

## **Indiana Medicaid Therapeutics Committee** **Therapeutic Class Review Summary**

### **Therapeutic Class:**

Narcotic Antitussive/1<sup>st</sup>-Generation Antihistamine Combinations

### **Overview:**

Tussionex<sup>®</sup> and promethazine with codeine are often used to relieve cough and upper respiratory symptoms associated with allergies or the common cold. Chlorpheniramine and promethazine competitively antagonize histamine at H<sub>1</sub>-receptor sites and produce sedative and anticholinergic effects, whereas codeine and hydrocodone cause suppression of cough via direct action on receptors in the cough center of the medulla.

Tussionex<sup>®</sup> is a schedule C-III controlled substance due to its hydrocodone component. Though psychological dependence, physical dependence, and tolerance may develop upon repeated administration of narcotics, psychological dependence is not likely to occur when Tussionex<sup>®</sup> is used for a short period of time for the treatment of cough. Hydrocodone is abused for its opiate-like effects, and is associated with significant addiction potential as well as increased sedation compared with codeine. Additionally, hydrocodone abuse has been escalating over the last decade. Tussicaps<sup>®</sup> (hydrocodone/chlorpheniramine) have recently been approved by the FDA and are available in either 10mg hydrocodone/4mg chlorpheniramine (full strength capsule, equivalent to 5mL of Tussionex suspension), or 5mg hydrocodone/4mg chlorpheniramine (half strength capsule). Tussionex<sup>®</sup> and Tussicaps<sup>®</sup> are contraindicated in children < 6 years of age due to the risk of fatal respiratory depression.

Promethazine with codeine, a schedule C-V controlled substance, has also been associated with possible psychological and physical dependence. However, the probability of these effects is low with use of oral codeine. Addiction remains a major risk with prolonged use of narcotics, with increasing doses often leading to loss of consciousness, abnormal breathing, and withdrawal symptoms that may last for months. Like Tussionex<sup>®</sup> and Tussicaps<sup>®</sup>, promethazine with codeine is contraindicated in children < 6 years of age due to the risk of fatal respiratory depression. Although Tussionex<sup>®</sup> and promethazine with codeine are effective treatments for cough and upper respiratory symptom relief, safer alternatives should be considered prior to their selection.

| Generic Name   | Brand Name   | Manufacturer           | Generic Available |
|--|--|------------------------|-------------------|
| Chlorpheniramine<br>Polistirex/Hydrocodone<br>Polistirex | Tussionex <sup>®</sup><br>Pennkinetic,<br>Tussicaps <sup>®</sup> | UCB Pharma             | N                 |
| Promethazine with<br>Codeine                             | Phenergan <sup>®</sup> with<br>Codeine*                          | Actavis US,<br>Various | Y                 |

\*Brand name product no longer available

### Summary:

Tussionex<sup>®</sup> and promethazine with codeine are effective treatments for the relief of cough and upper respiratory symptoms. However, the hydrocodone component of Tussionex<sup>®</sup> is associated with significant addiction potential and increased sedation compared with codeine. Both Tussionex<sup>®</sup> and promethazine with codeine are associated with the risk of fatal respiratory depression in children < 6 years of age, and are contraindicated in this age group. Therapy with narcotic/1<sup>st</sup>-generation antihistamine combinations may be most appropriate for patients who are unable to mitigate symptoms with safer alternatives. Selection for the preferred drug list should be based upon FDA-approved indications, efficacy, safety, and cost.