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Atripla (*efavirenz / emtricitabine / tenofovir disoproxil*)

An overview of Atripla and why it is authorised in the EU

What is Atripla and what is it used for?

Atripla is an antiviral medicine 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 previous HIV treatment combinations have not worked or have stopped working. Atripla must not be started in patients with HIV that is resistant to any of the three active substances in Atripla.

The three active substances in Atripla are: efavirenz (600 mg), emtricitabine (200 mg) and tenofovir disoproxil (245 mg).

How is Atripla used?

Atripla can only be obtained with a prescription and treatment should be started by a doctor who has experience in the management of HIV infection.

The recommended dose of Atripla is one tablet once a day. It is recommended that Atripla is taken on an empty stomach, preferably at bedtime. Patients should take the medicine regularly and not miss doses.

For more information about using Atripla, see the package leaflet or contact a doctor or pharmacist.

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 the virus to infect cells and make more viruses. Atripla keeps the amount of HIV in the blood at

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a low level. It does not cure HIV infection or AIDS, but it holds off damage to the immune system and the development of infections and diseases associated with AIDS.

In the European Union (EU), efavirenz has been approved since 1999, emtricitabine has been approved since 2003, and tenofovir disoproxil has been approved since 2002.

What benefits of Atripla have been shown in studies?

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 with that of continuing 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 study showed that 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.

Another study, which looked at how the combined tablet was absorbed in the body, showed that the combination tablet was absorbed in the same way as the separate medicines when they were taken on an empty stomach.

What are the risks associated with Atripla?

The most common side effects with Atripla (which may affect 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 side effects reported with Atripla, see the package leaflet.

Atripla must not be used in patients with severe liver disease and patients with a family member who has had QT prolongation (an alteration of the electrical activity of the heart) or has died unexpectedly. It must also not be used in patients who have had arrhythmia (abnormal heartbeat) and patients with abnormal levels of electrolytes in the blood (for example, potassium or magnesium).

Atripla must also not be used in patients who are taking any of the following:

- medicines that cause QT prolongation;
- certain medicines whose breakdown is blocked or accelerated by Atripla;
- St John's wort (a herbal preparation used to treat depression);
- voriconazole (used to treat fungal infections).

See the package leaflet for further details and for the full list of restrictions.

Why is Atripla authorised in the EU?

The European Medicines Agency noted that Atripla needs to be taken on an empty stomach to prevent certain side effects of one of its components, efavirenz. Because taking the medicine on an empty stomach could result in the component tenofovir being less effective, the Agency could not recommend Atripla for general use in patients with HIV and with high viral loads. Based on the data available it could only recommend Atripla as a convenient 'once-a-day tablet' treatment for maintaining viral loads in patients whose viral loads have already been reduced with other HIV treatment.

The Agency decided that Atripla's benefits are greater than its risks and recommended that it can be authorised for use in the EU.

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 medicines containing tenofovir disoproxil such as Atripla. The educational pack also contains recommendations for monitoring kidney function in patients taking the medicine.

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

As for all medicines, data on the use of Atripla are continuously monitored. Side effects reported with Atripla are carefully evaluated and any necessary action taken to protect patients.

Other information about Atripla

Atripla received a marketing authorisation valid throughout the EU on 18 December 2007.

Further information on Atripla can be found on the Agency's website ema.europa.eu/en/medicines/human/EPAR/Atripla.

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