



RILPIVIRINE (TMC 278)

GENERAL INFORMATION

- Therapeutic class: Non-nucleoside reverse transcriptase inhibitor (NNRTI).
- WHO guidelines: Not currently included in WHO guidelines.
- Originator company and product brand name: Tibotec (a subsidiary of Johnson & Johnson), Edurant.
- First approval by U.S. Food and Drug Administration (FDA): 20 May 2011.²³⁹
- WHO Model List of Essential Medicines (EML): Not included in the 17th edition.²⁴
- Janssen Pharmaceutica filed patents on rilpivirine in 2002 which are due to expire in 2022. Tibotec, one of the companies that compose the Janssen Pharmaceutical companies of Johnson & Johnson, further developed the drug and is now selling and managing it.²⁴

PRICE INFORMATION

Tibotec and generic companies were invited to contribute a price for this publication and communicated that they do not offer a lower price for developing countries.

SPOTLIGHT ON ACCESS ISSUES

Rilpivirine is approved for use in HIV-1 treatment-naïve patients in combination with other antiretrovirals.

The registration of rilpivirine in developing countries will be crucial for accessing the drug in the developing world. However, due to the complexities of use at the approved dose and interactions with TB drugs, it is uncertain²⁴⁰ to what extent rilpivirine will be useful for resource-limited settings.

Indeed, the approved dose of 25mg once a day comes with a heightened risk of virological failure when starting therapy for patients with high viral loads (>100,000 copies/ml). TMC 278 is also less robust compared to efavirenz. More research is needed to determine the safety and efficacy of higher doses.²⁴¹

Patents

Without patent barriers blocking generic manufacture in developing countries, rilpivirine could be

produced for as little as \$10 per patient per year. Although questions need to be surmounted concerning its lack of efficacy for patients starting at higher viral load and interactions with TB drugs, its usefulness in resource-limited settings comes from its potential for use in long-acting formulations, and its potential low price.

However patents and patent applications filed by two companies – Janssen Pharmaceutica and Tibotec – are preventing generic production.

Janssen Pharmaceutica applied for a basic patent on rilpivirine in 2003 in PCT,^{244,245} which was granted in Africa²⁴⁶ and countries like South Africa,²⁴⁷ China²⁴⁸ and India²⁴⁹ and is under review in countries like Brazil.²⁵⁰ In addition, Tibotec applied for a patent in PCT²⁵¹ that covers the combinations of rilpivirine/3TC/TDF and rilpivirine/FTC/TDF. This application is now pending review in Brazil²⁵² and India²⁵³ and

warrants a pre-grant opposition to prevent the extension of the patent monopoly by several years.

In 2010, Tibotec (now a subsidiary of Johnson & Johnson) signed voluntary licence (VL) agreements with generic producers to manufacture, market and distribute rilpivirine and its fixed-dose combination with other ARVs. Indian generic companies – Hetero, Emcure and Matrix – who signed the VL can manufacture and sell in India and to the countries listed in the VL (sub-Saharan Africa, Afghanistan, Bangladesh, Bhutan, Cambodia, Haiti, Kiribati, Laos, Maldives, Myanmar, Nepal, Samoa, Solomon Islands Timor-Leste, Tuvalu, Vanuatu, and Yemen). Aspen will have rights to market the product in sub-Saharan Africa including South Africa.^{242,243}

But the benefits will not be felt in Latin America, Central Asia and most Caribbean and South

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East Asian countries as they are ineligible to receive generic versions of the medicine under Tibotec's agreement.²⁵⁴ Among the middle-income countries with significant disease burden, besides India only South Africa can be supplied with the generic version.

Given these restrictive licensing policies, these countries may not be able to import generic versions from Indian companies, even if they override patents in their countries through compulsory licences.

Other conditions of the VL that impact the price or availability of rilpivirine can only be analysed once the terms of the VL are made public.

Paediatrics

The safety and efficacy of rilpivirine in paediatric patients have not been established. Studies are ongoing from 12 years old.²⁵⁵

As few treatment options exist for children with HIV, it is critical that paediatric studies of rilpivirine be completed and adapted formulations be made available.