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EPAR summary for the public

Atripla

efavirenz / emtricitabine / tenofovir disoproxil

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

What is Atripla?

Atripla is a medicine that contains three active substances: efavirenz (600 mg), emtricitabine (200 mg) and tenofovir disoproxil (245 mg). It is available as tablets.

What is Atripla used for?

Atripla 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 whose levels of HIV in the blood (viral loads) have been below 50 copies/ml for more than three months on their current HIV treatment combination. It must not be used in patients in whom any previous HIV treatment combinations have failed to work or have stopped working. Patients must not have been infected with HIV that was unlikely to respond to any of the three active substances in Atripla before they started their first HIV treatment combination.

The medicine can only be obtained with a prescription.

How is Atripla used?

Treatment with Atripla should be started by a doctor who has experience in the management of HIV infection. The recommended dose is one tablet once a day, swallowed whole with water. It is recommended that Atripla be taken on an empty stomach, preferably at bedtime. Patients should take the medicine regularly and avoid missing doses.
If patients need to stop taking efavirenz, emtricitabine or tenofovir disoproxil, or need to take different doses, they will need to take medicines containing efavirenz, emtricitabine or tenofovir disoproxil separately. Atripla should not be taken at the same time as other medicines that contain efavirenz, emtricitabine or tenofovir disoproxil, or lamivudine (another antiviral medicine). For more information, see the summary of product characteristics (also part of the EPAR).

**How does Atripla work?**

Atripla contains three active substances: efavirenz, which is a non-nucleoside reverse transcriptase inhibitor (NNRTI); emtricitabine, which is a nucleoside reverse transcriptase inhibitor; 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. Both nucleoside and nucleotide reverse transcriptase inhibitors are commonly known as NRTIs. All three active substances block the activity of reverse transcriptase, an enzyme produced by HIV that allows it to infect cells and make more viruses. Atripla keeps the amount of HIV in the blood at a low level. It 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.

All three active substances are already available in the European Union (EU): efavirenz has been approved as Sustiva and Stocrin since 1999, emtricitabine has been approved as Emtriva since 2003, and tenofovir disoproxil has been approved as Viread since 2002. The combination of tenofovir disoproxil and emtricitabine has been approved as Truvada since 2005.

**How has Atripla been studied?**

The main study of Atripla included 300 patients whose HIV infection was already being successfully treated with various combinations of antiviral medicines. The study compared the effectiveness of switching to Atripla tablets, taken on an empty stomach, with that of remaining on the successful HIV treatment combination. The main measure of effectiveness was the proportion of patients whose viral loads were below 200 copies/ml after 48 weeks.

The company also looked at the way the combined tablet was absorbed in the body in comparison with the separate medicines.

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

In the main study, switching to Atripla was as effective as remaining on the previous treatment combination. After 48 weeks, 89% of the patients taking Atripla (181 out of 203) and 88% of those remaining on previous treatment (85 out of 97) had viral loads below 200 copies/ml.

The combination tablet was absorbed in the body in the same way as the separate medicines, when they were taken without food.

**What is the risk associated with Atripla?**

The most common side effects with Atripla (seen in more than 1 patient in 10) are dizziness, headache, diarrhoea, nausea (feeling sick), vomiting, rash, asthenia (weakness), hypophosphataemia (low blood levels of phosphates) and elevated levels of creatine kinase (an enzyme found in muscles). For the full list of all side effects reported with Atripla, see the package leaflet.

Atripla must not be used in people who are hypersensitive (allergic) to efavirenz, emtricitabine, tenofovir disoproxil or any of the other ingredients. It must not be used in patients with severe liver disease or who are taking any of the following medicines:
- terfenadine, astemizole (commonly used to treat allergy symptoms – these medicines may be available without prescription);
- cisapride (used to relieve certain stomach problems);
- midazolam, triazolam (used to relieve anxiety or difficulty sleeping);
- pimozide (used to treat mental illnesses);
- bepridil (used to treat angina);
- ergot alkaloids such as ergotamine, dihydroergotamine, ergonovine and methylergonovine (used to treat migraine headache);
- St John’s wort (a herbal preparation used to treat depression);
- voriconazole (used to treat fungal infections).

Caution is also needed when Atripla is taken at the same time as other medicines. See the package leaflet for further details.

Why has Atripla been approved?

The CHMP noted that Atripla needs to be taken on an empty stomach to prevent certain side effects, but that this could result in low tenofovir levels in the blood. Therefore, the Committee concluded that Atripla could be a convenient ‘one-tablet once-a-day’ treatment when used to maintain low viral loads in patients already taking HIV treatment, but there is not enough information to be certain about its effects in patients who have not been treated before.

The Committee also noted that the demonstration of Atripla’s benefit is based mainly on 48-week data from a study in patients with stable suppression of HIV on an HIV treatment combination who then switched to Atripla. There is no information on its effects in patients who have not been treated before or who have been treated with many different anti-HIV medicines in the past. There is also no information on using Atripla with other anti-HIV medicines.

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

What measures are being taken to ensure the safe use of Atripla?

The company that markets Atripla will ensure that all doctors expected to prescribe the medicine are provided with an educational pack that includes information on the increased risk of kidney disease with tenofovir disoproxil-containing medicines such as Atripla. The educational pack also contains recommendations for monitoring kidney function in patients taking the medicine.

Other information about Atripla

The European Commission granted a marketing authorisation valid throughout the EU for Atripla on 13 December 2007.

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

This summary was last updated in 08-2012.