27 October 2017
EMA/707022/2017

PRAC recommends further restrictions for multiple sclerosis medicine Zinbryta due to risk of serious liver damage

Zinbryta to be used only in a restricted patient group, with strict liver monitoring

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) is recommending further restrictions on the use of the multiple sclerosis medicine Zinbryta (daclizumab) following a review of the medicine's effects on the liver.

The review found that unpredictable and potentially fatal immune-mediated liver injury can occur during treatment with Zinbryta and for up to 6 months after stopping treatment. In clinical trials, 1.7% of patients receiving Zinbryta had a serious liver reaction.

In order to reduce the risks, doctors should now only prescribe Zinbryta for relapsing forms of multiple sclerosis in **patients who have had an inadequate response to at least two disease modifying therapies (DMTs) and cannot be treated with other DMTs**.

In addition, doctors should monitor patients' liver function (ALT, AST and bilirubin) at least once a month as closely as possible before each treatment and continue monitoring them for up to 6 months after treatments have stopped.

If the patient does not comply with monitoring requirements or the response to treatment is inadequate, doctors should consider stopping treatment.

It is recommended that the doctor should stop treatment if a patient has liver enzyme levels over 3 times the normal limit and refer any patients with signs and symptoms of liver damage to a liver specialist.

Patients who test positive for hepatitis B or C infection should also be referred to a specialist.

Zinbryta must not be used in patients with pre-existing liver disease and should not be started in new patients with over 2 times the normal limit of liver enzymes. It is recommended that doctors do not use Zinbryta in patients with other autoimmune conditions.

The PRAC is also recommending that in addition to the current educational material, patients and healthcare professionals in the EU should be given an acknowledgment form. The form will be used to

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

confirm that doctors have discussed the risk with their patients and that the patients understand the importance of monitoring and checking for signs of liver damage.

These recommendations, which strengthen provisional measures introduced in July 2017, will now be sent to EMA's Committee for Medicinal Products for Human Use (CHMP), which will adopt the Agency's final opinion.

More about the medicine

Zinbryta is a medicine used to treat certain patients with relapsing forms of multiple sclerosis. Multiple sclerosis is a disease in which inflammation damages the protective sheath around the nerve cells in the brain and spinal cord. Relapsing means that the patient has flare-ups of neurological symptoms.

Zinbryta is available as a solution for injection in pre-filled pens and syringes. It is injected under the skin once a month.

Zinbryta contains the active substance daclizumab and was authorised in the EU in July 2016. More information can be found on the medicine's dedicated page on EMA's website.

More about the procedure

The review of Zinbryta was initiated on 9 June 2017 at the request of the European Commission under Article 20 of Regulation (EC) No 726/2004.

The review has been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which made a set of recommendations. The PRAC recommendations will now be sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt the Agency's 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.