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Codeine not to be used in children below 12 years for cough and cold

The CMDh[1] has agreed by consensus new measures to minimise the risk of serious side effects, including breathing problems, with codeine-containing medicines when used for cough and cold in children. As a result of these new measures:

- Use of codeine for cough and cold is now contraindicated in children below 12 years. This means it must not be used in this patient group.
- Use of codeine for cough and cold is not recommended in children and adolescents between 12 and 18 years who have breathing problems.

The effects of codeine are due to its conversion into morphine in the body. Some people convert codeine to morphine at a faster rate than normal, resulting in high levels of morphine in their blood. High levels of morphine can lead to serious effects, such as breathing difficulties.

The new measures follow a review by EMA's Pharmacovigilance Risk Assessment Committee (PRAC). The PRAC considered that, although morphine-induced side effects may occur in patients of all ages, the way codeine is converted into morphine in children below 12 years is more variable and unpredictable, making this population at special risk of such side effects. In addition, children who already have problems with their breathing may be more susceptible to respiratory problems due to codeine. The PRAC also noted that cough and cold are generally self-limiting conditions and the evidence that codeine is effective at treating cough in children is limited.

In addition to the new measures for children, codeine must also not be used in people of any age who are known to convert codeine into morphine at a faster rate than normal ('ultra-rapid metabolisers') nor in breastfeeding mothers, as codeine can harm the baby because it passes into breast milk.

This review comes after a previous review of codeine for pain relief in children, which resulted in several restrictions being introduced in order to ensure that the medicine was used as safely as possible. As it was realised that similar considerations could apply to the use of codeine for cough and cold in children, a second EU-wide review of such use was started. The restrictions for codeine for cough and cold are largely in line with the previous recommendations for codeine when used for pain relief.

[1] The CMDh is a medicines regulatory body representing the European Union (EU) Member States, Iceland, Liechtenstein and Norway.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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As the CMDh has now agreed the PRAC measures by consensus, the measures will be directly implemented by the Member States where the medicines are authorised, according to an agreed timetable.

Information for patients

- Following an EU-wide review of codeine when used for cough and cold, changes have been made to the way the medicine is used to ensure that the benefits continue to outweigh the risks in children and adolescents.
- Codeine-containing medicines for cough and cold must not be used in children below 12 years of age because of the risk of serious side effects, including breathing problems.
- In children and adolescents between 12 and 18 years who have problems with their breathing, codeine is not recommended as this population may be more susceptible to breathing problems due to codeine.
- Patients of all ages who are known to be 'ultra-rapid metabolisers', which means that they convert codeine into morphine very rapidly, must not use codeine for cough and cold as they are more at risk of serious side effects with codeine.
- Mothers who are breastfeeding must not take codeine as codeine can harm the baby because it passes into breast milk.
- Parents and caregivers who notice any of the following symptoms in a patient given codeine should stop giving the medicine and seek medical attention immediately: slow or shallow breathing, confusion, sleepiness, small pupils, feeling or being sick, constipation and lack of appetite.
- If you or your child are being treated with codeine and have any questions or concerns about your treatment, speak to your doctor or pharmacist.

Information for healthcare professionals

- Codeine for cough and cold is now contraindicated in children below 12 years, and not recommended in children between 12 and 18 years with compromised respiratory function.
- Codeine is also contraindicated in women during breastfeeding and patients known to be CYP2D6 ultra-rapid metabolisers.

These new measures follow a review of available safety and efficacy data on codeine when used for cough and cold, including data from clinical studies, observational studies and meta-analyses, post-marketing data in Europe and other published literature on the use of codeine in children.

In total, 14 cases of codeine intoxication in children (aged from 17 days to 6 years) related to the treatment of cough and respiratory infection were identified in the published literature, four of which had a fatal outcome.

The available data indicate that the way codeine is converted into morphine in children below 12 years is more variable and unpredictable, making this population at special risk of morphine-induced side effects. In addition, the evidence that codeine is effective at treating cough in children is limited and international guidelines emphasise that cough associated with viral infections may be satisfactorily managed with fluids and increased ambient humidity; in the case of chronic cough, treatment should be directed at the underlying disease.

More about the medicine

Codeine is an opioid medicine that is converted into morphine in the body. It is widely used for pain relief and for the treatment of the symptoms of coughs and colds. 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 active substances.

More about the procedure

The review of codeine when used for cough and cold in children was initiated in April 2014 at the request of the German medicines agency (BfArM), under Article 31 of Directive 2001/83/EC.

The review was carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), EMA's Committee responsible for the evaluation of safety issues for human medicines, which has made a set of recommendations. As codeine-containing medicines are all authorised nationally, the PRAC recommendations were forwarded to the CMDh for its position. The CMDh is a body representing EU Member States as well as Iceland, Lichtenstein and Norway, and is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.

On 22 April 2015 the CMDh adopted its position by consensus, so the measures recommended by the PRAC will be directly implemented by the Member States where the medicines are authorised, according to an agreed timetable.

Contact our press officer

Monika Benstetter

Tel. +44 (0)20 3660 8427

E-mail: press@ema.europa.eu