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NOTICE: DISCONTINUATION OF TILIDINE DROPS AND RECOMMENDED THERAPEUTIC ALTERNATIVES-UPDATED

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The Paediatric Hospital Level (2017 edition) Standard Treatment Guidelines (STGs) and Essential Medicines List (EML) currently recommends the use of sublingual tilidine (Valoron®) drops in children for a number of indications.

Tilidine is a weak opiate indicated for moderate to severe pain in children. There is often irrational fear of prescribing opiate analgesia, however it is important that this be addressed with clinicians, as children are vulnerable to inadequate pain management. Pain scoring tools for assessment of pain severity (NIPS/R-FLACC or Numerical Rating Scale) must be utilised so that an accurate diagnosis of pain can be made to guide appropriate therapy.

The sole supplier in South Africa is discontinuing the production of tilidine drops. The recommended therapeutic alternative for oral tilidine drops is outlined below:

Paediatric Hospital Level (2017): Chapter	Indications	Current recommendation in STGs and EML	Therapeutic alternative to tilidine drops*
Chapter 3: Blood and Blood Forming Organs	Haemophilia A and B – Moderate Pain	» Tilidine, oral, 1 mg/kg/dose (1 drop per 2.5 kg 6 hourly)	• Morphine, oral » If 0–1 month of age: 0.05 mg/kg 6 hourly » If > 1–12 months of age: 0.05 – 0.2 mg/kg/dose 4-6 hourly » If > 12 months of age: 0.2–0.4 mg/kg/dose 4-6 hourly
Chapter 20: Pain	Procedure associated with moderate pain	• Tilidine, sublingual, 1 mg/kg 45 minutes before procedure **OR** • Morphine, oral, 0.1-0.3 mg/kg 30 – 60 minutes before procedure **OR** • Ketamine, oral 4-6 mg/kg in a sweet drink 30 minutes before procedure	• Ketamine, oral 4-6 mg/kg in a sweet drink 30 min before procedure **OR** • Morphine, oral • If 0–1 month of age: 0.05 mg/kg 6 hourly • If > 1–12 months of age: 0.05 – 0.2 mg/kg/dose 4-6 hourly • If > 12 months of age: 0.2–0.4 mg/kg/dose 4-6 hourly Morphine, 30–60 minutes before procedure *To be used together with simple analgesia: oral paracetamol and oral ibuprofen (see STGs and EML for doses)*

Paediatric Hospital Level (2017): Chapter	Indications	Current recommendation in STGs and EML	Therapeutic alternative to tilidine drops*
	Management of Pain (intermediate efficacy opioid)	• Tilidine, oral, 6 hourly. » 1 drop per 2.5 kg of body weight (*i.e.* 1 mg/kg/dose)	• Morphine, oral » If 0–1 month of age: 0.05 mg/kg 6 hourly » If > 1–12 months of age: 0.05 – 0.2 mg/kg/dose 4-6 hourly » If > 12 months of age: 0.2–0.4 mg/kg/dose 4-6 hourly
Chapter 22: Anaesthesia	Post-operative analgesia – Moderate Pain	• Tilidine, oral, 1 mg/kg/dose (i.e. weight (kg) divided by 2.5 = number of drops) 6-hourly	• Morphine, oral » If 0–1 month of age: 0.05 mg/kg 6 hourly » If > 1–12 months of age: 0.05 – 0.2 mg/kg/dose 4-6 hourly » If > 12 months of age: 0.2–0.4 mg/kg/dose 4-6 hourly

**Morphine dosing in line with British National Formulary for Children 2021-2022.*

Oral Morphine extemporaneous preparation:

There is a lack of robust data on extemporaneous formulations for neonates and infants with available excipients and formulations in South Africa. It is thus recommended that for this group of patients a diluted morphine intravenous formulation be used orally (in consultation with specialists in units and your pharmacy department).

e.g. Add 1ml of 10mg/ml IV solution to 9ml normal saline (preservative-free), to make 1mg/ml concentration. (To be stored in fridge for no longer than 7 days)

For older children and adolescents the following formulation can be considered:

**NEMLC approved formulation listed in Adult Hospital Level STGs and EML, Appendix IV: extemporaneous compounding*

Morphine 0.1% (10mg/ml) solution

Formula:

Morphine hydrochloride/sulphate	50 g
Benzoic acid solution 5%	100 ml
Sorbitol 70%	1.5 L
Sterile water	add to 5000 ml

Benzoic acid solution 5%:

Benzoic acid	50 g
Propylene glycol	750 ml
Hot sterile water	add to 1000 ml

Preparation:

Dissolve the morphine in approximately 2000 ml of the purified water. Dissolve the benzoic acid solution 5% in this solution. Add the 70% sorbitol solution and a sufficient quantity of purified water to a volume of 5000 ml and mix well.

To make the benzoic acid 5% solution: Dissolve the benzoic acid in the propylene glycol, adding the hot purified water to a volume of 1000 ml.

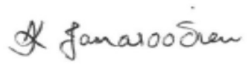
Declaration:

Active ingredient: Morphine hydrochloride/sulphate 10 mg per ml
Dosage form: Oral solution
Excipients: Benzoic acid, propylene glycol, sorbitol, purified water

Storage: Glass amber bottle, below 25 °C with an expiry date of 6 months. Quality requirements Identity: as stated under the section "Declaration", above. Content morphine hydrochloride: 90–110% of the declared amount, calculated as the pure substance. pH: ≤ 4 Appearance: The solution is clear and almost free of visible particles.

Provinces and Healthcare Facilities are requested to distribute and communicate this information in consultation with the Pharmaceutical and Therapeutics Committees. Kindly share with all healthcare professionals and relevant stakeholders.

Kind regards



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