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Measures to minimise risk of serious side effects of multiple sclerosis medicine Lemtrada

EMA is recommending restriction of the use of the multiple sclerosis medicine Lemtrada (alemtuzumab) due to reports of rare but serious side effects, including deaths. New measures to identify and manage the serious side effects are also recommended. The side effects include cardiovascular disorders (affecting the heart, circulation and bleeding as well as stroke) and immune-related disorders (caused by the body's defence system not working properly).

Lemtrada should now only be used to treat relapsing-remitting multiple sclerosis if the disease is highly active despite treatment with at least one disease-modifying therapy or if the disease is worsening rapidly. Lemtrada must also no longer be used in patients with certain heart, circulation or bleeding disorders or in patients who have autoimmune disorders other than multiple sclerosis.

The medicine should only be given in a hospital with ready access to intensive care facilities and specialists who can manage serious adverse reactions.

EMA has also recommended updating the physician's guide and the patient information pack with advice on minimising the risk of serious cardiovascular disorders, which may occur shortly after a Lemtrada infusion (drip), and immune-related conditions, which may occur many months and possibly years after the last treatment.

These recommendations were issued by the [EMA's safety committee \(PRAC\)](#) and have now been endorsed by the Agency's human medicines committee (CHMP). They will replace the [temporary measures](#) introduced in April 2019 while the review of Lemtrada was under way. The changes come into force when the European Commission issues its decision.

Information for patients

- Serious but rare side effects have been reported with Lemtrada, including disorders of the heart, blood vessels and problems of the immune system which may affect blood and organs such as the lungs and liver.
- Your doctor will review your treatment to check if treatment with Lemtrada remains appropriate.
- You will be watched closely in hospital when you receive Lemtrada and for a short period afterwards, but some side effects can develop days or months later. You must get medical help immediately if:

- you have any chest pain or breathing difficulty while Lemtrada is being given to you or in the next few days (signs of heart problem);
- you cough up blood or have breathing difficulty (signs of bleeding in the lungs);
- you have drooping of the face, severe headache, neck pain, weakness on one side or difficulty speaking (signs of stroke or damage to blood vessels in your brain);
- your skin or eyes turn yellow, or you have dark urine, pain in your belly or you bleed or bruise easily (signs of liver damage);
- you have fever, swollen glands, bruising or rash (signs of a dangerous immune disorder called haemophagocytic lymphohistiocytosis).
- Carefully read the updated Lemtrada patient guide and patient alert card because they contain important information and reminders about what to watch out for.
- Speak with your doctor or pharmacist if you have any questions or concerns about your treatment.

Information for healthcare professionals

- Rare but serious effects that can occur within 1 to 3 days of Lemtrada infusion include myocardial ischaemia, myocardial infarction, cerebral haemorrhage, cervicocephalic arterial dissection, pulmonary alveolar haemorrhage and thrombocytopenia.
- Autoimmune side effects occurring within 48 months or longer after the last dose of Lemtrada include autoimmune hepatitis and haemophilia A as well as immune thrombocytopenic purpura, thyroid disorders and, rarely, nephropathies. Haemophagocytic lymphohistiocytosis, a syndrome of immune activation characterised by fever, hepatomegaly and cytopenia, has also been reported.
- Serious infections as well as reactivation of Epstein-Barr virus can also occur.
- Lemtrada should now only be used as a single disease-modifying therapy in adults with relapsing-remitting multiple sclerosis with:
 - highly active disease despite a full and adequate course of treatment with at least one disease-modifying therapy or
 - rapidly evolving severe disease defined by 2 or more disabling relapses in one year, and with 1 or more gadolinium-enhancing lesions on brain MRI or a significant increase in T2 lesion load compared to a recent MRI.
- In addition to current contraindications, Lemtrada is now also contraindicated in:
 - severe active infections until complete resolution
 - uncontrolled hypertension
 - history of angina pectoris, myocardial infarction, stroke or dissection of the cervicocephalic arteries
 - coagulopathy, on antiplatelet or on anti-coagulant therapy
 - concomitant autoimmune diseases other than multiple sclerosis

- Patients should receive Lemtrada only in a hospital with ready access to intensive care and with specialists and equipment for diagnosing and managing cardiac and cerebrovascular reactions and cytokine release syndrome, as well as autoimmune disorders and infections.
- The summary of product characteristics includes updated information on monitoring for side effects, including instructions on evaluations before, during and after Lemtrada infusion.
- The guide for healthcare professionals will also be updated.
- The patient should be provided with the Lemtrada patient guide and patient alert card and be advised to seek medical help immediately if any signs of serious side effects occur.

More about the medicine

Lemtrada is a medicine used to treat adults with relapsing-remitting multiple sclerosis, a disease of the nerves in which the body's immune system acts incorrectly to destroy 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 was initiated on 10 April 2019 at the request of European Commission, under [Article 20 of Regulation \(EC\) No 726/2004](#).

The review was first carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines. While the review was ongoing, the PRAC had issued temporary recommendations restricting the use of the medicine. The PRAC issued its final recommendations on 31 October to replace the temporary measures. The PRAC recommendations were sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which adopted the Agency's opinion. The CHMP opinion will now be forwarded to the European Commission, which will issue a final legally binding decision applicable in all EU Member States in due course.