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Use of multiple sclerosis medicine Lemtrada restricted while EMA review is ongoing

EMA has started a review of the multiple sclerosis medicine Lemtrada (alemtuzumab) following new reports of immune-mediated conditions (caused by the body's defence system not working properly) and problems with the heart and blood vessels with the medicine, including fatal cases.

As a temporary measure while the review is ongoing, Lemtrada should only be started in adults with relapsing-remitting multiple sclerosis that is highly active despite treatment with at least two disease-modifying therapies (a type of multiple sclerosis medicine) or where other disease-modifying therapies cannot be used. Patients being treated with Lemtrada who are benefitting from it may continue treatment in consultation with their doctor.

In addition to the restriction, EMA's safety committee (PRAC) has recommended an update of the product information for Lemtrada to inform patients and healthcare professionals about cases of:

- immune-mediated conditions, including autoimmune hepatitis (with damage to the liver) and haemophagocytic lymphohistiocytosis (overactivation of the immune system which may affect different parts of the body);
- problems with the heart and blood vessels occurring within 1–3 days of receiving the medicine, including bleeding in the lungs, heart attack, stroke, cervicocephalic arterial dissection (tears in the lining of the arteries in the head and neck);
- severe neutropenia (low levels of neutrophils, a type of white blood cell that fights infections).

Healthcare professionals should consider stopping treatment in patients who develop signs of these conditions and patients should immediately seek medical help if they experience symptoms.

EMA will now evaluate all available data on the safety concerns with the medicine, and consider any additional measures necessary to protect patients and whether there should be changes in the authorised use.

Information for patients

- New cases of side effects have been reported with Lemtrada, including some affecting the heart, blood vessels, lungs and liver.
- You should get medical help immediately if you experience symptoms of:

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  - acute (sudden) heart problems (usually within 1–3 days of receiving the medicine): such as trouble breathing and chest pain
  - bleeding in lungs: such as trouble breathing and coughing up blood
  - stroke and tears in blood vessels supplying the brain: such as drooping of the face, sudden severe headache, weakness on one side, difficulty with speech or neck pain
  - liver problems: such as yellow skin or eyes, dark urine, and bleeding or bruising more easily than normal
  - an inflammatory condition known as haemophagocytic lymphohistiocytosis: such as fever, swollen glands, bruising and skin rash.
- If you have any of these symptoms, your doctor will examine you and may consider stopping Lemtrada and switching you to an alternative treatment.
- An in-depth review of Lemtrada is ongoing and further information will be provided as soon as it is available.
- While the review is ongoing, Lemtrada will only be prescribed to new patients if other medicines have not worked or are not suitable.
- Speak with your doctor if you have questions or concerns about your treatment.

Information for healthcare professionals

- Doctors are being informed in writing of temporary restrictions on the prescription of Lemtrada pending the conclusion of an ongoing review of the medicine and inclusion of new safety warnings in the product information of Lemtrada.
- New treatment should only be initiated in adults with relapsing-remitting multiple sclerosis that is highly active despite a full and adequate course of treatment with at least two other disease-modifying therapies, or in adults with highly active relapsing-remitting multiple sclerosis where all other disease-modifying therapies are contraindicated or otherwise unsuitable.
- For patients being treated with Lemtrada, vital signs should be monitored before and during the intravenous infusion. If clinically significant changes are observed, discontinuation of infusion and additional monitoring, including ECG, should be considered.
- Liver function tests should be carried out before and during treatment. If patients develop signs of liver damage, unexplained liver enzyme elevations or symptoms suggestive of hepatic dysfunction (e.g. unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, jaundice or dark urine), Lemtrada should only be re-administered following careful consideration.
- Patients who develop signs of pathological immune activation should be evaluated immediately, and a diagnosis of haemophagocytic lymphohistiocytosis considered. Symptoms of immune activation may occur up to 4 years after the start of treatment.
- Further information will be provided once the review of Lemtrada is concluded.

More about the medicine

Lemtrada is a medicine used to treat adults with relapsing-remitting multiple sclerosis, a disease of the nerves in which inflammation destroys the protective sheath surrounding the nerve cells. Relapsing-remitting means that the patient has attacks (relapses) in between periods with few or no symptoms (remissions). The medicine is used for patients with active disease. It is given by infusion (drip) into a vein.

The active substance in Lemtrada, alemtuzumab, is a monoclonal antibody (a type of protein) that has been designed to recognise and attach to a protein called CD52 found on white blood cells of the immune system (the body's defences). By attaching to CD52, alemtuzumab causes the white blood cells to die and be replaced, thereby reducing damaging activity of the immune system.

Lemtrada was authorised in the EU in 2013. More information about the medicine is available on the EMA website: ema.europa.eu/medicines/human/EPAR/lemtrada.

More about the procedure

The review of Lemtrada has been initiated at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004.

The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations.

At the start of the review, the PRAC has issued temporary recommendations to restrict the use of Lemtrada in new patients. The PRAC has also made recommendations to update the product information following routine safety monitoring.

The PRAC's final recommendations will be forwarded to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt an opinion. The final stage of the review procedure is the adoption by the European Commission of a legally binding decision applicable in all EU Member States.