Adult Service

Desferrioxamine chelation in patients with haemoglobin disorders: Clinical guideline

Indication

Desferrioxamine (Desferal) should continue to be considered the iron chelator of choice for the following patient groups:

- Those with significant adverse reaction to Deferasirox and Deferiprone.
- In combination with Deferiprone for patients with severe iron overload (LIC >15/mg/g dry weight, cardiac MRI T2* < 10ms). Desferrioxamine may be administered by continuous infusion **for severe cardiac siderosis** to suppress the generation of labile plasma iron/non-transfusion bound iron (LPI/NTBI).
- **For urgent surgery in patients with severe cardiac loading** and a history of previous/current organ dysfunction continuous intravenous desferrioxamine at 50-60mg/kg/day should be used, review Surgery protocol: http://nssg.oxford-haematology.org.uk/red-cell/documents/acute-management-thalassaemia/S56-surgery-in-adults-with-thalassaemia.pdf
- End stage renal failure.

Dose Range

Routine management

- Usual dose is between 20-50mg/kg/day.
- Administered as a subcutaneous infusion over 8-12 hours (usually overnight), typically 4-7 days per week.
- Ascorbic acid orally on days of chelation may increase urinary iron excretion**. The recommended dose is 200mg for adults and 100 mg for children. Caution** - There is a potential risk of increasing toxic iron levels and precipitating cardiac toxicity in patients who are heavily iron loaded and at risk of cardiomyopathy. Ascorbic acid should not be used on non-Desferrioxamine days in all patients and in the early stages of intensive chelation therapy for patients with cardiac failure or with myocardial T2* <10 msec.

Severe advanced iron overload

- Continuous intravenous Desferrioxamine infusion over 24 hours is preferred in patients with severe cardiac iron deposition, acute or chronic cardiac problems due to iron overload, early cardiomyopathy detectable by echo or other method even in absence of clinical symptoms or signs.

Emergency therapy/Cardiac siderosis

- Continuous infusion is usually given through an indwelling line for long-term management. For emergency management, before an indwelling line can be inserted, Desferrioxamine can be given through a peripheral vein, provided it is diluted in 250- 500 ml of 0.9% normal saline to avoid damage to the veins. A dose of at least 50 mg/kg/day and not exceeding 60 mg/kg/day is recommended as a 24-hour infusion.

The following table suggests appropriate doses, but please note that treatment should always be tailored to the individual patient and their response. The lowest effective dose should always be used:

From Guys and St Thomas's chelation guidelines, 2015:

Ferritin	Desferrioxamine dose (7 nights)	Desferrioxamine dose (5 nights)
<2000	25mg/kg/day	35mg/kg/day
2000-3000	35mg/kg/day	49mg/kg/day
>3000	Up to 50mg/kg/day	X

Administration

There are a variety of pumps available for administration of Desferrioxamine. Newer devices, including balloon pumps, are smaller, lighter, and quieter than their predecessors. For patients who find dissolving, mixing and drawing up Desferrioxamine a problem, pre-filled syringes or balloons may be useful. Some pumps are designed to monitor compliance.
Liaise with your local pharmacy/equipment department or medical devices library.

Practical details for intravenous infusions

10 % solutions of Desferrioxamine given to peripheral veins will damage and sclerose the vein. If infused (as an emergency) into a peripheral vein, the solution must be diluted – for example in 200-500 ml of 0.9% normal saline.
Intravenous Desferrioxamine with blood transfusion is not a recommended practice.

Relative contraindications

- Pre-existing sensory neural hearing loss.
- Pre-existing macular retinal pigment epithelial disease.
- First trimester of pregnancy. (NB. Safe during breastfeeding.)

Baseline investigations

- Liver function, renal function, ferritin, iron, transferrin saturation.
- Cardiac T2* MRI/Ferriscan.
- Baseline ophthalmology and audiometry assessment before treatment commences.

Monitoring

- Every three months – liver function, renal function, ferritin, iron, transferrin saturation.
- Ferritin target levels 500-1500 mcg/l
- Annually – audiometry, ophthalmology review, cardiac T2* MRI/Ferriscan scan.

Dose adjustment for adverse effects:

- Therapeutic (Porter) index: (Thalassaemia major only)

Therapeutic index= Mean daily dose (mg/kg) / ferritin (mcg/l).
Aim for index <0.025 at all times.
e.g. in a patient on 45mg/Kg of Desferrioxamine 5 nights per week who has a serum ferritin of 2500micrograms/l, the therapeutic index is calculated thus:
Mean daily dose: 45 x 5 ÷ 7= 32.14
Therapeutic index: 32.14 ÷ 2500 = 0.0128

Complications:

- Local skin reaction
  Persistent local skin reactions may be reduced by varying injection sites, lowering the strength of infusion, or in severe cases, by adding 5-10 mg of hydrocortisone to the infusion mixture. Application of topical low potency corticosteroid cream after injection can reduce local reactions.
  - Ensure correct dilution (10%) and rate of infusion.
  - Check for dressing allergy.
  - If ulceration of skin, ensure adequate depth of needle insertion.

- Allergic responses are rare but have been described; the first dose should always be given in hospital and under supervision

- Severe allergy
  - Consider desensitisation protocol or alternative iron chelator

- Febrile illness or diarrhoea: **Consider Yersinia**
  - Symptoms: Abdominal pain, vomiting and/or diarrhoea
  - Interrupt Desferrioxamine
  - Drug of choice: Ciprofloxacin 500mg BD po or 400mg BD iv
  - Severe and occasionally fatal Klebsiella infection has also been associated with Desferrioxamine
  - Patients developing high fever, diarrhoea and abdominal pains or other signs of infection should be instructed to stop Desferrioxamine chelation and seek medical advice as soon as possible.

- Audiology
  - If worsening symptoms of hearing loss or tinnitus, or progressive deterioration noted on pure audiometry, withhold Desferrioxamine and repeat audiogram every three months until deficit has stabilised before reintroducing chelation.
  - Base reintroduction dose on reassessment of hepatic iron concentration, Porter index or the previously tolerated dose.

- Vision
  - If worsening symptoms of visual loss (especially night blindness or central scotoma) or new lesions noted in an ophthalmic assessment consistent with chelator toxicity, hold off Desferrioxamine until symptoms and ophthalmic findings have completely resolved.
  - Base reintroduction of dose on the above variables.

- Pulmonary toxicity including respiratory distress syndrome and neurotoxicity have been described with higher than recommended doses.

Concomitant medication:
Caution is advised when Desferrioxamine mesilate is used in combination with any phenothiazine as it may lead to prolonged unconsciousness.

Specialist Referrals:
Thalassaemia HCC MDT: for discussion of complex patients
Email: emma.drasar@nhs.net

National Haemoglobinopathy Panel MDT: for discussion of novel therapies
Website: https://www.nationalhaempanel-nhs.net/mdtfunction

Documents:
Patient information: There is no Oxford based patient information available at this time. Please use: https://www.medicines.org.uk/emc/files/pil.3813.pdf

References:

Standards for the Clinical Care of Adults with Sickle Cell Disease in the UK © Sickle Cell Society 2018.

Dr R Kesse-Adu and Dr J Howard. Guy's and St Thomas' Guidelines for iron chelation in adults with a haemoglobinopathy or other inherited anaemia diagnosis. 2013.

A. Victor Hoffbrand, Ali Taher, and Maria Domenica Cappellini. How I treat transfusional iron overload. Blood, 2012, Volume 120, Number18.

United Kingdom Thalassaemia Society. Standards for the Clinical Care of Children and Adults with Thalassaemia in the UK. 3rd Edition, 2016.

John Porter, Vip Viprakasit, and Antonis Kattamis. Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT) [Internet]. 3rd edition Chapter 3. https://www.ncbi.nlm.nih.gov/books/NBK269373/#APP.001.

NHSE. Clinical Commissioning Policy 16070/P: Treatment of iron overload for transfused and non- transfused patients with chronic inherited anaemias. 26 August 2016.

Desferrioxamine (Des.feral ®) Summary of product characteristics. Last Updated on eMC 15-Nov-2016.

Farrukh T. Shah,John B. Porter,Nandini Sadasivam,Banu Kaya,James C. Moon,Mark Velangi,Emmanuel Ako,Shivan Pancham, BJH guidelines, *Guidelines for the monitoring and management of iron overload in patients with haemoglobinopathies and rare anaemias*, 06

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Review

Name	Revision	Date	Version	Review date
Wale Atoyebi	Pre-peer review	Jan 2013	1.0	Jan 2015
Deborah Hay	Routine review	Aug 2015	1.2	Aug 2015
Dr Magbor Akanni Nadjoua Maouche	Full review	Mar 2017	2.0	March 2019
Dr Noemi Roy	Review, HCC updates	July 2020	2.1	July 2022
Wale Atoyebi	Full review	October 2023	3.0	October 2025