INDICATION

1.1 **Background**: Infantile haemangiomas are the most common benign tumour of infancy, affecting 5-10% of the population. They have a predictable natural history, with a proliferative phase occurring over several months after birth, then a gradual involution over several years. In 90% of cases, they require no treatment as they regress leaving no long-term scarring. In 10% of cases, their location can lead to serious or life-threatening complications, and it is this group of patients where intervention is required.

1.2 **Who to treat?** Infants and children with complicated haemangiomas. This includes haemangiomas around the eyes (which may impair visual development if left to involute spontaneously) or ulcerative lesions.

Children with large haemangiomas are at potential risk of developing decompensated cardiac failure when being treated with propranolol and should be referred to a paediatric cardiologist for assessment prior to commencing treatment.

Children with airway haemangiomas would be managed by tertiary paediatric respiratory and ENT specialists.

Uncomplicated haemangiomas resolve spontaneously, and treatment in these children is not justified, given the risk of side effects of propranolol.

AREAS OF RESPONSIBILITY FOR SHARED CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of propranolol can be shared between the specialist setting and the patient's GP (if different). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.
REFERRAL AND INITIATION

1.1 **Treatment:** There are currently no gold standards for systemic treatments of haemangiomas. Previously, treatments including systemic or intra-lesional corticosteroids, α-interferon, vincristine, laser therapy and surgical resection have been used, but there are no comparative studies of their effectiveness.

Haemangioma endothelial cells express β2 adrenergic receptors, and propranolol is thought to work by a combination of vasoconstriction, inhibition of angiogenesis and induction of apoptosis. There are several small studies and case series showing favourable results of haemangioma reduction or resolution with oral propranolol treatment. Given that propranolol has a more favourable side effect profile than other treatments (especially systemic steroids), oral propranolol is increasingly being used as first-line therapy.

1.2 **Commencing Oral Propranolol Treatment:** Patients under 2 years of age should be admitted electively to the paediatric day ward for 4 hours of monitoring, unless there are specific additional concerns that need admission (e.g. PHACES/parental literacy issues or issues with administering medication) though the decision on the type of admission rests with the admitting consultant. If this monitoring period is acceptable, the child may go on home leave, to return the next week for the dose increase and a further 4 hours of monitoring. Patients 2 years of age or over should be admitted as a day case to the paediatric day ward for 4 hours of monitoring.

All patients should undergo a full history and examination and an ECG taken and examined prior to treatment starting. Children should be well – those with an inter-current illness are at increased risk of hypoglycaemia from propranolol. Children have their heart rate, blood pressure and blood sugar monitored as treatment commences.

1.3 **Stopping treatment:** Treatment is usually continued for up to 6 months with a clinical review every month, but longer courses may be needed.

Propranolol should be temporarily discontinued during inter-current illness or reduced calorie intake due to the risk of hypoglycaemia.

On stopping propranolol at the end of treatment, the dose should be tapered off over 2-4 weeks to prevent a rebound tachycardia. Propranolol may need to be discontinued if children develop bronchospasm on treatment (usually those with an atopic tendency).

### Specialist Responsibilities

<table>
<thead>
<tr>
<th>No.</th>
<th>Task</th>
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<tbody>
<tr>
<td>1</td>
<td>Diagnose haemangioma needing treatment</td>
</tr>
<tr>
<td>2</td>
<td>Initiate treatment and prescribe first treatment course</td>
</tr>
<tr>
<td>3</td>
<td>Ensure treatment is undertaken for 6 months with a clinical review every month (but longer courses may be needed).</td>
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<tr>
<td>4</td>
<td>Monitor response and communicate with GP</td>
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### General Practitioner Responsibilities

<table>
<thead>
<tr>
<th>No.</th>
<th>Task</th>
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<tr>
<td>1</td>
<td>Prescribe ongoing propranolol 5mg/5ml and liaise with secondary care if any queries</td>
</tr>
<tr>
<td>2</td>
<td>Maintain awareness of reviews and discontinue when advised to.</td>
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</table>
**Monitoring**
Pre-treatment photography may be required so that success of treatment can be monitored – this will be determined by the dermatology or ophthalmology team managing the patient.

**Dosage and Administration**
Children under 2 years of age commence therapy at \(1\text{mg/kg/day}\) divided into 8 hourly doses and increase to \(2\text{mg/kg/day}\) divided into 8 hourly doses after a week if tolerated. Children 2 years of age or over can start at \(2\text{mg/kg/day}\) divided into 8 hourly doses directly.

Propranolol for young children is given as a liquid. The liquid is usually given as a 5mg/5ml strength. Propranolol can come in higher strengths of liquid so ideally any strength other than 5mg/5ml should be avoided to minimize the risk of giving the wrong dose.

**Cautions + Contraindications to Propranolol Treatment:**

- Caution needed if history of asthma or bronchospasm, or existing diabetes.
- Contra-indicated if marked bradycardia, hypotension, second- or third-degree AV block, uncontrolled heart failure, metabolic acidosis, severe peripheral arterial disease, phaeochromocytoma.

**Side effects**
Propranolol has a well-documented safety and side effect profile, after its long-term use in children with cardiovascular problems. The most serious side effect is hypoglycaemia, which can be exacerbated by illness, or preceding treatment with systemic steroids prior to starting propranolol. It can cause either hypo- or hyper-glycaemia in children with or without diabetes. Bradycardia and hypotension rarely cause symptoms in therapeutic doses but can cause problems in overdose.
Other side effects include diarrhoea, sleep disturbance (nightmares), fatigue, coldness of the extremities and rashes.

**Interactions: please see BNF for children**

This list is not exhaustive. The manufacturer’s summary of product characteristics (SPC) and the most current edition of the British National Formulary should be consulted for full information on contra-indications, warnings, side-effects and drug interactions.

**Patient Information:** see Appendix 1

**Drug costs:**
Propranolol 5mg/5ml oral solution sugar free: 150 ml prescription only medicine
No NHS indicative price available: Drug Tariff (Part VIII A Category A) price = £23.51
References


Minutes from the Paediatric Clinical Governance meeting, and Haemangioma Audit presentation Oct 2016, and from Drugs and Therapeutics Apr 2018
Appendix 1: Patient Information

Treating Haemangiomas with Propranolol

What are Infantile Haemangiomas?

Haemangiomas (also known as strawberry birthmarks) are very common, affecting around 5 in 100 babies. They are a benign overgrowth of blood vessels in the skin which usually enlarge quite rapidly over the first 3 months and then stop growing by around 6-12 months of age. Haemangiomas naturally shrink slowly over 5 or more years and usually only a small patch of extra skin or normal skin is left by 7 years of age. Most haemangiomas do not need treatment but some can cause problems, for instance those around the eye, which can affect the baby’s vision, or haemangiomas around the mouth that may interfere with feeding. In these babies, we prefer to treat the haemangioma with propranolol and this leaflet explains what the treatment involves.

What is propranolol?

Propranolol is a type of medication called a beta-blocker. It has traditionally been used in the treatment of a fast heart rate or high blood pressure, but it has also been found to be very effective at reducing the size of haemangiomas more quickly than if no treatment is given. Most children and babies do not have any side effects with propranolol at all but it may rarely cause the following problems:

- Low blood pressure
- Low heart rate
- Low blood sugar
- Worsening of asthma, coughing or wheeze
- Sleep disturbance
- Cold extremities
- Constipation

If you have any concerns about these side effects, please discuss them with your doctor, nurse or pharmacist.

What will happen when my child starts treatment?

We will assess your child before starting propranolol and will ask you to stay in hospital for a period of observation when the medication is started.

You will be given a date to bring your child to the Paediatric Day Case unit. Children under 2 years old will need to come in for around half a day for their first dose and again on the following week for a dose increase. Children over 2 years will come in for half a day.

When you come to the Paediatric Day Case unit, your child will be weighed, have a blood pressure and heart rate check, and have a finger-prick or heel-prick blood test to check the blood sugar. They will be seen by one of the paediatric doctors, who will discuss any other medical problems, and examine your child.

They will then have the first dose of the medicine, which is a liquid. Following this dose they will have regular blood pressure, heart rate and blood sugar checks. If there are no problems, your child will be allowed home, for you to give the second and third doses of the day. If they are over two years, they will then continue the medicine at home 3 times a day. If they are under 2 years of age, your child will need to continue on the starting dose at home.
3 times a day for a week to ensure they tolerate the medication, and then come back to repeat the process with a higher dose the following week. If there are problems with the first dose they may need to stay a little longer and have further blood pressure/blood sugar checks. A few children may not be able to tolerate propranolol in which case the medicine would be stopped.

**How is propranolol taken?**

Propranolol is usually given by mouth three times a day.

Propranolol can cause low blood sugar particularly in very young babies. To avoid this, give the medicine with a feed and we would advise giving at least 2oz of milk with the evening dose. Babies should have a milk feed during the night. If your child is unwell and not eating/feeding you should not give propranolol until they are feeding again.

Your child should not have the anti-wheezing medicine salbutamol (by inhaler or nebuliser) while taking propranolol as the two medicines have opposing effects.

Teething gels containing lignocaine should not be given to babies taking propranolol. Some pharmacies sell teething powders that do not contain lignocaine and are safe. Paracetamol does not react with propranolol so can be given safely according to the instructions on the bottle.

Always check with your doctor or pharmacist before giving your child any other medicine, including medicines on prescription from your family doctor (GP), medicines bought from a pharmacy (chemist) or any herbal or complementary medicines.

**What dose is given?**

Your child’s dose of propranolol is worked out based on their weight, and is likely to increase as your child grows. Propranolol for young children is given as a liquid. The liquid is usually given as a 5mg/5ml strength (meaning that 5ml of liquid contains 5mg of propranolol). Propranolol can come in higher strengths of liquid so ideally any strength other than 5mg/5ml should be avoided to minimize the risk of giving the wrong dose. **It is very important to check the dose with the pharmacist** if you are receiving a new bottle of medicine. If you are unsure about the correct dose to give, please check with your doctor.

**What happens next?**

You are likely to notice an improvement in the appearance of the haemangioma within a few days of starting propranolol, however it can take some months to see the full effect of treatment. The treatment works for most but not all children with haemangiomas. Treatment is usually given for around one year and is then gradually weaned down over a period of 2-4 weeks at the end of the course.

If you have any queries or concerns, please ring your consultant, or the paediatric day assessment unit on 01202 442613.