# Deferasirox (Exjade) chelation therapy in patients with haemoglobin disorders: Clinical Guideline

## Indication

Deferasirox should be considered first line therapy for all patients with major haemoglobinopathies requiring chelation therapy, especially if the cardiac T2* < 10ms. Prior to starting treatment, provide patient information leaflet on Exjade.

## Dose Range

**ATTENTION**: Dosing is **DIFFERENT** depending on the formulation whether film-coated tablets or dispersible tablets.

**Formulations are NOT INTERCHANGEABLE.** The dose of film-coated tablets should be 70% the dose of dispersible tablets, rounded to the nearest whole tablet.
Check local formulary for available formulation.

Treatment should be commenced after ~20 units of packed red cells, or when the ferritin is consistently >1000 microgram/l.

Starting doses and dose adjustments vary between transfusion-dependent iron overload and non-transfusion dependent thalassaemia syndrome; refer to tables 1 and 2 respectively for dosing information.

## Administration

**Film coated tablets** should be taken once a day, preferably at the same time each day, and may be taken on an empty stomach or with a light low fat meal.
Tablets should be swallowed whole with water. For patients who are unable to swallow, tablets may be crushed and sprinkled onto soft food, e.g. yogurt. The tablets come in 90mg, 180mg and 360mg strengths.

**Dispersible tablets** should be taken once a day on an empty stomach at least 30 minutes before food at approximately the same time each day, preferably morning and not with any antacids. Tablets should be dissolved in 100-200mL of water, orange or apple juice. (It must not be dissolved in fizzy drinks). The tablets come in 125mg, 250mg, or 500mg strengths. This formulation is now used rarely.

## Table 1: Dosing in Transfusional Iron Overload

| | Film-coated tablets | Dispersible tablets | Transfusions/SF |
|---|---|---|---|
| **Starting dose** | **14 mg/kg/day** | **20 mg/kg/day** | After 20 units of PRBC or SF >1,000 µg/l |
| **Alternative starting doses** | 21 mg/kg/day | 30 mg/kg/day | >14ml/kg/month of PRBC (approx. >4 units/month for an adult) |
| | 7 mg/kg/day | 10 mg/kg/day | <7 ml/kg/month of PRBC (approx. <2 units/month for an adult) |
| **Dose adjustments** (every 3-6 months) | **Dose increase**<br>• When SF persistently >2,500 µg/l and not showing a decreasing trend over time | | |
| | Adjust in 3.5 - 7 mg/kg/day increments<br><br>Up to maximum of 28 mg/kg/day | Adjust in 5-10 mg/kg/day increments<br><br>Up to maximum of 40 mg/kg/day | Depending on response and therapeutic target |
| | **Dose decrease:** consider in,<br>• Patients treated with doses >30 mg/kg (if dispersible tablets) and > 21mg/kg/day (if film-coated tablets), with a SF <2,500 µg/l and showing a decreasing trend over time.<br>• Patient whose serum ferritin level has reached the target (usually between 500 and 1,000 µg/l).<br>• Consider Interruption if SF falls consistently <500 µg/l, | | |
| | Adjust in 3.5 - 7 mg/kg/day increments | Adjust in 5-10 mg/kg/day increments | |
| **Switching from desferrioxamine in stable patients** | Use One third of desferrioxamine dose | Use Half of desferrioxamine dose | |

PRBC= Packed Red Blood Cells
SF= Serum Ferritin

## Table 2: Dosing in Non-transfusion dependent Thalassaemia Syndromes

| | Film-coated tablets | Dispersible tablets | LIC*/SF |
|---|---|---|---|
| **Starting dose** | **7 mg/kg/day** | **10 mg/kg/day** | LIC ≥5 mg Fe/g dw or SF >800 µg/l |
| **Dose adjustments** (every 3-6 months) | Adjust in 3.5 - 7 mg/kg/day increments | Adjust in 5-10 mg/kg/day increments. | |
| | **Dose increase:**<br>• Consider if LIC ≥7 mg Fe/g dw or SF >2,000 µg/ l and not showing a downward trend<br>• If patient LIC was not assessed and serum ferritin is ≤2,000 µg/l, dosing should not exceed 10 mg/kg (if dispersible tablet) or 7mg/kg (if film-coated tablet).<br>• Doses above 20mg/kg//day (if dispersible tablet) or 14mg/kg/day (if film-coated tablets) not recommended.<br><br>**Dose decrease:**<br>• Consider when LIC <7 mg Fe/g dw or SF ≤2,000 µg/l<br>• Discontinue when LIC <3 mg Fe/g dw or serum ferritin <300 µg/l | | |

LIC=Liver Iron concentration
SF= Serum Ferritin. dw= dry weight

**Relative contraindications:**

- Pre-existing renal disease (CrCl < 60 ml/min renal replacement therapy)
- Pre-existing liver disease (ALT>5 x ULN unless due to hepatic iron overload)
- Severe lactose intolerance
- Pregnancy
- In combination with other iron chelator therapies as the safety of such combinations has not been established and is not commissioned.

**Baseline investigations prior to initiating therapy:**

- FBC, reticulocyte count
- LFT, creatinine, Calcium, phosphate, vitamin D, CRP, AFP, protein: creatinine ratio, ferritin, iron, transferrin saturation, zinc
- Check Creatinine Clearance if borderline renal function, extremes of body weight or history of renal issues. (Cockroft &Gault calculation https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation )
- Ophthalmology assessment
- Audiometry assessment

**Monitoring:**

- Serum creatinine weekly for the first month of therapy and during first month after dose modification, then monthly thereafter.
- Check Creatinine Clearance weekly if borderline renal function, extremes of body weight or history of renal issues. (Cockroft &Gault calculation https://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation )
- Initially monthly - Bone, CRP, Urinalysis
- LFTs: every 2 weeks during the first month then monthly thereafter
- 3 Monthly – Ferritin, Zn
- Annually - Cardiac T2* MRI
- Annually – Ophthalmology and Audiology review

**See S7.21 Monitoring chart** http://nssg.oxford-haematology.org.uk/red-cell/documents/iron-overload-and-chelation/S7-21-deferasirox-chelation-drug-management-table.pdf

**Dose adjustments for Adverse Effects:**

Increase in serum creatinine

- If > 33% above pre-treatment average, or proteinuria > 0.3 on two occasions and no other cause can be found, reduce dose by 5-10mg/kg and repeat after 2-4 weeks.
- Discontinue if elevation persists and consider renal unit referral.
- Dose can be increased (in 5mg/kg increments) if creatinine stable at <33% above pre-treatment average for one month.

Elevated LFTs

- In case of president and progressive elevations in serum transaminases levels, treatment should be interrupted and dose modifications should be considered. Deferasirox can be cautiously reintroduced at reduced doses once transaminase levels return to baseline.

- Not recommended in patients with severe hepatic impairment (Child-Pugh Class C). In patients with moderate hepatic impairment (Child-Pugh Class B), the dose should be considerably reduced followed by progressive increase up to a limit of 50%
- Monitor weekly
- Consider rechallenging at reduced dosage when LFTs return to normal.

**Diarrhoea /GI upset (abdominal pain, nausea/vomiting)**
Is the most common reported side effect and may respond to changing the time of day of administration or the diluents or timing with food. It seems to be best tolerated in the evening on a full stomach. If the patient is lactose intolerant, suggest lactase supplementation. Also consider split dosing. In case of diarrhoea, patient should take an antidiarrheal for up to 2 days and keep hydrated.

**Skin rash**
Usually resolves without requiring dose reduction
If severe, discontinue until rash settles and rechallenge with antihistamines.

**Dose adjustment according to iron stores:**
This is indicated for increasing serum ferritin levels (>1500), increasing liver or cardiac loading or development of new clinical complications of iron overload. See table above.

In general, for patients with high and increasing iron burden consider treating with alternative regimens.

Once targets have been achieved for hepatic iron (< 2mg/g dry weight) and cardiac T2* (> 20ms), dosage should be maintained.

If serum ferritin falls consistently < 500 then institute a drug holiday and continue to monitor Ferrtin monthly.

**Documents:**
Patient information:

- Novartis patient information, (2019) or
- https://www.medicines.org.uk/emc/files/pil.4329.pdf

**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

**References:**

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

A. Victor Hoffbrand, Ali Taher, and Maria Domenica Cappellini. How I treat transfusional iron overload. Blood, 2012, Volume 120, Number 18.

Deferasirox (Exjade ®) film-coated tablets. Summary of Product Characteristics. Last Updated on eMC 17-Oct-2019,

Deferasirox (Exjade ®) dispersible tablets. Summary of Product Characteristics. Last Last Updated on eMC 17-Oct-2016.

NHSE. Clinical Commissioning Policy 16070/P: Treatment of iron overload for transfused and non- transfused patients with chronic inherited anaemias. 26 August 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 October 2021

**Author:**
Dr Wale Atoyebi, Clinical Lead for Haemoglobinopathies

**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 | Jan 2017 |
| Dr Magbor Akanni, MKUH.<br>Nadjoua Maouche, Pharmacist.<br>Sandy Hayes, ANP. | Full review, new formulation, ODN format, development of monitoring table | January 2017 | 2.0 | Oct 2018 |
| Dr Noemi Roy | Review, HCC details, NHP MDT details | October 2020 | 2.1 | October 2022 |
| Wale Atoyebi | Full review | October 2023 | 3.0 | October 2025 |