*The Commonwealth of Massachusetts*





*Executive Office of Health and Human Services*

*Office of Medicaid*

*100 Hancock Street, 6th Floor*

*Quincy, MA 02171*

DEVAL L. PATRICK

Governor

 JOHN W. POLANOWICZ

 Secretary

KRISTIN THORN

Medicaid Director

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Subject: Prior authorization for codeine use in members under 10 years of age

**Key points:**

* Medical literature and FDA warnings suggest risk of opioid toxicity with codeine use in some children.
* Metabolism of codeine to morphine is highly variable; outcomes may range from ineffective analgesia to toxicity.
* Prescribers may want to consider avoiding the use of codeine for pediatric pain.
* Effective with the November/December 2014 MassHealth Drug List update, MassHealth will require prior authorization for products containing codeine prescribed to members under 10 years of age.

Dear Prescriber,

This letter is a follow-up to a notification sent in August 2013 regarding pediatric codeine use, which warned prescribers of the potential dangers associated with the use of codeine in children. As you may know, the medical literature has reported cases of respiratory depression and death in pediatric patients who were administered codeine within recommended dosing ranges after undergoing tonsillectomy and/or adenoidectomy for treatment of obstructive sleep apnea (OSA).1,2 In August 2012, the Food and Drug Administration (FDA) issued a safety announcement which was later strengthened in February 2013 after 13 cases of pediatric death (N=10) or opioid overdose (N=3) had been reported through 2012 in children ages 21 months to nine years. Most of these deaths were in the setting of adenotonsillectomy or respiratory infection, and the announcement indicated that codeine should not be used for pain in children following tonsillectomy and/or adenoidectomy, and resulted in the addition of a Boxed Warning to drug labels of codeine-containing products.3 The updated FDA announcement also states that codeine should be used in other types of pediatric pain only if the benefits outweigh the risks, and should be used only on an as-needed basis.3

Codeine metabolism can be unpredictable and potentially dangerous in patients considered ultra-rapid CYP2D6 metabolizers, including up to 29% of patients of certain ethnic backgrounds and approximately 1% to 7% of the general population.3 Ultra-rapid CYP2D6 metabolism may enhance the conversion of codeine to morphine at a rate that may lead to unanticipated, and sometimes life-threatening opiate overdoses, especially in young children.4 Conversely, the percentage of patients considered poor CYP2D6 metabolizers can range from approximately 1% to 30%, depending on ethnic group, and there is little to no analgesic effect from codeine in these individuals.2,5 In addition to these concerns, there is the high rate of side effects associated with codeine use and a lack of clinical trials demonstrating its efficacy for treatment of pain and for use as an antitussive.6

Several organizations and professional societies have discouraged the use of codeine in children, including the World Health Organization (WHO)and the American Academy of Pediatrics.7 However, these warnings have not always been heeded. For example, a study by Kaiser, et. al. evaluated national trends in the prescribing of codeine in children.8 This study found that between 2001 and 2010, the proportion of emergency department visits in the U.S. for patients ages 3 to 17 years that resulted in codeine prescriptions showed a statistically significant decrease from 3.7% to 2.9%; however, there was no statistically significant decrease in the frequency of codeine prescriptions specifically for injury visits (1.8% to 1.6%, *P*=0.72), or upper respiratory infection/cough visits (0.5% to 0.4%, *P*=0.28), or in opioid prescriptions for all visits (8.5% to 10.5%, *P*=0.06).7 The authors also compared codeine prescribing since the 2006 issuance of warnings against codeine use for cough and/or upper respiratory infection from the American Academy of Pediatrics and American College of Chest Physicians, and found that there was no statistically significant change.8

**Given the above referenced safety and efficacy concerns, effective** **with the November/December 2014 MassHealth Drug List update, MassHealth will require prior authorization for products containing codeine prescribed to members under 10 years of age.** MassHealth encourages prescribers to carefully consider the risks of codeine when evaluating analgesic options for their pediatric patients. Acetaminophen and ibuprofen have shown analgesic efficacy comparable or superior to codeine in acute pain situations.9-11 If opioid use is required, options such as morphine or oxycodone may represent alternatives with more reliable metabolism than codeine, which has properties that may make prediction of both safety and efficacy more difficult. If CYP2D6 genotyping has been performed, that information must be submitted with any prior authorization request for codeine.

We appreciate your continued support and dedication to providing care to MassHealth members. The MassHealth Drug List, including Therapeutic Class Table 8 outlining the coverage status of codeine and other opioids, can be found on the MassHealth Pharmacy website at [www.mass.gov/masshealth/pharmacy](http://www.mass.gov/masshealth/pharmacy).

Sincerely,



Paul L. Jeffrey, PharmD

Pharmacy Director

MassHealth

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