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October 12, 2012

Elizabeth Miller, Pharm. D.
Director of the Division of Nonprescription Drugs and Health Fraud
Food and Drug Administration
10903 New Hampshire Avenue, WO51 Room 5176
Silver Spring, MD 20993-0002

Re: **Request for agency exercise of enforcement discretion regarding addition of new Warning language to *Drug Facts* labeling for Over-the-Counter benzocaine liquid/gel products indicated for relieving oral discomfort**

Dear Dr. Miller:

The Consumer Healthcare Products Association (CHPA) is the national trade association representing the leading manufacturers and distributors of over-the-counter (OTC) medicines and dietary supplements in the United States. CHPA and its member companies marketing OTC benzocaine oral liquid and gel topical products indicated for relief of oral discomfort are writing to address the agency's recently expressed concern regarding reports of methemoglobinemia observed in association with liquid/gel benzocaine use in children ≤2 years of age. Specifically, we request that the agency exercise its enforcement discretion and not take enforcement action against companies that wish to include a warning relating to the possible risk of methemoglobinemia on product labels.

Despite its long history of safe and effective use, benzocaine has been rarely associated with the development of methemoglobinemia, a condition in which the ability of red blood cells to deliver oxygen throughout the body is reduced, in certain susceptible individuals. Although the majority of these events have been reported following professional use of a benzocaine spray product (*i.e.*, administration by a healthcare professional in patients undergoing a diagnostic procedure), cases have also been observed following the use of OTC benzocaine oral liquid/gel topical formulations, particularly in children ≤2 years of age.

Member companies that manufacture and/or market oral liquid/gel benzocaine products propose adding language to the Warning section of the *Drug Facts* panel that will describe the common symptoms of methemoglobinemia (*e.g.*, difficulty breathing; pale, gray or blue colored skin; weakness, confusion, or headache) and will instruct consumers to stop use and seek immediate medical attention if these symptoms occur.

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Products containing the local anesthetic benzocaine are available OTC in both oral liquid and gel form for use in children and adults to relieve pain due to a number of etiologies including teething, sore throat, toothache, canker sores, and mouth or gum irritation.

The current labeling for OTC benzocaine products used for the treatment of oral discomfort, as outlined in the Tentative Final Monograph for Oral Healthcare Drug Products (56 Fed. Reg. 48302-48347, September 24, 1991) indicates that infants < 4 months of age should not be treated with benzocaine except under the advice and supervision of a dentist.

We are recommending the following warning statement be added under a separate subheading:

> Stop use and seek immediate medical attention if you have ■ difficulty breathing ■ pale, gray or blue colored skin ■ weakness, confusion, or headache
>
> These may be signs of a rare, but serious condition and may appear within minutes to hours after benzocaine use.

Below, we provide a representative example of what the updated label will look like following adoption of the proposed language.

Drug Facts

Active ingredient ***Purpose***

Benzocaine XX%.....Oral pain reliever

Use

For the temporary relief of sore gums due to teething in infants and children 4 months of age and older

Warnings

Allergy Alert: Do not use this product if your child has a history of allergy to local anesthetics such as procaine, butacaine, benzocaine, or other "caine" anesthetics

Do not use this product for more than 7 days unless directed by a dentist or doctor

When using this product

- do not exceed recommended dosage
- fever and nasal congestion are not symptoms of teething and may indicate the presence of infection. If these symptoms persist, consult your doctor

Stop use and ask a doctor or dentist if

- sore mouth symptoms do not improve in 7 days
- irritation, pain, or redness persists or worsens
- swelling, rash, or fever develops

Stop use and seek immediate medical attention if you have

- difficulty breathing
- pale, gray, or blue colored skin
- weakness, confusion, or headache

These may be signs of a rare, but serious condition and may appear within minutes to hours after benzocaine use.

Keep out of reach of children. If more than used for pain (or teething) is accidentally swallowed, get medical help or contact a Poison Control Center right away.

Directions

- Apply to affected area not more than four times daily or as directed by a dentist or doctor
- For infants under 4 months of age there is no recommended dosage or treatment except under the advice and supervision of a dentist or doctor

We respectfully request that the agency provide a written response to this letter, stating the agency's intentions to use enforcement discretion where manufacturers of OTC benzocaine oral liquid/gel topical products choose to modify the *Drug Facts* language.

Sincerely,

Jay E. Sirois, Ph.D.
Director, Regulatory & Scientific Affairs

cc: Michael S. Furness, Ph.D., Director, Division of Nonprescription Drug Regulation Development