


Alert	<p>Only small, superficial (flat to raised 5 mm above the surface) infantile haemangiomas (IH) of less than 10 mm size (maximum 50 mm) respond to topical timolol.</p> <p>Timolol is not to be applied on ulcerated areas.</p> <p>If timolol is commenced less than 5 weeks post-term, infant needs to be monitored as if on oral beta-blocker to ensure no bradycardia, hypoglycaemia or hypotension, especially with any intercurrent illnesses.</p> <p>Use timolol 0.5% (5 mg/mL) preparation for this particular indication.</p>
Indication	<p>Topical treatment of small, superficial infantile haemangiomas (IH) of less than 5 cm in diameter.</p>  <p>(With permission from Prof Orli Wargon, Sydney Children's Hospital)</p>
Action	<p>Non-selective β_1 and β_2 adrenoceptor antagonist. Hypothesised mechanisms of action include decreased nitric oxide and vasoconstriction early during treatment; blockage of pro-angiogenic signals (e.g. vascular endothelial growth factor and basic fibroblastic growth factor) in the intermediate term, causing arrest of IH growth; and finally, induction of apoptosis causing IH regression (Chambers 2012). Local experience suggests better response in flatter lesions.</p>
Drug Type	Nonselective β adrenoceptor antagonist.
Trade Name	Nyogel Eye gel [Aspen Pharma], Tenopt Eye drops [Aspen], Timoptol Eye drops [Mundipharma], Timoptol-XE Gel forming eye drops [Merck Sharp & Dohme]
Presentation	Timolol maleate 0.5% (5 mg/mL) ophthalmic solution/gel.
Dosage/Interval	1 drop twice daily from 5 weeks post-term up to 24 weeks or longer at patient/clinician discretion, depending on the IH progression.
Route	Topical
Maximum Daily Dose	2 drops
Preparation/Dilution	
Administration	<p>Rub the solution into the area twice daily and spread it gently with a glove coloured finger to cover the entire lesion. Parents can use ungloved finger and wash with soap and water after application.</p>
Monitoring	<p>If treatment is commenced 5 weeks post-term, usually well tolerated with no specific routine monitoring required.</p> <p>If treatment is to be commenced before 5 weeks post-term, monitor blood pressure, heart rate, respiratory rate, blood glucose, and electrocardiograph at the screening visit and then every 2–4 days until 5 weeks post-term or at the discretion of the clinician.</p>
Contraindications	Ulceration of the lesion. Application on mucous membranes.
Precautions	Less than 5 weeks post-term
Drug Interactions	Co-administration with systemic beta-blocker (e.g. propranolol) may exacerbate the side effects of beta-blockade.
Adverse Reactions	Very rare. Bradycardia, hypotension, hypoglycaemia.
Compatibility	Not applicable.
Incompatibility	Not applicable.
Stability	Discard within 28 days of opening.
Storage	Preferably refrigerate after opening. However it can be stored in room temperature.
Special Comments	Thick or deep lesions are likely to require systemic treatment.
Evidence summary	<p>Infantile hemangiomas (IHs) are common paediatric lesions. Topically administered β adrenoceptor antagonists are an effective treatment for uncomplicated, superficial IHs. (LOE I, GOR B)(Ovadia SA 2015⁹).</p> <p>In Ovadia et al's systematic review, on superficial IHs response rates for topical propranolol and topical timolol were not significantly different, 76% and 83% respectively (P = 0.45).⁹</p>

	<p>Prospectively conducted studies reported lower response rates compared to retrospective studies for both topical propranolol ($P = 0.06$) and topical timolol ($P < 0.01$). When only prospectively conducted studies were included, response rates for topical propranolol and topical timolol were not significantly different, 72% and 72% respectively ($P = 0.98$). Significant adverse effects were rare. Only 1 case of sleep disturbance was reported across 554 patients from all studies. The strength (0.1% to 0.5%), dose (daily to 5 times a day) and duration of treatment (fixed duration or based on IH progression) varied among the studies.</p> <p>The only randomised, placebo-controlled trial on timolol was performed by Chan et al in infants aged 5 to 24 weeks and indicates that up to 2 drops per day of topical timolol maleate 0.5% gel for 24 weeks' duration is a safe and effective therapy for the treatment of IH not requiring systemic treatment.¹⁶ The onset of action appears to be slower than oral propranolol chloride with significant improvements in absolute volume reduction, proportional growth and clinical appearance noted only after 12 to 16 weeks. The efficacy of topical timolol maleate 0.5% gel appears to be more pronounced for lesions with a mean diameter of < 11.3 mm (i.e. < 100 mm³ in volume). The side-effect profile of topical timolol maleate 0.5% gel in the 5- to 24-week age group is favourable, with no significant differences in heart rate or blood pressure.</p>
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