

Practitioner Information Sheet by Pure Integrative Pharmacy
Benzocaine / Lidocaine / Tetracaine (BLT) or Lidocaine/Tetracaine (LT) compounded numbing creams
NOT FOR DISSEMINATION TO THE PUBLIC

General Information

Benzocaine/Lidocaine/Tetracaine (BLT) and Lidocaine/Tetracaine are a combination of topical anesthetics used in application to accessible mucous membranes except the eyes. These products are compounded (made from raw powders and ingredients) and are used for topical anesthesia, mild pain control, and to reduce discomfort of many dermatological procedures. These include application prior to vaccinations, and procedures, such as electrolysis and laser hair removal.¹²³

Compounded products do not have official indications by Health Canada or the US FDA. They are considered when commercial products are ineffective, not tolerated, not available, or when patients seek medications with fewer “unnecessary” excipients. BLT and LT creams are an alternative to commercial products when they are too costly (30g of Emla costs \$70+) or when their low concentrations (~5% for most products) are not effective.

People have varying responses to anesthetics, so it is hard to know which option (BLT or LT) will work best. The concentrations of numbing agents in the compounded creams provided by Trans Care BC for pain relief related to medically-necessary hair removal prior to gender-affirming genital surgery are:

- BLT: 20% Benzocaine, 6% Lidocaine, 4% Tetracaine
- LT: 23% Lidocaine, 7% Tetracaine

Mechanisms of action

Benzocaine, lidocaine, and tetracaine are local anesthetics that decrease nerve membrane permeability to sodium, thereby blocking nerve conduction. This reduction of membrane depolarization rate increases the threshold for electrical excitability. Clinically this leads to reduction or loss of function in nerves innervating pain, temperature, touch, proprioception, and skeletal muscle tone. All nerves are affected, but the blockade first affects autonomic, then sensory, then motor neurons. Systemic use can affect cardiovascular and central nervous systems, but systemic absorption of BLT or LT is expected to be minimal when used appropriately.

Warnings, Precautions, and Contraindications

- Benzocaine, lidocaine and tetracaine have a greater association with contact sensitization than other local anesthetics. These products are not intended for prolonged application time or use.
- *It is contraindicated to apply BLT or LT to large areas of inflamed or denuded tissue* as excessive absorption can occur, increasing the risk of systemic toxicity. BLT or LT can be applied to recently shaven areas that are not inflamed. Avoid application to burns, skin abrasions, and areas of atrophy. BLT and LT are intended only for short term topical administration to relatively healthy, small areas of skin. ¹²³
- *It is contraindicated to cover the site of BLT application with occlusive dressings, or gauze/cotton rolls.* Despite low risks, this increases retention of the active ingredients on the skin, which increases systemic absorption, risk of toxicity, and may even cause methemoglobinemia and skin necrosis.¹²³
- BLT and LT products are intended only for topical administration. Do not administer through ophthalmic or any parenteral routes. If you require administration in these routes, please contact our sterile lab at pure20@purepharmacy.com. ¹²³
- BLT products are contraindicated for use in patients with cholinesterase deficiencies, including pseudocholinesterase deficiency.¹²³

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Warnings, Precautions, and Contraindications continued:

- Do not use BLT products 72 hours before having pancreatic function tests with bentiromide, as benzocaine could interfere with results.
- Excess methemoglobin concentrations have been reported in connection with benzocaine-containing products. Use care to assure the maximum dose of BLT is not exceeded during a procedure or an appointment. During procedures and for at least 2 hours post-application, monitor the patient for signs of methemoglobinemia (increased respiratory rate, shortness of breath, decreased blood oxygen saturation levels, cyanotic skin or lips; of note, methemoglobinemia renders 2-wavelength pulse oximetry results unreliable and a co-oximeter should be used instead).
 - If a patient becomes cyanotic or if elevated methemoglobin concentrations are suspected, immediately initiate treatment to counteract methemoglobinemia (such as administration of methylene blue) as oxygen delivery is ineffective throughout the body until the condition is reversed. Symptom onset may occur within minutes to 1-2 hours after benzocaine application and can occur with the first or subsequent applications. Severe cases of methemoglobinemia can result in death.
 - It would be prudent to consider a different or a lower strength local anesthetic in patients who have a reduced oxygenation status as, compared to healthy individuals, they may have signs and symptoms of methemoglobinemia at lower serum methemoglobin concentrations. Reduced oxygenation status can be seen with cardiac disease, asthma, chronic obstructive pulmonary disease (COPD), or tobacco smoking.
- Patients who have glucose-6-phosphodiesterase or G6PD deficiency, hemoglobin-M disease, methemoglobin reductase deficiency, or pyruvate-kinase deficiency should consider an alternative to benzocaine. These individuals have reduced concentrations or a complete absence of enzymes that help reverse methemoglobinemia, and may have a greater tendency for elevated concentrations of methemoglobin with benzocaine use. Advise patients and caregivers of the signs and symptoms associated with cyanosis (such as: pale, gray, or blue-colored skin; headache; lightheadedness; dyspnea; anxiety; fatigue; and tachycardia), and instruct that they should seek immediate medical attention if they suspect methemoglobinemia.
- Health Canada reminds healthcare professionals to NOT use benzocaine-containing products for children < 2 years old, due to the risk of benzocaine-induced methemoglobinemia. Children in this age are also not able to communicate that they are experiencing symptoms of methemoglobinemia. In children ≥ 3 years and adolescents, use with caution as an appropriate dose has not been established; manufacturers recommend using a reduced dose in very young patients

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Beyond-Use Date (BUD) / Storage

- Store this medication in its original container at room temperature 20°C to 25°C away from heat, moisture and light.
- Keep out of the reach of children.
- Clinical experience at Pure Pharmacy confirms stability beyond 180 days, but without analytical data, we may default to the 30 or 180 day BUD per USP guidelines. USP and clinical guidelines recommend throwing away any unused medicine after the beyond use date (BUD). However, BUD is not the same as expiry. That is, a BUD means that we lack data beyond that date, so we estimate conservatively e.g., Sandoz makes a hydrocortisone 2.5% cream with over 1 year expiry, while our compound has a 30-day BUD. For a longer BUD, we would need data for that specific strength or we must send it for a \$400+ analysis, which is impractical. Patients or practitioners could use past the BUD at their own risk.
 - BLT 20/6/4% in Lipoderm has stability data from PCCA indicating the potency remains within a 90-110% range for **180 days** when stored at a controlled room temperature of 20°-25°C in a stated closure system and protected from light. Changes in the ratio or the base are unlikely to alter this BUD.

Prescription Requirement

As of February 1, 2021, BLT and LT topical formulas in British Columbia are classified as a Schedule II drug and do not require a prescription, except when the mixture contains an equal amount of lidocaine and tetracaine in concentrations of 7% or higher. That is, lidocaine 10%/tetracaine 10% will require a prescription, but BLT 20/6/4% and lidocaine 23%/tetracaine 7% do not. Consult BC Laws for the most recent requirements:

https://www.bclaws.gov.bc.ca/civix/document/id/complete/statreg/9_98

It can be helpful for the patient to have a prescription. If the patient experiences any complications or concerns, the compounding pharmacy will be able to see the percentages of the products they have been using and the base they were compounded in, and help make adjustments based on patient needs.

Pharmacokinetics

- Benzocaine: Hepatic metabolism. Metabolites are renally excreted.
- Lidocaine: Hepatic metabolism by CYP3A4. 95% is dealkylated to the pharmacologically active metabolites monoethylglycinexylidide (MEGX) then to the inactive glycine xylidide.
- Tetracaine: Absorption is dependent on dose, tissue vascularity, and degree of vasodilation. Plasma pseudocholinesterases hydrolyzes tetracaine to para-aminobenzoic acid (PABA). It has the slowest rate of hydrolysis of the ester type local anesthetics and its metabolites are primarily renally excreted.¹²³

Route-specific Pharmacokinetics:

- Topical Route: BLT contains ester anesthetics, which are metabolized to para-aminobenzoic acid (PABA), and thus should not be used in anyone with ester local anesthetic hypersensitivity or para-aminobenzoic acid, PABA hypersensitivity.¹²³

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Pregnancy

Safe use of BLT or LT during pregnancy has not been established with respect to possible adverse effects upon fetal development. Manufacturers state that these products should not be used during early pregnancy, unless the healthcare provider judges the potential benefits outweigh the unknown hazards; routine precaution for the use of any topical anesthetic should be observed.¹²³ A study by the American Dental Association provides some evidence that, when needed, the use of dental local or topical anesthetics at 13 weeks to 21 weeks of pregnancy or later is likely safe and does not raise incidences of adverse pregnancy outcomes or other adverse events; the study analyzed data from the Obstetrics and Periodontal Therapy (OPT) trial, a multicenter study of over 800 pregnant patients in the early to mid-second trimester who received required dental procedures.⁷

Breastfeeding/Chestfeeding

- It is not known whether the components of BLT or LT are excreted in human milk. However, when used appropriately, as a single dose applied topically to mucosal tissue, systemic absorption is expected to be minimal and unlikely to affect the nursing infant.
- BLT or LT should never be applied on or near the breast/chest tissue or nipple of a person who is breastfeeding.
 - Benzocaine has been associated with life threatening cases of methemoglobinemia in infants and children ≤ 2 years of age.
 - This drug combination has not been evaluated by the American Academy of Pediatrics (AAP), however lidocaine is classified as usually compatible with breastfeeding if an alternative is needed.
- Consider the benefits of breastfeeding/chestfeeding, the risk of potential infant drug exposure, and the risk of an untreated or inadequately treated condition. If a breastfeeding/chestfeeding infant experiences an adverse effect related to a drug ingested by the chest or breast-feeding parent, healthcare providers are encouraged to report the adverse effect to Health Canada.¹²³⁶⁸⁹

Interactions

- Benzoyl Peroxide: Concurrent use of benzoyl peroxide and topical anesthetics may decrease the efficacy of the anesthetic. In a clinical study, an estimated 75% increase in patient-reported, prick-induced pain was noted in areas treated with both 5% benzoyl peroxide and 6% benzocaine cream as compared to areas treated with 6% benzocaine cream alone. Investigators attributed the decreased anesthetic effect to a breakdown of the benzocaine molecule by either or both benzoyl peroxide or benzoyl peroxide-derived free radicals. It is recommended that the skin area that is to be topically anesthetized have no previous treatment with benzoyl peroxide or that the skin is thoroughly washed prior to the application of the anesthetic.¹⁰

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Interactions continued:

Other local anesthetics: Dibucaine; Ethyl chloride; Pramoxine: Caution is advised if combining local anesthetics. The toxic effects of local anesthetics are additive. A major cause of adverse reactions appears to be excessive plasma concentrations, which may be due to accidental intravascular administration, slow metabolic degradation, or overdosage. In addition to additive toxic effects, rare and sometimes fatal cases of methemoglobinemia have been reported with the use of topical or oromucosal benzocaine-containing products. Clinicians should closely monitor patients for the development of methemoglobinemia when a combination local anesthetic is used during a procedure. If a patient becomes cyanotic or if elevated methemoglobin concentrations are suspected, immediately institute treatment to counteract methemoglobinemia (such as administration of methylene blue) as oxygen delivery is ineffective throughout the body until the condition is reversed. Patients who are receiving other drugs that can cause methemoglobin formation, such as prilocaine, are at greater risk for developing methemoglobinemia.¹²³⁵⁶¹¹ Adverse reactions are minimal with appropriate use of BLT products (i.e., as a single dose applied topically to mucosal tissue by a healthcare practitioner).¹²³

Adverse reactions

Adverse reactions caused by local anesthetics are more likely to occur in patients following prolonged self-medication (which is contraindicated), and present as a contact dermatitis characterized by erythema and pruritus which may progress to vesiculation and oozing. Localized allergic reactions may occur after prolonged or repeated use of any aminobenzoate anesthetic. Prolonged or occluded contact of the anesthetic to any site is not recommended as it increases the possibility of a serious allergic reaction, dehydration of the epithelium, or an escharotic effect. If manifestations of an allergic reaction such as rash (unspecified), urticaria, or edema occur, the drug should be discontinued. Unpredictable adverse reactions such as hypersensitivity or anaphylactoid reactions are extremely rare.¹²³ Excess methemoglobin concentrations have been reported in connection with benzocaine-containing products. If a patient receiving BLT becomes cyanotic or if elevated methemoglobin concentrations are suspected, immediately institute treatment to counteract methemoglobinemia (such as administration of methylene blue) as oxygen delivery is ineffective throughout the body until the condition is reversed. Symptom onset may occur within minutes to 1—2 hours after application and can occur with the first or subsequent applications. Closely monitor the patient for signs of methemoglobinemia (increased respiratory rate, shortness of breath, decreased blood oxygen saturation levels, cyanotic skin or lips) during the procedure and for at least 2 hours post-application. Of note, methemoglobinemia renders 2-wavelength pulse oximetry results unreliable and a co-oximeter should be used instead. Additionally, if a spray formulation is being used it should be applied judiciously as several factors influence the amount of benzocaine contained in a single spray (including manufacturer differences, varying concentrations, length of time actuator is depressed, residual container volume, and orientation of the spray). Development of methemoglobinemia may not be dose dependant as symptoms have been reported following a single spray. Severe cases of methemoglobinemia can result in death. Advise patients and caregivers of the signs and symptoms associated with cyanosis (such as: pale, gray, or blue-colored skin; headache; lightheadedness; dyspnea; anxiety; fatigue; and tachycardia), and instruct that they should seek immediate medical attention if they suspect methemoglobinemia. In April 2011, the FDA alerted the public and healthcare professionals of the risk of methemoglobinemia associated with the use of benzocaine oromucosal products. Benzocaine sprays used during medical procedures to numb the mucous membranes of the mouth and throat have been associated with methemoglobinemia. A total of 319 cases, including 32 life-threatening cases and 7 deaths, have been reported to the FDA.¹²³⁴⁵

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Adapted from <https://www.empowerpharmacy.com/drugs/blt-cream>

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