

Safety of Promethazine in Children

KEY POINTS

- ❖ **All promethazine products carry a black box warning contraindicating use in children less than 2 years and strongly cautioning use in children age 2 and older.**
- ❖ **The FDA recently released a statement advising against the use of promethazine with codeine cough syrups in children less than 6 years of age.**
- ❖ **Serious adverse events associated with promethazine use have been reported for all routes of administration at a variety of weight-based dosages.¹**
- ❖ **Idaho Medicaid no longer covers any promethazine-containing products for children less than 2 years or promethazine with codeine in children less than 6 years.**

Due to its antihistamine, antiemetic, and sedative properties, promethazine (Phenergan) has been used for a variety of indications in children including postoperative nausea and vomiting, nausea and vomiting associated with gastroenteritis, and cough and cold symptoms. However, adverse events associated with promethazine have been reported including respiratory depression, cardiac arrest, sleep apnea, seizures, and other neurologic disorders.

The package labeling of all promethazine-containing products includes a black box warning stating its use is contraindicated in children less than 2 and strongly cautioned in children 2 years and older, due to the risk of fatal respiratory depression. Recently, the FDA discouraged the use of combination promethazine and codeine cough and cold products in children less than 6.

Idaho Medicaid no longer covers any promethazine-containing products in children less than 2 or any cough and cold product (including promethazine with codeine) in children less than 6. In addition, dose and quantity limits have been set for these products in children 6 years of age or older and can be found on the preferred drug list at: <http://healthandwelfare.idaho.gov/Providers/PrescriptionDrugProviders/tabid/205/Default.aspx>.

There are a number of pharmacologic and non-pharmacologic treatment options with more favorable adverse event profiles and/or better efficacy than promethazine which may be appropriate alternatives in many cases—examples of these are shown in the table on the next page. The 5HT₃ receptor antagonists (e.g ondansetron [Zofran]) are effective for the prevention and treatment of both postoperative vomiting and gastroenteritis-associated nausea and vomiting in children.³ Unfortunately, options for the treatment of cough and cold symptoms are limited due to a lack of safety and efficacy data for many cough and cold products in young children. In addition, a number of these products have recently been removed from the market.

If promethazine is clinically indicated, the lowest effective dose is recommended, and particular care should be exercised to avoid concomitant use of other drugs with respiratory effects. Children with underlying respiratory conditions should be prescribed promethazine with great

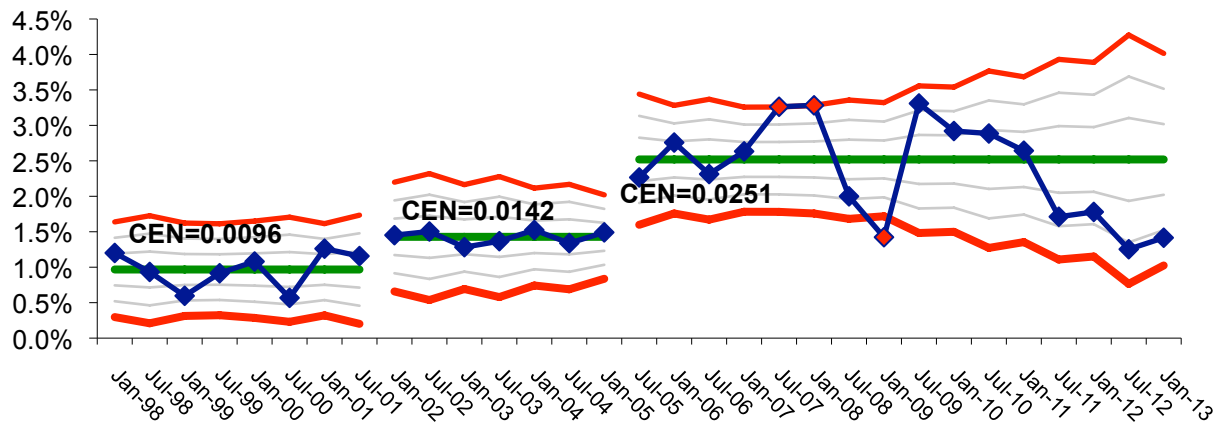
caution.

Table: Alternatives to Promethazine in Children^{3,4}

| GASTROENTERITIS-ASSOCIATED VOMITING | |
|-------------------------------------|---|
| Mild to Moderate | <p><u>Oral rehydration therapy (ORT):</u> Preferred treatment for most Pedialyte, Infalyte, or a generic rehydration solution in small volumes every 10-60 min Avoid liquids that may cause diarrhea (e.g. cola, chicken broth, apple juice, sports drink) Continue breastfeeding and/or age appropriate diet as tolerated</p> |
| Severe/Intractable | <p><u>Anti-emetics:</u> 5HT₃ receptor antagonists (e.g ondansetron [Zofran]) may be used, but are expensive Use only in those at risk for hospitalization or when vomiting hinders ORT</p> |
| COUGH AND COLD SYMPTOMS | |
| Congestion | <p>Humidifier OTC nasal saline (¼ tsp salt and 4 oz warm water) Bulb syringe (suction no more than twice daily to avoid irritation)</p> |
| Cough | Adequate hydration |
| Fever/Pain | Acetaminophen and/or ibuprofen |

Over 6,000 Idaho Medicaid children received a promethazine-containing product in the last year, and about one-quarter of them were under the age of six. The figure below shows that the proportion of these children with associated respiratory depression is 2.5% and has doubled in the last 15 years. The most commonly used product was promethazine with codeine.

Figure: Proportion of Idaho Medicaid Children Age 0-5 Receiving Promethazine that had an Adverse Respiratory Event



References:

1. Starke P, Weaver J, Chowdhury B. Boxed warning added to promethazine labeling for pediatric use. N Eng J Med. 2005;352(5):2653.
2. Promethazine HCl and Codeine Phosphate Oral Solution November 2008. *Detailed View: Safety Labeling Changes Approved By FDA Center for Drug Evaluation and Research (CDER)*. Available at: <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyRelatedDrugLabelingChanges/ucm121083.htm> (Cited 9/09).
3. Practice parameter: the management of acute gastroenteritis in young children. American Academy of Pediatrics, Provisional Committee on Quality Improvement, Subcommittee on Acute Gastroenteritis. Pediatrics. 1996 Mar;97(3):424-35.
4. Leung AK, Robson WL. Acute gastroenteritis in children: role of anti-emetic medication for gastroenteritis-related vomiting Paediatr Drugs. 2007;9(3):175-84.
(Available online at <http://idahodur.isu.edu>, information current as of September 2009)