



# TIPRANAVIR (TPV)

## GENERAL INFORMATION

- Therapeutic class: Protease inhibitor (PI).<sup>5</sup>
- WHO guidelines: Not currently included in WHO guidelines. TPV is indicated for combination treatment of HIV-1 infected adult patients who are treatment-experienced and infected with HIV-1 strains resistant to more than one protease inhibitor.<sup>300</sup>
- Originator company and product brand name: Boehringer Ingelheim (BI), Aptivus.
- First approval by U.S. Food and Drug Administration (FDA): June 2005.<sup>23</sup>
- WHO Model List of Essential Medicines (EML): Not included in the 17th edition.<sup>24</sup>
- World sales of originator product: There are no sales figures listed in the company's annual report.
- Patents: The basic patent was applied for by Upjohn in May 1995,<sup>301</sup> and is due to expire in 2015. In 1998, Pharmacia & Upjohn applied for additional patents related to pharmaceutical formulations suitable for the oral administration of TPV.<sup>302, 303</sup> In January 2000, BI acquired worldwide rights for TPV.

## PRICE INFORMATION

**Boehringer Ingelheim was invited to contribute a price for this publication and has communicated it does not offer a reduced price for developing countries.**

## SPOTLIGHT ON ACCESS ISSUES

In 2010, WHO recommendations for second-line therapy included two 'preferred' protease inhibitors (PI), to be taken in combination with two NRTIs. They are atazanavir (ATV) boosted with ritonavir (RTV) and lopinavir/ritonavir (LPV/r). As tipranavir (TPV) was not identified as one of the priority products, its use in the developing world will be limited.<sup>7</sup>

TPV, like all PIs (with the exception of nelfinavir (NFV)), requires boosting with RTV. Abbott's heat-stable ritonavir received marketing approval in the U.S. and Europe in early 2010. Registering this new formulation in developing countries will be crucial in order to allow the use of other PIs than lopinavir. A generic heat-stable RTV is now available and was WHO prequalified in late 2010.

One further limitation concerning TPV is that the capsules require refrigeration until dispensing.

Boehringer Ingelheim has communicated that TPV is available through its Compassionate Use Program and that the company is currently filing for registration in various countries.

### Patents

TPV patents have been filed widely in developing countries with generic production capacity, such as Brazil and China.<sup>38</sup>

In Brazil, where the patent applications are under review, the drug regulatory agency (ANVISA), which has to give 'prior consent' for any patent application related to a medicine, advised for the rejection of the basic patent application.<sup>304</sup> In early 2007, civil society expressed concerns over the delays to the registration procedure of TPV in Brazil – the medicine had been tested in Brazilian patients in 14 research centres since February 2004, but the drug was not actually registered in the country. After

considerable civil society pressure, the registration was eventually filed with ANVISA at the end of February 2008, almost three years after US FDA and EMA approvals. The intervention by Brazilian civil society was partly based in response to suspicions that Boehringer Ingelheim did not want to register the product in the country, unless they had the guarantee that the patent would be granted by the patent office.<sup>305, 306, 307</sup>

### Paediatrics

TPV is currently approved for use in children from two years of age and older.<sup>23</sup>

A paediatric oral solution exists. However, TPV must be given with a RTV booster, but the RTV solution currently available has a bitter aftertaste and contains 43% alcohol, and is thus not adapted for children, limiting the use of TPV in this population.