



MALE GENITAL DESENSITIZERS

This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredient.

Notes

- ▶ Text in parentheses is additional optional information which can be included on the PLA and product label at the applicant's discretion.
- ▶ The solidus (/) indicates that the terms are synonyms or the statements are synonymous. Either term or statement may be selected by the applicant.

Date January 22, 2013

Proper name(s)

4-aminobenzoic acid ethyl ester (Merck 2012)

Common name(s)

benzocaine (USP 35; Merck 2012; CTFA 2008)

Source material(s)

p-aminobenzoic acid (Merck 2012; CTFA 2008)

Route(s) of administration

topical

Dosage form(s)

Those pharmaceutical dosage forms suited to topical administration. Metered dose and chlorofluorocarbons (CFCs)-based aerosols/aerosol sprays and metered-dose pump sprays are unacceptable dosage forms.

Use(s) or Purpose(s) Statement(s) to the effect of

- ▶ For reducing oversensitivity in advance of intercourse (US FDA 1992).
- ▶ For temporary male genital desensitisation, helping to slow the onset of ejaculation (US FDA 1992).
- ▶ Helps in temporarily retarding the onset of ejaculation/temporarily slowing the onset of ejaculation/temporarily prolonging the time until ejaculation (US FDA 1992).
- ▶ Helps in the prevention of premature ejaculation (US FDA 1992).

Dose(s)

Quantity(ies)

3–7.5% in a water-soluble base (US FDA 1992)

Directions for use Statement(s) to the effect of

- ▶ Apply a small amount to head and shaft of penis 5-10 minutes before intercourse, or use as directed by a health care practitioner (CPhA 1996; US FDA 1992).
- ▶ Avoid contact with eyes. If this happens, immediately flush thoroughly with water.
- ▶ For external use only.
- ▶ Keep out of reach of children.
- ▶ Use smallest amount possible to achieve desired result.
- ▶ Wash product off after intercourse (CPhA 1996; US FDA 1992).
- ▶ Wipe off any excess gel before commencing intercourse (CPhA 1996).

Duration of use

No statement required.

Risk information Statement(s) to the effect of

Caution(s) and warning(s)

Premature ejaculation may be due to a condition requiring medical supervision. If this product, used as directed, does not provide relief, discontinue use and consult a health care practitioner (US FDA 1992).

Contraindication(s)

If the following symptoms appear: weakness, confusion, headache, difficulty breathing and/or pale, gray or blue coloured skin, stop use and consult a health care practitioner. These symptoms may be signs of methemoglobinemia, a rare disorder, which may appear up to 2 hours after use (HC 2011a,b).

Known adverse reaction(s)

Hypersensitivity/allergy has been known to occur; in which case, discontinue use (HC 2011a,b; US FDA 1992).

Non-medicinal ingredients

Must be chosen from the current NHPD *Natural Health Products Ingredients Database* and must meet the limitations outlined in the database.

Storage conditions

Statement(s) to the effect of

Aerosols/aerosol sprays and pump sprays:
Store below 40°C (USP DI 2006)

All products:
Store in airtight container. Protect from light. (Martindale 2010)

Semi-solid preparations (e.g. gels):
Store between 15-30°C (USP DI 2006).

Solutions:
Store below 30°C (USP DI 2006).

Specifications

- ▶ The finished product specifications must be established in accordance with the requirements described in the NHPD *Quality of Natural Health Products Guide*.
- ▶ The medicinal ingredient must comply with the requirements outlined in the *Natural Health Products Ingredients Database* (NHPID). In addition, the medicinal ingredient may comply with the specifications outlined in the pharmacopoeial monographs listed in Table 1 below.

Table 1 Benzocaine monographs published in the United States (USP) Pharmacopeia, British (BP) and European (Ph.Eur.) Pharmacopoeias

Pharmacopoeia	Monograph
BP	Benzocaine

Pharmacopoeia	Monograph
Ph. Eur.	Benzocaine
USP	Benzocaine Benzocaine cream Benzocaine gel Benzocaine topical solution Benzocaine topical aerosol

References cited

BP 2012: British Pharmacopoeia 2012. London (GB): The Stationary Office on behalf of the Medicines and Healthcare products Regulatory Agency (MHRA); 2011.

CPhA 1996: Carruthers-Czyzewski P, Gillis C, Letwin D, editors. Nonprescription Drug Reference for Health Professionals. Ottawa (ON): Canadian Pharmaceutical Association; 1996.

CTFA 2008: Gottschalck TE, Bailey JE, editors. International Cosmetic Ingredient Dictionary and Handbook. 12th edition. Washington (DC): Cosmetic, Toiletry and Fragrance Association; 2008.

HC 2011a: Health Canada 2011. Health risks associated with the use of topical benzocaine products. Internal document. [Available on Request.]

HC 2011b : Health Canada reminds Canadians of health risks associated with topical benzocaine products. About Health Canada, Information update, Canada Vigilance Program, Marketed Health Products Directorate [Date modified : 2011-04-19; Accessed : 2012 July 10]. Available from: http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2011/2011_59-fra.php

Martindale 2010: Sweetman SC, editor. Martindale: The Complete Drug Reference. 37th edition [Internet]. London (GB): Pharmaceutical Press; 2010. [benzocaine: ethyl 4-aminobenzoate, CAS: 94-09-7, 20101127; Accessed 2012 July 30]. Available from: <http://ovidsp.tx.ovid.com/>

Merck 2012: O'Neil MJ, Heckelman PE, Koch CB, Roman KJ, editors. The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals (14th Edition - Version 14.9). Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.; 2006, 2012. Available from: <http://www.knovel.com/>

Ph.Eur. 2012: European Pharmacopoeia. 7th edition. Strasbourg (FR): Directorate for the Quality of Medicines and HealthCare of the Council of Europe (EDQM), 2012.

US FDA 1992: US Department of Health and Human Services, Food and Drug Administration. 21 CFR Part 348. [Docket No. 78N-0301]. Male Genital Desensitizing Drug Products for Over-the-Counter Human Use; Final Monograph. ACTION: Final Rule; DATES: This final rule is effective June 19, 1993 [Internet]. Federal Register, Volume 57, Number 119, June 19, 1993. [Accessed 2011 December 8]. Available from:

<http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Over-the-CounterOTCDrugs/StatusofOTCRulemakings/UCM078147.pdf>

USP 35: United States Pharmacopeia and the National Formulary (USP 35 - NF 30). Rockville (MD): The United States Pharmacopeial Convention; 2012.

USP DI 2006: Drug Information for the Health Care Professional. 26th edition, Volume 1. Greenwood Village (CO): Thomson Micromedex; 2006.

References reviewed

Abu-Laban RB, Zed PJ, Pursell RA, Evans KG. Severe methemoglobinemia from topical anesthetic spray: case report, discussion and qualitative systematic review. *Canadian Journal of Emergency Medicine* 2001;3(1):51-56.

Ash-Bernal R, Wise R, Wright SM. Acquired methemoglobinemia. A retrospective series. *Medicine* 2004;83(5):265-273.

Balicer RD, Kitai E. Methemoglobinemia caused by topical teething preparation: a case report. *Scientific World Journal* 2004 July 15;4:517-520.

Barker SJ, Tremper KK, Hyatt J. Effects of methemoglobinemia on pulse oximetry and mixed venous oximetry. *Anesthesiology* 1989;70(1):112-117.

Benzocaine Topical Products: Sprays, Gels and Liquids - Risk of Methemoglobinemia. [Posted 04/07/2011] U.S. Food and Drug Administration MedWatch The FDA Safety Information and Adverse Event Reporting Program. [Internet]. [Accessed 2011 December 21]. Available from: <http://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm250264.htm>

Birchem SK. Benzocaine-induced methemoglobinemia during transesophageal echocardiography. *Journal of the American Osteopathic Association* 2005;105(8):381-384.

Chung N-Y, Batra R, Itzkevitch M, Borochoy D, Balduf M. Severe methemoglobinemia linked to gel-type topical benzocaine use: a case report. *The Journal of Emergency Medicine* 2010;38(5):601-606.

Clary B, Skaryak L, Tedder M, Hilton A, Botz G, Harpole D. Methemoglobinemia complicating topical anesthesia during bronchoscopic procedures. *Journal of Thoracic and Cardiovascular Surgery* 1997;114(2):203-205.

Dahshan A, Donovan K. Severe methemoglobinemia complicating topical benzocaine use during endoscopy in a toddler: a case report and review of the literature. *Pediatrics* 2006;117(4):e806-809.

Darracq M, Daubert P. A cyanotic toddler. *Pediatric Emergency Care* 2007;23(3):195-199.

Dinneen SF, Mohr DN, Fairbanks BF. Methemoglobinemia from topically applied anesthetic spray. *Mayo Clinic Proceedings* 1994;69(9):886-889.

Douglas WW, Fairbanks VF. Methemoglobinemia induced by a topical anesthetic spray (cetacaine). *Chest* 1977;71(5):587-591.

El-Husseini A, Azarov N. Is threshold for treatment of methemoglobinemia the same for all? A case report and literature review. *The American Journal of Emergency Medicine* 2010;28(6):748.e5-748.e10.

Fisher MA, Henry D, Gillam L, Chen C. Toxic methemoglobinemia: A rare but serious complication of transesophageal echocardiography. *Canadian Journal of Cardiology* 1998;14(9):1157-1160.

Grauer SE, Giraud GD. Toxic methemoglobinemia after topical anesthesia for transesophageal echocardiography. *Journal of the American Society of Echocardiography* 1996;9(6):874-876.

Gray TA and Hawkins S. A PACU crisis: A case study on the development and management of methemoglobinemia. *Journal of PeriAnesthesia Nursing* 2004;19(4):242-253.

Guay J. Methemoglobinemia related to local anesthetics: A summary of 242 episodes. *Anesthesia & Analgesia* 2009;108(3):837-845.

Health Canada advises Canadians of health risks involved with using benzocaine. About Health Canada, Advisory 2006-115 November 24, 2006. [Internet]. [Accessed 2011 December 21]. Available from: http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2006/2006_115-eng.php

Khorasani A, Candido KD, Ghaleb AH, Saatee S, Appavu SK. Canister tip orientation and residual volume have significant impact on the dose of benzocaine delivered by Hurricane spray. *Anesthesia & Analgesia* 2001;92:379-383.

Moore TJ, Walsh CS, Cohen MR. Reported adverse event cases of methemoglobinemia associated with benzocaine products. *Archives of Internal Medicine* 2004 June 14;164:1192-1196.

Nguyen, ST, Cabrales RE, Bashour CA, Rosenberger TE Jr, Michener JA, Yared J-P, Starr NJ. Benzocaine-induced methemoglobinemia, *Anesthesia & Analgesia* 2000;90(2):369-371.

O'Donohue WJ Jr, Moss LM, Angelillo VA. Acute methemoglobinemia induced by topical benzocaine and lidocaine. *Archives of Internal Medicine* 1980;140(11):1508-1510.

Olson MI, McEvoy GK. Methemoglobinemia induced by local anesthetics. *American Journal of Hospital Pharmacy* 1981;38(1):89-93.

Orr TM, Orr DL II. Methemoglobinemia secondary to over-the-counter Anbesol. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 1997;84(1):79-81.

Osterhoudt K. Methemoglobinemia. In: Erickson TB, Ahrens WR, Aks S, Baum C, Ling L, editors. *Pediatric Toxicology*. 1st edition. New York, NY: McGraw-Hill; 2005.

Public Health Advisory: Benzocaine Sprays marketed under different names, including Hurracaine, Topex, and Cetacaine. [Internet]. [Accessed 2011 June 6]. Available from: <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHealthcareProfessionals/PublicHealthAdvisories/ucm124350.htm>

Rodriguez LF, Smolik LM, Abehlik AJ. Benzocaine-induced methemoglobinemia: report of a severe reaction and review of the literature. *The Annals of Pharmacotherapy* 1994;28(5):643-649.

Sachdeva R, Pugada JG, Casale LR, Meizlish JL, Zarich SW. Benzocaine-induced methemoglobinemia. A potentially fatal complication of transesophageal echocardiography. *Texas Heart Institute Journal* 2003;30(4):308-310.

So T-Y, Farrington E. Topical benzocaine-induced methemoglobinemia in the pediatric population. *Journal of Pediatric Health Care* 2008;22(6):335-339.

Spiller HA, Revolinski DH, Winter ML. Multi-center retrospective evaluation of oral benzocaine exposure in children. *Veterinary and Human Toxicology* 2000;42(4):228-231.

Stoelting RK, Miller RD. *Basics of Anesthesia*. 4th edition. Publisher: Elsevier Science Health Science Division; 2000.

Tantisattamo E, Suwantarat N, Vierra JR, Evans SJ. Atypical presentations of methemoglobinemia from benzocaine spray. *Hawai'i Medical Journal* 2011;70(6):125-126.

Townes PL, Geertsma MA and White MR. Benzocaine-induced methemoglobinemia. *American Journal of Diseases of Children* 1977;131(6):697-698.

Tsigrelis C, Weiner L. Methemoglobinemia revisited: an important complication after transesophageal echocardiography. *The European Society of Cardiology* 2006;7(6):470-472.

Vallurupalli M, Das M, Manchanda S. Infection and the risk of topical anesthetic induced clinically significant methemoglobinemia after transesophageal echocardiography. *Echocardiography* 2010;27(3):318-323.

Vessely MB, Zitsch RP III. Topical anaesthetic-induced methemoglobinemia: A case report and review of literature. *Otolaryngology-Head and Neck Surgery* 1993;108(6):763-767.

VHA Pharmacy Benefits Management Strategic Healthcare Group and the Medical Advisory Panel and the National Center for Patient Safety. A Guidance on the Use of Topical Anesthetics for Naso/Oropharyngeal and Laryngotracheal Procedures; 2006.

Wong DH, Wilson SE. Avoiding topical anesthesia-induced methemoglobinemia. *Obesity Surgery* 2005;15(7):1088.

Wright R, Lewander W, Woolf A. Methemoglobinemia: etiology, pharmacology, and clinical management. *Annals of Emergency Medicine* 1999;34(5):646-56.