PROVINCIAL STANDARDS & GUIDELINES

BCRenal
Provincial Health Services Authority

Use of Intradermal Lidocaine & Topical Anaesthetics to Ease Cannulation Pain

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Approved by the BCR Hemodialysis Committee

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IMPORTANT INFORMATION

This BC Renal guideline/resource was developed to support equitable, best practice care for patients with chronic kidney disease living in BC. The guideline/resource promotes standardized practices and is intended to assist renal programs in providing care that is reflected in quality patient outcome measurements. Based on the best information available at the time of publication, this guideline/resource relies on evidence and avoids opinion-based statements where possible; refer to www.bcrenal.ca for the most recent version.

For information about the use and referencing of BC Renal provincial guidelines/resources, refer to bcrenal.ca/health-info.

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1.0 Scope

Pain related to cannulation is a significant concern for some patients. This guideline provides recommendations for the use of intradermal lidocaine and topical anaesthetics for the purposes of reducing pain associated with cannulation of fistulas and grafts.

This guideline applies to both adult and paediatric patient populations.

Related Guidelines (BC, Canada and International):

- BC Renal (BCR): Available at BCRenal.ca/health-professionals/clinical-resources/vascular-access#Resources
  - Rope Ladder Cannulation of AV Fistulas and Grafts.
  - Buttonhole Cannulation of AV Fistulas and Grafts.
- Canadian Association of Nephrology Nurses and Technologists (CANNT). Nursing Recommendations for the Management of Vascular Access in Adult HD Patients, 2015 Update. cannt-acitn.ca/en/standards-of-practice/vascular-access-guidelines (available for purchase).
- European Society of Vascular Surgery (ESVS), Vascular Access: Clinical Practice Guidelines, 2018. Available at ejves.com/article/S1078-5884(18)30080-7/abstract (brief mention of anaesthesia in 6.3.1.2. Does not recommend specific agents, but lists options (lidocaine 2.5% and prilocaine 2.5%, intradermal lidocaine injection and coolant sprays)).
- Apart from those identified above, national and international nephrology guidelines make little or no mention of the use of intradermal lidocaine or topical anaesthetics including those published by: National Kidney Foundation (KDOQI CPG for Vascular Access, 2019 Update), UK Renal Association (Vascular Access, 2015, Kidney Health Australia Vascular Access (2013), Canadian Society of Nephrology (Vascular Access, 2012), and Netherlands (Vascular Access, 2007).

2.0 Recommendations & Rationale

Recommendation 1: Consider using topical anaesthetics [lidocaine 2.5%/prilocaine 2.5% (EMLA®) or liposomal lidocaine 4% (Maxilene-4®)] in the following:

1. ***Patients in whom cannulation has been attempted using intradermal lidocaine* and the patient continues to complain of significant pain; or***
2. ***Patients who have small, shallow or young fistulas (difficult to inject intradermal lidocaine®); or***
3. ***Patients who have a severe fear of needles (precluding the use of intradermal lidocaine); or***
4. ***Children ages 19 and under.***

*With the exceptions noted above, intradermal lidocaine should be considered first for cost reasons.

Patients on HD are repeatedly exposed to stress and pain from approximately 300 punctures per year to their arteriovenous fistula (AVF) or arteriovenous graft (AVG). Considerable patient discomfort and stress can be associated with this procedure. Several studies have concluded that cannulation causes mild to moderate pain in HD patients[1, 2]. One study (n=449) reported that 24% of patients had severe pain[3] while another (n=25) estimated that 49% experienced moderate pain and 12% experienced severe puncture-related pain[4]. Therefore, pain control during AVF needling should be a priority in dialysis care.

Some studies have reviewed the use of non-pharmacological strategies to alleviate cannulation pain in HD patients and have been shown to be of benefit. Examples include programmed distraction, aromatherapy and cryotherapy[5,6,7]. Some patients, however, may also require pharmacological strategies, including intradermal lidocaine or topical anesthetics (which will be the focus of the remainder of this guideline).

Rationale for limiting the use of intradermal lidocaine and topical anaesthetics

Many patients do not report experiencing severe discomfort with cannulation and do not require intradermal lidocaine or a topical anaesthetic. Intradermal lidocaine and topical anaesthetics are expensive and there is no published evidence to support widespread or universal use. Moreover, the use of these agents has been associated with transient cutaneous vasoconstriction, which has posed concerns of potentially more difficult venous access8. They have, however, been shown to be effective in patients where significant pain or a fear of needles may be an impediment to successful dialysis.

Topical anaesthetics that have been approved for use in Canada are:

(1) lidocaine 2.5%/prilocaine 2.5% (EMLA®);
(2) liposomal lidocaine 4% (Maxilene-4®); and
(3) tetracaine (Ametop®).

The first two are funded by BCR for patients who meet the specified criteria to support the goal of "fistula first." BCR does not fund the use of tetracaine (AMETOP®); while it is effective, it is higher cost than the other two.

Characteristics of topical anaesthetics & intradermal lidocaine 2%

Refer to Table 1 for an overview and Appendix 1 for a summary of the literature

Table 1: Topical Anaesthetics and Intradermal Lidocaine 2% [8, 9, 10]

Characteristics of Topical Anaesthetics & Intradermal Lidocaine 2%			
	TOPICAL ANAESTHETICS		**Intradermal Lidocaine 2% ampoule (Xylocaine®)**
	Liposomal lidocaine 4% (Maxilene 4®)	**Lidocaine 2.5% / prilocaine 2.5% (EMLA®)**	
When to apply	30+ min prior to cannulation	60 min prior to cannulation	~2 min prior to cannulation
Duration of action	1-2 hrs (> 30 min after removal)	2-3 hrs (1- 2 hrs after removal)	5 min - 1 hr
Pre-cannulation dose [1]	0.5 in (~ size of nickel) onto each needling site, with or without occlusive dressing	0.5 in (~size of nickel) onto each needling site with occlusive dressing	0.2 mL intradermal injection at each needling site
Prescription required?	No	No	No
Availability	5g & 30g tubes	5g & 30g tubes	5mL single use ampoule
Use in children (cautions)	Children < 2 yrs old: Consult a physician	• Contraindicated in pre-term infants (gestational age < 37 weeks). • Contraindicated in infants < 1 yr old if on concurrent drugs which increase the risk for methemoglobinemia (e.g., sulphonamides, other drugs – see product monograph in CPS).	Yes – approved for use in children
Cost /3 months [2]	$55-$60[3] (30 g tube)	$58-$68[i] (30 g tube)	$50 - $55[4] ($1.40/5mL amp) Excludes cost of syringe and alcohol swab –$0.33 per dose

[1] See CPS product monograph for dosing in children.
[2] Supply of topical anaesthetic for outpatient hemodialysis patients is obtained through renal pharmacies in the community and BCR would be charged the retail cost as opposed to the base cost (hospital cost). For intradermal lidocaine, supply is obtained through pharmacy dispensary and BCR would be charged the base cost (hospital cost).
[3] Outpatient supply is obtained through renal pharmacies and is based on retail cost, which varies depending on retailer.
[4] Intradermal lidocaine is supplied by hospital and is based on hospital cost.

Recommendation 2: For patients who meet the criteria for topical anaesthetics, utilize the protocol in tables 2 and 3 for ordering and filling orders.

Table 2: Protocol for Ordering Topical Anaesthetic Cream (Algorithm)

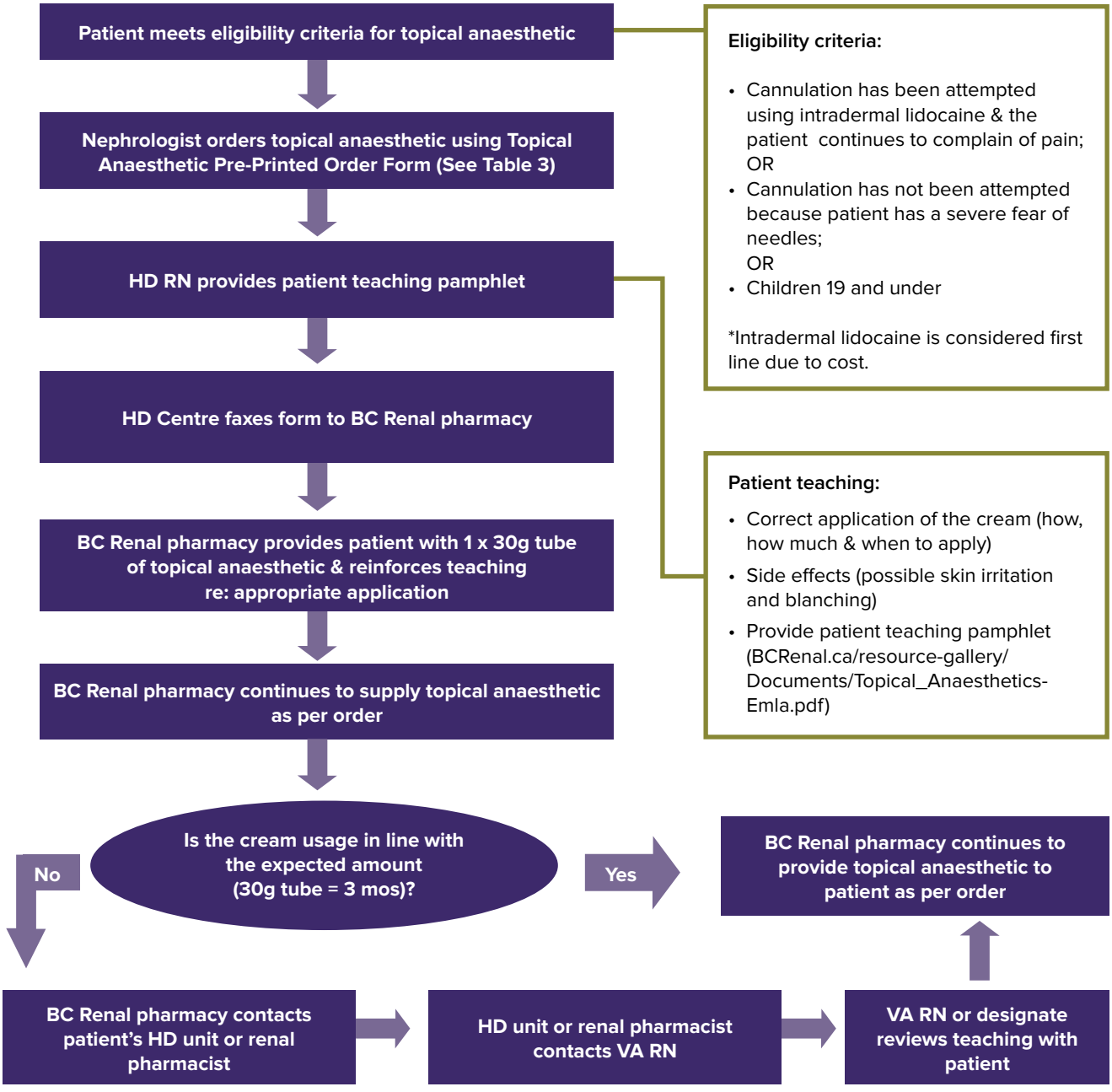

Table 3: Pre-printed Order Form for Topical Anaesthetic Cream (Optional Form)

Add HA/Hospital Logo	Add Label/Addressograph
PRESCRIBER'S ORDERS Refer to Guideline: *Use of Topical Anaesthetic to Ease Cannulation Pain* (www.bcrenal.ca)	

Date and Time	**Topical Anaesthetic Orders: Easing Cannulation Pain** (Items with check boxes must be selected to be ordered) (Page 1 of 1)

Dialysis Modality ☐ In-Center HD ☐ Community HD ☐ Home HD

Rationale for ordering (check all that apply):

- ☐ Cannulation has been attempted using intradermal lidocaine and patient continues to complain of significant pain; OR
- ☐ Patient has a small, shallow or young fistula; OR
- ☐ Patient has a severe fear of needles.
- ☐ Child ages 19 and under

Teaching completed:
RN to provide teaching & teaching sheet to patient re application of topical anaesthetic.

Prescription:

- ☐ Lidocaine 2.5%/prilocaine 2.5% (EMLA®), dispense 1 x 30 g tube.
- ☐ Liposomal lidocaine 4% (Maxilene-4®), dispense 1 x 30 g tube.

Instructions for patients: www.bcrenal.ca (vascular access section)
Apply at least 1 hour before each hemodialysis run.

- ☐ 1. Squeeze about 1.25 cm (0.5 in) of cream or the size of nickel onto the access above or below previous needle sites. Spread the cream along the access.
  2. Cover with a clear plastic wrap.
  OR
- ☐ 1. Place a thick layer of cream on the inside of each cap (nurse to provide cap and ensure metal has been removed prior to giving to patient).
  2. Place the caps onto the access above or below previous needle sites. Secure the caps.

FAX order to the BCPRA pharmacy (fax #: ____-_____).

Enter medication into PROMIS.

_____	_____	_____	_____
Printed Name	Signature	College ID	Pager

Recommendation 3: For patients using topical anaesthetics, provide teaching about the correct application (where to apply, how much and when to apply) and the side effects.

Correct application of a topical anaesthetic maximizes the effectiveness of the medication in reducing needling pain. See BCRenal.ca/resource-gallery/Documents/VA-Use_of_Topical_Anaesthetic_Cann_Pain.pdf for patient teaching pamphlet.

Important points to include in teaching include:

- Timing of application and onset of duration.
- Correct application.
- Side effects: redness /rashes or whitening at the site of the application.

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4.0 Sponsors

Developed by:

1. Vascular Access Working Group of multidisciplinary care providers from across BC (2011 version)
2. Vascular Access Educators Group (updates since 2011 version)

Approved by:

1. BC Renal Hemodialysis Committee (2011 & 2021)
2. BC Renal Pharmacy & Formulary Committee (2011 & 2021)
3. BC Renal Medical Advisory Committee (2011 version; minor updates in 2017 and 2021)

5.0 Appendices

Appendix 1: Summary of the Literature

Appendix 1: Summary of the Literature

Most studies on the use of topical anaesthetics to reduce needling pain have focused on pain associated with venipuncture, particularly in children. Aside from the buttonhole technique, few have focussed on pain associated with cannulation of fistulas and grafts in hemodialysis (HD). The following is a summary of the current evidence to support our recommendations for topical anaesthetics for AVF/AVG cannulation based on literature reviews conducted by BCR vascular access in 2005, 2008 and 2019.

EMLA cream, applied on average 60-90 minutes prior to needling, is an effective topical anaesthetic and the most studied topical agent for reducing pain associated with AVF cannulation in HD. Adverse effects include mild transient skin blanching and, less frequently, allergic contact dermatitis or hypersensitivity reactions.

EMLA has been demonstrated to be more effective than placebo in reducing AVF cannulation pain among adolescents (12 to 18 years old) and adult (≥ 18 years old) HD patients in 4 double-blinded, randomized, placebo-controlled crossover studies and 1 randomized controlled trial (RCT)[4, 11, 12, 13]. Most studies measured pain based on a 100mm visual analogue scale (VAS). In the study by Celik et al (n=41), patients in the EMLA arm reported less moderate pain (9.8% vs. 56.1%, p=0.00) and none reported severe pain (0% vs. 19.5%, p=0.00) compared to placebo4. Overall, mean VAS scores were 33.4± 19.5(0-77) in the placebo arm vs. 10.7± 10.6 (0-44) in the EMLA arm (p=0.00). Similarly, using a 10-point VAS, a median 3-point reduction in pain was seen with EMLA in the RCT[14].

The most commonly reported side effect of EMLA was mild, transient skin blanching, which had an incidence of 16% in the single RCT (n=75)[11]. This effect is thought to be secondary to vascular constriction and has been reported to be temporary and self-limiting in literature[15]. There have been concerns whether repeated EMLA application would result in more difficult subsequent cannulations. However, this has not been established in studies. In a multicentre, prospective observational study in children without renal impairment receiving venepuncture, after single application of EMLA, no difference in successful cannulation at first attempt were noted between EMLA and placebo. Nonetheless, further studies with repeated applications are needed.

Although less common, allergic contact dermatitis or hypersensitivity reactions from EMLA cream have also been reported[4, 13, 16, 17]. Perez-Perez et al. reported a case of allergic contact dermatitis after 5 months of EMLA application, which presented as an itchy, erythematous, and desquamative lesion over the brachial AVF17. Patch testing confirmed sensitivity to prilocaine and symptoms resolved after EMLA withdrawal and topical predcarbinate (corticosteroid) treatment. Other less commonly reported reactions included erythema, itching, burning, edema, and temporary eczematous skin[11].

There is also an increased risk of methemoglobinemia with EMLA® use in patients less than 3 months of

age and less than 1 year of age if on concurrent drugs that increase the risk for methemoglobinemia (e.g. sulfonamides). These adverse effects were not reported in the studies reviewed as young children were excluded from them.

It is important to note that the above studies are limited in study size (n<75 in all efficacy trials) and duration, with most studies involving only 1-3 EMLA applications[11, 12, 18]. Only 2 studies involved repeated EMLA application for 3 months and up to 1.5 years[11, 12].

Comparison of EMLA to other alternatives:

EMLA has been compared to cryotherapy, intradermal lidocaine, as well as other topical anaesthetics. In comparison to piroxicam gel, lidocaine spray, ice pack, and vapocoolant spray, EMLA cream has significantly lower total pain scores during AVF cannulation in crossover studies and 1 RCT[4, 14, 18]. We did not further explore these options given that they are less efficacious than EMLA, commericially unavailable in Canada, and/or more costly.

Intradermal Lidocaine

- ***Intradermal lidocaine has a more rapid onset of action (1-3mins vs. 30-60mins), but may be more costly than EMLA or Maxilene depending on the quantity of topical anaesthetics used (see Table 1)[10, 19].***
- ***Although EMLA has been compared to intradermal lidocaine for AVF cannulation, it is inconclusive whether EMLA is more effective in reducing AVF cannulation associated pain. In general venipuncture of children, effects of the two interventions were comparable.***
- ***Transient skin reactions including itching and skin blanching were more frequently reported with EMLA, but there is insufficient data to comment on differences in long-term adverse effects.***

Only 2 studies have compared EMLA and intradermal lidocaine:

A single crossover study (n=26) by Watson et al. compared EMLA to intradermal lidocaine and concluded that EMLA provided improved ease of insertion of fistula needles and greater pain relief[13]. However, statistical significance in pain reduction with EMLA was only demonstrated at the venous site on a 10-point VAS and no difference was found at the arterial site using VAS or a 3-category verbal rating. Skin reactions were clinically insignificant except for 1 patient who developed severe itching and rash at the EMLA site 10 hours later. Based on this study, it is inconclusive whether EMLA is more effective for AVF cannulation associated pain.

In contrast, general venepuncture of children (7-12 years old) scheduled for minor ambulatory surgical procedures, 0.2mL of 1% intradermal lidocaine was found to be comparable to 2.5g of EMLA in pain reduction20. The study (n=40) also noted mild itching and transient blanching that spontaneously resolved with EMLA. No adverse effects were mentioned for intradermal lidocaine. A limitation of this study is that the pain caused by general venepuncture may

potentially be different from AVF cannulation (e.g. different bore size of needle, the need for cannulation of both arterial and venous sites in close proximity).

Liposomal lidocaine 4% (Maxilene-4®) and tetracaine (Ametop®)

- ***EMLA has not been directly compared to liposomal lidocaine 4% (Maxilene-4®) or tetracaine (Ametop®) for AVF cannulation associated pain.***
- ***Based on studies conducted in venepuncture and other procedures, in comparison to EMLA, liposomal lidocaine 4% has comparable efficacy and tetracaine has superior anaesthetic effects.***
- ***Liposomal lidocaine 4% has a faster onset (30mins), lower cost (see Table 1), and possibly lower incidence of skin blanching compared to EMLA.***
- ***Tetracaine also has a faster onset (30mins) and is more effective, but is significantly more costly, requires refrigeration, and may cause more erythema. It may be a more favourable option for young children due to its lack of association with methemoglobinemia. Its significantly higher cost and need for refrigeration are factors that may limit its role as a first-line option.***

In a systematic review of RCTs (n= 2096) that examined children (3 years and older) and adults who received venepuncture, liposome-encapsulated lidocaine was found to have comparable analgesic efficacy to EMLA while tetracaine had more favorable anaesthetic effects over EMLA[21]. This systematic review did not report on adverse effects.

A second systematic review comparing tetracaine to EMLA, also demonstrated superiority of tetracaine to EMLA in intravenous cannulation, venipuncture, Port-a-Cath puncture, and laser therapy when both agents were applied for the same duration[22]. Moreover, it found that tetracaine was more commonly associated with erythema, likely due to its vasodilatory effects, while EMLA was more associated with skin blanching.

Among 3 double-blinded RCTs and crossover studies in pediatrics (1 month to 17 years old), only 1 RCT found similar incidence of adverse effects between liposomal lidocaine 4% and EMLA, which included blanching, erythema and itchiness[23]. The other 2 studies found that EMLA caused more skin blanching, particularly when it was occluded, but there was no difference in anaesthesiologist's rating of the difficulty of IV insertion[24, 25].

Although the above evidence is based on large patient populations, extrapolation of anaesthetic effects from other venepuncture procedures can potentially result in a different degree of pain stimulus than that of AVF cannulation.