RonanRx
PERSONALIZED MEDICINE

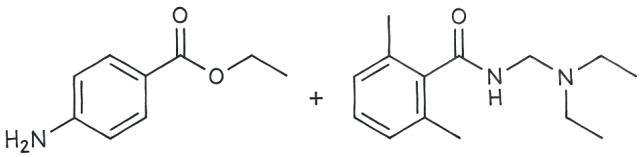
CLINICAL MONOGRAPH · DERMATOLOGY

Compounded Topical Anesthetics (BLT, LET)

Custom topical anesthetic combinations for procedural use

Topical anesthetics are creams, gels, ointments, or patches placed on the skin to numb it before a small procedure. Some, EMLA, LMX-4, LMX-5, Synera, and Pliaglis, are FDA-approved over-the-counter or prescription products with defined application areas and times. Others, such as BLT (benzocaine/lidocaine/tetracaine) and LET (lidocaine/epinephrine/tetracaine), are compounded by pharmacies for specific clinical uses that the FDA-approved products cannot cover [fda_consumer_2007; mccleskey2013].

Compounded high-strength numbing creams have a real safety record: the FDA has documented patient deaths and serious reactions after people applied these creams at home over large skin areas, often before laser hair removal, and absorbed too much medicine. For that reason, RonanRx only dispenses high-strength compounded topical anesthetics on a patient-specific prescription for provider-administered use, with clear limits on how much area can be covered and how long the cream stays on [sobanko2012]. We do not send these creams home with patients to apply on their own [kouba2016].



EVIDENCE POSTURE FDA APPROVED WELL STUDIED REVIEWED **2026-05-11**

State-licensed 503A | Pharmacist reviewed | Doctor led | Cold-chain ready | Patient choice preserved

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FOR CLINICIANS

Compounded topical anesthetics are pharmacy-prepared creams, gels, and ointments containing one or more local anesthetics (most commonly lidocaine, tetracaine, benzocaine, prilocaine, with or without epinephrine), used to anesthetize intact skin or mucosa before needle procedures, laser and light-based procedures, laceration repair, and superficial dermatologic interventions [fda503a] [eichenfield2002; croxtall2010]. The dominant mechanism across agents is reversible voltage-gated sodium channel blockade in cutaneous nerve endings [becker2012, becker2006]. The FDA-approved landscape includes EMLA (lidocaine 2.5% / prilocaine 2.5%), LMX-4 (liposomal lidocaine 4%, OTC), LMX-5 (liposomal lidocaine 5%, OTC), Synera (lidocaine 70 mg / tetracaine 70 mg heated patch), and Pliaglis (lidocaine 7% / tetracaine 7% peel-off cream) [fda_label_emla; fda_label_lmx4; fda_label_synera]. Each approved product has defined site, area, and contact-time labeling.

The 503A compounded role is narrow and provider-anchored. LET (lidocaine 4% / epinephrine 0.1% / tetracaine 0.5%) is the workhorse compounded formulation for pediatric and adult laceration repair, supported by randomized trials [schilling1995; resch1998; singer2000] and Cochrane systematic reviews [eidelman2011; tayeb2017]; it is functionally a replacement for the now-obsolete TAC. BLT-class high-strength combinations (benzocaine / lidocaine / tetracaine, typically 20/6/4 with variants) are used in dermatology for fractional laser, ablative laser, tattoo, and microneedling procedures where FDA-approved products are insufficient on intact skin [railan2007]. The safety record of compounded high-strength topical anesthetics applied at home, with or without occlusion, over large body-surface areas, before laser hair removal, includes documented patient deaths and serious systemic local anesthetic toxicity [doshi2003; kouba2016]. FDA issued a public health advisory in 2007 [fda_consumer_2007] and a 2014 patient safety communication specifically addressing this hazard. McCleskey and colleagues [mccleskey2013] documented detectable serum lidocaine after a 23% lidocaine / 7% tetracaine ointment was applied to facial surfaces, with the accompanying Sobanko commentary [sobanko2013] framing the clinical implications [fda_label_pliaglis]. RonanRx restricts dispensing of high-strength compounded topical anesthetics to provider-administered use with documented application-area limits [fda503a] [friedman1999; sobanko2012].

Why Personalized Compounded Topical Anesthetics (BLT, LET)

The FDA-approved cutaneous anesthetics were each designed for one job. EMLA was approved for a 60-minute application over 25 square centimeters of intact skin before a needle stick. LMX-4 was approved for a thin layer before venipuncture. Synera is a patch for a single small site. Pliaglis is an air-drying peel for adult dermatologic procedures. None of those labels were written for an ablative fractional laser pass across a full face, a four-hour tattoo on a back, a microneedling session on a chest, or a pediatric laceration on a scalp that needs hemostasis at the wound edge. The variables that matter, body surface area, contact time, occlusion, whether the skin is intact or open, the patient's age and weight, methemoglobin reductase and G6PD status, and what other oxidant or sodium-channel-active drugs are on board, are not parameters the manufactured tube accounts for.

Compounding is how those variables get fitted to a real patient and a real procedure. The prescriber and pharmacist can pick the active mix the procedure actually needs: LET for an open laceration where epinephrine slows bleeding and limits systemic uptake, a BLT-class cream when an FDA-approved product cannot achieve the depth or duration a fractional laser pass requires, a benzocaine-free formulation for an infant or a G6PD-deficient patient, or a single-agent lidocaine preparation for mucosa where tetracaine would be too aggressive. Strength, vehicle (gel versus cream versus ointment), application area, contact time, and occlusion are all specified per patient per procedure, with the area, the total mass dispensed, and the removal protocol written on the label. The molecules are the same ones the FDA reviewed in EMLA, LMX, Synera, and Pliaglis. What changes is the formulation that fits the operator, the procedure, and the skin in front of them.

This is the older arrangement, a prescriber who knows the patient and the procedure, a pharmacist who prepares the cream for that one use, and a label with the patient's name on it. Modern oversight, state pharmacy inspection, named-patient prescriptions, and the documented harm record from at-home unsupervised use, are why compounded high-strength topical anesthetics stay provider-administered.

Quick Facts About Compounded Topical Anesthetics (BLT, LET)

Category: Topical amide / ester local anesthetic combinations (sodium-channel blockade)

Active ingredients: Most commonly compounded combinations include BLT (benzocaine 20% / lidocaine 6% / tetracaine 4%, with concentration variants), LET (lidocaine 4% / epinephrine 0.1% /

tetracaine 0.5%), and historical TAC (tetracaine / adrenaline / cocaine). Custom single-agent or combination creams, gels, and ointments are also prepared.

FDA-approved branded forms (alternatives): EMLA (lidocaine 2.5% / prilocaine 2.5% cream), LMX-4 and LMX-5 (liposomal lidocaine 4% and 5% OTC creams), Synera (lidocaine 70 mg / tetracaine 70 mg heated patch), and Pliaglis (lidocaine 7% / tetracaine 7% cream activated by air drying). Each FDA-approved product has a defined application area, time, and patient population.

Route: Topical, provider-administered to defined, limited areas of intact skin or mucosa, typically followed by occlusion and wiped off prior to procedure

Evidence posture: Multiple randomized trials and Cochrane systematic reviews support LET for pediatric and adult laceration repair; FDA-approved EMLA, LMX-4, Synera, and Pliaglis are well studied for needle procedures and superficial dermatologic procedures. Compounded high-strength BLT and similar combinations have published procedural-efficacy data but a documented serious-harm record when used outside controlled administration.

FDA-approval status: EMLA, LMX-4, LMX-5, Synera, and Pliaglis are FDA-approved. Compounded BLT, LET, TAC, and other custom topical anesthetic combinations are not FDA-approved.

Compounded under: 503A, patient-specific prescription only, dispensed for provider-administered use where an FDA-approved topical anesthetic cannot meet a documented procedural need

Critical safety boundary: RonanRx does NOT dispense compounded high-strength topical anesthetics (BLT and equivalents) for unsupervised home application. The FDA has documented patient deaths and serious systemic toxicity (seizures, arrhythmias, methemoglobinemia) following home application of compounded high-strength topical anesthetics, particularly under occlusion or over large body-surface areas before laser hair removal. Provider-administered use with defined area, contact time, and occlusion limits is required.

Methemoglobinemia caution: Benzocaine and prilocaine can cause methemoglobinemia, particularly in infants and patients with G6PD deficiency or methemoglobin reductase deficiency. The FDA expanded the benzocaine boxed warning and contraindicated benzocaine sprays and oral products under 2 years of age in 2018.

SPECIALS: PATIENT-SPECIFIC PRESCRIPTION ONLY

Compounded Topical Anesthetics (BLT, LET) described in this monograph is a 503A compounded preparation. Every dose is made on a prescription, for a named patient, by a licensed pharmacist. It is not a stocked, mass-manufactured product.

- **Made to order, not off a shelf.** No batch sits in a warehouse waiting for buyers. Your prescription triggers the prep.
- **Named-patient label.** The bottle carries one patient's name. The batch records carry one prescription.
- **Dose, strength, and route chosen for the patient.** A prescriber decides what gets compounded, not a manufacturer who set the strength for a trial population.
- **Licensed pharmacist on the hook.** A real person, with a license that can be pulled, signs off on every prep. State inspectors check the facility.
- **Compounded drugs are not FDA-approved.** They should not be evaluated using branded-drug trial data alone. Availability varies by state and prescribed medication.

How This Differs from a Research-Use-Only Website

A research-use-only website ships a vial from a warehouse. There is no prescription, no pharmacist, no facility inspection, and no way to recall the product if something is wrong with it. If the vial is mislabeled, contaminated, or under-potent, there is nobody whose license is at stake.

A 503A compounding pharmacy is the other thing. The doctor writes the prescription. A licensed pharmacist, whose name is on the label, prepares the medicine in a facility the state inspects. If something goes wrong, there is a person and a license on the hook, and a documented chain of custody on every lot. That accountability is what makes it safe.

What is Compounded Topical Anesthetics (BLT, LET)?

A compounded topical anesthetic is a pharmacy-prepared cream, gel, ointment, or solution containing one or more local anesthetic active ingredients in a vehicle designed for cutaneous or mucosal application [fda_label_pliaglis]. The dominant active ingredients are the amide anesthetics lidocaine and prilocaine, the ester anesthetics tetracaine and benzocaine (and historically cocaine), and the adrenergic vasoconstrictor epinephrine [schilling1995; singer2000; fda_label_emla]. Combinations are formulated to broaden onset, depth, and duration of cutaneous anesthesia, and, when epinephrine is included, to reduce systemic absorption and provide hemostasis at the application site [becker2012, becker2006, kouba2016].

Two combinations dominate compounded practice. LET (lidocaine 4% / epinephrine 0.1% / tetracaine 0.5%) is a solution or gel used principally for laceration repair in pediatric and adult emergency settings; it replaced the prior TAC (tetracaine / adrenaline / cocaine) formulation on safety and controlled-substance grounds [resch1998; eidelman2011; tayeb2017]. BLT (benzocaine 20% / lidocaine 6% / tetracaine 4%, with multiple concentration variants in clinical use) is a high-strength cream used in dermatology and aesthetic medicine for topical anesthesia of intact skin before laser resurfacing, fractional laser, tattoo,

microneedling, and similar superficial procedures where FDA-approved EMLA, LMX, Synera, and Pliaglis are insufficient in depth or duration [doshi2003; railan2007; sobanko2012].

Compounded topical anesthetics are not FDA-approved and are not bioequivalent to the FDA-approved EMLA, LMX-4, LMX-5, Synera, or Pliaglis products [friedman1999; fda_label_lmx4; fda_label_synera]. They are prepared under section 503A of the FD&C Act on patient-specific prescriptions in state-licensed compounding pharmacies under USP <795> standards for nonsterile preparations [usp_795] [fda503a].

How Compounded Topical Anesthetics (BLT, LET) Works

Local anesthetics produce reversible loss of sensation by binding inside voltage-gated sodium channels (Nav) of peripheral nerves, blocking the inward sodium current that propagates action potentials. The protonated cationic form of the anesthetic accesses the intracellular pore through the open channel; binding is use-dependent and blocks small unmyelinated C and thinly myelinated Aδ pain fibers preferentially over large myelinated motor fibers, producing analgesia before motor block [becker2012, becker2006].

Topical application requires the anesthetic to cross the stratum corneum, the rate-limiting barrier to cutaneous absorption. Strategies to enable transcutaneous penetration include (1) eutectic mixtures (EMLA, lidocaine plus prilocaine), where the freezing-point depression at the eutectic ratio yields a liquid-phase oil-in-water emulsion of higher base anesthetic concentration than either agent alone [fda_label_emla]; (2) liposomal encapsulation (LMX-4 / LMX-5) [eichenfield2002, nestor2006]; (3) heat-augmented delivery (Synera patch, with an iron-air oxidation heating element that drives diffusion) [croxtall2010]; (4) air-drying peel formulations that form an occlusive layer (Pliaglis); and (5) high-concentration compounded combinations of benzocaine, lidocaine, and tetracaine (BLT) under occlusion [sobanko2012, kouba2016, railan2007].

Adding a vasoconstrictor (epinephrine in LET; historically cocaine, which is itself a vasoconstrictor, in TAC) reduces cutaneous blood flow, slows systemic absorption, and prolongs local effect, a design choice that is particularly useful in open wounds where systemic uptake would otherwise be rapid [schilling1995, resch1998, eidelman2011].

Biological Role of Compounded Topical Anesthetics (BLT, LET)

Voltage-gated sodium channels mediate the depolarization phase of the action potential in all excitable tissues, including peripheral sensory nerves, autonomic fibers, motor nerves, the central nervous system, and cardiac myocytes. Local anesthetic block of cutaneous nerve endings produces the desired analgesic effect; systemic absorption produces the undesired CNS and cardiac toxicity that determines maximum safe doses. The Klein tumescent literature [klein1990, klein2016] established that under specific formulation conditions (highly dilute lidocaine in a large volume of buffered crystalloid with epinephrine, infiltrated

subcutaneously), total lidocaine doses well above the historical 4.5 mg/kg / 7 mg/kg-with-epinephrine ceilings are tolerated; this work informed the broader understanding that local anesthetic systemic toxicity is driven by free-fraction plasma concentration, not by total administered dose in isolation [becker2012].

Vasoconstriction at the application site (whether by added epinephrine in LET or by cocaine itself in historical TAC) reduces blood flow, slows systemic uptake of the anesthetic, prolongs duration of action, and provides hemostasis, a useful property in dermal laceration repair where the operator benefits from a relatively dry surgical field [schilling1995, resch1998] [becker2012].

Detailed Mechanism of Compounded Topical Anesthetics (BLT, LET)

Voltage-gated sodium channels are tetrameric transmembrane proteins responsible for the depolarization phase of the neuronal action potential. Local anesthetics bind to a site in the inner vestibule of the channel pore, accessible from the cytoplasmic side, in the open or inactivated state. Binding stabilizes the inactivated conformation and prevents recovery to the resting state on the timescale of repetitive firing, producing use-dependent block. Sensory C and Aδ fibers, small-diameter, slower-conducting, high-firing-rate pain fibers, are blocked at lower anesthetic concentrations than large myelinated Aα motor fibers, accounting for the differential analgesia / motor sparing observed clinically [becker2012, becker2006].

Cutaneous penetration is governed by the stratum corneum. Anesthetic free-base (uncharged) penetrates lipid bilayers more readily than the protonated cation; once in the more aqueous cytoplasm of nociceptive nerve endings, the equilibrium shifts back toward the cationic form, which is the active blocking species. Formulation strategies that increase the proportion of free base (e.g., EMLA's eutectic mixture, which exists as a liquid at room temperature and increases effective base concentration; high-concentration compounded BLT under occlusion that warms and hydrates the stratum corneum) increase transcutaneous flux [fda_label_emla, sobanko2012, kouba2016]. Liposomal encapsulation (LMX-4 / LMX-5) reduces the apparent diffusion barrier by partitioning lidocaine into a lipid carrier that fuses with stratum corneum lipids [eichenfield2002, nestor2006]. Heat (Synera's iron-air oxidation heating element) raises skin temperature by approximately 3°C and accelerates diffusion across the stratum corneum [croxtall2010]. Air-drying peel formulations (Pliaglis) form an occlusive film over the application site that traps moisture and elevates anesthetic free-base availability.

Tetracaine and benzocaine are ester anesthetics hydrolyzed by plasma butyrylcholinesterase; lidocaine and prilocaine are amide anesthetics hepatically metabolized by CYP3A4 / CYP1A2 with first-pass clearance after systemic absorption. The clinically relevant safety pharmacology is governed by free-fraction plasma exposure: at low systemic concentrations (lidocaine <5 μg/mL), patients experience light-headedness, tinnitus, and circumoral numbness; at higher concentrations (5, 10 μg/mL), seizures and respiratory depression; at the highest concentrations (>10 μg/mL), cardiovascular collapse and arrhythmia [becker2012; klein2016]. Prilocaine and benzocaine are oxidizing agents that convert hemoglobin Fe(II) to Fe(III) (methemoglobin), with clinically significant methemoglobinemia documented after EMLA

application in infants and after benzocaine oral and spray products in patients of all ages [sinisterra2002; russell1997].

Compounded Topical Anesthetics (BLT, LET) Research History

Topical anesthesia of intact skin and mucosa has a long history, but practical formulations enabling reliable cutaneous block emerged in the late 20th century. TAC (tetracaine / adrenaline / cocaine) was widely used for pediatric laceration repair in the 1980s and into the 1990s, then displaced by LET on safety, cost, and controlled-substance grounds. Schilling and colleagues in 1995 [schilling1995] randomized children with facial and scalp lacerations to TAC versus LET and found equivalent anesthetic efficacy with a substantially better safety and regulatory profile for LET [nestor2006]. Resch and Schilling in 1998 [resch1998] subsequently compared LET solution and gel formulations in pediatric lacerations and reported equivalent efficacy with the gel offering practical advantages for application without runoff. Singer and Stark in 2000 [singer2000] extended the LET evidence to adult laceration triage, demonstrating that pre-treatment with LET at the time of triage reduced subsequent injection pain and facilitated repair. Cochrane systematic reviews [eidelman2011, tayeb2017] consolidated the LET literature and identified it as a first-line topical option for repair of dermal laceration.

FDA-approved cutaneous topical anesthetics emerged in parallel. EMLA (eutectic mixture of lidocaine and prilocaine) was approved in the U.S. in 1992 for topical anesthesia of intact skin and became the reference product for needle procedures, particularly pediatric venipuncture and IV cannulation [fda_label_emla]. Liposomal lidocaine 4% (ELA-Max, later LMX-4) was demonstrated in a randomized trial by Eichenfield and colleagues in 2002 [eichenfield2002] to provide non-inferior analgesia for pediatric venipuncture compared with EMLA, with a shorter onset (30 minutes versus 60 minutes for EMLA). LMX-4 became available over-the-counter; LMX-5 followed for short-duration applications. The Sawyer / Synera heated lidocaine-tetracaine patch was approved as a prescription product for needle and superficial dermatologic procedures and reviewed by Croxtall in 2010 [croxtall2010]. Pliaglis (lidocaine 7% / tetracaine 7%, peel-off cream) was approved for procedural anesthesia in dermatology with an air-drying occlusive vehicle [nestor2006].

The compounded high-strength topical anesthetic literature is anchored in dermatology. Friedman, Fogelman, and colleagues in 1999 [friedman1999] performed a comparative study of four topical anesthetics in advance of pulsed dye laser treatment, establishing the principle that higher-concentration compounded combinations could achieve depth of anesthesia not reliably provided by EMLA on intact skin. Doshi and Friedman in 2003 [doshi2003] reported a 30-minute application of the S-Caine peel (a lidocaine 70 mg / tetracaine 70 mg precursor to Pliaglis) before nonablative laser [nestor2006]. Sobanko and colleagues in 2012 [sobanko2012] reviewed the topical anesthetic landscape for dermatologic procedures, and Kouba and the American Academy of Dermatology guideline panel in 2016 [kouba2016] published consensus guidelines for local anesthesia in office-based dermatologic surgery covering both injected and

topical agents and explicitly addressing the role of compounded BLT-class preparations under provider-administered conditions.

The compounded topical anesthetic safety record is the counterweight to the procedural-efficacy literature. The FDA's 2007 public health advisory [fda_consumer_2007] and the 2007 FDA warning letters to several compounding pharmacies followed reports of patient deaths after at-home application of high-strength compounded topical anesthetics, typically applied over large body-surface areas under plastic wrap occlusion before laser hair removal. The 2014 FDA patient safety communication on compounded topical anesthetics reinforced the at-home-application hazard. The McCleskey 2013 study [mccleskey2013] documented detectable serum lidocaine concentrations after a 23% lidocaine / 7% tetracaine ointment was applied to facial surfaces, with the accompanying Sobanko commentary [sobanko2013] discussing the clinical implications [nestor2006]. Methemoglobinemia from benzocaine (and from prilocaine in EMLA in infants) is documented in case reports and pediatric pharmacovigilance [sinisterra2002; russell1997; shachor2008] and led to the 2018 FDA boxed warning expansion contraindicating benzocaine sprays and oral products under 2 years of age.

Compounded Topical Anesthetics (BLT, LET) Timeline

1990 • Klein (J Dermatol Surg Oncol), tumescent technique permits lidocaine doses of 35 mg/kg for liposuction; establishes the modern framework for local-anesthetic safe-dose pharmacology [klein1990]

1992 • FDA approves EMLA (lidocaine 2.5% / prilocaine 2.5% cream) for topical anesthesia of intact skin; eutectic-mixture formulation becomes the reference product for needle procedures [fda_label_emla]

1995 • Schilling et al [schilling1995]. (Ann Emerg Med), randomized trial of TAC vs LET in pediatric facial and scalp lacerations demonstrates equivalent anesthetic efficacy with better safety profile for LET

1997 • Russell and Doyle (Drug Saf), risk-benefit assessment of topical percutaneous local anesthetics in children, including the methemoglobinemia signal for prilocaine and benzocaine [russell1997]

1998 • Resch and Schilling (Ann Emerg Med), LET solution vs gel for pediatric laceration repair shows equivalent efficacy; gel preferred for handling [resch1998]

1999 • Friedman et al [friedman1999]. (Dermatol Surg), comparative study of four topical anesthetics in advance of pulsed dye laser treatment establishes high-strength compounded combinations for dermatology

2000 • Singer and Stark (Acad Emerg Med), LET pretreatment at triage in adult lacerations reduces injection pain and facilitates repair [singer2000]

2002 • Eichenfield et al [eichenfield2002]. (Pediatrics), ELA-Max (liposomal lidocaine 4%) non-inferior to EMLA for pediatric venipuncture with shorter onset

2002 • Sinisterra et al [sinisterra2002]. (J Pediatr), methemoglobinemia in an infant after eutectic mixture of local anesthetic (EMLA) use during nitric oxide therapy

2003 • Doshi and Friedman (Dermatol Surg), 30-minute application of S-Caine peel (lidocaine/tetracaine precursor to Pliaglis) before nonablative laser [doshi2003]

2005 • FDA approves Synera (lidocaine 70 mg / tetracaine 70 mg heated patch) for topical anesthesia of intact skin in adults and children ages 3 and older [fda_label_synera]

2006 • Becker and Reed (Anesth Prog), Essentials of local anesthetic pharmacology; sodium channel block, structure-activity, and systemic toxicity framework [becker2006]

2006 • Nestor (J Drugs Dermatol), safety of occluded 4% liposomal lidocaine cream documents pharmacokinetic profile of LMX-4 under occlusion [nestor2006]

2007 • FDA Public Health Advisory and FDA Consumer warnings (Meadows), life-threatening side effects from compounded topical anesthetics following at-home application, particularly before laser hair removal; FDA warning letters to several compounding pharmacies [fda_consumer_2007]

2007 • Railan and Alster (J Drugs Dermatol), topical lidocaine for cosmetic dermatologic procedures reviews compounded high-strength preparations and FDA-approved alternatives [railan2007]

2008 • Shachor-Meyouhas et al [shachor2008]. (J Emerg Med), application of topical analgesia in triage: a potential for harm; case-based safety discussion

2010 • Croxtall (Drugs), review of the lidocaine/tetracaine medicated plaster (Synera/Rapydan) in minor dermatologic and needle-puncture procedures [croxtall2010]

2011 • Eidelman and Weiss (Cochrane Database Syst Rev), topical anaesthetics for repair of dermal laceration; systematic review supports LET as a first-line topical option [eidelman2011]

2012 • Sobanko et al [sobanko2012]. (Dermatol Surg), topical anesthetics for dermatologic procedures: a review covers EMLA, LMX, Synera, Pliaglis, and compounded BLT-class preparations

2012 • Becker and Reed (Anesth Prog), local anesthetics: review of pharmacological considerations updates the safe-dose and toxicity framework [becker2012]

2013 • McCleskey et al [mccleskey2013; sobanko2013]. (Dermatol Surg), serum lidocaine levels and cutaneous side effects after application of 23% lidocaine / 7% tetracaine ointment to the face; accompanying Sobanko commentary

2014 • FDA Patient Safety Communication on compounded topical anesthetics, reinforces the at-home-application hazard, particularly before laser hair removal

2016 • Kouba et al [kouba2016]. (J Am Acad Dermatol), American Academy of Dermatology guidelines for the use of local anesthesia in office-based dermatologic surgery, including topical and compounded BLT-class preparations

2016 • Klein and Jeske (Anesth Analg), estimated maximal safe dosages of tumescent lidocaine, updating the safe-dose framework for dilute infiltration [klein2016]

2017 • Tayeb and Eidelman (Cochrane Database Syst Rev), updated systematic review of topical anaesthetics for pain control during repair of dermal laceration [tayeb2017]

2018 • FDA expands the benzocaine boxed warning and contraindicates benzocaine oral and spray products in children under 2 years of age following methemoglobinemia case accumulation

Clinical Contexts for Compounded Topical Anesthetics (BLT, LET)

Topical anesthesia of intact skin for needle procedures (venipuncture, IV cannulation, vaccination, lumbar puncture) FDA APPROVED

FDA-approved indication for EMLA, LMX-4, LMX-5, and Synera. Compounded preparations are not appropriate first-line for routine needle procedures.

EMLA (lidocaine 2.5% / prilocaine 2.5% cream) is FDA-approved for topical anesthesia of intact skin and is the long-standing reference product for needle procedures, with 60-minute application time under occlusion [fda_label_emla]. LMX-4 (liposomal lidocaine 4%) provides non-inferior analgesia for pediatric venipuncture with a 30-minute application time and is OTC [eichenfield2002, fda_label_lmx4]. Synera (lidocaine 70 mg / tetracaine 70 mg heated patch) reaches anesthesia in approximately 20, 30 minutes for adults and children ages 3 and older [croxtall2010, fda_label_synera]. Compounded topical anesthetics are not appropriate first-line for routine needle procedures because adequate FDA-approved options exist.

Branded product: EMLA (lidocaine/prilocaine cream); LMX-4 / LMX-5 (liposomal lidocaine); Synera (lidocaine/tetracaine heated patch)

Topical anesthesia of intact skin for superficial dermatologic procedures (dermal filler injection, superficial laser, light-based therapy) FDA APPROVED

FDA-approved indication for Pliaglis (lidocaine 7% / tetracaine 7%) and Synera; compounded BLT used when FDA-approved depth or duration is insufficient.

Pliaglis (lidocaine 7% / tetracaine 7% peel-off cream) is FDA-approved for topical anesthesia in adults prior to superficial dermatologic procedures, with a 20, 30 minute application and an air-drying occlusive vehicle [fda_label_pliaglis] [friedman1999; doshi2003]. Synera covers superficial procedures including dermal filler injection and minor superficial laser [croxtall2010, fda_label_synera]. Compounded BLT-class preparations (most commonly benzocaine 20% / lidocaine 6% / tetracaine 4% with concentration variants) are used in dermatology and aesthetic medicine for procedures where the FDA-approved products do not provide adequate depth or duration on intact skin, particularly fractional laser, ablative laser resurfacing, tattoo, and microneedling, as discussed in the Sobanko 2012 review [sobanko2012], Railan and Alster 2007 [railan2007], and Kouba 2016 AAD guidelines [kouba2016]. RonanRx dispenses compounded BLT only for documented provider-administered use with defined application-area and contact-time limits.

Branded product: Pliaglis (lidocaine/tetracaine cream); Synera (lidocaine/tetracaine heated patch)

Topical anesthesia of dermal lacerations for repair (pediatric and adult) WELL STUDIED

Well-studied off-label / compounded use, LET is the workhorse formulation supported by randomized trials and Cochrane systematic reviews.

LET (lidocaine 4% / epinephrine 0.1% / tetracaine 0.5%) is the standard compounded topical anesthetic for repair of dermal laceration in pediatric and adult emergency settings. Schilling and colleagues [schilling1995] randomized children with facial and scalp lacerations to TAC vs LET and found equivalent anesthetic efficacy with a substantially better safety and regulatory profile for LET. Resch and Schilling [resch1998] compared LET solution vs gel and reported equivalent efficacy with gel preferred for handling. Singer and Stark [singer2000] extended the LET evidence to adult laceration triage. The Cochrane systematic reviews by Eidelman [eidelman2011] and the updated Tayeb [tayeb2017] reviews position LET as a first-line topical option for laceration repair. LET is not FDA-approved as a finished product but is widely compounded under 503A for this established procedural use.

Topical anesthesia of intact skin before tattoo, microneedling, fractional laser, and ablative laser procedures WELL STUDIED

Well-studied compounded use, high-strength BLT-class preparations under provider-administered conditions. FDA-approved products are insufficient on intact skin for these procedures.

Compounded BLT (benzocaine 20% / lidocaine 6% / tetracaine 4% and concentration variants) is used in dermatology and aesthetic medicine to anesthetize intact skin before procedures that require deeper or longer-duration topical anesthesia than the FDA-approved EMLA, LMX, Synera, or Pliaglis products reliably provide [mccleskey2013]. Friedman and colleagues [friedman1999] documented comparative efficacy in advance of pulsed-dye-laser treatment. Doshi and Friedman [doshi2003] reported 30-minute application of the S-Caine peel (precursor to Pliaglis) before nonablative laser. Sobanko 2012 [sobanko2012] reviewed compounded BLT formulations in the procedural dermatology context. Railan and Alster 2007 [railan2007] reviewed topical lidocaine specifically for cosmetic dermatologic procedures. Kouba 2016 AAD guidelines [kouba2016] address provider-administered compounded BLT as part of office-based dermatologic surgery practice. RonanRx restricts dispensing to documented provider-administered use; high-strength compounded topical anesthetics are NOT dispensed for unsupervised home application before laser hair removal or any other procedure.

Topical anesthesia of mucosal surfaces (oral, urethral, ophthalmic), provider-administered diagnostic and procedural use WELL STUDIED

Well-studied; FDA-approved single-agent preparations exist (e.g., lidocaine 4% oral solution, tetracaine ophthalmic, benzocaine sprays). Compounded combinations are dispensed only when FDA-approved products cannot meet documented procedural need.

Mucosal absorption of topical anesthetics is more rapid and complete than absorption through intact skin because the mucosal barrier is markedly thinner than the cornified stratum corneum. FDA-approved single-agent lidocaine, tetracaine, and benzocaine preparations cover most mucosal procedural needs (urethral lidocaine jelly, ophthalmic tetracaine drops, dental and oropharyngeal benzocaine sprays) [becker2012; becker2006]. Compounded mucosal anesthetic preparations are dispensed when a specific concentration, vehicle, or combination is not available commercially and a documented procedural need exists. Methemoglobinemia from benzocaine sprays is well documented, particularly with repeat or prolonged application; the FDA contraindicated benzocaine sprays and oral products in children under 2 years of age in 2018.

Off-Label Uses of Compounded Topical Anesthetics (BLT, LET)

Topical anesthesia for dermal laceration repair (LET) WELL STUDIED

Compounded off-label use supported by randomized trials and Cochrane systematic reviews; LET is not FDA-approved as a finished product.

LET (lidocaine 4% / epinephrine 0.1% / tetracaine 0.5%) is the standard topical anesthetic for dermal laceration repair in U.S. emergency departments. Schilling 1995 [schilling1995], Resch 1998 [resch1998], and Singer 2000 [singer2000] randomized trials and the Cochrane systematic reviews [eidelman2011, tayeb2017] support its use; not FDA-approved as a finished product.

Topical anesthesia before tattoo, microneedling, and laser procedures on intact skin (BLT) WELL STUDIED

Compounded off-label provider-administered use; FDA-approved products may be insufficient in depth or duration. Not appropriate for unsupervised at-home application.

Compounded BLT (and concentration variants) is used in dermatology and aesthetic medicine for procedures requiring deeper or longer topical anesthesia than EMLA, LMX, Synera, or Pliaglis reliably provide [friedman1999; doshi2003; railan2007; sobanko2012]. Compounded high-strength topical anesthetics applied at home over large areas under occlusion have caused patient deaths and serious systemic toxicity [fda_consumer_2007; mccleskey2013; sobanko2013] [kouba2016].

FDA-Approved Uses of Compounded Topical Anesthetics (BLT, LET)

Brand	Indication	Year	Route
EMLA	Topical anesthesia of intact skin in conjunction with local anesthetic infiltration and venipuncture, and superficial dermatologic procedures, in adults and children	1992	Topical cream (lidocaine 2.5% / prilocaine 2.5%)
LMX-4 / LMX-5	OTC topical anesthesia of intact skin for temporary relief of minor pain and itch; widely used for needle procedures in pediatrics	1998	Topical liposomal cream (lidocaine 4% and 5%)
Synera	Topical local analgesia for superficial venous access and superficial dermatologic procedures in adults and children ages 3 and older	2005	Topical heated patch (lidocaine 70 mg / tetracaine 70 mg with iron-air heating element)
Pliaglis	Topical local analgesia in adults prior to superficial dermatologic procedures including dermal filler injection,	2006	

Brand	Indication	Year	Route
	pulsed-dye laser, facial laser resurfacing, and laser-assisted tattoo removal		Topical peel-off cream (lidocaine 7% / tetracaine 7%)

Four FDA-approved cutaneous topical anesthetic products cover most clinical needs: EMLA (lidocaine 2.5% / prilocaine 2.5% cream, approved 1992), LMX-4 / LMX-5 (liposomal lidocaine 4% and 5% OTC creams), Synera (lidocaine 70 mg / tetracaine 70 mg heated patch, approved 2005), and Pliaglis (lidocaine 7% / tetracaine 7% peel-off cream, approved 2006) [fda_label_emla; fda_label_lmx4; fda_label_synera]. Each has defined application area, time, occlusion, and patient-age labeling [doshi2003; kouba2016]. EMLA, LMX-4, LMX-5, and Synera are appropriate first-line products for needle procedures; Pliaglis and Synera cover superficial dermatologic procedures [fda_label_pliaglis; schilling1995; singer2000].

Compounded topical anesthetic preparations are not FDA-approved. They are dispensed under section 503A on patient-specific prescriptions only when an FDA-approved product cannot meet a documented procedural need [fda503a]. LET (for laceration repair) and BLT-class preparations (for procedures where FDA-approved products are insufficient on intact skin) are the established compounded indications [sobanko2012]. The FDA has issued specific safety communications about compounded high-strength topical anesthetics applied at home, particularly before laser hair removal [fda_consumer_2007] [resch1998; friedman1999].

Compounded Compounded Topical Anesthetics (BLT, LET) (503A)

Compounded topical anesthetics occupy a defined and bounded role under section 503A [becker2012]. The FDA-approved cutaneous topical anesthetic market (EMLA, LMX-4, LMX-5, Synera, Pliaglis) covers most clinical needs in needle procedures, superficial dermatologic procedures, and many laser and light-based procedures [fda_label_lmx4; croxtall2010; railan2007]. Compounding is appropriate only where an FDA-approved product cannot meet a documented patient-specific procedural need [fda_essentially_a_copy, fda503a].

RonanRx prepares compounded topical anesthetics in two principal scenarios: (1) LET (lidocaine 4% / epinephrine 0.1% / tetracaine 0.5%) solution or gel for dermal laceration repair, a well-studied procedural use without an FDA-approved finished-product equivalent; and (2) BLT-class high-strength combinations (most commonly benzocaine 20% / lidocaine 6% / tetracaine 4%, with prescriber-specified concentration variants) for provider-administered topical anesthesia in dermatology and aesthetic medicine where Pliaglis, Synera, EMLA, or LMX cannot achieve the depth or duration required on intact skin for procedures such as fractional laser, ablative laser, tattoo, or microneedling [fda_label_emla; fda_label_synera; fda_label_pliaglis]. Custom single-agent or allergen-free preparations are also dispensed when a documented excipient or vasoconstrictor sensitivity makes the FDA-approved product unusable [singer2000; klein2016].

CRITICAL safety boundary: RonanRx does not dispense compounded high-strength topical anesthetics (BLT and equivalents) for unsupervised at-home application [sobanko2012; eidelman2011; tayeb2017]. The FDA has documented patient deaths and serious systemic local anesthetic toxicity (seizures, cardiac arrhythmia, methemoglobinemia) following at-home application of compounded high-strength topical anesthetics, particularly when applied over large body-surface areas under plastic-wrap occlusion before laser hair removal [fda_consumer_2007] [friedman1999; doshi2003]. McCleskey and colleagues [mccleskey2013] documented detectable serum lidocaine concentrations after a 23% lidocaine / 7% tetracaine ointment was applied to facial surfaces under controlled conditions; the accompanying Sobanko commentary [sobanko2013] discussed the clinical implications [eichenfield2002]. RonanRx requires every prescription for a compounded high-strength topical anesthetic to identify a controlled administration plan, provider-administered application with defined area, contact time, and removal protocol, and we do not fill prescriptions that read as routine at-home use [kouba2016; schilling1995; resch1998].

Compounded topical anesthetic preparations are not bioequivalent to EMLA, LMX-4, LMX-5, Synera, or Pliaglis [becker2006]. Absorption, onset, depth, duration, and systemic exposure depend on the specific combination, concentration, vehicle, occlusion, application area, contact time, and integrity of the skin barrier. Procedural efficacy data summarized from compounded BLT publications is generated under defined clinical conditions and does not transfer to arbitrary at-home application.

Compounded Topical Anesthetics (BLT, LET) Formulations and Routes

Form	Concentration	Description
Compounded LET solution or gel (lidocaine 4% / epinephrine 0.1% / tetracaine 0.5%)	Lidocaine 4% / epinephrine 1:1,000 / tetracaine 0.5%	Nonsterile topical liquid or gel under USP <795>, dispensed in a single-use applicator quantity for provider-administered application to a dermal laceration prior to repair. Standard application is 1, 3 mL applied with a cotton ball or gauze and held in place for 20, 30 minutes before suturing.
Compounded BLT cream (benzocaine / lidocaine / tetracaine)	Benzocaine 20% / lidocaine 6% / tetracaine 4% is the conventional baseline; prescriber-specified variants are dispensed on documented procedural need	Nonsterile cream under USP <795> for provider-administered topical anesthesia of intact skin before laser, tattoo, microneedling, and similar superficial dermatologic procedures. Dispensed with a defined application-area limit, contact-time limit, and removal protocol; NOT dispensed for unsupervised home application.
Compounded custom single-agent or allergen-free topical anesthetic	Custom per prescriber order, most commonly lidocaine 4, 10% in an inert vehicle for patients with	Nonsterile cream, gel, or ointment under USP <795> for documented excipient sensitivity to an FDA-approved product, or for a concentration or vehicle not commercially available.

Form	Concentration	Description
	documented sensitivity to EMLA, LMX, Synera, or Pliaglis excipients	
Manufactured EMLA cream (reference product)	Lidocaine 2.5% / prilocaine 2.5%	FDA-approved eutectic mixture for topical anesthesia of intact skin. Apply under occlusion for 60 minutes for venipuncture; 120 minutes for deeper procedures. Approved 1992.
Manufactured LMX-4 / LMX-5 cream (reference product)	Liposomal lidocaine 4% (LMX-4) or 5% (LMX-5)	OTC liposomal lidocaine creams for topical anesthesia. Faster onset than EMLA (~30 minutes for LMX-4 venipuncture per Eichenfield 2002).
Manufactured Synera patch (reference product)	Lidocaine 70 mg / tetracaine 70 mg per patch, with iron-air oxidation heating element	FDA-approved heated patch for topical local analgesia in adults and children ages 3 and older. 20, 30 minute application typical.
Manufactured Pliaglis cream (reference product)	Lidocaine 7% / tetracaine 7% peel-off cream	FDA-approved air-drying peel-off cream for topical local analgesia in adults before superficial dermatologic procedures.

Routes used in published literature: topical.

Compounded Topical Anesthetics (BLT, LET) Dosing

Route	Population	Range	Duration	Study type
Topical	Children and adults, dermal laceration repair (LET)	1, 3 mL of LET solution or gel applied to the wound with a cotton ball or gauze; held in place for 20, 30 minutes prior to repair. Maximum total LET dose generally limited to 3 mL for children weighing <20 kg.	Single application per procedure	Randomized controlled trials and Cochrane systematic review
Topical	Adults, provider-administered BLT for dermatologic and aesthetic procedures	Application area, total mass of cream, contact time, and occlusion are specified by the prescriber on a per-procedure basis and limited to ensure cumulative lidocaine + benzocaine + tetracaine systemic exposure remains below systemic-toxicity thresholds. Compounded BLT 20/6/4 is typically applied as a thin layer over a defined procedural area for 20, 45 minutes under provider supervision	Single procedural application; not for repeat at-home dosing	Procedural-dermatology case series and review

Route	Population	Range	Duration	Study type
		and removed before the procedure. NOT for unsupervised home application.		
Topical	Adults and children, FDA-approved EMLA for needle procedures (reference product)	2.5 g of cream over 20, 25 cm² of skin, under occlusion, for 60 minutes prior to venipuncture; up to 60 g over 600 cm² for larger procedures. Maximum application area and dose vary by age and body weight.	Single application per procedure	FDA-approved labeled regimen
Topical	Adults and children, FDA-approved LMX-4 / LMX-5 (reference product)	Thin layer applied to intact skin and gently rubbed in; typically 30-minute application for needle procedures per Eichenfield 2002 study results.	Single application per procedure	FDA-approved labeled regimen
Topical	Adults and children ≥3 years, FDA-approved Synera patch (reference product)	One patch applied to intact skin; activates on opening; 20, 30 minute application typical.	Single application per procedure	FDA-approved labeled regimen
Topical	Adults, FDA-approved Pliaglis cream (reference product)	Thin layer applied to intact skin; air-dries to a peel-off film over 20, 30 minutes prior to procedure.	Single application per procedure	FDA-approved labeled regimen

Doctor-prescribed and procedurally administered. Topical anesthetic application planning depends on the procedure, the patient's age and body weight, the application area, occlusion, contact time, and the integrity of the skin barrier. The Kouba 2016 AAD guidelines [kouba2016] provide consensus recommendations for office-based dermatologic surgery covering both compounded and FDA-approved topical anesthetics. The Becker 2006 / 2012 reviews [becker2006, becker2012] frame systemic local-anesthetic toxicity and free-fraction-driven safe-dose principles, and the Klein tumescent literature [klein1990, klein2016] anchors the safe-dose framework for dilute lidocaine infiltration.

For compounded BLT-class preparations, RonanRx requires the prescription to specify (1) the procedure, (2) the application-area limit (typically described in cm² or by anatomic region), (3) the maximum total cream mass dispensed, (4) the maximum contact time, (5) whether occlusion is permitted, and (6) the controlled administration setting (clinic, OR, or supervised procedure room). Prescriptions that lack a

controlled administration plan are not filled. The FDA's compounded topical anesthetic safety communications [fda_consumer_2007] are the regulatory anchors for this practice.

Compounded Topical Anesthetics (BLT, LET) Safety

Topical anesthetic safety is dominated by systemic local-anesthetic toxicity and methemoglobinemia. Systemic toxicity occurs when free-fraction plasma anesthetic concentrations reach CNS- or cardiac-toxic thresholds; clinical manifestations progress from light-headedness, tinnitus, and circumoral numbness (lidocaine <5 μg/mL), to seizures and respiratory depression (5, 10 μg/mL), to arrhythmia and cardiovascular collapse (>10 μg/mL) [17][16]. Free-fraction is a function of total absorbed dose, anesthetic, application area, occlusion, skin integrity, and individual pharmacokinetics; the Klein tumescent literature [18][19] established that the safe ceiling depends on formulation conditions rather than total milligram dose in isolation.

Compounded high-strength topical anesthetics applied at home over large body-surface areas under occlusion are the dominant documented safety hazard. The FDA's 2007 public health advisory and the 2007 FDA Consumer warnings [23] followed patient deaths and seizures after at-home application of compounded preparations before laser hair removal. The 2014 FDA patient safety communication reinforced this hazard. McCleskey and colleagues [13] documented detectable serum lidocaine concentrations after a 23% lidocaine / 7% tetracaine ointment was applied to facial surfaces under controlled conditions, with the Sobanko commentary [14] discussing clinical implications. The Shachor-Meyouhas case-based review [22] discussed topical-analgesia harm in the triage context.

Methemoglobinemia is the second major hazard. Benzocaine and prilocaine are oxidizing agents that convert hemoglobin Fe(II) to Fe(III), particularly in infants (immature methemoglobin reductase) and in patients with G6PD deficiency or congenital methemoglobinemia. Sinisterra and colleagues [21] reported methemoglobinemia in an infant after EMLA application during nitric oxide therapy; Russell and Doyle [20] reviewed the risk-benefit profile of topical percutaneous local anesthetics in children including the methemoglobinemia signal. In 2018 the FDA expanded the benzocaine boxed warning and contraindicated benzocaine oral and spray products in children under 2 years of age.

Local site reactions, erythema, transient blanching (from epinephrine in LET), edema, pruritus, are common, generally mild, and self-limited. Contact dermatitis and allergic reactions to individual anesthetics, vasoconstrictors, or vehicle excipients occur. Application to broken skin, mucosa, or large body-surface areas substantially increases systemic absorption and risk. RonanRx does not dispense compounded high-strength topical anesthetics for application to non-intact skin without a procedural indication and supervised administration. Compounded preparations are not bioequivalent to FDA-approved products; manufactured-product safety data summarized above does not transfer to arbitrary compounded combinations without local stability and PK assessment.

Contraindications

Topical anesthetic combinations are contraindicated in patients with known hypersensitivity to any component (amide anesthetic, ester anesthetic, epinephrine, or vehicle excipient). LET and other epinephrine-containing combinations are contraindicated for application to terminal arteries, fingers, toes, nose, penis, and ear pinna, where vasoconstriction could precipitate ischemia [151].

Benzocaine-containing products are contraindicated in children under 2 years of age (FDA 2018) for oral and spray indications, with the same methemoglobinemia hazard applying to high-concentration cutaneous benzocaine in young children and in patients with G6PD deficiency or congenital methemoglobinemia [2120]. Prilocaine (EMLA) carries the same methemoglobinemia caution.

Compounded high-strength BLT-class preparations are contraindicated for unsupervised at-home application, particularly under occlusion or over large body-surface areas before laser hair removal [23]. RonanRx does not fill prescriptions that lack a controlled provider-administered administration plan.

Drug interactions

Systemic absorption of topical anesthetics is generally low when applied as labeled to intact skin, but rises substantially with large application areas, occlusion, broken skin, mucosal application, or high-concentration compounded preparations. Patients receiving systemic class I antiarrhythmics (mexiletine, tocainide), other local anesthetics, or amide anesthetic infusions are at additive risk for CNS and cardiac toxicity from absorbed topical lidocaine [1716].

Epinephrine in LET interacts with non-selective beta blockers (potential for unopposed alpha vasoconstriction with hypertension) and with monoamine oxidase inhibitors and tricyclic antidepressants (potentiated sympathomimetic response); these interactions are most relevant when LET is applied over substantial open-wound surface area. Methemoglobin-inducing co-administration (dapsone, nitrates, sulfonamides) compounds the prilocaine and benzocaine methemoglobinemia hazard [2021].

Adverse events

Common local adverse events are mild and self-limited: transient erythema, pallor or blanching (from epinephrine in LET), edema, pruritus, and burning at application site. Contact dermatitis and allergic hypersensitivity are reported [1215].

Serious adverse events are systemic local anesthetic toxicity (CNS, light-headedness, tinnitus, perioral numbness, agitation, seizures; cardiac, arrhythmia, conduction block, cardiovascular collapse) and methemoglobinemia (cyanosis, hypoxia, headache, fatigue, dyspnea). The dominant documented serious-harm pattern in the U.S. compounded topical anesthetic literature involves at-home application of high-strength BLT-class creams over large body-surface areas under occlusion before laser hair removal, with patient deaths documented in FDA safety communications [23]. McCleskey 2013 [13] documented measurable serum lidocaine after controlled facial application of a 23/7 lidocaine/tetracaine ointment. Methemoglobinemia from EMLA (prilocaine) has been documented in infants [21] and the FDA expanded the

benzocaine boxed warning in 2018 contraindicating benzocaine sprays and oral products in children <2 years.

Monitoring Compounded Topical Anesthetics (BLT, LET) Therapy

For provider-administered topical anesthetic procedures, baseline assessment includes the procedure plan, application area, occlusion plan, contact time, and identification of methemoglobinemia risk factors (age <2 years, G6PD deficiency, congenital methemoglobinemia, concurrent oxidant medication). During the procedure, monitor for early signs of systemic toxicity (light-headedness, tinnitus, agitation, perioral paresthesia) and for cutaneous adverse events (urticaria, marked edema). Pulse oximetry is appropriate when benzocaine or prilocaine exposure is substantial, particularly in pediatric patients.

Post-procedure, the application site is cleansed of residual cream and inspected. Patients are educated to report delayed neurologic, cardiac, or cyanotic symptoms; emergency contact information is provided. Compounded preparations are not bioequivalent to FDA-approved products [becker2012, klein2016, kouba2016].

Compounded Topical Anesthetics (BLT, LET) in Special Populations

Compounded Topical Anesthetics (BLT, LET) Evidence Quality

Evidence supporting FDA-approved cutaneous topical anesthetics (EMLA, LMX-4, LMX-5, Synera, Pliaglis) is well established. EMLA is supported by 30+ years of pediatric and adult procedural literature [fda_label_emla]. LMX-4 (liposomal lidocaine) is supported by the Eichenfield 2002 randomized trial vs EMLA [eichenfield2002] and the Nestor 2006 occlusion safety study [nestor2006] [fda_label_lmx4]. Synera is supported by the Croxtall 2010 review [croxtall2010, fda_label_synera]. Pliaglis is supported by FDA labeling for superficial dermatologic procedures [fda_label_pliaglis]. The procedural-dermatology landscape is summarized by the Sobanko 2012 review [sobanko2012] and the Kouba 2016 AAD guidelines [kouba2016].

Evidence supporting compounded LET for dermal laceration repair is strong: randomized trials [schilling1995, resch1998, singer2000] and Cochrane systematic reviews [eidelman2011, tayeb2017] position LET as a first-line topical option without an FDA-approved finished-product equivalent [fda_label_lmx4]. Evidence supporting compounded BLT-class high-strength combinations for procedural dermatology is documented in case series and procedural-efficacy comparisons [friedman1999, doshi2003, railan2007] and discussed in the Sobanko 2012 review and Kouba 2016 AAD guidelines [sobanko2012, kouba2016]; these data are generated under provider-administered conditions and do not transfer to at-home application.

The compounded-topical-anesthetic safety literature is anchored by FDA safety communications [fda_consumer_2007], by the McCleskey 2013 facial-application study [mccleskey2013] and accompanying Sobanko commentary [sobanko2013], and by pediatric and infant methemoglobinemia signals [sinisterra2002; russell1997; shachor2008] [fda_label_lmx4]. The Klein tumescent literature [klein1990; klein2016] and the Becker 2006 / 2012 pharmacology reviews [becker2006; becker2012] frame the safe-dose pharmacology that underlies the boundary between provider-administered procedural use and unsupervised at-home application.

Major Compounded Topical Anesthetics (BLT, LET) Clinical Studies

Study	Design	Participants	Duration	Finding
Schilling TAC vs LET (1995, Ann Emerg Med)	Randomized double-blind trial of tetracaine/adrenaline/cocaine (TAC) vs lidocaine/epinephrine/tetracaine (LET) for anesthesia of pediatric facial and scalp lacerations	171	Single procedural application	Equivalent anesthetic efficacy for TAC and LET; LET preferred on safety, cost, and controlled-substance grounds, established LET as the modern compounded standard for laceration repair [schilling1995]
Resch LET solution vs gel (1998, Ann Emerg Med)	Randomized trial of LET solution vs LET gel for pediatric facial and scalp laceration repair	95	Single procedural application	Equivalent anesthetic efficacy between solution and gel formulations; gel preferred for handling and reduced runoff [resch1998]
Singer LET adult triage (2000, Acad Emerg Med)	Randomized double-blind trial of LET pretreatment at triage vs placebo in adult lacerations	49	Single procedural application	LET pretreatment at triage reduced subsequent injection pain and facilitated repair in adult patients [singer2000]
Eidelman Cochrane topical anesthetics for laceration repair (2011)	Cochrane systematic review of topical anaesthetics for repair of dermal laceration	—	—	LET is comparable to TAC and supports use as a first-line topical option for laceration repair; injection anesthetics remain alternatives when topical is insufficient [eidelman2011]

Study	Design	Participants	Duration	Finding
Tayeb Cochrane update (2017)	Updated Cochrane systematic review of topical anaesthetics for pain control during repair of dermal laceration	—	—	Confirms LET as a first-line topical option for dermal laceration repair; supports continued compounded use in pediatric and adult emergency settings [tayeb2017]
Eichenfield ELA-Max vs EMLA (2002, Pediatrics)	Randomized, double-blind, multicenter trial of ELA-Max (liposomal lidocaine 4%) 30-minute application vs EMLA 60-minute application before venipuncture in children	120	Single procedural application	ELA-Max (liposomal lidocaine 4%) for 30 minutes provided non-inferior analgesia compared with EMLA for 60 minutes; established the LMX-4 product profile [eichenfield2002]
Nestor occluded 4% liposomal lidocaine safety (2006, J Drugs Dermatol)	Pharmacokinetic and safety study of 4% liposomal lidocaine cream applied under occlusion	—	—	Documented serum lidocaine concentrations and tolerability profile of LMX-4 under occlusion conditions [nestor2006]
Croxtall Synera/ Rapydan review (2010, Drugs)	Therapeutic review of lidocaine/tetracaine medicated plaster (Synera/Rapydan) in minor dermatological and needle puncture procedures	—	—	Heated lidocaine/tetracaine patch produces topical anesthesia within 20, 30 minutes for adult and pediatric needle procedures and superficial dermatologic interventions [croxtall2010]
Friedman comparative four topical anesthetics (1999, Dermatol Surg)	Comparative study of four topical anesthetics in advance of pulsed dye laser treatment	—	—	Higher-concentration compounded combinations achieved depth of anesthesia not reliably provided by EMLA on intact skin for dermatologic laser procedures; established the rationale for compounded BLT-class preparations in procedural dermatology [friedman1999]

Study	Design	Participants	Duration	Finding
Doshi S-Caine peel before nonablative laser (2003, Dermatol Surg)	Clinical study of 30-minute S-Caine peel (lidocaine 70 mg / tetracaine 70 mg precursor to Pliaglis) before nonablative laser	—	—	30-minute application produced adequate topical anesthesia for nonablative laser, supporting subsequent FDA approval of Pliaglis [doshi2003]
Railan and Alster topical lidocaine for cosmetic dermatology (2007, J Drugs Dermatol)	Review of topical lidocaine and compounded BLT-class preparations for cosmetic dermatologic procedures	—	—	Reviews compounded high-strength topical anesthetics and FDA-approved alternatives for cosmetic dermatology and frames the role of provider-administered application [railan2007]
Sobanko topical anesthetics for dermatologic procedures review (2012, Dermatol Surg)	Narrative review covering EMLA, LMX, Synera, Pliaglis, and compounded BLT-class preparations for dermatologic procedures	—	—	Synthesizes the procedural-dermatology evidence base and frames the controlled use of compounded high-strength topical anesthetics under provider-administered conditions [sobanko2012]
Kouba AAD guidelines for local anesthesia in office-based dermatologic surgery (2016, J Am Acad Dermatol)	American Academy of Dermatology consensus guideline	—	—	Consensus recommendations for injected and topical local anesthetics in office-based dermatologic surgery, including compounded BLT-class preparations under provider-administered conditions [kouba2016]
McCleskey 23% lidocaine / 7% tetracaine on the face (2013, Dermatol Surg)	Pharmacokinetic study of serum lidocaine concentrations and cutaneous side effects after controlled facial application of a 23% lidocaine / 7% tetracaine ointment	—	—	Documented measurable serum lidocaine after facial application of high-strength compounded lidocaine/tetracaine; clinically interpreted by the accompanying Sobanko commentary as supporting controlled-administration

Study	Design	Participants	Duration	Finding
				limits [mccleskey2013; sobanko2013]
Becker and Reed local anesthetic pharmacology essentials (2006, Anesth Prog)	Educational review of local anesthetic pharmacology	—	—	Frames sodium-channel-block mechanism, structure-activity, and systemic toxicity for amide and ester local anesthetics [becker2006]
Becker and Reed local anesthetics pharmacological considerations (2012, Anesth Prog)	Educational review update	—	—	Updated pharmacology framework including topical absorption and free-fraction-driven safe-dose principles [becker2012]
Klein tumescent technique 35 mg/kg (1990, J Dermatol Surg Oncol)	Clinical pharmacology study of tumescent lidocaine for liposuction	—	—	Tumescent infiltration of dilute lidocaine with epinephrine permits total lidocaine doses of 35 mg/kg without systemic toxicity; established formulation-dependent safe-dose framework [klein1990]
Klein and Jeske maximal safe tumescent lidocaine (2016, Anesth Analg)	Updated PK analysis of safe lidocaine dosages with tumescent technique	—	—	Provides updated maximal safe dosage estimates for tumescent lidocaine; reinforces formulation-dependent safety pharmacology [klein2016]
Russell and Doyle topical local anesthetics in children (1997, Drug Saf)	Risk-benefit assessment review	—	—	Reviews pediatric topical local anesthetic safety including methemoglobinemia signal for prilocaine and benzocaine [russell1997]
Sinisterra EMLA methemoglobinemia in an infant (2002, J Pediatr)	Case report	—	—	Documents methemoglobinemia in an infant after EMLA application during nitric oxide therapy, case-level evidence for the prilocaine pediatric safety concern [sinisterra2002]

Study	Design	Participants	Duration	Finding
Shachor-Meyouhas topical analgesia in triage potential for harm (2008, J Emerg Med)	Case-based safety discussion	—	—	Frames the potential for harm when topical analgesia is applied without controlled administration [shachor2008]

Compounded Topical Anesthetics (BLT, LET) Pharmacokinetics & Pharmacodynamics

Pharmacokinetics

Systemic absorption of topical anesthetics is determined by anesthetic identity and concentration, vehicle, occlusion, application area, contact time, and skin-barrier integrity. Lidocaine free-base permeates the stratum corneum and partitions into cutaneous nerve endings; once in the more aqueous cytoplasm, the equilibrium shifts back to the cationic form which is the active blocking species [becker2012, becker2006]. Lidocaine systemic half-life is approximately 90 minutes; metabolism is hepatic (CYP3A4 and CYP1A2). Prilocaine is the most rapidly absorbed of the common topical anesthetics and the principal contributor to methemoglobinemia in EMLA exposure [russell1997, sinisterra2002].

Tetracaine and benzocaine are ester anesthetics hydrolyzed by plasma butyrylcholinesterase; benzocaine is poorly water-soluble and is therefore typically formulated at high concentrations for compounded BLT-class preparations to drive partitioning into the stratum corneum. McCleskey and colleagues [mccleskey2013] documented measurable serum lidocaine after controlled application of a 23% lidocaine / 7% tetracaine ointment to facial surfaces, demonstrating that high-concentration compounded preparations produce systemic exposure even with controlled application conditions.

Compounded preparations are not bioequivalent to the FDA-approved EMLA, LMX-4, LMX-5, Synera, or Pliaglis products. Vehicle (cream vs gel vs ointment), occlusion, application area, and contact time substantially modify absorption [sobanko2012, kouba2016]. Compounded preparations should not be assumed to produce the published PK of any approved product.

Pharmacodynamics

Onset of cutaneous anesthesia depends on stratum-corneum permeation and varies with product: LMX-4 (~30 minutes) [eichenfield2002], EMLA (~60 minutes under occlusion) [fda_label_emla], Synera (20, 30 minutes with the integrated heating element) [croxtall2010], Pliaglis (20, 30 minutes air-drying) [fda_label_pliaglis], LET (20, 30 minutes under occlusion) [schilling1995, resch1998], and compounded BLT (typically 20, 45 minutes under occlusion in procedural dermatology). Depth of anesthesia depends on contact time, concentration, and occlusion [friedman1999; doshi2003; sobanko2012; kouba2016].

Comparing Compounded Topical Anesthetics (BLT, LET) Formulations

FDA-approved products: EMLA (lidocaine 2.5% / prilocaine 2.5% cream, eutectic mixture, 60-minute application), LMX-4 / LMX-5 (liposomal lidocaine 4% and 5%, OTC, ~30-minute application), Synera (lidocaine 70 mg / tetracaine 70 mg heated patch, 20, 30 minute application), Pliaglis (lidocaine 7% / tetracaine 7% peel-off cream, 20, 30 minute air-dry application) [fda_label_emla; fda_label_lmx4; fda_label_synera; resch1998]. Each has defined application-area and patient-age labeling [doshi2003; railan2007; kouba2016; singer2000].

Compounded products: LET (lidocaine 4% / epinephrine 0.1% / tetracaine 0.5%) solution or gel for laceration repair; BLT (benzocaine 20% / lidocaine 6% / tetracaine 4% with concentration variants) cream for procedural dermatology under provider-administered conditions; custom single-agent or allergen-free preparations for documented excipient sensitivity [fda_label_pliaglis; eichenfield2002; croxtall2010; schilling1995; tayeb2017]. Compounded preparations are not bioequivalent to FDA-approved products [fda_essentially_a_copy, sobanko2012] [friedman1999; eidelman2011].

Compounded Topical Anesthetics (BLT, LET) Storage and Handling

Manufactured EMLA, LMX-4, LMX-5, Synera, and Pliaglis are stored at controlled room temperature (20, 25°C, with excursions permitted to 15, 30°C) per labeling [fda_label_lmx4]. Synera patches are stored in original sealed foil pouches; the iron-air oxidation heating element activates on exposure to air [fda_label_synera, croxtall2010].

Compounded LET solution and gel and compounded BLT cream are stored per pharmacy stability assignment under USP <795>, typically at controlled room temperature with beyond-use dating determined by validated stability data [fda_label_emla; fda_label_pliaglis]. Epinephrine-containing LET is light- and oxidation-sensitive and is dispensed in amber containers with appropriate beyond-use limits [usp_795].

Compounded Topical Anesthetics (BLT, LET) Compounding & Operations

503A compounding

Compounded topical anesthetics are prepared under 503A on patient-specific prescriptions in state-licensed compounding pharmacies [fda503a]. RonanRx prepares nonsterile cutaneous creams, gels, ointments, and solutions per USP General Chapter <795> with documented active ingredient sourcing, gravimetric verification, content-uniformity assessment for compounded batches, and full lot traceability [usp_795]. Each compounded batch is documented per state board of pharmacy retention requirements.

Beyond-use dating, ingredient identity verification, and stability assessment follow USP <795> requirements. Each compounded BLT-class prescription includes a controlled administration plan specifying procedure, application area, contact time, occlusion plan, and removal protocol, consistent with FDA safety communications on compounded topical anesthetics [fda_consumer_2007] and the Kouba 2016 AAD guidelines for office-based dermatologic surgery [kouba2016] [fda503a].

Pharmacist review

Each prescription for a compounded topical anesthetic undergoes pharmacist review prior to dispensing [fda_essentially_a_copy]. The review confirms: a documented patient-specific clinical reason that an FDA-approved EMLA, LMX-4, LMX-5, Synera, or Pliaglis product is not appropriate (procedural depth or duration insufficient; documented excipient sensitivity; application site or age not covered by labeling); for LET prescriptions, the procedural indication (dermal laceration repair) and avoidance of terminal-artery sites; for BLT-class prescriptions, the controlled administration plan (provider-administered, defined area and contact time, removal protocol); absence of contraindications including age-restricted benzocaine in young children, G6PD deficiency, and concurrent oxidant medication [russell1997; sinisterra2002]; and total dispensed mass appropriate to the planned procedural application [fda_label_emla].

RonanRx does not fill prescriptions for compounded high-strength BLT-class topical anesthetics that read as routine at-home use, consistent with FDA safety communications and the documented serious-harm history [fda_consumer_2007; mccleskey2013; sobanko2013]. Prescriptions that do not specify a controlled administration plan are returned to the prescriber for clarification [fda_label_lmx4; fda_label_synera; fda_label_pliaglis].

Quality and traceability

Active pharmaceutical ingredients are sourced from FDA-registered facilities with documented certificates of analysis. Each batch is recorded with lot numbers traceable to API source, compounding date, beyond-use date, and dispensing pharmacist of record. Finished product lot records are retained per state board of pharmacy retention requirements.

Cold chain

Compounded topical anesthetic preparations are room-temperature products in routine practice. LET solutions and gels containing epinephrine are protected from light and stored within manufacturer/pharmacy beyond-use-date limits; refrigeration is used only when pharmacy-validated stability data require it [fda_label_pliaglis]. Manufactured EMLA, LMX-4, LMX-5, Synera, and Pliaglis are room-temperature products [fda_label_emla; fda_label_lmx4; fda_label_synera].

Frequently Asked Questions About Compounded Topical Anesthetics (BLT, LET)

Is compounded BLT the same as EMLA, LMX, Synera, or Pliaglis?

No. EMLA, LMX-4, LMX-5, Synera, and Pliaglis are FDA-approved manufactured topical anesthetics with defined labeling for application area, time, occlusion, and patient age [fda_label_lmx4]. Compounded BLT (benzocaine/lidocaine/tetracaine) is pharmacy-prepared on a patient-specific prescription and is not bioequivalent to any FDA-approved product [fda_label_emla; fda_label_synera; fda_label_pliaglis]. Compounded drugs are not FDA-approved [fda503a].

Why would anyone use compounded BLT when EMLA, LMX, Synera, and Pliaglis exist?

For most needle procedures and superficial dermatologic procedures, the FDA-approved products are appropriate first-line [sobanko2012; railan2007]. Compounded BLT is used in dermatology and aesthetic medicine for procedures where the FDA-approved products do not provide the depth or duration of cutaneous anesthesia required on intact skin, most commonly fractional laser, ablative laser resurfacing, tattoo, and microneedling [doshi2003; kouba2016]. Use is provider-administered with defined application-area and contact-time limits [friedman1999].

Can I take a tube of compounded BLT home and apply it before laser hair removal?

No. RonanRx does not dispense compounded high-strength topical anesthetics for unsupervised at-home application. The FDA has documented patient deaths and serious systemic toxicity following at-home application of compounded BLT-class creams, particularly under occlusion or over large body-surface areas before laser hair removal [fda_consumer_2007]. Provider-administered application with defined area, contact time, and removal protocol is required [mccleskey2013].

What is LET and how is it used?

LET is a compounded combination of lidocaine 4%, epinephrine 0.1%, and tetracaine 0.5%, used as a topical anesthetic for dermal laceration repair in pediatric and adult emergency settings [schilling1995; singer2000; eidelman2011]. It is applied to the wound with a cotton ball or gauze for 20, 30 minutes prior to suturing. Randomized trials and Cochrane systematic reviews support LET as a first-line topical option for laceration repair [resch1998] [tayeb2017]. LET is not used on terminal arteries (fingers, toes, nose, penis, ear pinna).

What are the dangers of compounded topical anesthetics?

The dominant documented hazards are systemic local anesthetic toxicity (light-headedness, seizures, arrhythmia, cardiovascular collapse) and methemoglobinemia (from benzocaine or prilocaine)

[sinisterra2002]. The serious-harm record in the U.S. is concentrated in at-home application of high-strength compounded creams over large body-surface areas under occlusion before laser hair removal [mccleskey2013]. The FDA issued safety communications in 2007 and 2014, and expanded the benzocaine boxed warning in 2018 contraindicating benzocaine sprays and oral products in children under 2 years [fda_consumer_2007].

Why was TAC replaced by LET?

TAC contained cocaine, which is a Schedule II controlled substance subject to DEA regulation, and presented documented toxicity in pediatric use. The Schilling 1995 randomized trial demonstrated equivalent anesthetic efficacy between TAC and LET for pediatric facial and scalp lacerations, with LET preferred on safety, cost, and regulatory grounds [schilling1995; resch1998]. LET is now the modern compounded standard.

Does RonanRx sell compounded BLT directly to patients?

No. Compounded topical anesthetics require a patient-specific prescription from a licensed prescriber identifying the patient and the procedural use, plus pharmacist review before dispensing. RonanRx is not a direct-to-consumer storefront and does not dispense compounded high-strength topical anesthetics for at-home unsupervised application [fda503a; fda_essentially_a_copy].

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How to Access Compounded Topical Anesthetics (BLT, LET)

Compounded Compounded Topical Anesthetics (BLT, LET) is dispensed under 503A on a patient-specific prescription. Depending on your role, the next step looks different.

FOR PRESCRIBING CLINICIANS

Offer this medication

A pharmacist will follow up within two business days. We'll cover state availability, supported formulations, and what integration looks like for your clinic.

ronanrx.com/request-partnership-call

PATIENT WITH A DOCTOR

Receive your prescription

If your doctor has prescribed Compounded Topical Anesthetics (BLT, LET), sign up so we can prepare and ship your medication. The signup wizard collects intake and connects you to the prescribing workflow.

ronanrx.com/patients

PATIENT WITHOUT A DOCTOR

Find a partner clinic

RonanRx prescribes through partner clinics — we don't initiate prescriptions on this site. Read how the referral process works and how to find a partner clinic in your state.

ronanrx.com/find-clinic

Other compounds RonanRx makes

This monograph is one of many in the RonanRx formulary. Every compound below is prepared under 503A on a patient-specific prescription. Browse the full catalog at ronanrx.com/medications and ronanrx.com/peptides, or scan the codes at right for each index.

Medications Peptides

MEDICATIONS (40)

Alpha-Lipoic Acid (ALA) — Antioxidant & mitochondrial
Coenzyme Q10 (CoQ10) — Antioxidant & mitochondrial
Glutathione — Antioxidant & mitochondrial
NAD+ / NMN — Antioxidant & mitochondrial
Compounded Topical Anesthetics (BLT, LET) — Dermatology
Topical Minoxidil — Dermatology
Topical Tretinoin — Dermatology
Compounded Magnesium — Energy & nutritional
Cyanocobalamin — Energy & nutritional
High-Dose Vitamin D — Energy & nutritional
Hydroxocobalamin — Energy & nutritional
Iron (Compounded) — Energy & nutritional
L-Carnitine — Energy & nutritional
Methylcobalamin (B12) — Energy & nutritional
Methylfolate — Energy & nutritional
Anastrozole — Hormone optimization
Clomiphene & Enclomiphene — Hormone optimization
DHEA — Hormone optimization
Estradiol — Hormone optimization
Estriol — Hormone optimization
Human Chorionic Gonadotropin (HCG) — Hormone optimization
Pregnenolone — Hormone optimization
Progesterone — Hormone optimization
Testosterone — Hormone optimization
Compounded Metformin — Metabolic & weight
Compounded Semaglutide — Metabolic & weight
Compounded Tirzepatide — Metabolic & weight
Lipotropic Injection (MIC, MICC) — Metabolic & weight
Low-Dose Naltrexone (LDN) — Metabolic & weight
Naltrexone-Bupropion Combination — Metabolic & weight
Topiramate — Metabolic & weight
Bremelanotide / PT-141 — Sexual health
Compounded Sildenafil — Sexual health
Compounded Tadalafil — Sexual health
Trimix Injection — Sexual health
Compounded Gabapentin — Sleep & recovery
Compounded Melatonin — Sleep & recovery
Compounded T3 (Liothyronine) — Thyroid
Compounded T3/T4 Combinations — Thyroid
Compounded T4 (Levothyroxine) — Thyroid

PEPTIDES (21)

Sermorelin — Available now

Tesamorelin — Available now

AOD-9604 — Growth-hormone axis (under FDA review)

CJC-1295 — Growth-hormone axis (under FDA review)

GHRP-2 / GHRP-6 — Growth-hormone axis (under FDA review)

Hexarelin — Growth-hormone axis (under FDA review)

Ipamorelin — Growth-hormone axis (under FDA review)

MK-677 / Ibutamoren — Growth-hormone axis (under FDA review)

5-Amino 1MQ — Metabolic & longevity (under FDA review)

Epitalon / Epithalon — Metabolic & longevity (under FDA review)

MOTS-C — Metabolic & longevity (under FDA review)

Thymosin Alpha-1 / Thymalin — Metabolic & longevity (under FDA review)

DSIP, Delta Sleep-Inducing Peptide — Neuro & cognitive (under FDA review)

Selank — Neuro & cognitive (under FDA review)

Semax — Neuro & cognitive (under FDA review)

Vasoactive Intestinal Peptide (VIP) — Neuro & cognitive (under FDA review)

BPC-157 — Tissue repair (under FDA review)

KPV — Tissue repair (under FDA review)

LL-37 — Tissue repair (under FDA review)

Pentadeca Arginate (PDA) — Tissue repair (under FDA review)

TB-500 / Thymosin Beta-4 — Tissue repair (under FDA review)