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EPAR summary for the public

Eviplera

emtricitabine / rilpivirine / tenofovir disoproxil

This is a summary of the European public assessment report (EPAR) for Eviplera. 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 Eviplera.

What is Eviplera?

Eviplera is a medicine that contains the active substances emtricitabine (200 mg), rilpivirine (25 mg) and tenofovir disoproxil (245 mg). It is available as tablets.

What is Eviplera used for?

Eviplera is used to treat adults infected with human immunodeficiency virus-1 (HIV-1), a virus that causes acquired immune deficiency syndrome (AIDS).

It is only used in patients where the virus has not developed resistance to certain anti-HIV medicines called non-nucleoside reverse transcriptase inhibitors (NNRTIs), tenofovir or emtricitabine, and who have HIV levels in the blood (viral load) of no more than 100,000 HIV-1 RNA copies/ml.

The medicine can only be obtained with a prescription.

How is Eviplera used?

Treatment with Eviplera should be started by a doctor who has experience in the management of HIV infection. The recommended dose is one tablet once a day and it must be taken with food.

If patients need to stop taking one of the active substances or if they need to modify their dose, patients should be switched to separate medicines containing emtricitabine, rilpivirine or tenofovir disoproxil. If Eviplera is given together with rifabutin, the doctor should prescribe an additional 25 mg of rilpivirine per day during rifabutin treatment.

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How does Eviplera work?

Eviplera contains three active substances: emtricitabine, which is a nucleoside reverse transcriptase inhibitor; rilpivirine, which is a non-nucleoside reverse transcriptase inhibitor (NNRTI); and tenofovir disoproxil, which is a 'prodrug' of tenofovir, meaning that it is converted into the active substance tenofovir in the body. Tenofovir is a nucleotide reverse transcriptase inhibitor.

All three active substances block the activity of reverse transcriptase, a viral enzyme that allows HIV-1 to replicate in the cells it has infected. By blocking this enzyme, Eviplera reduces the amount of HIV-1 in the blood and keeps it at a low level. Eviplera does not cure HIV-1 infection or AIDS, but it may slow the damage to the immune system and the development of infections and diseases associated with AIDS.

All three active substances are already available in separate medicines in the EU.

How has Eviplera been studied?

Eviplera has been studied in two main studies in patients with HIV-1 who had not received HIV treatment before. In the first main study involving 690 patients, Eviplera was compared with a similar combination that had efavirenz in place of rilpivirine. The second main study involving 678 patients compared rilpivirine with efavirenz, both being taken with emtricitabine and tenofovir disoproxil or two other nucleotide reverse transcriptase inhibitors.

The main measure of effectiveness was based on the reduction in viral load. Patients who attained a viral load of less than 50 HIV-1 RNA copies/ml after 48 weeks of treatment were considered to have responded to treatment.

Eviplera has also been evaluated in 532 patients who were switched from their current HIV treatment to Eviplera. Patient's previous treatment consisted either of two nucleotide reverse transcriptase inhibitors and another HIV medicine called a boosted protease inhibitor, or the medicine Atripla. The main measure of effectiveness was based on the maintained reduction in viral load.

The company also presented studies showing that the tablet containing all three substances is absorbed in the body in the same way as the separate tablets given concurrently under similar conditions.

What benefit has Eviplera shown during the studies?

The Eviplera combination compared well with combinations containing efavirenz. In the first study in previously untreated patients, 83% of the patients taking the Eviplera combination responded to treatment compared with 84% of the patients taking a combination with efavirenz. In the second study, 87% of the patients in the rilpivirine group (which included patients taking the Eviplera combination) responded to treatment. This compared with 83% of patients in the efavirenz group.

The two studies evaluating the effects of switching patients to Eviplera showed that Eviplera was as effective as the previous treatment and maintained the reduction in viral load.

What is the risk associated with Eviplera?

The most common side effects with Eviplera in patients who had not received previous HIV treatment (seen in more than 5 patients in 100) were nausea (feeling sick), dizziness, abnormal dreams, headache, diarrhoea and insomnia. In patients who had received previous HIV treatment, the most

common side effects (seen in more than 2 patients in 100) were tiredness, diarrhoea, nausea and insomnia. Rarely, kidney problems may occur in patients taking tenofovir disoproxil. Patients who have HIV and hepatitis B may see a worsening of their liver problems when stopping Eviplera.

Eviplera must not be used with the following medicines as they may lead to reduced blood levels of rilpivirine, and thereby reduce the effectiveness of Eviplera:

- carbamazepine, oxcarbazepine, phenobarbital, phenytoin (medicines for epilepsy);
- rifampicin, rifapentine (antibiotics);
- omeprazole, esomeprazole, lansoprazole, pantoprazole, rabeprazole (proton pump inhibitors for reducing stomach acid);
- systemic dexamethasone (a steroid anti-inflammatory and immunosuppressant medicine) except when used as a single dose treatment;
- St John's wort (a herbal medicine to treat depression and anxiety).

For the full list of side effects and restrictions with Eviplera, see the package leaflet.

Why has Eviplera been approved?

The CHMP concluded that Eviplera was as effective as combinations containing efavirenz. It also causes fewer side effects in the early stages of treatment and offers the benefit of being taken as one tablet once per day. However, the CHMP noted that there was some risk of HIV-1 developing resistance to rilpivirine and that this risk appeared to be lower in patients with a lower viral load. Therefore, the CHMP considered that the benefits of Eviplera outweigh its risks in patients with a low HIV-1 viral load, and recommended that it be granted marketing authorisation for this group of patients.

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

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Eviplera have been included in the summary of product characteristics and the package leaflet.

Other information about Eviplera

The European Commission granted a marketing authorisation valid throughout the European Union for Eviplera on 28 November 2011.

The full EPAR for Eviplera 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 Eviplera, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 06-2016.