Lemtrada for multiple sclerosis: use restricted while EMA review is ongoing

23.04.2019 | Circular Number P05/2019

Information on Lemtrada

- Lemtrada (alemtuzumab) is a monoclonal antibody (a type of protein) which recognises and attaches to CD52, a protein present on white blood cells of the immune system. Attaching CD52, alemtuzumab causes the white blood cells to die and be replaced, thereby reducing damaging activity of the immune system
- Lemtrada is administered via intravenous infusion to treat adults with active relapsing-remitting multiple sclerosis, in which the protective sheath surrounding the nerve cells is destroyed due to inflammation. Relapsing remitting means that the patient has attacks (relapses) in between periods with few or no symptoms (remissions).

Information from the EMA about the safety concern

The Pharmacovigilance Risk Assessment Committee (PRAC) started a review on Lemtrada 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, including fatal cases.

As a temporary measure 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.

PRAC is also recommending an update of the product information of 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).

The PRAC's recommendation will be forwarded to the CHMP which will adopt an opinion.

In Malta

For Healthcare Professionals

- New treatment with Lemtrada 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.

A DHPC letter about the safety concern has been disseminated to HCPs in Malta. Archived DHPC letters are available online at http://www.medicinesauthority.gov.mt/dhpc

Advice 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:
  - 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.

For more information, visit the European Medicines Agency's Lemtrada referral page

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on Lemtrada. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 or online to **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.>

Post-Licensing Directorate
Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Feedback Form

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this formt (address side up), stapling the ends and then posting (no stamp required)

Feedback:

We thank you for your interest and look forward to hearing your opinion.

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Pharmacovigilance Section

Post-Licensing Directorate

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