EDURANT® (rilpivirine): A New Treatment for People Newly Diagnosed with HIV

EDURANT® (rilpivirine) is the latest innovation in HIV therapy from Janssen. It is a new treatment for once daily use with other antiretroviral (ARV) agents in treatment-naïve adults with HIV-1 infection with a viral load ≤ 100,000 HIV-1 RNA copies/mL. EDURANT is a non-nucleoside reverse transcriptase inhibitor (NNRTI) and is the smallest ARV tablet currently available. NNRTIs work by blocking reverse transcriptase, a key enzyme that the HIV-1 virus uses to replicate. In clinical studies, EDURANT offered a better tolerability profile with respect to central nervous system (CNS) side effects (including insomnia, depression and dizziness), rash, triglyceride elevations and severe vitamin D deficiency compared to the standard of care (efavirenz).

EDURANT is the third ARV to enter Janssen’s HIV treatment portfolio, alongside PREZISTA® (darunavir) and INTELENCE® (etravirine), meaning that Janssen can now offer treatment options for most people living with HIV at every stage of their disease.

Indication and regulatory status

- EDURANT (rilpivirine) received marketing authorisation from the European Commission on November 28 for the treatment of HIV-1 infection in ARV treatment-naïve adult patients with a viral load ≤ 100,000 HIV-1 RNA copies/mL, in combination with other ARV agents.
- EDURANT (rilpivirine) was approved by the US Food and Drug Administration (FDA) in May 2011 and by the Canadian Health authorities in July 2011.
- Marketing authorisation applications have also been submitted in countries around the world including Russia, Japan and Switzerland.

Treatment administration

EDURANT (rilpivirine) is a white, 25mg tablet which should be taken once daily with a meal at the same time each day, in combination with other ARVs.

Rilpivirine is also part of Gilead Sciences’ EVIPLERA®, a complete once daily single-tablet regimen of emtricitabine 200mg/rilpivirine 25mg/tenofovir disoproxil 245mg, which received marketing authorisation from the European Commission on November 28 for use in HIV-1 infection in ARV naïve patients with a viral load ≤ 100,000 HIV-1 RNA copies/mL.

Key clinical data

The efficacy and safety of rilpivirine has been demonstrated in ECHO and THRIVE, two Phase 3 trials involving over 1,350 treatment-naïve HIV-1 patients. ECHO and THRIVE were randomised, double-blind, placebo-controlled trials that compared rilpivirine plus emtricitabine/tenofovir disoproxil to efavirenz plus emtricitabine/tenofovir disoproxil.

\(^\text{* Efficacy Comparison in treatment-naive HIV-infected subjects of rilpivirine and efavirenz}^\text{† TMC278 against HIV, in a once daily Regimen versus Efavirenz}^\)
blinded, active controlled, global trials comparing the efficacy, safety and tolerability of rilpivirine (25mg) versus efavirenz (standard of care).3,4

Key results1,5
The below table shows the efficacy, safety and tolerability results at 48 weeks for patients treated with rilpivirine and patients treated with efavirenz from the pooled data (ITT-TLOVR*) from the ECHO and THRIVE trials. All patients also took a background regimen (BR) of two N(t)RTIs.

<table>
<thead>
<tr>
<th></th>
<th>Rilpivirine + BR N=686</th>
<th>Efavirenz + BR N=682</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall response (&lt; 50 HIV-1 RNA copies/mL)</td>
<td>84.3%</td>
<td>82.3%</td>
</tr>
<tr>
<td>Overall virologic failure</td>
<td>9.0%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Response by baseline viral load ≤ 100,000 HIV-1 RNA copies/mL†</td>
<td>90.2%</td>
<td>83.6%</td>
</tr>
<tr>
<td>Virologic failure by baseline viral load ≤ 100,000 HIV-1 RNA copies/mL#</td>
<td>3.8%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Discontinued due to adverse drug reactions (ADRs)</td>
<td>2.0%</td>
<td>6.7%</td>
</tr>
<tr>
<td>Most common ADRs (grade 2-4) were:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Dizziness</td>
<td>8.0%</td>
<td>26.2%</td>
</tr>
<tr>
<td>• Abnormal dreams/nightmares</td>
<td>8.2%</td>
<td>12.8%</td>
</tr>
<tr>
<td>• Rash</td>
<td>3.1%</td>
<td>13.6%</td>
</tr>
</tbody>
</table>

*Intent-to-treat time to virologic response
#Licensed indication population
†In the population with a baseline viral load > 100,000 HIV-1 RNA copies/mL, there were more virologic failures with rilpivirine than with efavirenz.

Overall, rilpivirine demonstrated non-inferiority compared to efavirenz, with similar rates of virologic failure in patients with ≤ 100,000 HIV-1 RNA copies/mL, and a better tolerability profile in adult treatment naïve HIV-1 infected patients with respect to central nervous system (CNS) side effects (including insomnia, depression and dizziness), rash, triglyceride elevations and severe vitamin D deficiency.4,5

EDURANT (rilpivirine) provides more treatment choice for patients initiating HIV therapy and may provide an alternative option for treatment-naïve patients who may not be suitable to take other NNRTIs, such as those with certain pre-existing psychiatric conditions.3

About HIV Treatment
Since the late 1980’s more than 20 ARVs have been introduced, providing HIV-infected people with treatment regimens designed to reduce the amount of virus in the body and reduce its replication. While there is currently no cure for HIV, these advances have created the potential to dramatically change the health and life expectancy for many people living with HIV today.6

The aim of treatment for patients with HIV is to achieve an undetectable viral load, meaning there is very little HIV present in the body and an adequate or ‘normal’ CD4 count, meaning the immune system is doing well.7,8 An undetectable viral load is defined as < 50 HIV-1 RNA copies/mL of blood.
Treatment consists of taking several drugs together which reduce the virus’ ability to replicate. This is known as combination therapy or Highly Active Anti-Retroviral Therapy (HAART). HAART combines three or more anti-HIV medications, some from different drug classes, in a daily regimen. The combination of drugs from different classes helps to ensure that the virus is being attacked at multiple phases in its life cycle.

Adherence to therapy has been shown to affect how well anti-retroviral medications suppress HIV. In fact, adherence is so important in the treatment of HIV that researchers have found that optimal suppression of the virus typically requires 95 percent adherence. Treatments that are more tolerable, with simpler dosing regimens, can facilitate adherence.

**Global Access**
The primary focus of the Janssen Global Access & Partnerships Program is to provide sustainable and affordable access to HIV medicines in sub-Saharan Africa (SSA) and least developed countries (LDCs). Current licensing agreements cover countries that are home to three out of every four people in the world living with HIV.

In 2011 Janssen entered into five agreements with multiple generic manufacturers to register, manufacture, market and distribute a 25mg generic version of rilpivirine in SSA and LDCs and India as both a single agent medicinal product and a fixed-dose combination (FDC) product with 300mg tenofovir disoproxil fumarate and 300mg lamivudine. Four of these agreements were signed before any regulatory approvals in the US or Europe, allowing generic manufacturers to move more quickly in developing formulations and seek regulatory approvals of rilpivirine.

*Please see full Summary of Product Characteristics or visit [http://www.emea.europa.eu](http://www.emea.europa.eu) for more details.*

**References**