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Questions and answers on the review of Vimpat (lacosamide) 15mg/ml syrup

Outcome of a procedure under Article 20 of Regulation (EC) No 726/2004

The European Medicines Agency has completed a review of Vimpat 15 mg/ml syrup, following a quality issue in some batches leading to an uneven distribution of the active substance lacosamide in the syrup. A voluntary recall was initiated on 15 September 2011 as a precautionary measure. The Agency's Committee for Medicinal Products for Human Use (CHMP) has now concluded that in light of the quality defect the benefits of Vimpat 15 mg/ml syrup do not outweigh its risks and this formulation should therefore be permanently discontinued.

What is Vimpat?

Vimpat is a medicine containing the active substance lacosamide.

Vimpat is an antiepileptic that is used to treat partial-onset seizures (epileptic fits starting from one specific part of the brain) as an add-on to other antiepileptic medicines in patients with epilepsy aged 16 years and older. It can be used in patients with partial-onset seizures with or without secondary generalisation (where the seizure subsequently spreads to the whole brain).

Vimpat has been authorised in the EU since 29 August 2008[1]. Vimpat is available as film coated tablets, a 15mg/ml syrup and a solution for intravenous use. The review only concerned Vimpat syrup.

Why was Vimpat 15 mg/ml syrup reviewed?

On 17 June 2011, the Agency was made aware of a quality defect in several batches of Vimpat 15 mg/ml syrup, in which the syrup was reported to contain flake-like precipitates (small solid particles) of the active substance, lacosamide. It was not a product contamination and to date, no adverse effects that could be attributed to the precipitate (such as overdose or lack of effect) were observed.

The company carried out an investigation in bottles with precipitate which showed that lacosamide was not evenly distributed in the solution. It was concerned that this could affect the dose of lacosamide

1 Vimpat 15 mg/ml syrup was marketed in Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, the Netherlands, Spain, Sweden, the United Kingdom as well as, Norway

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that patients receive, leading them to receive too much or too little. An analysis of affected batches showed that this problem could not be remediated.

At its July meeting, the CHMP agreed to the company's proposal to initiate a recall on 15 September 2011 as a precautionary measure.

Consequently, the European Commission asked the CHMP to assess the quality concerns with Vimpat 15 mg/ml syrup and to issue an opinion on whether its marketing authorisation should be maintained, varied, suspended or withdrawn across the EU.

Which data has the CHMP reviewed?

The CHMP requested data from the company to carry out a benefit-risk assessment. These included analytical data of affected batches and tests carried out with Vimpat 15mg/ml syrup under different storage conditions to see if this could prevent the precipitation.

What are the conclusions of the CHMP?

Based on the evaluation of the available data and the scientific discussion within the Committee, the CHMP concluded that in light of the quality defect the benefits of Vimpat 15 mg/ml syrup do not outweigh its risks, and therefore recommended that the marketing authorisation for Vimpat should be varied and the 15 mg/ml syrup formulation should be discontinued. Vimpat remains available as film coated tablets and a solution for intravenous use. The company has recently submitted an application to obtain approval for a 10 mg/ml liquid formulation. The application is currently under review by the CHMP.

What are the recommendations for patients?

- On 15 September 2011 a recall for Vimpat 15 mg/ml syrup was started and this formulation therefore became unavailable.
- Patients should note that no cases of adverse effects or lack of effect due to the quality defect of Vimpat 15 mg/ml syrup have been reported and the recall is a precautionary measure.
- Patients should not stop taking their current medication or change their dose, without medical supervision.
- Patients currently using Vimpat 15 mg/ml syrup should speak to their doctor to discuss their treatment.
- Patients who have any questions should speak to their doctor or pharmacist.

What are the recommendations for pharmacists and prescribers?

- On 15 September 2011 a recall for Vimpat 15 mg/ml syrup was initiated. Prescribers have been sent a letter to inform them of the recall and to provide guidance on how to manage patients on Vimpat 15 mg/ml syrup.
- Doctors should no longer prescribe Vimpat 15 mg/ml syrup.
- Doctors should contact patients currently on Vimpat 15mg/ml syrup as soon as possible in order to switch them to an alternative treatment.
- Patients on Vimpat 15 mg/ml syrup should be switched to Vimpat film coated tablets whenever possible. For patients who cannot take the tablets, it may be possible to obtain the US approved

Vimpat 10 mg/ml liquid formulation which does not have this quality defect on a named patient basis, or alternative antiepileptic treatment may have to be considered.

- For patients on doses above 200 mg/day of Vimpat the dose must gradually be tapered down as per official recommendations.
- Pharmacists should refer any patients on Vimpat 15 mg/ml syrup to their doctor.
- Pharmacists should return any bottles of Vimpat 15 mg/ml syrup to their supplier.

A European Commission decision on this opinion will be issued in due course.

The current European public assessment report for Vimpat can be found on the Agency's website ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports.