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Lorazepam Macure (lorazepam, 4 mg/ml solution for injection): control of status epilepticus to be added to product information

On 27 June 2024, the European Medicines Agency (EMA) completed a review of Lorazepam Macure following disagreement among EU Member States about an application to update the medicine's product information to include the control of status epilepticus (epileptic seizure lasting longer than 5 minutes or recurrent seizures without recovery in between) in adults, adolescents and children from 1 month old.

The Agency agreed that this use can be added to the product information in the Member States of the EU where the medicine is authorised. However, the product information should include information to minimise the potential risk of toxicity in young children linked to the combined use of three alcohol-based excipients.

What is Lorazepam Macure?

Lorazepam Macure, a medicine of the benzodiazepine class, is used in several EU countries as a sedative before surgery or extensive physical examinations. It is also used to relieve severe fear or tension in people who cannot swallow tablets.

Lorazepam Macure contains the active substance lorazepam and is a generic medicine. A generic medicine contains the same active substance and works in the same way as a reference medicine authorised in the EU. The reference medicine for Lorazepam Macure is called Xilmac.

Lorazepam Macure is authorised in Austria, Belgium, Denmark, Finland, Germany, Ireland, Italy, the Netherlands, Norway, Slovenia and Sweden.

The company that markets Lorazepam Macure is Macure Pharma ApS.

Why was Lorazepam Macure reviewed?

Lorazepam Macure was authorised in the EU via national procedures.

In June 2022, Macure Pharma ApS submitted an application to the Dutch medicines agency as part of a mutual recognition procedure to update the product information for Lorazepam Macure in line with that

of the reference medicine Xilmac. The update involved the addition of a new use to control status epilepticus in adults, adolescents, children and infants from 1 month of age.

The company wanted this update to be recognised in all the other Member States where the medicine is authorised. However, the Member States were not able to reach an agreement and the matter was therefore referred to EMA for arbitration on 1 February 2024.

The Swedish medicines agency had concerns about the measures in place to minimise the risks associated with the medicine in infants below 5 years of age. They considered that the product information for Lorazepam Macure should be updated to better highlight and minimise the risk of accumulation of three alcohol-based excipients (benzyl alcohol, propylene glycol and polyethylene glycol) in these infants.

What is the outcome of the review?

The Agency recommended approving the update to the product information of Lorazepam Macure to add the control of status epilepticus in adults, adolescents, children and infants from 1 month of age. However, the product information should also provide additional information about the potential risk of toxicity in young children exposed to the combination of benzyl alcohol, propylene glycol and polyethylene glycol. In particular, the product information will underline that the medicine must not be given to newborn infants to control status epilepticus. It will also include a warning on the risk of cumulative exposure in children under 5 years with the combined use of the three alcohol excipients and advice not to repeat the maximum dose within 24 hours in these children.

More about the procedure

The review of Lorazepam Macure was initiated on 22 February 2024 at the request of the Netherlands under Article 13 of Regulation (EC) No 1234/2008.

The review was carried out by EMA's Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use.

The European Commission issued an EU-wide legally binding decision to implement these changes on 29 August 2024.