SANOFI GENZYME

Direct Healthcare Professional Communication 23rd April 2019

Alemtuzumab (Lemtrada): Restriction of use due to serious safety concerns

Dear Healthcare professional,

This letter is sent in agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) to inform you of the following:

EMA is reviewing the benefits and risks of Lemtrada (alemtuzumab) for the treatment of multiple sclerosis following reports of serious cardiovascular reactions, newly identified autoimmune hepatitis, and haemophagocytic lymphohistiocytosis.

The following measures have been agreed until this review is finalised.

Summary

- Treatment of new patients should only be initiated in adults with highly active relapsing remitting multiple sclerosis (RRMS), despite a full and adequate course of treatment with at least two other disease-modifying treatments (DMTs), or in adult patients with highly active RRMS where all other DMTs are contraindicated or otherwise unsuitable.

- Vital signs should be monitored, including blood pressure, before and periodically during alemtuzumab infusion. If clinically significant changes in vital functions are observed, discontinuation of infusion and additional monitoring, including ECG, should be considered.

- Liver function should be evaluated before and during treatment.

- In case of symptoms of hepatic injury, or other serious immune mediated reactions, treatment should only be re-administered following careful consideration.

- Patients should be advised to immediately seek medical help if they experience symptoms occurring within a few days of the infusion or symptoms of hepatic injury.

Background information

On 11 April 2019, EMA started a review of the benefit-risk balance of Lemtrada in the approved indication. This is due to new findings of serious safety concerns from post-marketing use, including fatal cases, cardiovascular adverse events in close temporal association with Lemtrada infusions, and immune-mediated adverse reactions. There are currently serious questions as to whether the current risk minimisation measures are sufficient to adequately manage these risks.

During this review, treatment in new patients should only be initiated in adult patients with highly active relapsing remitting multiple sclerosis (RRMS), despite a full and adequate course of treatment with at least two other disease modifying treatments (DMTs), or in adult patients with highly active RRMS where all other DMTs are contraindicated or otherwise unsuitable.

Patients being treated with Lemtrada who are benefitting from it may continue treatment in consultation with their prescriber.

In light of these emerging post-marketing data, alemtuzumab is suspected to be related to the following:

Autoimmune hepatitis and hepatic injury

Cases of hepatic injury including elevations of serum transaminases and autoimmune hepatitis (including fatal cases) have been reported in patients treated with alemtuzumab. Liver function should be evaluated before and during treatment. Patients should be informed about the risk of hepatic injury and related symptoms. In case of these symptoms, treatment should only be re-administered following careful consideration.

Other serious reactions temporally associated with alemtuzumab infusion

During post-marketing use, cases of pulmonary alveolar haemorrhage, myocardial infarction, stroke (including ischaemic and haemorrhagic stroke) and cervicocephalic (e.g. vertebral, carotid) arterial dissection have been reported. Reactions may occur following any of the doses during the treatment course. In the majority of cases, time to onset was within 1-3 days of Lemtrada infusion. Patients should be informed about the signs and symptoms, and advised to seek immediate medical attention if any of these symptoms occur.

Vital signs, including blood pressure, should be monitored before and periodically during Lemtrada infusion. If clinically significant changes in vital functions are observed, discontinuation of infusion and additional monitoring, including ECG, should be considered.

Haemophagocytic lymphohistiocytosis

During post-marketing use, haemophagocytic lymphohistiocytosis has been reported in patients treated with Lemtrada. Haemophagocytic lymphohistiocytosis is a life-threatening syndrome of pathologic immune activation characterised by clinical signs and symptoms of extreme systemic inflammation. It is associated with high mortality rates if not recognised early and treated. Symptoms have been reported to occur within a few months to 4 years following the initiation of treatment. Patients who develop early manifestations of pathologic immune activation should be evaluated immediately, and a diagnosis of haemophagocytic lymphohistiocytosis should be considered.

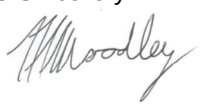
Call for reporting
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the appropriate national reporting system and contact Sanofi. Contact details below.

It is easiest and quickest to report suspected adverse reactions online via the Yellow Card website - https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store.

Alternatively, prepaid Yellow Cards for reporting are available by writing to FREEPOST YELLOW CARD (no other address details necessary), by emailing yellowcard@mhra.gov.uk, at the back of the British National Formulary (BNF), by telephoning the Commission on Human Medicines (CHM) free phone line: 0800 731 6789, or by downloading and printing a form from the Yellow Card section of the MHRA website.

Further Information:
If you require any further information, please contact Sanofi Medical Information department.
Telephone: 0845 372 7101 or email UK-medicalinformation@sanofi.com

Yours Sincerely



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