LRI Children's Hospital

Treating Infantile Haemangiomas (IH) with Oral Propranolol Guidelines

Staff relevant to:	Medical & Nursing staff working within UHL Children's Hospital
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1. Introduction and who this guideline applies to

Infantile hemangiomas (IH) are the most common vascular tumors, affecting around 4% of infants. They are more common in premature or low birth weight infants, females and those from White ethnicities. Placental anomalies are an important risk factor. IH typically appear in the first few weeks of life and grow rapidly for the first few months. Thereafter, slow proliferation can continue for up to 6-12 months. Due to their spontaneous involution, the majority of IH do not require treatment. Nonetheless, about 15% of IH result in complications, such as **obstruction, ulceration, or disfigurement**, and then require therapeutic intervention. In 2008, the first report of the successful use of propranolol radically changed the treatment of IH and since then propranolol has become the first-line therapeutic agent in the management of complex IH. Studies have shown that propranolol is a safe and effective treatment for IH in most patients.[1]

Note: If there is any clinical doubt about the diagnosis (i.e., IH versus congenital hemangiomas), please arrange with the Plastics Team for a biopsy to be taken to check if GLUT1 is positive (which is the case in IH).

2. Initiating Treatment with Oral Propranolol

2a. Criteria for oral propranolol therapy

At least one of the following:

1. Vision compromise
2. Airway IH with potential or actual airway compromise
3. Nasal IH with actual or potential obstruction
4. Lip IH causing potential or actual functional impairment and/or disfigurement
5. Involvement of the auditory canal causing recurrent infection
6. Ulcerated IH, especially where topical treatment would not be appropriate or has not been effective
7. Risk of permanent disfigurement
8. Spinal cord compression by IH
9. Liver IH in conjunction with cutaneous IH in selected cases in collaboration with other specialists

Absolute contra-indications:

1. Recent or on-going hypoglycemic episodes
2. Second- and third-degree heart block
3. Hypersensitivity to propranolol hydrochloride

Relative contra-indications:

1. Frequent wheezing
2. Blood pressure outside normal range for age – treatment in conjunction with paediatrician
3. HR outside normal range for age – treat in conjunction with paediatrician

If the patient is suitable for oral propranolol therapy:

1. Discuss treatment with parents and give a British Association of Dermatologists (BAD) patient information leaflet "***Propranolol for Infantile Hemangiomas***" and **"*Propranolol: Information for Parents" (Appendix B)***

2. Examine the lesion with a dermatoscope (to make sure it is vascular), document **size of IH** and the **size of any ulcerated area** if present

3. Arrange clinical photographs (via **Consultant Connect/ Nervecentre**)

4. Arrange investigations if required (**See below 2B**)

5. If suspected segmental hemangioma/PHACES please refer to **section 5**

6. Refer child to Paediatrician for examination (CVS and to rule out organomegaly)*****

7. If child is suitable for outpatient initiation, write script and ask nurses to place in Propranolol folder in the drug cupboard in Paediatric Outpatients. **DO NOT GIVE TO PARENTS until the child has had a normal CVS examination**

8. If child is not suitable for outpatient initiation, discuss with the dermatology on call team who will liaise with paediatric on-call team so that they can arrange admission to children's day-case, Ward 19******

9. If a second opinion is needed, contact Lea.SolmanKosutic@gosh.nhs.uk and mary.glover@gosh.nhs.uk (Great Ormond Street) to obtain a usually quicker reply or bch-tr.derm2@nhs.net (Birmingham Children's Hospital). Please include NHS number and DOB and copy Leicester Consultant you previously discussed case with, and document your request for referral and advice received on Dit3.

*** Contact the Paediatric Dermatology admin team via extension 16308/16041 and book the patient onto Dr. Nichani's clinic (code: SN1F1N) asking to use the FX slot. If no FX slot available, and the child needs to be seen urgently then contact Dr. Nichani directly via the trust**

email to discuss. If Dr. Nichani is on leave, please contact Dr Sridhar or another Pediatrician. Please note the paediatric dermatology mailbox is now PaedsNeuroMetaDerm@uhl-tr.nhs.uk and its admin team leader is sally.n.smith@uhl-tr.nhs.uk (the Yellow team mailbox should not be used)

**** If the referral is URGENT/ INPATIENT ADMISSION is REQUIRED, then:**

1. **Contact the Dermatology On call Registrar via switchboard on the day with patient details. They will arrange for the patient to be reviewed urgently by the paediatric on-call team who will contact a paediatric cardiologist for CVS assessment and investigations.**
2. **The Dermatology on Call Registrar will need to ensure photographs are uploaded to Nerve Centre and Consultant Connect**
3. **Dermatology on-call Registrar to liaise with on-call paediatrician /SPR if admission is needed.**

2b.Pre-treatment investigations

Healthy babies do not require investigations before the initiation of propranolol, however, consider FBC, U&Es, LFTs and TFTs in complex cases.

A pre-treatment **ECG** is not required routinely but **should be performed** in patients with **a heart rate below the 5th percentile for age, a strong family history of sudden death/arrhythmia, episodes of loss of consciousness and maternal history of connective tissue disease**.

1. Outpatients: Paediatric team to email Emchc@uhl-tr.nhs.uk requesting ECG (see Appendix 7 for request form)
2. Inpatients : Paediatric team to request ECG via ICE

A pre-treatment **ECHO** is required in patients with **bradycardia, a heart murmur detected on auscultation and in patients with a segmental IH**.

Assessing Paediatrician will arrange ECG and ECHO at LRI, if indicated, in discussion with paediatric cardiology (please see below).

An **USS spine** should be considered **for plaque haemangioma in the lumbosacral area crossing the midline** or **perianal haemangioma extending into the gluteal cleft to assess for underlying spina bifida**.

An **USS liver** should be requested for babies **with more than 5 cutaneous haemangiomas to look for liver haemangiomas**.

Dermatologists might need to discuss with neonatologists/ paediatricians who might be better placed to request and act on results of these investigations if needed.

Paediatric Outpatient Cardiac Investigation Requests

Referrals for investigations from non-cardiology departments performed at the EMCHC require auditing. Any requests for a stand-alone test should be requested through ICE(inpatients) or email referral made to Emchc@uhl-tr.nhs.uk (outpatients). The test will then be booked.

Investigation	Accepted source of referral	Notes
12-Lead ECG	Paediatric Cardiologist or Registrar* General Paediatrics Child and Adolescent Psychiatry Community Paediatrics	Interpretation of the ECG and communicating the result lies with the referring clinician If an ECG with a report is required, then this should be done as a referral to the Paediatric Cardiology Service (with the exception of CAMHS referrals). Please specify in the referral to the paediatric cardiology service that is for an ECG with a report.
Echocardiogram	Paediatric Cardiologist or Registrar* Paediatric Oncology Paediatric Nephrology	In most cases, children requiring outpatient echocardiograms should be referred to the Paediatric Cardiology Service Exceptions are routine screening for patients undergoing chemotherapy

2c. If you need to refer a patient with IH to Dermatology Paediatric Outpatients to be seen soon (within 6-8 weeks):

- Please ring the pediatric dermatology admin team (Ext 16308/16041) to alert them that you will be emailing a referral to **PaedsNeuroMetaDerm@uhl-tr.nhs.uk with copy to its admin team leader sally.n.smith@uhl-tr.nhs.uk** as urgent with patient details, the referral information and photos of the lesions. Parents are able to email you photographs securely to either **mychildphotos@uhl-tr.nhs.uk; skinphotos@uhl-tr.nhs.uk** or you can alert the team photos are on Nervecenter. Please copy email to Wendy Swanson, Paediatric Dermatology Specialist Nurse (wendy.h.swanson@uhl-tr.nhs.uk).
- Please send parents patient information leaflets (Wendy Swanson might be able to assist you) on:

- Infantile Haemangiomas(https://www.bad.org.uk/shared/get-file.ashx?id=86&itemtype=document)
- and Propranolol (https://www.bad.org.uk/shared/get-file.ashx?id=177&itemtype=document)
- NB: These can also be found on www.bad.org.uk, following quick links to patient information leaflets.

If the referral is more URGENT (rapidly growing in critical areas) then contact the Dermatology On call Registrar via switchboard on the day with this information. They will arrange for the patient to be reviewed urgently if needed. The Dermatology On call registrar will need to ensure photographs are uploaded to Consultant Connect/Nervecentre (photos might have been sent to mychildphotos@uhl-tr.nhs.uk or Skinphotos@uhl-tr.nhs.uk). The Dermatology On-call Registrar will need to discuss the case with the dermatology consultant on call to assess suitability for Propranolol initiation.

2d. Outpatient Initiation

The patient is a suitable candidate for initiation in outpatients if the following criteria are fulfilled:

ALL of the following apply:

Born at term (37 weeks plus)
Older than 4 weeks
Has established feeds and appropriate weight gain
Non segmental haemangioma
Normal cardiovascular and respiratory assessment by paediatricians
No family history of sudden cardiac death or arrhythmia
No maternal connective tissue disease
No history of loss of consciousness or hypoglycaemia.
No history of frequent wheezing
No other significant comorbidities

Prescribe **Propranolol oral solution 5 mg/5 ml** in the outpatient clinic:

Day 1: 1mg/kg daily in 3 divided doses (i.e. 0.33mg/kg tds)
Day 2 and beyond: 2mg/kg daily in 3 divided doses (i.e. 0.66mg/kg tds)

Place script into the propranolol folder in drug cupboard in Paediatric Outpatients. DO NOT GIVE TO THE PARENTS. Dr Nichani (or assessing Paediatrician) will issue this script if the CVS exam is normal**.**

In the event that there are abnormalities detected by the Paediatrician, the Paediatrician should destroy the script, and contact the initiating doctor, document their findings on Dit3 and make the necessary referrals.

Follow ups

1. Arrange a follow up appointment with the referring team.

2. **For dermatology patients**:

A. With the doctor who initiated propranolol **at 4 weeks**
B. With our paediatric dermatology Specialist Nurse **in 8-12 weeks or once the IH is showing signs of regression.**

2e. Inpatient Initiation

Reasons to initiate therapy in hospital include:

Pre term
Less than 4 weeks of age
Poor weight gain
Segmental haemangioma/ concern re PHACES(see Section 5)
Significant comorbidities or family history
History of frequent wheeze (relative contraindication to propranolol)
BP or HR below 5th centile (following paediatric cardiology assessment)
If requested by paediatrician following assessment

Refer patient to the neonatology team or paediatric team who should liaise with the paediatric admission unit / Children's Day Case unit, Ward 19 LRI (0116 258 6317**)** and parents for the admission of these either small or unwell babies/children that at not fit to start propranolol as an outpatient (you might be able to obtain support from SpNurses Sue Flaherty neonatology-or neonatology Specialist Nurse Sue– neonatology- or Wendy Swanson if they are available). Once baby is on the ward and fit to start, if a clear plan is in place, then the neonatologists or paediatricians should go ahead and prescribe propranolol. The dermatology on call team should be contacted to review the baby as well. They should be informed of the day/time of admission as early as possible if their input is need (to suggest propranolol doses to be used and/or consent parents on admission, if this is still pending), as they might not be available immediately (Thursday morning is the best time for dermatology for a planned admission). Please note the dermatology department is now based out of LRI, at St Peter's Healthcare centre.

On day of admission:

Paediatric Nurse will:

-Measure baseline **weight, temperature, pulse** and **BP**.
-Blood **glucose** will be measured if preterm infant/ neonate/ low weight/ poor weight gain or history of hypoglycaemia.

Paediatric Doctor will:

- Review patient is well (no concurrent illness) and feeding normally.
- Ensure paediatric assessments have been done and any investigations requested are complete. (Check on ICE)
- Check parents have read the BAD leaflet '***Propranolol for Infantile Haemangiomas****'* and are happy to proceed.
- Review baseline observations.
- If all is well, prescribe:

Propranolol oral solution 5mg/5ml 0.33 mg/kg stat dose

Nurse to measure BP and pulse every 30 mins for 4 hours.

If all is well discharge child on 1mg/kg/daily in 3 divided doses (i.e. 0.33mg/kg tds) to be increased to 2mg/kg/daily in 3 divided doses (i.e. 0.66mg/kg tds) after 24 hours. This comes in a 150ml bottle.

Arrange out-patient follow up with referring team in 4 weeks. For dermatology patients, organize a follow up with dermatology consultant /Reg who initiated propranolol in 4 weeks and with dermatology specialist nurse (Wendy Swanson) in 8-12 weeks if appropriate.

3. FOLLOW UP FOR PATIENTS TAKING ORAL PROPRANOLOL.

Patients should be monitored on a regular basis in the outpatient clinic. It is not necessary to monitor pulse or blood pressure. If the haemangioma is slow to respond to treatment, the dose can be increased to a maximum of 3mg/kg.[2]

Optional: use the Global Assessment Score to assess response to treatment.

Consider twice daily dosing of propranolol or a more concentrated solution at the clinician's discretion for older babies (you might need to contact pharmacy to make them aware and discuss).

4. STOPPING PROPRANOLOL.

Propranolol should be temporarily discontinued **in the setting of significantly reduced oral intake** or **if the patient has wheezing that requires treatment.**

Treatment of IH should extend beyond the proliferative period of IH to avoid rebound growth and the decision when to stop treatment will have to be guided by clinical features. There is no uniform cut off age that determines the risk of rebound growth, although a European study suggested that children aged 17 months or older had a significantly lower risk of rebound growth compared to younger age groups.[3]

5. SEGMENTAL HAEMANGIOMAS AND PHACES

- **Cervicofacial segmental IH** can be associated with **PHACES** (**P**osterior fossa anomalies, **H**aemangioma, **A**rterial anomalies, **C**oarctation of the aorta/Cardiac anomalies, **E**ye anomalies, **S**ternal cleft and **S**upraumbilical raphe). This group of patients poses a distinctive treatment challenge, as they frequently require prompt treatment for airway and peri ocular IH, but propranolol may increase the haemodynamic risks associated with an otherwise asymptomatic cerebral arteriopathy. Please contact the paediatric on call team who should support you on the actions below:

- All patients with segmental IH of the head and neck require cardiac assessment, including ECG and ECHO before starting propranolol. **The**

paediatric on call team to discuss with paediatric cardiology SpR / consultant on call and dermatology on call team.

- Ideally, **a cerebral magnetic resonance angiogram (MRA)** should also be performed ***before*** propranolol treatment is initiated. Please discuss with paediatric radiologist. If it is not possible to obtain an urgent MRA, the starting dose of propranolol should be no more than **0.5 mg/kg/day in three divided doses. If MRA shows arterial stenosis, discussion with a paediatric neurologist is required prior to starting propranolol.[1]**

6. Education and Training

No additional education or training is required to implement this guideline.

7. Monitoring Compliance

None

8. References:

1. Solman,L et al (2017) Propranolol in the treatment of infantile haemangiomas: The British Society for Paediatric Dermatology consensus guidelines.

2. Leaute-Labreze C, Hoeger P, Mazereeuw-Hautier J, Guibaud L et al. (2015) A randomized, controlled trial of oral propranolol in infantile haemangioma. N Engl J Med ; **372**: 735-46.

3. Wedgeworth E, Glover M, Irvine AD, et al. (2016) Propranolol in the treatment of infantile haemangiomas: lessons from the European Propranolol In the Treatment of Complicated Haemangiomas (PITCH) Taskforce survey. The British Journal of Dermatology **174**(3):594-601.

6. Key Words

Propranolol, Infantile Haemangioma

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

Contact and review details	
Guideline Leads (Names and Titles) Dr Ingrid Helbling, Dr Sanjiv Nichani	**Executive Lead** Chief Medical Officer
Details of Changes made during review: January 2023; Update ECG referral process	

Appendix 1: Template for inpatient initiation of oral propranolol.

Date _____

Patient Sticker

Weight (kilos) _____

Blood Glucose _____
(*Only required for neonates/ preterm infants/ poor weight gain/ hypoglycaemic episodes)*

	0	0.5hr	1 hr.	1.5hr	2 hr.	2.5hr	3 hr.	3.5hr	4 hr.
BP									
HR									

Pre- treatment checklist:

Parents have read and understood BAD Leaflet	
Baby has been examined by a paediatrician	
ECG and ECHO normal (organized by paeds if indicated)	
Segmental haemangioma/ PHACES *not* suspected	
Baby is well and feeding normally	
Baseline observations satisfactory	
Prescribe test dose **propranolol oral solution 5mg/5ml** 0.33mg/kg stat	

If any concerns during observation stage please discuss with the on call paediatric team.

Post observation checklist:

Observations satisfactory	
Complete TTO	
Prescribe **propranolol oral solution 5mg/5ml** 0.33mg/kg tds increasing to 0.66mg/kg tds after 24 hours (150 ml bottle)	
Advice to parents: Give medicine with feeds. Stop temporarily if baby taking significantly reduced feeds. For any concerns contact Specialist Nurse 0116 258 6910 (office hours) or ring 111 (999 in an emergency)	
Arrange outpatient follow up in 4 weeks with referring team (for dermatology patients, FU with referring doctor in 4 weeks and with Dermatology Specialist Nurse in 8-12 weeks)	

Signed _____ (Paediatric Nurse)

Signed _____ (Speciality CT/SPR)

Appendix 2: Dosing regimen for oral propranolol 5mg/5ml.

Weight (kg)	1mg/kg daily in 3 divided doses. (0.33mg/kg tds)	2mg/kg daily in 3 divided doses. (0.66mg/kg tds)
3.0	1 ml tds	2ml tds
3.5	1.2 ml tds	2.3 ml tds
4.0	1.3 ml tds	2.7 ml tds
4.5	1.5 ml tds	3.0 ml tds
5.0	1.7 ml tds	3.3 ml tds
5.5	1.8 ml tds	3.7 ml tds
6.0	2.0 ml tds	4.0 ml tds
6.5	2.2 ml tds	4.3 ml tds
7.0	2.3 ml tds	4.7 ml tds
7.5	2.5 ml tds	5.0 ml tds
8.0	2.7 ml tds	5.3 ml tds
8.5	2.8 ml tds	5.7 ml tds
9.0	3.0 ml tds	6.0 ml tds
9.5	3.2 ml tds	6.3 ml tds
10.0	3.3 ml tds	6.7 ml tds

NB: Segmental haemangioma/ suspected PHACE syndrome: 0.5mg/kg/ in 3 divided doses. Do not increase until clinic review by experienced paediatric dermatologist, cardiologist and neurologist.

Normal Observation Values for Infants (0-12 months)

Heart Rate 110 - 160

Respiratory Rate 30 - 40

Systolic BP 70 - 90

Appendix 3: Propranolol: Information for Parents.

Propranolol information for parents

Your baby has been prescribed Propranolol. A low dose is given for the first 24 hours (3 doses) to reduce the risk of side effects. The dose is then increased from the 4th dose onwards. This will be clearly stated on the label.

IMPORTANT: please check you have been given the correct concentration from the pharmacist each time you start a new bottle of propranolol. This is propranolol oral solution **5mg/5ml.**

The dose of medication depends on the baby's weight. As your baby grows, the dose will need to be increased. We will arrange for your baby to be weighed regularly in clinic and the dose will be adjusted accordingly.

If your baby stops feeding normally for any reason, or is vomiting, please STOP the medication until they are back to feeding normally again.

Sometimes babies can develop a wheezing noise when breathing. This is usually due to a viral infection. If this happens, please stop the medication and contact your GP or ring 111.

Your baby will be seen in clinic in 4 weeks.

For any concerns regarding your child's treatment please contact Specialist Paediatric Dermatology nurse on 0116 258 6910, or the Paediatric Secretaries on 0116 258 6126.

Appendix 4: Checklist for out-patient initiation of oral propranolol.

Oral Propranolol is indicated: **Functional Impairment** **Ulceration** **Risk of permanent disfigurement**	
No absolute contraindications: **Hypoglycaemia** **2nd or 3rd Heart Block** **Hypersensitivity to propranolol**	
Born at 37 weeks or more	
Older than 4 weeks	
Established feeds and appropriate weight gain	
Non segmental haemangioma	
No FH sudden cardiac death or arrhythmia	
No history of loss of consciousness	
No history of hypoglycaemia	
No history of frequent wheezing	
No other significant comorbidities	

Clinical photographs arranged (Consultant Connect/Nervecentre)	
Parents have BAD and Propranolol information leaflets	
Refer to paediatricians for CVS and RESP exam.	
Outpatient follow up at 4 weeks after starting treatment with initiating doctor, and specialist nurse at 8 weeks.	

Prescribe Propranolol oral solution 5mg/5ml in the outpatient clinic:

Day 1: 1mg/kg daily in 3 divided doses (i.e. 0.33mg/kg tds)
Day 2 and beyond: 2mg/kg daily in 3 divided doses (i.e. 0.66mg/kg tds)

Place script into the propranolol folder. **DO NOT GIVE TO THE PARENTS**. Dr Nichani (or assessing Paediatrician) will issue this script if the CVS exam is normal. In the event that there are abnormalities detected by the Paediatrician, the script will be destroyed and the initiating doctor contacted.

Appendix 5: Guidance for Paediatric Dermatology Specialist Nurse.

Babies under dermatology will be reviewed at 4 weeks following the initiation of oral propranolol by a doctor and at 8-12 weeks by the Sp Nurse. The following areas should be addressed:

1. How is the haemangioma responding to treatment? Compare with previous photos and organise for new photos to be taken.

2. Has the child had any new illnesses or medications prescribed since the last attendance?

3. Is the child having any medication related side effects? *E.g. sleep disturbance, wheeze, cold extremities, floppy, and lethargy.*

4. Are there any other parental concerns?

5. Document Global Assessment Score (optional)

6. Please weigh the child and titrate dose accordingly.

Propranolol oral solution 5mg/5ml.

Weight (kg)	Dose*
3.0	**2.0** ml three times daily
3.5	**2.3** ml three times daily
4.0	**2.7** ml three times daily
4.5	**3.0** ml three times daily
5.0	**3.3** ml three times daily
5.5	**3.7** ml three times daily
6.0	**4.0** ml three times daily
6.5	**4.3** ml three times daily
7.0	**4.7** ml three times daily
7.5	**5.0** ml three times daily
8.0	**5.3** ml three times daily
8.5	**5.7** ml three times daily
9.0	**6.0** ml three times daily
9.5	**6.3** ml three times daily
10.0	**6.7** ml three times daily

Dose 2mg/kg in 3 divided doses

Follow up: standard review is 8 weeks for a child with no side effects and a good response to treatment. If there are concerns, arrange a sooner review at 2-4 weeks and discuss with the Dermatology team in clinic.

Appendix 6: Global Assessment Score

SIZE:

-5 -4 -3 -2 -1 0 1 2 3 4 5

(-5 = doubled in size; 0= no change; 5 = complete resolution)

COLOUR

-5 -4 -3 -2 -1 0 1 2 3 4 5

(-5= Twice as red; 0= no change; 5 = normal skin)

Appendix 7: Paediatric ECG referral form

East Midlands Congenital Heart Centre

Paediatric ECG Referral

NHS University Hospitals of Leicester NHS Trust
Caring at its best

Referrer details	**Patient details**
Drs name:	Name:
Address:	Date of Birth:
Telephone:	Address:
Fax	NHS number

ECG request for:

All paediatric referrals (under 16yrs old)

Any queries 0116 2563926 or Emchc@uhl-tr.nhs.uk

An Appointment will be arranged by the EMCH Cardiac Investigations at LRI and sent directly to the patient.

Urgent cardiology referrals via paediatric consultant on call

Please indicate below the reason for referral with a brief history.

Clinical details

- ☐ Suspected Arrhythmia
- ☐ Chest pain
- ☐ ADHD treatment
- ☐ Other (please specify)

Relevant past history:

- ☐ Known CHD
- ☐ Hypertension
- ☐ Pacemaker
- ☐ Other (please specify):

Relevant drug history:

- ☐ Please specify :

Degree of Urgency _____

Today's date: _____ **Name** _____

Signature _____

Title: Treating Infantile Haemangiomas with oral Propranolol
V: 3 Approved by Children's Quality and Safety Board on: March 2023 Trust Ref: C22/2018
Next Review: March 2026