



Deferasirox treatment for iron overload

A patient's guide

What is deferasirox?

- Deferasirox is an iron chelation medication.
- Chelation is a small molecule that binds iron and removes it from the body.

Why is too much body iron a bad thing?

- Too much body iron is harmful to the tissues where it accumulates.
- Blood transfusion results in iron overload because each unit of blood contains iron as part of the haemoglobin in red blood cells.
- The body has no natural way of removing all the extra iron so the iron is stored in cells.
- The liver is the main site for iron storage but once the liver is full of iron it will start to be deposited in other organs such as the hormone glands and the heart.
- In transfusion-dependent thalassaemia patients, iron can also deposit in the heart, leading to heart failure.
- Excess iron can also affect:
 - the glands that control growth, sexual development and fertility
 - insulin production, causing diabetes
 - the glands that control thyroid hormone
 - bone formation.
- **Liver complications**
 - Although the liver is better equipped to deal with iron overload than some other tissues, poor control of liver iron will cause liver scarring and eventually liver failure (cirrhosis) – although this can take many years to develop.
 - Liver cancer is a late complication.
 - Removing iron from the liver reduces these risks.
- **Hormone problems**
 - Iron can cause serious complications when it is deposited in the hormone glands. If iron is deposited in the pituitary gland which controls the hormones regulating growth and sexual development, young people may fail to enter puberty naturally.
 - Older people may have difficulties conceiving because the hormones oestrogen (in women) and testosterone (in men) will stop being produced.
 - Other glands that are affected are the thyroid gland (resulting in hypothyroidism), the pancreas (resulting in diabetes), and the parathyroid gland (resulting in low calcium levels in the blood).
 - Unfortunately damage to the hormone glands is not reversible.



- **Heart problems**

- Iron can be deposited in the heart and, if severe levels are reached, can result in heart failure or abnormal heart rhythms (palpitations) which are both serious and can be life threatening.
- Heart failure is reversible with intensive chelation, but it is completely avoidable if you follow treatment correctly.

- The aim is to prevent problems developing in the first place. Therefore, the best strategy for managing iron overload is avoiding high levels of iron.
- In general, liver iron values of above 7mg/g dry weight on a type of MRI called FerriScan liver iron assessment are the levels above which complications start to develop.
- We keep a liver iron target of below 5mg/g dry weight for our patients to ensure that iron overload complications do not develop.
- All chelation drugs are effective if used appropriately and we will adjust chelation treatments, so they are tolerable and fit in with your lifestyle, as well as achieving the desired treatment goal.

When can deferasirox be a useful treatment?

- Deferasirox is designed to eliminate excess iron from the body.
- It can be used in children and adults who have iron overload as a result of blood transfusions.
- Deferasirox is also licensed for some other thalassaemia patients who develop too much body iron even without blood transfusion.

How does deferasirox work?

- Deferasirox is small enough to be absorbed through the gut and enter the blood stream.
- Binding of iron can occur in the blood stream or within tissues such as the liver or heart.
- Once iron is bound to deferasirox, the iron complex is eliminated from the body through the bile and some in the faeces.
- Very little is eliminated in the urine, so the urine does not go red as with other chelators that eliminate iron in the urine (such as desferrioxamine or deferiprone).

How is deferasirox taken?

- Deferasirox now comes as a film-coated tablet to take by mouth.
- Please note that the old formulation is no longer available in the UK.
- It is usually taken once a day, either on an empty stomach or with a light meal.
- Taking deferasirox at the same time each day will help you to remember when to take your tablets.
- If you are unable to swallow the whole tablet, you can crush it and sprinkle the full dose on to soft food, such as yogurt or apple puree.
- You will need to eat the food immediately and finish the whole portion – you should not keep it to eat later.



- The effective and safe dose depends on how much iron is already in your body, and how rapidly iron is accumulating from blood transfusions or from absorption in the diet. For example, if you are receiving quite a lot of blood regularly, a high dose of deferasirox will usually be needed to keep pace with the iron loading rate. This doesn't always apply if the blood is given as an automated exchange transfusion, which is the case for some sickle cell disease patients.
- If the iron has accumulated in the past but the current rate of iron loading is slow, a smaller dose will be effective in reducing the amount of iron in the body.
- It is also very important to understand that as the amount of iron falls with deferasirox treatment, the dose of deferasirox may need to be reduced. Doses often need to decrease when ferritin falls below 1000µg/L or if the fall in ferritin is too rapid.
- If the deferasirox doses remain high when the levels of iron fall, there is a risk of 'over-chelation'. This could increase the risk of side effects from deferasirox (please see below). To prevent this, we will monitor you carefully and adjust the doses accordingly.

How much should be taken and how often?

- Deferasirox is taken once daily (seven days a week), and the dose needs to be adjusted from time to time to ensure effective chelation.
- If the goal is to maintain a safe level of iron, then we will normally use a dose of around 15-20 mg/kg/day.
- We may use doses of up to 28mg/kg/day if the goal is to reduce the total iron burden or if someone is on a very heavy transfusion programme.
- Sometimes, when iron is only accumulating slowly from exchange transfusion or in transfusion independent patients, doses as low as 10mg/kg/day are more appropriate.
- It is very important to understand that an effective and safe dose depends on how much iron is already in the body, and on how rapidly iron is accumulating from blood transfusion or from iron absorption in the diet.
- If you are missing a couple of doses a week it will significantly reduce the impact of iron chelation and you could end up maintaining a high iron burden rather than reducing it.
- It is also very important to understand that as the amount of iron falls with deferasirox treatment, the dose needs to be decreased.
- If the doses given remain high when the iron level falls, there is a risk of 'over-chelation'. This could increase the risk of side effects from deferasirox and that is why we monitor all patients on iron chelation carefully so doses can be adjusted from the ferritin trend.
- If the Deferasirox® doses remain high when the levels of iron fall, there is a risk of 'over-chelation'. This could increase the risk of side effects from deferasirox (please see below). To prevent this, we will monitor you carefully and adjust the doses accordingly.

Can deferasirox be given with other iron chelators?

- Combining deferasirox with another chelator may be useful when iron control is inadequate during the treatment with deferasirox alone.



Monitoring for effectiveness of deferasirox

- As with other chelators, the serum ferritin levels and trend is the most convenient way to monitor iron overload.
- An MRI scan of the liver and heart can be used for dose and regime adjustment and for risk assessment. These are typically performed about once a year.

How frequent are unwanted effects and what are they?

- Like any medicine, deferasirox can have unwanted effects. These are more likely if the dose given is too high for the level of iron overload or the rate of iron loading.
- Fortunately, the side effects of deferasirox have been looked at in very large clinical trials so the frequency at which these occur are well known.
- **Effects on the gut**
 - These occur in about 15% of patients, are typically mild and do not persist.
 - They include stomach pain, nausea, and vomiting, diarrhoea or constipation.
 - These symptoms rarely require dose adjustment or stopping treatment and tend to settle down over a few weeks.
 - If these persist or you suffer from severe vomiting or diarrhoea every time you take deferasirox, the Doctor prescribing the treatment should be informed.
 - Mostly these symptoms can be managed effectively by adjusting the time of day the medication is taken or taking it with food.
 - Stomach ulcers have rarely occurred.
- **Skin rashes**
 - These occur in about 11% of patients.
 - Skin rashes are typically red and itchy and sometimes raised.
 - They may occur all over the body or can be confined to the palms and feet.
 - The rash typically develops within two weeks of starting treatment and responds well to temporary dose reduction.
 - Sometimes steroids can be given for the rash
 - Very rarely, you may need to permanently stop taking this medicine.
- **Kidney function tests**
 - Doctors monitor kidney function with a blood test called 'serum creatinine'.
 - The serum creatinine increases by about 30% in about one third of patients on deferasirox and is not usually a cause for concern.
 - However, in some cases deferasirox may need to be interrupted or given at a lower dose.
- **Effects on the liver function tests**
 - Usually, liver function tests improve as body iron is decreased.
 - Less than 1% of patients may have an increase in liver enzymes greater than twice the upper limit of normal. In these cases, we may need to test the blood more frequently.



- If the liver enzymes rise more severely (more than five times the upper limit of normal) we may require interruption of treatment and occasionally permanent discontinuation.

- **Other effects**

- Occasionally there have been reports of a problem known as metabolic acidosis occurring in patients who had pre-existing renal kidney problems or diarrhoea. We would consider interrupting deferasirox in patients who develop metabolic acidosis.
 - Rarely patients have developed a severe allergic reaction known as anaphylaxis.
 - Unlike deferiprone, deferasirox is not linked to joint pains and does not affect the white cell count, so weekly blood count monitoring is not required.
 - Unlike desferrioxamine, deferasirox over-treatment is not typically associated with hearing or eyesight problems, although all patients are still monitored as a precaution.
 - Rarely, cataracts have been reported with both Desferal and deferasirox.
 - Also, unlike desferrioxamine, the use of deferasirox at current recommended doses does not seem to affect growth in children.
- In clinical trials, patients using deferasirox reported better satisfaction, convenience of use and quality of life compared to patients using desferrioxamine.

Monitoring for side effects of deferasirox

- It is important to monitor all patients on chelation treatment regularly to avoid under or over-treatment.
- There are some specific monitoring tests that need to be done for patients taking deferasirox:
 - **Kidney function:** This should usually be monitored using the serum creatinine every time a sample is taken for a cross match (typically every three to four weeks).
 - **Urine protein** can also be monitored at these visits
 - **Liver function tests:** These should be done at the time of the cross match, at weekly intervals for four weeks after starting treatment and after a dose increase.
 - **Eye and ear tests:** Ear tests are done about every one to two years. Eye tests are done when your Doctor thinks it is necessary.
- These tests need to be done more often when the treatment is first started or if the dose is changed (particularly when the dose is increased).

For more information about chelation therapy, please see our leaflet, '**Treatment options for iron overload**'



Contact details

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- Network website:

<https://www.uclh.nhs.uk/theredcellnetwork/subscribe>

If you or your family have any other questions, please do not hesitate to contact any of the above medical team at Whittington Health.

Where can I get more information?

The UK Thalassaemia Society

19 The Broadway, London N14 6PH

Tel: 020 8882 0011

Website: www.ukts.org

The Sickle Cell Society

54 Station Rd, London NW10 4UA

Tel: 020 8861 7795

Website: <http://www.sicklecellsociety.org>

NHS 111

Tel: 111

www.nhs.uk/NHSEngland/AboutNHSservices/Emergencyandurgentcareservices/Pages/NHS-111.aspx



Patient advice and liaison service (PALS)

If you have a compliment, complaint or concern please contact our PALS team on 020 7288 5551 or whh-tr.PALS@nhs.net

If you need a large print, audio or translated copy of this leaflet please email whh-tr.patient-information@nhs.net. We will try our best to meet your needs.

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