Lemtrada for multiple sclerosis: measures to minimise risk of serious side effects

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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).

In Malta Lemtrada is authorised through a centralised procedure.

Information from the EMA about new measures to minimise risks

Results from the review carried out from the Pharmacovigilance Risk Assessment Committee (PRAC) show that Lemtrada (alemtuzumab) authorised to treat multiple sclerosis can cause serious side effects, including cardiovascular disorders (affecting the heart, circulation and bleeding as well as stroke), immune-related disorders (caused by the body's defence system not working properly) and deaths. Following the review, EMA's recommendations are:

- Treatment with Lemtrada are to be used in adults with relapsing-remitting multiple sclerosis that is highly active disease despite a full and adequate course of treatment with at least one disease-modifying therapy or if the disease is worsening rapidly
- Lemtrada must 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
- To update 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

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.

In Malta

For Healthcare Professionals

- Between 1 and 3 days of Lemtrada infusion, rare but serious adverse reactions can occur including myocardial ischaemia, myocardial infarction, cerebral haemorrhage, cervicocephalic arterial dissection, pulmonary alveolar haemorrhage and thrombocytopenia
- Within 48 months or longer after the last dose of Lemtrada, autoimmune side effects can occur including autoimmune hepatitis and haemophilia A, as well as immune thrombocytopenic purpura, thyroid disorders and, rarely, nephropathies. Hemophagocytic 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 is to 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 two 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
- Lemtrada should only be given in hospital with ready access to intensive care facilities and 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.

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

Information for Patients

- Serious side effects occurring with Lemtrada have been reported, including deaths, 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 ensure it remains appropriate
- When you receive Lemtrada you will be closely monitored in hospital and for a short period afterwards, but some side effects can develop after days or months. You must immediately get medical help 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 have trouble breathing or if you cough up blood (signs of bleeding in the lungs)
    - You have drooping of the face, severe headache, weakness on one side, difficulty with speech or neck pain (signs of stroke or damage to blood vessels in your brain)
    - You have 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).
- Patients should read carefully the updated Lemtrada patient guide and patient alert card because they contain important information and reminders about what to watch out for
- If you have any questions or concerns about your treatment, speak with your doctor or pharmacist

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 (alemtuzumab). 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:

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Pharmacovigilance Section

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