Amethocaine (Tetracaine)

Newborn use only

2022

Alert	Prolonged ophthalmic use is not recommended due to risk of severe keratitis and corneal adverse effects. Safety data is lacking and therefore use the lowest concentration available.
Indication	Local anaesthesia for eye examination (including RetCam) and procedures (laser) in newborn infants in conjunction with other pharmacological and/or non-pharmacological analgesic methods.
Action	Local anaesthetic.
Drug type	Ester-type local anaesthetic.
Trade name	Minims Amethocaine Eye Drops (Tetracaine (amethocaine) hydrochloride)
Presentation	Single use eye drops 0.5% (5 mg/mL), 1% (10 mg/mL) approximately 0.5 mL.
Dose	One drop each eye as required 1–5 minutes prior to examination. Further drops may be needed to achieve a complete anaesthetic effect
Dose adjustment	No information.
Maximum dose	No information.
Total cumulative dose	
Route	Topical instillation into the eyes from the container or use a microdrop (5–7 microL) cannula.
Preparation	Not required
Administration	Apply pressure to the lacrimal sac during and for 60 seconds after instillation of eye drop to minimise systemic absorption. Wipe away excess medication. Normal corneal sensitivity can be expected after approximately 1 hour of administration.
Monitoring	
Contraindications	Hypersensitivity to any of the components of the preparation. Eye infection.
Precautions	The cornea may be damaged by prolonged or frequent application of anaesthetic eye drops. Prolonged use of topical ophthalmic local anaesthetics has been associated with severe keratitis and permanent corneal opacification and scarring with accompanying reduction of visual acuity or visual loss. Systemic toxicity typical of local anaesthetics could occur if sufficient amounts were absorbed systemically. Systemic absorption of tetracaine (amethocaine) may be reduced by compressing the lacrimal sac at the medial canthus for a minute during and following the instillation of the drops
Drug interactions	Metabolism may be inhibited by anticholinesterases with prolongation of the effects of tetracaine (amethocaine). May competitively enhance the neuromuscular blocking action of suxamethonium.
Adverse reactions	Local burning and stinging sensation. Blurred vision, keratitis, hyperaemia, lacrimation and allergic conjunctivitis. Systemic (if systemic absorption occurs) – Rare. Apnoea, cardiac arrest, ventricular arrhythmias, irritability and excitation. Prolonged ophthalmic use may lead to severe keratitis and corneal adverse effects (13). For decontamination after eye exposure, irrigate eyes with sodium chloride 0.9%.
Compatibility	Cyclopentolate, phenylephrine, tropicamide
Incompatibility	No information.
Stability	Discard immediately after use.
Storage	Store at 2°C to 8°C. (Refrigerate. Do not freeze.) Protect from light. Each Minims unit should be discarded after a single use.
Excipients	Hydrochloric acid and purified water. No preservatives.
Special comments	Not approved for use in preterm infants by FDA (Food and Drug Administration of USA) in view of the immaturity of the enzyme system that metabolises the ester type of local anaesthetic (14). The American Academy of Ophthalmology in January 2013 suggested the use of proparacaine to assess premature infants (15). Proparacaine is not registered in Australia. Consensus among Australian ophthalmologists during the development of this formulary was to continue to use tetracaine (amethocaine) as no reported adverse effects in neonates in Australia.
Evidence	**Efficacy:** Retinopathy of prematurity screening is a painful and stressful procedure (1-2). No clinical trial has assessed the effect of tetracaine (amethocaine) topical eye drops in newborn infants undergoing eye examination for ROP. Three RCTs in newborn infants evaluated the effects of topical anaesthetic eye drops (proparacaine HCL 0.5% ophthalmic solution) during ROP examination (3-5). Proparacaine eye drops prior to examination were found effective in reducing pain responses and/or the

	number of infants with high pain scores on eye examination. However, the effect was not great and a substantial proportion of infants still had high pain scores. Another RCT compared topical anaesthetic eye drops (proparacaine HCL 0.5% ophthalmic solution) to oral sucrose during ROP examination. (6) There was no difference between pain scores. Three systematic reviews found that although there is evidence that topical eye anaesthetic reduces pain, its effect is incomplete and screening remains a painful procedure (7). No single pain intervention is optimal for ROP examination, a multi-modal approach involving a topical anaesthetic and multisensory interventions is required (8, 9). **Conclusion:** Pain Study Group of the Italian Society of Neonatology 2009 recommended, in the case of RetCam screening, applying local anaesthesia with oxybuprocaine 0.4% or tetracaine (amethocaine) 1% eye drops. For laser therapy for ROP, in general, combine a local anaesthetic with a general anaesthesia (10). **Safety:** There are no safety data for the use of topical amethocaine eye drops in newborn infants. Systematic review of the use of topical tetracaine (amethocaine) gel 4% for procedural pain in newborn infants found three studies reported a statistically significant reduction in pain compared to placebo during venepuncture and one study reported a statistically significant reduction in pain compared to placebo during cannulation (11). One study reported no statistical difference between the two groups during intramuscular injection. There was no increased risk of local redness, swelling or blanching after use of tetracaine (amethocaine) gel. In adults, instillation of tetracaine (amethocaine) eye drops had a longer and more severe duration of stinging than proxymetacaine 0.5% eye drops (12). Prolonged ophthalmic use may lead to severe keratitis and corneal adverse effects (13). **Pharmacokinetics/pharmacodynamics:** No pharmacokinetics reported in newborn infants. Onset of anaesthesia after instillation into the eye is 10 to 20 seconds, and duration of anaesthesia is 10 to 20 minutes (Minims Amethocaine Eye Drops product information).
Practice points	
References	1. Avila-Alvarez A, Pertega-Diaz S, Vazquez Gomez L, et al. Pain assessment during eye examination for retinopathy of prematurity screening: Skin conductance versus PIPP-R. Acta Paediatr. 2020 May; 109(5):935-942. 2. Moral-Pumarega MT, Caserío-Carbonero S, De-La-Cruz-Bértolo J. et al. Pain and stress assessment after retinopathy of prematurity screening examination: indirect ophthalmoscopy versus digital retinal imaging. BMC Pediatr. 2012 Aug 28; 12:132. 3. Cogen MS, Parker JS, Sleep TE, Elsas FJ, Metz TH, McGwin G. Masked trial of topical anesthesia for retinopathy of prematurity eye examinations. Journal of American Association for Pediatric Ophthalmology and Strabismus 2011; 15(1):45-8. 4. Marsh VA, Young WO, Dunaway KK, Kissling GE, Carlos RQ, Jones SM, Shockley DH, Weaver NL, Ransom JL, Gal P. Efficacy of topical anesthetics to reduce pain in premature infants during eye examinations for retinopathy of prematurity. Annals of Pharmacotherapy 2005; 39(5):829-33. 5. Mehta M, Mansfield T, VanderVeen DK. Effect of topical anesthesia and age on pain scores during retinopathy of prematurity screening. Journal of perinatology 2010; 30(11):731-5. 6. Nesargi SV, Nithyanandam S, Rao S, Nimbalkar S, Bhat S. Topical anesthesia or oral dextrose for the relief of pain in screening for retinopathy of prematurity: a randomized controlled double-blinded trial. Journal of tropical pediatrics 2014; 61(1):20-4. 7. Dempsey E, McCreery K. Local anaesthetic eye drops for prevention of pain in preterm infants undergoing screening for retinopathy of prematurity. Cochrane Database of Systematic Reviews 2011. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007645.pub2/abstract. 8. Francis K, Gephart S. What Is Best Practice for Providing Pain Relief During Retinopathy of Prematurity Eye Examinations? Advances in Neonatal Care 2016; 16(3):220-8. 9. Disher T, Cameron C, Mitra S, Cathcart K, Campbell-Yeo M. Pain-Relieving Interventions for Retinopathy of Prematurity: A Meta-analysis. Pediatrics. 2018 Jul; 142(1):e20180401. 10. Lago P, Garetti E, Merazzi D, Pieragostini L, Ancora G, Pirelli A, Bellieni CV. Guidelines for procedural pain in the newborn. Acta Paediatrica 2009; 98(6):932-9. 11. Foster JP, Taylor C, Spence K. Topical anaesthesia for needle-related pain in newborn infants. The Cochrane Library. 2017 Jan 1. 12. Shafi T, Koay P. Randomised prospective masked study comparing patient comfort following the instillation of topical proxymetacaine and amethocaine. Br J Ophthalmol 1998; 82:1285-7. 13. Micromedex solutions. Tetracaine. Accessed on 17 February 2022.

	14. MIMS Online. Tetracaine (Amethocaine) Hydrochloride. Accessed on 13 December 2017. 15. American Academy of Pediatrics Section on Ophthalmology. Screening examination of premature infants for retinopathy of prematurity. Pediatrics. 2013; 131(1):189-95

VERSION/NUMBER	DATE
Original 1.0	13/03/2018
Revised 2.0	17/02/2022
REVIEW	17/02/2027

Authors Contribution

Original author/s	David Osborn
Current review	Nilkant Phad
Evidence Review	David Osborn, Nilkant Phad
Expert review of the original	Mark Jacobs, Hughie Tsang, Kimberley Tan
Nursing Review	Eszter Jozsa, Priya Govindaswamy, Sarah Neale
Pharmacy Review	Jing Xiao
ANMF Group contributors	Srinivas Bolisetty, Bhavesh Mehta, John Sinn, Mohammad Irfan Azeem, Simarjit Kaur, Carmen Burman, Helen Huynh, Thao Tran, Hannah Bell, Michelle Jenkins, Lisa Kremer
Final editing of the original	Ian Whyte
Electronic version	Cindy Chen, Ian Callander
Facilitator	Srinivas Bolisetty