



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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EMA restricts use of multiple sclerosis medicine Zinbryta

Restrictions are provisional measures while review of liver safety is ongoing

The European Medicines Agency (EMA) has provisionally restricted the use of the multiple sclerosis medicine Zinbryta (daclizumab) to patients with highly active relapsing disease that has failed to respond to certain other treatment, and to patients with rapidly evolving relapsing disease who cannot be treated with other medicines.

In addition, patients with liver injury must not be given the medicine. Starting treatment with Zinbryta is not recommended for patients with autoimmune diseases other than multiple sclerosis and caution should be used when giving Zinbryta together with medicines that can damage the liver. Doctors should continue to monitor the liver function of patients receiving the medicine and closely watch patients for signs and symptoms of liver injury.

These provisional measures have been taken, as a precaution, to ensure that Zinbryta continues to be used as safely as possible while a review of its liver safety is ongoing.

This medicine was authorised in the EU in July 2016 to treat adults with relapsing forms of multiple sclerosis (a disease in which inflammation damages the protective sheath around the nerve cells in the brain and spinal cord).

The review of Zinbryta started after the death from liver injury (fulminant liver failure) of a patient involved in an ongoing observational study, as well as four cases of serious liver injury. The risk of liver damage with the medicine was already known at time of its approval in the EU, and several measures were in place to manage this risk, including the requirement to monitor liver function and provide educational materials to healthcare professionals and patients on the risk of liver damage.

Healthcare professionals have been informed in writing about the provisional measures to be followed by doctors. Once the review is concluded, EMA will communicate further and provide updated guidance to patients and healthcare professionals.

Information for patients

The safety of the multiple sclerosis medicine Zinbryta is being reviewed. As a precaution, changes have been made to the way the medicine is used while this review is ongoing:



- The use of Zinbryta has been restricted to patients with highly active relapsing disease that has failed to respond to other treatment, and to patients with rapidly evolving relapsing disease who cannot be treated with other medicines.
- Patients who already have liver injury will not be treated with this medicine.
- Zinbryta treatment is not recommended in multiple sclerosis patients who have autoimmune diseases other than multiple sclerosis.
- If you are already being treated with this medicine, your doctor will check whether you should continue or switch to an alternative treatment.
- Your doctor will test your liver function at least monthly, and check for signs and symptoms of liver injury. If you have signs of liver injury, your doctor will refer you to a liver specialist.
- While on treatment with this medicine, you should contact your doctor immediately if you develop any symptoms of liver problems, such as unexplained nausea (feeling sick), vomiting, abdominal pain, tiredness, loss of appetite, yellowing of the skin and eyes and dark urine.
- Speak to your doctor or pharmacist before you start taking any other medicines, including medicines obtained without a prescription and herbal supplements.
- You should not stop treatment before speaking to your doctor. If you are being given Zinbryta and have any questions or concerns, speak to your doctor or pharmacist.
- Once the review of Zinbryta is concluded, further information will be provided.

Information for healthcare professionals

- The ongoing safety review was triggered following the death from fulminant liver failure of a patient who was treated with Zinbryta in an ongoing observational study, as well as four cases of serious liver injury.
- Cases of liver injury with Zinbryta have occurred early after treatment initiation, following repeated treatment courses and several months after discontinuation.
- As a precaution and while the review is ongoing, Zinbryta's use has been restricted to adult patients with highly active relapsing disease despite a full and adequate course of treatment with at least one disease modifying therapy (DMT) or with rapidly evolving severe relapsing multiple sclerosis who are unsuitable for treatment with other DMTs.
- In addition, the medicine has been contraindicated in patients with pre-existing hepatic disease or hepatic impairment.
- Healthcare professionals should review promptly any patients who are currently taking Zinbryta to assess whether this medicine continues to be appropriate for them.
- Treatment initiation is not recommended in patients with concurrent autoimmune conditions other than multiple sclerosis and in patients with serum transaminases (ALT or AST) that are at least twice the upper limit of normal (≥ 2 times the ULN).
- Caution is recommended before giving Zinbryta in combination with medicinal products of known hepatotoxic potential, including non-prescription medicines and herbal supplements.
- Prior to treatment initiation, ALT, AST and bilirubin levels should be measured. Serum transaminase and bilirubin levels should be monitored at least monthly, and more frequently if clinically indicated, during treatment and for up to 4 months after the last dose.

- Patients should be informed about the potential risk of serious liver problems and how to recognise them.
 - All patients on Zinbryta should also be monitored for signs and symptoms of hepatic injury during treatment. In case of signs and symptoms suggestive of hepatic injury, the patient should be promptly referred to a hepatologist.
 - If an adequate therapeutic response has not been achieved, discontinuation of therapy should be considered.
 - Further details on these provisional measures have been provided in writing to healthcare professionals and the product information has been updated accordingly.
 - Further information will also be provided once the review is concluded.
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More about the medicine

Zinbryta is a medicine used to treat adults 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 the 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 [here](#).

More about the procedure

The review of Zinbryta has been initiated at the request of the European Commission, under [Article 20 of Regulation \(EC\) No 726/2004](#).

The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines. During the review, the PRAC made a set of provisional recommendations to protect public health. These were forwarded to the European Commission (EC), which on 14 July 2017 issued a provisional legally binding decision applicable in all EU Members States.

Once the PRAC review is concluded, any further recommendations will be forwarded to the Committee for Medicinal Products for Human Use (CHMP), responsible for evaluating medicines for human use, which will adopt a final 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.