reason, it is critical to have EFV studied for use in children below three years of age.

An oral suspension is available. As of May 2011, two generic sources were quality-assured by either US FDA or WHO prequalification. One generic source of NVP 50mg tablet is quality-assured by US FDA.

The WHO Paediatric Antiretroviral Working Group suggests a new formulation of NVP 20mg scored tablet be developed for the new WHO PMTCT guidelines for infant prophylaxis.²²

Generic manufacturers have been developing triple fixed-dose combinations including NVP, and as of May 2011, three paediatric triple FDCs that include NVP were quality-assured by either US FDA or WHO prequalification. All are produced by generic companies.