Community Care of North Carolina

Attention Medical Providers - Codeine in Children Safety Alert

December 2016

Codeine has been prescribed to pediatric patients for many decades as both an analgesic and an antitussive agent. Codeine is a prodrug with minimal pharmacologic activity until metabolized in the liver into morphine, which is responsible for codeine's analgesic effects. In children, there is substantial genetic variability in the activity of the responsible hepatic enzyme, CYP2D6, and, as a consequence, individual patient response to codeine varies from no therapeutic effect to high sensitivity and potential toxicity.

In recent years, various public health organizations and regulatory bodies, including the American Academy of Pediatrics, the World Health Organization, the US Food and Drug Administration, and the European Medicines Agency, have issued pointed warnings regarding the potential occurrence of adverse effects with codeine in children. These and other groups have or are considering issuing a contraindication notice for the use of codeine for children as either an analgesic or an antitussive. Adverse drug event surveillance has documented the occurrence of unanticipated respiratory depression and death after receiving codeine in children, many of whom have been shown to be ultra-rapid metabolizers. With increasing rates of childhood obesity and associated comorbidities, those with documented or suspected obstructive sleep apnea appear to be at particular risk. One report outlined the deaths of three children ages 4-10 years due to codeine toxicity. The children were obese, however the codeine doses were within recommended dose ranges for adjusted lean weight.

Due to the concerns mentioned above, less problem-prone alternatives to codeine are preferable. If codeine is prescribed, parents and caregivers should be warned about the risks associated with codeine use in children. Bringing these concerns to our attention, the American Academy of Pediatrics recently issued a clinical report which states that **"Codeine should no longer be prescribed to children due to its poor analgesic effect and risk of opioid toxicity and oversedation."**

Additional clinical research is needed to improve the understanding of the risks and benefits in children of both opioid and non-opioid alternatives for orally administered pain management and cough suppression. Until this is available, consistent with the American Academy of Pediatrics recommendation, alternatives with more predictable effects should be used as first-line therapy for pain management in children.

Thank you for your support in serving our Medicaid and Health Choice communities!

Friedrichsdorf SJ, Nugent AP, Strobl AQ. Codeine-associated pediatric deaths despite using recommended dosing guidelines: three case reports. J Opioid Manag. 2013 Mar-Apr;9(2):151-5. doi: 10.5055/jom.2013.0156.

Tobias JD, Green TP, Coté CJ –Section on Anesthesiology and Pain Medicine-Committee on Drugs. Codeine: Time To Say "No". Pediatrics. 2016 Sep 19. pii: e20151648. [Epub ahead of print]