



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Review of codeine-containing medicines started

On 3 October 2012, the European Medicines Agency started a review of codeine-containing medicines. Codeine is a widely used analgesic (a medicine for pain relief) which is authorised for use in adults and children. Codeine is converted into morphine in the body by an enzyme called CYP2D6.

It is well-known that some patients who are 'CYP2D6 ultra-rapid metabolisers' convert codeine to morphine at a faster than normal rate, resulting in higher than normal levels of morphine in their blood. High levels of morphine can lead to toxic effects such as breathing difficulties. Up to approximately 6.5% of Caucasians are CYP2D6 ultra-rapid metabolisers but prevalence differs according to racial or ethnic group.

Recent concerns have arisen over an increased risk of morphine toxicity when codeine is given to children after surgery. In particular, a very small number of cases have been reported of fatal or life-threatening respiratory depression in children who are ultra-rapid metabolisers and were given codeine after surgical removal of the tonsils or adenoids in the treatment of obstructive sleep apnoea (frequent interruption of breathing during sleep).

The European Medicines Agency will evaluate the impact of the new information on the benefit-risk balance of codeine-containing medicines when these medicines are used for pain relief in children.

More about the medicine

Codeine is a widely used opioid medicine for pain relief. It is also used in the treatment of coughs. In the EU, codeine-containing medicines have been approved via national procedures, and are available either on prescription or over the counter in the different Member States. Codeine is marketed as a single-ingredient medicine or in combination with other substances such as aspirin or paracetamol.

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More about the procedure

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, which will make a set of recommendations. As the review only covers nationally authorised medicines, the PRAC recommendation will be forwarded to the Co-



ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a final position. The CMDh is a regulatory body that represents national competent authorities of EU Member States.

The review was initiated on 3 October 2012, at the request of the UK medicines agency under Article 31 of Directive 2001/83/EC. After discussions, on 31 October 2012 the scope of the review was extended from post-surgery pain relief in children to pain relief in children.