Isentress
raltegravir

This document is a summary of the European Public Assessment Report (EPAR) for Isentress. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Isentress.

What is Isentress?

Isentress is a medicine that contains the active substance raltegravir. It is available as 400 mg tablets, 25 and 100 mg chewable tablets and granules for an oral suspension (in sachets, each containing 100mg).

What is Isentress used for?

Isentress is used in combination with other anti-HIV medicines to treat adults and children from the age of 4 weeks who are infected with human immunodeficiency virus (HIV-1), a virus that causes acquired immune deficiency syndrome (AIDS).

The medicine can only be obtained with a prescription.

How is Isentress used?

Treatment with Isentress should be started by a doctor who has experience in the management of HIV infection.

The oral granules are used to make oral suspensions for children aged 4 weeks and older weighing at least 3 kg. The chewable tablets are for bigger children weighing at least 11 kg, while the 400-mg tablets are for adults and children from six years of age weighing more than 25 kg.
Equivalent doses of these different forms do not produce the same levels of raltegravir in the body, so they must not be used interchangeably. Information on the doses and formulations to give to different patients can be found in the summary of product characteristics (also part of the EPAR).

**How does Isentress work?**

The active substance in Isentress, raltegravir, is an integrase inhibitor. It blocks an enzyme called integrase, which is involved in a step in the reproduction of HIV. When the enzyme is blocked, the virus cannot reproduce normally, slowing down the spread of infection. Isentress, taken in combination with other anti-HIV medicines, reduces the amount of HIV in the blood and keeps it at a low level. Isentress does not cure HIV infection or AIDS, but it may delay the damage to the immune system and the development of infections and diseases associated with AIDS.

**How has Isentress been studied?**

Isentress has been studied in five main studies:

- two studies involved a total of 699 ‘treatment-experienced’ patients who were already receiving treatment for HIV infection that was not working. The studies compared Isentress with placebo (a dummy treatment), which were added to ‘optimised background therapy’ (a combination of other anti-HIV medicines chosen for each patient as it had the best chances of reducing the levels of HIV in the blood). The main measure of effectiveness was the reduction in the levels of HIV in the blood (viral load) after 16 weeks;

- a third study involved 566 patients who had not taken HIV treatment before and compared Isentress with efavirenz (another anti-HIV medicine). All of the patients also took tenofovir and emtricitabine (other anti-HIV medicines). The main measure of effectiveness was the number of patients who had ‘undetectable’ viral loads (below 50 copies per millilitre of blood) after 48 weeks;

- Isentress has also been studied in a fourth study involving 126 HIV-1 infected children between 2 and 18 years whose existing treatment for HIV infection was not working. The study looked at the blood levels and the safety of Isentress.

- A fifth study included 26 children aged 4 weeks to 2 years who were given Isentress oral granules made into a suspension. This study looked at viral load after 24 and 48 weeks.

**What benefit has Isentress shown during the studies?**

In treatment-experienced patients, Isentress was more effective than placebo: 77% of the patients who took Isentress had viral loads below 400 copies/ml after 16 weeks, compared with 42% of those who took placebo. The response was sustained for at least 48 weeks.

In patients who had not taken HIV treatment before, Isentress was as effective as efavirenz. After 48 weeks, 86% of the patients taking Isentress had viral loads below 50 copies/ml (241 out of 281), compared with 82% of those taking efavirenz (230 out of 282).

The study in children between 2 and 18 years showed that Isentress was safe in children and levels of the medicine obtained in the blood in children were similar to those obtained in adults. Therefore, the effectiveness observed in adults is also expected in children.

In the study in children aged 4 weeks to 2 years Isentress treatment led to a reduction in viral load and after 48 weeks 53% of the children had viral loads below 50 copies/ml.
What is the risk associated with Isentress?

The most common side effects with Isentress (seen in between 1 and 10 patients in 100) are abnormal dreams, nightmares, insomnia (difficulty sleeping), depression, abnormal behaviour, dizziness, headache, psychomotor hyperactivity (restlessness), vertigo (a spinning sensation), decreased appetite, abdominal distension (swollen tummy), abdominal pain (stomach ache), diarrhoea, flatulence (gas), nausea (feeling sick), vomiting, dyspepsia (indigestion), rash, asthenia (weakness), fatigue (tiredness), pyrexia (fever), atypical lymphocytes (abnormal white blood cells), and increased blood levels of some enzymes (alanine aminotransferase, aspartate aminotransferase, lipase and pancreatic amylase) and triglycerides (a type of fat). Side effects in children were comparable to those in adults. For the full list of all side effects reported with Isentress, see the package leaflet.

Isentress must not be used in people who are hypersensitive (allergic) to raltegravir or to any of the other ingredients.

Why has Isentress been approved?

The CHMP decided that Isentress’s benefits are greater than its risks and recommended that it be given marketing authorisation.

What extra measures are being taken to ensure the safe and effective use of Isentress?

A risk management plan has been developed to ensure that Isentress is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Isentress, including the appropriate precautions to be followed by healthcare professionals, patients and care givers.

Other information about Isentress:

The European Commission granted a conditional marketing authorisation valid throughout the European Union for Isentress on 20 December 2007. This was switched to a full marketing authorisation on 14 July 2009.

The full EPAR for Isentress can be found on the Agency’s website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports. For more information about treatment with Isentress, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

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