Review of Codeine containing products started

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Information on Codeine

Codeine is a widely used opioid medicine for pain relief in both adults and children. It is also used in the treatment of coughs. In Malta codeine-containing medicines are either prescription only medicines or available as over the counter medicines depending on the indication authorised. Codeine is marketed as a single-ingredient medicine or in combination with other substances such as aspirin or paracetamol. The medicinal products authorised in Malta affected by this review are listed in a **list published** by the European Medicines Agency.

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.

Information from European Medicines Agency about the safety concern

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 rare but 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). [1,2]

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The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, will evaluate the impact of the new information on the benefit-risk balance of codeine-containing medicines when these medicines are used for post-operative pain relief in children. The PRAC will then 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.

For Healthcare Professionals and Patients

For more information on the review of codeine containing medicines please see the **press release** issued by the European Medicines Agency. The list of questions by the PRAC, addressed to the Marketing Authorisation Holders of codeine-containing medicines can also be found **here**.

Reporting adverse drug reactions

Healthcare professionals and patients are encouraged to maintain vigilance on codeine containing products. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority yellow card scheme or online at **http://www.medicinesauthority.gov.mt/pub/adr.doc** or to the marketing authorisation holder or their local representatives. '

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

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[1] Ciszkowski C. et al; Codeine, Ultrarapid-Metabolism Genotype, and Postoperative Death. N Eng J Med 2009 http://www.nejm.org/doi/full/10.1056/NEJMc0904266

[2] Kelly LE. et al; More codeine fatalities after tonsillectomy in North American children. Paediatrics 2012 http://www.ncbi.nlm.nih.gov/pubmed/22492761

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