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Aubagio (*teriflunomide*)

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

What is Aubagio and what is it used for?

Aubagio is a medicine that contains the active substance teriflunomide. It is used to treat patients from the age of 10 years with multiple sclerosis (MS), a disease in which inflammation destroys the protective sheath around the nerves.

Aubagio is used in the type of MS known as relapsing-remitting MS, when the patient has flare-ups of symptoms (relapses) followed by periods of recovery (remissions).

How is Aubagio used?

Aubagio can only be obtained with a prescription and treatment should be started and supervised by a doctor who has experience in the management of MS.

Aubagio is available as tablets. The recommended dose for adults is 14 mg once a day. The dose for children depends on their body weight. For more information about using Aubagio, see the package leaflet or contact your doctor or pharmacist.

How does Aubagio work?

In MS, the body's immune system malfunctions and attacks parts of the central nervous system (the brain and spinal cord), causing the inflammation that damages the nerve sheaths. The active substance in Aubagio, teriflunomide, blocks an enzyme called 'dihydro-orotate dehydrogenase' which is necessary for cells to multiply. The exact way teriflunomide works in MS is not known but it is thought to reduce the number of lymphocytes which form part of the immune system and are involved in the inflammation process. With fewer lymphocytes, there is less inflammation, helping to control the symptoms of MS.

What benefits of Aubagio have been shown in studies?

Aubagio has been studied in five main studies involving over 2,900 patients with relapsing-remitting MS.

One study involving 179 adults compared the effects of Aubagio with placebo (a dummy treatment) on the number of active lesions (developing areas of damage) in the brain detected by a brain scan.

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Aubagio was found to be more effective than placebo: after around 9 months (36 weeks), the number of active lesions was around 1 per scan in patients who were taking Aubagio compared with around 2.7 in patients taking placebo.

Two studies involving 2,257 adults compared the effects of Aubagio with placebo in reducing the number of relapses per patient per year (called the 'annualised relapse rate'). Treatment lasted for up to about three years (152 weeks). Aubagio was found to be more effective than placebo: in patients taking Aubagio, relapses were reduced by around 30% more than in patients taking placebo (the annualised relapse rate was 0.35 for Aubagio compared with 0.53 for placebo). The studies also looked at the effect of Aubagio on the changes in the patients' level of disability and showed that the risk of disability getting worse was reduced by 30% in comparison with placebo after around two and a half years (132 weeks) of treatment.

The fourth study involving 324 adults compared the effects of Aubagio with interferon beta-1a (another treatment for MS) on the rate of treatment failure, by looking at the time until patients had their first relapse or permanently stopped their treatment. The study lasted for up to two years. The results of the study were inconclusive. A 13.5% rate of permanent discontinuation was seen in patients taking Aubagio, compared with 24% in patients taking interferon beta-1a. However, the rate of relapse was 23.4% with Aubagio compared with 15.4% with interferon beta-1a. Overall, no conclusion could be reached from this study on any differences between Aubagio and interferon beta-1a for MS treatment.

Another study, involving 166 children (aged 10-17 years), was inconclusive but it did indicate that Aubagio extended the time for a relapse or a lesion to develop in the brain (which was about 72 weeks for Aubagio compared with 37 weeks for placebo). Overall, the data from adults and the results of this study support use of Aubagio in children (aged 10 and older) with relapsing-remitting MS.

What are the risks associated with Aubagio?

The most common side effects with Aubagio (which may affect more than 1 in 10 people) are headache, diarrhoea, increased liver enzymes, nausea (feeling sick), and alopecia (hair loss). In general, headache, diarrhoea, nausea and alopecia are mild to moderate, resolve with time and do not usually lead to treatment being stopped. For the full list of side effects reported with Aubagio, see the package leaflet.

Aubagio must not be used in patients with:

- severe liver disease;
- severe immunodeficiency states, such as acquired immune deficiency syndrome (AIDS);
- poor bone marrow function or low blood cell counts (red cells, white cells or platelets);
- severe active infections;
- severe kidney disease that requires dialysis;
- severe hypoproteinaemia (low blood protein levels).

Aubagio must also not be used in pregnant women or during breast-feeding. Women who can become pregnant must not take Aubagio without using reliable contraceptive measures. For the full list of restrictions, see the package leaflet.

Why is Aubagio authorised in the EU?

The European Medicines Agency decided that Aubagio's benefits are greater than its risks and it can be authorised for use in the EU. In studies, Aubagio was shown to reduce relapses and delay the progression of disability in patients with relapsing-remitting MS. Although the effects were modest,

they were considered to be significant and similar to other MS treatments, although there were no conclusive results available from a direct comparison with interferon beta-1a. Aubagio is given by mouth which was considered to be an advantage over other medicines such as interferon beta-1a. Regarding its safety, side effects were similar to the immunosuppressant leflunomide, as leflunomide is converted into teriflunomide in the body. The risk of serious side effects affecting the liver and bone marrow was considered manageable and adequately addressed by risk minimisation measures.

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

The company that markets Aubagio must ensure that all healthcare professionals who are expected to use Aubagio receive an information pack containing important safety information, including the tests and monitoring that should be carried out in patients before and after starting treatment. The pack will also include information on a registry the company will set up to collect data on babies born to women treated with Aubagio, as well as a patient reminder card with key safety information for patients.

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

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

Other information about Aubagio

Aubagio received a marketing authorisation valid throughout the EU on 26 August 2013.

Further information on Aubagio can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/aubagio

This overview was last updated in 05-2021.