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Questions and answers on the suspension of the marketing authorisations for oral meprobamate-containing medicines

Outcome of a procedure under Article 107 of Directive 2001/83/EC

The European Medicines Agency has completed a review of the safety and effectiveness of oral meprobamate-containing medicines, due to serious side effects seen with the medicine. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that the benefits of meprobamate do not outweigh its risks, and that all marketing authorisations for oral medicines containing meprobamate should be suspended throughout the European Union (EU). The Committee recommended that the suspension should be implemented gradually to avoid the risk of severe withdrawal symptoms in patients stopping treatment abruptly.

What is meprobamate?

Meprobamate is a sedative medicine used to treat the symptoms of anxiety and related conditions, including anxiety states, alcohol withdrawal, migraine attacks, digestive disorders, muscle tension or cramps and insomnia. Oral meprobamate-containing medicines have been authorised in a number of EU Member States for several decades via national procedures. They are available as tablets containing meprobamate on its own or in combination with other medicines. These medicines are currently authorised in France, the Netherlands, Finland, Hungary, Italy, Romania and the United Kingdom, as well as Iceland and Norway, under the invented name Equanil and other trade names. Meprobamate-containing medicines can only be obtained with a prescription.

Why was meprobamate reviewed?

In July 2011, the French medicines regulatory agency announced its intention to suspend the marketing authorisations for oral meprobamate-containing medicines because of serious side effects seen with these medicines. These included confusion and loss of consciousness, particularly in elderly people, and the risk of addiction to the medicine when used for prolonged periods, with severe withdrawal symptoms on stopping treatment abruptly. The French medicines agency was also concerned by reports of these medicines being taken for longer than recommended and cases of overdose (sometimes in combination with other medicines) leading to coma or death.



Measures to minimise the risks with meprobamate had already been taken in France. These included restricting these medicines to patients who could not use alternative medicines and limiting treatment to a maximum of twelve weeks. The French medicines agency concluded in July 2011 that these measures had not been sufficient to prevent overdose and serious side effects from occurring in France.

As required by Article 107, France informed the CHMP of its intention to suspend the marketing authorisations in France, so that the Committee could prepare an opinion on whether the marketing authorisations for products containing meprobamate should be maintained, changed, suspended or withdrawn across the EU.

Which data has the CHMP reviewed?

The CHMP considered the benefit-risk assessment carried out by the French medicines agency for meprobamate-containing medicines marketed in France, covering data from the period 2009 to 2011. The Committee also considered information requested from the companies that market meprobamate-containing medicines in the EU. This included data from studies, post-marketing surveillance and the published literature, as well as from poison control centres on cases of poisoning with meprobamate.

What are the conclusions of the CHMP?

The CHMP noted that there was a risk of serious and potentially fatal side effects in patients taking meprobamate-containing medicines under normal conditions of use, including coma. The Committee considered that these risks were increased by the danger of unintentional overdose due to the small difference between the treating dose and the dose that can harm patients, including elderly people. The CHMP also noted that some patients can become addicted to the medicine, leading to serious side effects if they stop treatment abruptly after using it for a long time. Finally, the CHMP considered that there was limited data on the benefits of meprobamate.

Based on the evaluation of the currently available data and the scientific discussion within the Committee, the CHMP concluded that the benefits of oral meprobamate-containing medicines do not outweigh their risks, and therefore recommended that all marketing authorisations for oral meprobamate-containing medicines should be suspended throughout the EU. All oral meprobamate-containing medicines will be withdrawn from the EU market until any further data show that the benefits outweigh the risks.

The Committee acknowledged that it is important to allow for patients currently taking meprobamate-containing medicines to be transferred gradually to alternative treatments, particularly due to the risks of severe withdrawal symptoms on stopping treatment abruptly. To ensure prescribers have enough time to determine the most appropriate treatments for individual patients, the Committee recommended that the withdrawal of the medicines from the market be carried out gradually, within 15 months of the adoption of the European Commission decision. It will be the responsibility of each Member State to set the precise timeframe for this market withdrawal at national level, within the 15 month framework, and to assess the need for other activities, such as recommendations for prescribers and patients on safe and effective alternatives.

What are the recommendations for patients?

- Patients currently using meprobamate-containing medicines should speak to their doctor at their next scheduled appointment to review their treatment.

- Patients should not stop their treatment without speaking to their doctor, since stopping treatment abruptly may lead to severe withdrawal symptoms.
- Patients who have any questions should speak to their doctor or pharmacist.

What are the recommendations for prescribers?

- Doctors should not start new patients on meprobamate-containing medicines.
- Doctors should review the treatment of patients currently taking meprobamate-containing medicines with a view to switching them to alternative treatments, in line with national recommendations for the condition being treated.
- Prescribers should be aware that the availability of meprobamate-containing medicines will decrease as the withdrawal from the market takes place according to national timeframes.

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