

Patient Safety Alert

Veterans Health Administration Warning System Published by VA Central Office

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February 8, 2006
ATTACHMENT A Updated 8/11/06

- Item:** **Cessation of Topical Spray Benzocaine Usage to Anesthetize the Surfaces of the Nasopharynx, Oropharynx, Laryngotracheal Region and Airway. Affected products include, but are not limited to:**
- Hurricaine[®] Spray (benzocaine 20%)
 - Cetacaine[®] Spray (benzocaine 14%, butyl aminobenzoate 2% and tetracaine 2%)
 - Topex[®] Spray (benzocaine 20%)
- Specific Incidents:** Several cases have been reported where benzocaine used as a topical anesthetic on the surfaces of the nasopharynx, oropharynx, laryngotracheal region, and airway has resulted in severe, and in some cases fatal, methemoglobinemia (MHb).
- General Information:** Benzocaine is a topical anesthetic that is frequently used in metered or unmetered spray form to anesthetize the surfaces of the nasopharynx, oropharynx, laryngotracheal region, and airway. Among its many applications, it is employed to facilitate endoscopies of the upper GI tract and airway, and is utilized in many otorhinolaryngologic procedures. One of the well documented serious side effects of benzocaine is the induction of MHb, which reduces oxygen-carrying capacity of the blood. The therapeutic index of benzocaine is sufficiently low such that dangerous levels of MHb can be easily induced in the course of clinical practice. MHb also renders routine 2-wavelength pulse oximetry unreliable, thus reducing a clinician's ability to detect a critical level of hypoxia. Many cases of benzocaine induced MHb have been reported in the medical literature that have resulted in injury or death.
- Actions:**
1. Each VISN Director will ensure that benzocaine-containing topical spray products used to anesthetize the surfaces of the nasopharynx, oropharynx, laryngotracheal region and airway are removed from their VISN Drug Formularies (if listed) by April 1, 2006.
 2. All such benzocaine-containing topical spray products must be removed from inventory and patient treatment areas no later than April 1, 2006 and returned to pharmacy for disposal / return. Lidocaine will be used in their place as a topical anesthetic and appropriate dispensing and administration materials must be provided as well as lidocaine packaged in appropriate volumes and concentrations before this deadline.
 3. All medical facility Directors will ensure that the following actions are accomplished:
 - a. Immediately, and no later than February 17, 2006, the Chief of Staff or other responsible clinician in charge will ensure that:
 - i. Notification to Anesthesia, Critical Care, Dental, ENT, Emergency Room Practitioners, GI, Pharmacy, Pulmonary, Supply, Processing and Distribution, Acquisition and Materiel

Management and any other disciplines /areas that are impacted by this change is accomplished. Technicians working in these areas must be included in the notification.

ii. Clinicians in all clinical areas where benzocaine-containing topical spray is currently employed (e.g., locations where endoscopies are performed) and used, prior to the transition to lidocaine by April 1, 2006, will be furnished with access to Attachment A. Attachment A outlines the highest benzocaine dose that may routinely be administered during the transition period, and the steps necessary to address a toxic dose that causes a clinically significant episode of MHb.

iii. Clinicians begin, as soon as possible and not later than April 1, 2006, to use lidocaine in place of benzocaine-containing topical spray to anesthetize the surfaces of the nasopharynx, oropharynx, laryngotracheal region, and airway. Attachment B provides information on dispensing techniques, lidocaine doses and concentrations as well as equipment that is available. Information on how to procure these items is also provided in Attachment B.

b. That appropriate steps are taken to assure that coordination with clinicians, Supply, Processing and Distribution departments, Acquisition and Materiel Management Services and Pharmacies takes place so that all benzocaine-containing topical spray products used to anesthetize the surfaces of the nasopharynx, oropharynx, laryngotracheal region and airway will be removed from service and that techniques, equipment, orientation, and training are in place to insure transition to lidocaine or other topical agents no later than April 1, 2006.

Additional Information:

<http://www.pbm.va.gov/criteria/benzocaine.pdf>

Moore TJ, Walsh CS, Cohen MR. Reported adverse event cases of methemoglobinemia associated with benzocaine products. Arch Intern Med 2004;164:1192-1196.

Wright R, Lewander W, Woolf A. Methemoglobinemia: etiology, pharmacology, and clinical management. Annals of Emergency Medicine. 1999; Nov, 34(5).

Sachdeva R, Pugeda J, Casale L, Meizlish J, Zarich S. Benzocaine-induced methemoglobinemia. Texas Heart Institute. 2003;30(4):308-310.

Groeper K, Katcher K, Tobias J. Anesthetic management of a patient with methemoglobinemia. Southern Medical Journal. 2003 May, 96(5):504-509

Hurford W, Kratz A. Case 23-2004: A 50-year-old woman with low oxygen saturation. The New England Journal of Medicine. 2004 Jul, 351(4): 380-387.

ISMP Medication Safety Alert; www.ismp.org/Newsletters/acutecare/articles/20021003.asp?ptr=y

Source: VA National Center for Patient Safety

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What You Should Know About Methemoglobinemia (MHb) as You Transition From Using Benzocaine to Anesthetize the Surfaces of the Oropharynx, Nasopharynx, Laryngotracheal Region and Airway.

Methemoglobinemia caused by Benzocaine

- Benzocaine, a topical anesthetic frequently used in its spray form on the surfaces of the oropharynx, nasopharynx, laryngotracheal region and airway, can induce MHb.
- In MHb, affected hemoglobin cannot carry oxygen, or carbon dioxide. This is caused by oxidizing ferrous iron (Fe⁺⁺) to ferric iron (Fe⁺⁺⁺) within the hemoglobin molecule.
- MHb has been shown in the medical literature to lead to hypoxia, resulting in death.

The Medication

- Benzocaine is found in Hurricaine[®] and Topex[®] sprays at 20%, Cetacaine[®] spray at 14%, as well as a variety of other products.
- For Hurricaine[®] spray, the manufacturer recommends 1 spray of the drug in a less-than-1-second burst.
- *Hurricaine[®] Topical Anesthetic spray delivers approximately 51.2 mg of benzocaine in a 1 second spray.**
- *In Cetacaine[®] spray, the product delivers 28 mg of benzocaine in each second of spray. Spray in excess of two seconds is contraindicated.**
- *While many of the reports show benzocaine-acquired MHb following more than 1 spray in the allotted period, several reports identify MHb in patients receiving normal doses.**
- There have been reports of high variability of the dose of benzocaine administered due to varying fullness of non-metered spray bottles.
- For Topex[®] spray, the manufacturer indicates that 2 to 3 metered sprays (50mg per metered spray) are commonly used. The manufacturer's Material Safety Data Sheet recommends no more than 5 sprays be administered. However, even a metered dose product will not prevent overdose if excessive sprays are used.

Warning Signs

- Cyanosis is a primary sign of MHb; however, in individuals with a darker complexion, or patients with anemia, cyanosis may not be consistently noticed prior to an adverse event occurring.
- Hypoxia, dyspnea, cyanosis, tachypnea, fatigue, tachycardia, change in mental status, headache, and chest pressure are some of the signs/symptoms of MHb.
- Anecdotally, tachycardia may be misinterpreted as a response to pain for which additional benzocaine is then given, when in fact, the increase in heart rate may be secondary to MHb.
- Anemic patients may be at higher risk for adverse events due to benzocaine-induced MHb.

Making the Diagnosis

- **DO NOT RELY ON ROUTINE 2-WAVELENGTH PULSE OXIMETRY TO DETECT HYPOXEMIA IN THE PRESENCE OF MHb.**
- To measure MHb, blood samples should be analyzed using a co-oximeter (multiwavelength *in vitro* oximeter).
- A blood sample appears "chocolate" in color.
- The onset of MHb may occur quickly, or can be delayed as long as 20 to 60 minutes following administration of benzocaine. MHb can persist for many hours after onset.

* 8/11/06 ATTACHMENT A updated text in italics

Treatment

- Treatment of choice is methylene blue 1% solution (10 mg/ml). The recommended dose is 1 to 2 mg/kg (0.1-0.2 mL/kg of a 1% solution, which would be 70mg to 140mg or 7mL to 14 mL of a 1% solution for a 70kg patient) infused intravenously over 3 to 5 minutes. **Note: Patients with G6PD deficiency require lower doses of methylene blue and should be started at 0.3-0.5 mg/kg (0.03-0.05 mL/kg of a 1% solution) and then titrated upward as needed. If they don't improve, methylene blue treatment should be abandoned and exchange transfusion should be considered. A reduced dose of methylene blue should be considered in patients with renal impairment.**
- Methylene blue should be given when clinical judgment dictates; in addition, when MHB levels are available literature indicates methylene blue should be given when MHB reaches 20% in symptomatic patients and 30% in asymptomatic patients.
- Consideration may be given to administering supplemental oxygen, depending on the patient's underlying respiratory status and/or other pertinent medical condition(s).
- Excessive doses of methylene blue can also result in MHB.

References:

Moore TJ, Walsh CS, Cohen MR. Reported adverse event cases of methemoglobinemia associated with benzocaine products. Arch Intern Med 2004;164:1192-1196.
Wright R, Lewander W, Woolf A. Methemoglobinemia: etiology, pharmacology, and clinical management. Annals of Emergency Medicine. 1999; Nov, 34(5).
Sachdeva R, Pugada J, Casale L, Meizlish J, Zarich S. Benzocaine-induced methemoglobinemia. Texas Heart Institute. 2003;30(4):308-310.
Groeper K, Katcher K, Tobias J. Anesthetic management of a patient with methemoglobinemia. Southern Medical Journal. 2003 May, 96(5):504-509
Hurford W, Kratz A. Case 23-2004: A 50-year-old woman with low oxygen saturation. The New England Journal of Medicine. 2004 Jul, 351(4): 380-387.
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Dispensing Techniques and Equipment for Use of Lidocaine when Anesthetizing the Surfaces of the Nasopharynx, Oropharynx, Laryngotracheal Region and Airway

Local medical and pharmacy staff may choose to assemble kits for use in anesthesia of the nasopharynx, oropharynx, laryngotracheal region and airway by applying the following guidelines:*

- **Kit Contents**
 - Two 5 mL lidocaine 4% ampules (i.e., 10 mL = 400mg of lidocaine)
 - DO NOT dispense 50 mL vials of 4% Lidocaine!
 - Appropriate mucosal atomization or spray device
 - Four isopropyl alcohol prep pads
 - Two 5mL syringes
 - Two filter needles to draw up lidocaine from ampule
 - Instructions on appropriate use of lidocaine (See **Table 2** below)
- **Kit Characteristics**
 - Kit container should be clear, so contents can be examined without opening the kit
 - Kit should have a tamper evident seal
 - Kit should have an expiration date the same as the earliest expiring individual item.
- **Kit Quality Control**
 - Before the kits are available for dispensing, a pharmacist must check the contents for accuracy and initial and date the kit

} (See **Table 1** below)

* Kit contents should be tailored to meet local needs

TABLE 1: Drugs and Supplies for Kit

PRODUCT DESCRIPTION	ORDERING and PRODUCT INFORMATION	VA PRICE
Lidocaine HCl 4%, 5mL Ampules (preservative free) NDC # 00409-4283-01	Order: VA Pharmaceutical Prime Vendor	\$27.94 / 25
MAD[®]100 Nasal Drug Delivery with 3ml Syringe	Order: (801) 281-3000 or http://www.wolfetory.com/orders-us.html Product info: http://www.wolfetory.com/nasal.html	\$78.00 / 25
MAD[®]300 Nasal Drug Delivery without Syringe	Order: (801) 281-3000 or http://www.wolfetory.com/orders-us.html Product info: http://www.wolfetory.com/nasal.html	\$65.00 / 25
MADgic[®] MAD600 Laryngo-Tracheal Drug Delivery System with 3ml Syringe	Order: (801) 281-3000 or http://www.wolfetory.com/orders-us.html Product info: http://www.wolfetory.com/madgic.html	\$118.00 / 25
MADgic[®] MAD700 Laryngo-Tracheal Drug Delivery Device without Syringe	Order: (801) 281-3000 or http://www.wolfetory.com/orders-us.html Product info: http://www.wolfetory.com/madgic.html	\$104.75 / 25
Laryng-O-Jet[®] Prefilled 4% lidocaine HCl topical solution with syringe and cannula (160mg/4mL)NDC 0548-6300-00	Order: VA Pharmaceutical Prime Vendor. Product info: http://www.ims-limited.com/deliverysystems.htm	\$65.50 / 25
LTA[®] Prefilled 4% lidocaine HCl topical solution with syringe and cannula (160mg/4mL) NDC 0074-4698-01	Order: VA Pharmaceutical Prime Vendor. Product info: http://www.hospira.com/products/productcatalog.aspx	\$86.52 / 25

Table may not include all commercially available devices and products. Consult available suppliers for alternate devices and products
MAD = METERED ATOMIZATION DEVICE (SEE IMAGES)

Note: Cost of all MAD devices is based on retail cost. Wolfe Tory accepts Government credit cards. Orders can be placed by calling (801) 281-3000 or <http://www.wolfetory.com/orders-us.html>

TABLE 2:**Lidocaine Dosage and Administration Instructions for 4% Topical Lidocaine Using Either 5ml Ampules of 4% Lidocaine Injection, or Prefilled Topical Solution Devices****Instructions**Dosing for KIT:

- Adult initial dose = 40mg to 200mg (1-5mL of a 4% solution).
- Adult maximum dose = 400 mg (10mL of a 4% solution). If patient weighs less than 70kg, do not exceed 6 mg/kg OR 400 mg, whichever dose is less.

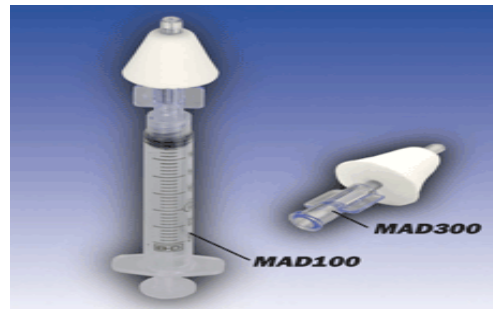
Onset of Action: 2-5 minutesDuration of Action: 30-60 minutesMethod of Application For MAD[®] devices:

- Select appropriate device from list of device images
- Clean neck of lidocaine ampule with alcohol prep pads prior to opening
- Draw lidocaine into syringe using a filter needle
- Remove needle
- Attach MAD[®] device
- ***Atomization devices require sufficient pressure on plunger of syringe to atomize solution***

Cautions:

Use extreme caution if there is sepsis or severely traumatized mucosa in the area of application since under such conditions there is the potential for rapid systemic absorption.

Although the rate of absorption is relatively slow after spraying the laryngotracheal mucosa, there is the attendant risk that some solution may gravitate into the lower respiratory tract where surface area for absorption and tissue blood flow are much greater, resulting in unexpectedly rapid and high blood levels.

Device Images**Nasopharynx:**Use MAD[®]100 and 300 Nasal Delivery Devices

<http://www.wolfetory.com/nasal.html>

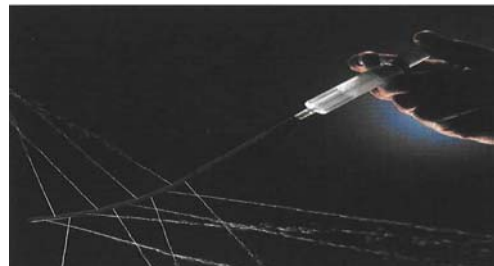
Oropharynx, Laryngotracheal Region or Airway:

Atomization: Use MAD 600 or 700

Spray: LARYNG-O-JET[®]LTA[®] Kit (not shown)MAD[®] 600 and 700 Laryngo-Tracheal Devices

<http://www.wolfetory.com/madgic.html>

LARYNG-O-JET Laryngo-Tracheal Device



<http://www.ims-limited.com/deliverysystems.htm>

This guidance is based on the best clinical evidence currently available. The recommendations in this document are dynamic, and will be revised as new clinical information becomes available. This guidance is intended to assist practitioners in providing consistent, high quality, cost effective drug therapy. These criteria are not intended to interfere with clinical judgment. The clinician must ultimately decide the course of therapy based on individual patient situations.