EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

11 April 2012
EMA/CHMP/763180/2011 Corr* to Rev 1
EMEA/H/A-31/1284

Questions and answers on the review of suppositories containing terpenic derivatives

Outcome of a procedure under Article 31 of Directive 2001/83/EC as amended

The European Medicines Agency has completed a review of the safety and effectiveness of suppositories containing terpenic derivatives. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that the use of these medicines should be contraindicated in children under 30 months old, children with a history of epilepsy or febrile convulsion and children with a recent history of anorectal lesion (precancerous growths in the anus or rectum).

What are suppositories containing terpenic derivatives?

Suppositories containing terpenic derivatives are medicines given rectally used to treat various conditions. The medicines concerned by this review are used to treat coughs and colds in children and adolescents. The approved indications vary in different EU countries, but typically include supportive treatment for mild, sudden bronchial disorders, particularly productive and non-productive cough.

Terpenic derivatives are mainly obtained from natural substances originating from plants such as conifers. They include camphor, cineole, terpineol, terpine, citral and menthol. They are often found in herbal substances and herbal preparations, such as pine needle or turpentine. They are also found in essential oils obtained from plants, such as niaouli, wild thyme or eucalyptus.

Medicines containing terpenic derivatives are available in various forms, including solutions to be inhaled or rubbed into the skin as well as suppositories. In the EU, suppositories containing terpenic derivatives are authorised by national procedures and are available without prescription. They are currently marketed in Belgium, France, Luxembourg, Finland, Italy, Portugal and Spain under various trade names.

Why were suppositories containing terpenic derivatives reviewed?

The French medicines regulatory agency had concerns about the safety of suppositories containing terpenic derivatives, particularly the risk of serious neurological side effects in young children such as

* Editorial revisions have been made in the description of terpenic derivatives to ensure accuracy.

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convulsions. The French agency was also concerned that reliable data on the effectiveness of these medicines were not available, and that the medicines did not fulfil the latest clinical recommendations for treating cough in children.

Consequently, on 27 October 2010 the French agency asked the CHMP to carry out a full assessment of the benefit-risk balance of suppositories containing terpenic derivatives in children younger than 30 months of age and to issue an opinion on whether the marketing authorisations for these medicines should be maintained, varied, suspended or withdrawn across the EU in this population.

Which data has the CHMP reviewed?

The CHMP looked at the benefit-risk assessment carried out by France, and information requested from the companies that market suppositories containing terpenic derivatives in the EU. This included study data supporting the marketing authorisations and safety data including reports of side effects from post-marketing surveillance and the published literature.

What are the conclusions of the CHMP?

Based on the evaluation of the currently available data and the scientific discussion within the Committee, the CHMP concluded that there was a risk of these medicines inducing neurological disorders, especially convulsions, in infants and small children. The CHMP noted that children aged up to 30 months and children with a history of epilepsy or febrile convulsion were most at risk of these neurological side effects because their nervous system is not yet fully developed. It also decided that there was a risk of these medicines causing local anorectal lesions.

The Committee noted that the effectiveness of these medicines had not been clearly demonstrated, as no clinical trials with suppositories containing terpenic derivatives had been performed and there were no studies focused on infants and children.

The Committee therefore recommended that the use of suppositories containing terpenic derivatives be contraindicated in children under 30 months old, children with a history of epilepsy or febrile convulsion and children with a recent history of anorectal lesion.

What are the recommendations for patients and carers?

- Suppositories containing terpenic derivatives should not be used in children under 30 months old, children with a history of epilepsy or febrile convulsion and children with a recent history of anorectal lesion.
- Terpenic derivatives in other forms, such as solutions to be inhaled or rubbed into the skin, may continue to be used as currently approved.
- Patients and carers who have any questions should speak to their doctor or pharmacist.

The European Commission issued a decision on 20 January 2012.