Scottish Paediatric & Adult Haemoglobinopathy Network

Paediatric Guideline - Iron Overload and Chelation Guideline

It is important to educate the patient and family about the potential complications of iron overload and the need for chelation therapy and monitoring. Patients and other family members should be encouraged to be involved in the self-administration of medications at home.

When to start

For those on regular transfusions with a rising ferritin, chelation should commence when ferritin reaches 1000 mcg/l, usually after 10-20 transfusions. Ferritin is an acute phase reactant and should be elevated on 2 occasions when the patient is well.

What to start

Age	1st line	2nd line
<2 years	Desferrioxamine	Deferasirox
2-6 years	Desferioxamine OR Deferasirox	
>6 years	Deferasirox OR desferrioxamine	Deferiprone

Chelators, dose, toxicities and drug safety monitoring

- for full list of side effects and up to date dosing consult BNF and SPC

Desferrioxamine	
Dose range	Starting dose 20-30 mg/kg/d for 8-12 hours 3-7 days/week by subcutaneous infusion, increasing to maximum 40mg/kg/d 7 days/week After one month Vitamin C at a dose of 2 mg/kg/day (maximum 100 mg/day) should be given on treatment days
Side effects	Ototoxicity Lens opacities Yersinia infection – abdominal pain and fever Growth impairment Contraindicated if Creat clearance <60

Desferrioxamine	
Safety monitoring	Monthly liver function tests Monthly creatinine Annual audiometry and ophthalmology from age 5 Stop drug and admit for investigation and treatment if patient develops diarrheoa or abdominal pain and fever (consider Yersinina – start ciprofloxacin) Sitting and standing height, baseline bone age

Deferiprone	
Dose range	75mg/kg/d in 3 divided doses, may increase to 100mg/kg/d
Side effects	Neutropenia and agranulocytosis (2%) GI upset, transaminitis Joint pains Zinc deficiency
Safety monitoring	Weekly FBC for 12 months then 2 weekly Patient advice re fever Monthly liver function tests Monthly creatinine and urine PCR

Deferasirox	
Dose range	Initially 7-21mg/kg once daily (film coated tablet – can be crushed in apple sauce or yoghurt) Adjust by 3.5-7mg/kg every 3-6 months according to serum ferritin. Max 28mg/kg/d, usual maximum 21mg/kg/day
Side effects	GI upset Transaminitis Reversible increase in creatinine, proteinuria Rash
Safety Monitoring	Creatinine monthly (weekly 1st 4 weeks or after dose change) Urine protein:creatinine ratio (monthly) LFTs monthly (weekly 1st 4weeks) Annual audiometry and ophthalmology from age 5

Monitoring of iron overload and secondary organ toxicity

Serum ferritin	– monthly
LFTs	– monthly
Liver ferriscan	– by age 8 (when MRI tolerated without sedation)
	– annually (or more often as clinically indicated eg>15mg/g dw)
MRI Cardiac T2*	– by age 8 (when MRI tolerated without sedation)
LVEF by ECHO	– by age 8
	– annually; (6 monthly if T2* <10ms)

For full details of endocrine monitoring see link to Endocrine Guideline available on the SPAH Paediatric Guideline website page.

Optimal levels of LIC, Drug choice and Dose adjustment

Adequacy of chelation depends on chelator dose, adherence, and transfusion requirements. Children <6 years of age have a relatively greater transfusion requirement which decreases with age.

The target for LIC requires a balance between avoidance of iron toxicity and prevention of chelator-induced toxicity. Normal LIC is 0.2-1.8 mg/g dry weight (dw), but maintaining levels within this range may increase the risk of chelator toxicity. Levels between 3-7 mg/g dw should not result in hepatic or endocrine toxicity Levels above 15 mg/g dw in thalassaemia patients have been associated with an increased risk of morbidity and mortality from iron overload.

Optimal levels of cardiac iron

Risk (If untreated)	T2*
No cardiac iron, low risk of heart failure (HF)	≥ 20 milliseconds
Mild to moderate cardiac iron, low risk of HF	10 – 19 milliseconds
High cardiac iron, moderate risk of HF	6 – 9 milliseconds
High cardiac iron, high risk of HF	< 6 milliseconds

Recommendation - Aim to keep ferritin around 500-1000mcg/l with LIC 3 – 7 mg/g dw and myocardial T2* > 20 ms

Review chelation regimen every 3 months and consider serum ferritin, LIC ferriscan value and cardiac T2* when making dose adjustments and choosing the most appropriate regimen. If ferritin is not decreasing iron balance may be improved by better adherence.

Intensification of therapy

Monotherapy dose increase

Increase dose 3 monthly if ferritin consistently >1000 mcg/l and rising or >1500 mcg/l

Change of chelator

Consider change of chelation therapy to alternative 1st line or second line therapy or combination therapy if

- ferritin>1000 mcg/l and rising or consistently over 1500 mcg/l without improvement despite maximum tolerated dose of single agent.
- unacceptable toxicity at adequate doses to achieve negative iron balance

Combination therapy

Consider use of combination therapy if

- monotherapy at maxiumum tolerated licensed dose is insufficient,
- compliance with monotherapy at required frequency is inadequate
- combination has potential to increase rate of iron removal

Options for combination therapy – see ref 1 for further details
Deferiprone and desferrioxamine particularly if negative iron balance is not achieved with deferiprone alone
Desferrioxamine and deferasirox – effective and well tolerated
Deferiprone and deferasirox - limited experience but may be highly effective at improving cardiac T2* (consider bd regimen for both to aid compliance)

Emergency intensification
This is indicated when there is evidence of cardiac decompensation (LVEF<56%) or a high risk of this occurring T2*<8ms
See Ref 1 for further guidance

Dose reduction
In general chelator toxicities are increased when ferritin falls.
Consider dose reduction/or interruption when ferritin <500mcg/l.

References
1. Guidelines for monitoring and management of iron overload in patients with haemoglobinopathies and rare anaemias. Shah et al British Journal of Haematology 2021
2. UK Thalassemia Society - Standards for the Clinical Care of Children and Adults with Thalassaemia in the UK 2016
3. Management of iron overload in children BJH 2014

NOTE
This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.