Deferiprone – treatment for iron overload

A patient’s guide

What is deferiprone?
Deferiprone 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 the body starts to deposit iron in other organs such as the hormone glands and the heart.

Liver complications
Although the liver is better equipped to deal with iron overload than 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 this risk.

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 not enter puberty naturally.

Older people may develop secondary infertility because the hormones oestrogen (in women) and testosterone (in men) will stop being produced. Other affected glands are the thyroid gland resulting in hypothyroidism, the pancreas resulting in diabetes, and the parathyroid gland resulting in low calcium levels in the blood. Endocrine damage 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 palpitations of the heart. These 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.
Therefore the best strategy for managing iron overload is to avoid high levels of iron. In general we know that liver iron values of above 7mg/g dry weight on a type of MRI called FerriScan MRI (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.

All chelation drugs are effective if used appropriately. We will adjust treatment regimes so they are tolerable and fit in with your lifestyle, as well as achieving the desired therapeutic goal.

**When can deferiprone be a useful treatment?**

Deferiprone is used to chelate iron in patients with thalassaemia major who have been unable to tolerate desferrioxamine, or in patients who are in need of combination therapy with desferrioxamine.

It is used outside the remit of its licence in patients with sickle cell anaemia and in patients with rare inherited anaemias and more recently in patients with neurodegenerative conditions such as Frederichs ataxia and superficial siderosis.

You should not take deferiprone if:
- You are pregnant, trying for a baby or breast-feeding
- You have ever been told you have a low number of white blood cells
- You have previously had a low white cell count on deferiprone.

**How does deferiprone work?**

Deferiprone is small enough to be absorbed though 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 deferiprone, the iron complex is eliminated from the body though the urine. The urine turns a reddish colour.

**How is deferiprone taken?**

Deferiprone is available as 500mg tablets, 1,000mg tablets and an oral solution. It is taken orally as three divided doses a day. Allow at least a four hour interval between deferiprone and other medications or supplements containing aluminium, or zinc.

**How much should be taken and how often?**

Deferiprone is taken orally and can be taken with or without food. If you miss a dose, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose and then continue with your regular schedule. Do not try to catch up or take two doses at the same time to make up for a missed dose.

If the goal is to maintain a safe level of iron then we will normally use a dose of around 75mg/kg/day. We may use doses of up to 100mg/kg/day if the goal is to reduce the total iron burden or if someone is on a very heavy transfusion programme. We may also recommend that deferiprone is used with desferrioxamine infusions in a combination regime. This combination can be used in patients with iron in the heart or in patients with high levels of liver iron.
As the iron burden comes down the doses will be reduced so that we can maintain the iron at a safe level.

**Can deferiprone be given with other iron chelators?**
Deferiprone is often used as a single chelation treatment or as part of a combination treatment with desferrioxamine. Experience of combining deferiprone with Exjade is fairly limited, although there are now some trials that show this can be useful and well tolerated. We will consider combination very occasionally in those patients where iron burden is difficult to control.

**Monitoring for effectiveness of deferiprone**
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 drug, deferiprone can have unwanted effects.

**Agranulocytosis or neutropenia**
Deferiprone can cause a serious side effect resulting in a very low white blood cell count. One type of white blood cell, called a neutrophil, is important for fighting bacterial infections. If you have a low neutrophil count (called neutropenia) you may be at risk of developing serious infection. Neutropenia is quite common with deferiprone and around four per cent of patients may have a low neutrophil count occasionally. If the low neutrophil count continues to fall, it can become a serious problem.

Severe neutropenia is known as agranulocytosis (one per cent of patients may get this) and if you develop agranulocytosis, you will be at risk of developing serious infections that can lead to death unless promptly identified and appropriately treated.

It is very important that you have **weekly blood tests** to check the neutrophil count while taking deferiprone.

If you develop neutropenia, your healthcare professional should check your blood counts every day until your white blood cell count improves.

**Should you develop a fever or a sore throat while taking deferiprone you should not take the next dose and should attend hospital urgently for a full blood count to exclude neutropenia or agranulocytosis.**

If you are unwell you will need to be admitted to hospital and will require antibiotics and sometimes growth factor injections to help bring the neutrophil count back up.
Effects on the gut
These occur in about 15 to 30 per cent of patients, are typically mild and do not persist. These include stomach pain (often described as hunger cramps), nausea, and vomiting. 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 nausea every time you take deferiprone, the medical team prescribing the treatment should be informed.

Mostly these symptoms can be managed effectively by taking the deferiprone with food or by starting at a low dose and increasing the dose every few days until you are on the correct dose. Occasionally you may need anti-nausea medication to help you.

Deferiprone can cause increased liver enzymes in your blood. Your medical team should do a monthly blood test to check your liver function during treatment. Mostly these are mild increases and no change is needed but if there is a large increase in the value of the liver enzymes, the medical team may stop the deferiprone and consider investigations.

Joint pains
These can occur in about 15 per cent of patients and are mostly mild or moderate. These tend to occur in large joints such as the knee or ankle. If you get such pains or if the joint becomes swollen let your medical team know. These side effects can occur even after many years on deferiprone.

Red urine
This is a very common side effect and most patients will get reddish coloured urine after taking deferiprone. This is the iron to drug complex and reflects the impact of chelation.

Monitoring for side effects of deferiprone
Monitoring is important to assess for side effects. You should have the following tests done on a regular basis:
1. Full blood count weekly for monitoring the neutrophils
2. Liver function tests once a month to look for liver problems with deferiprone
3. All the routine monitoring for iron overload including ferritin tests, MRI assessments of liver and heart iron as scheduled by the medical team.
Your medical team is:

- Dr Farrukh Shah (thalassaemia lead)
- Dr Bernard Davis (sickle cell lead)
- Dr Ali Rismani (consultant haematologist)
- Dr Emma Drasar (consultant haematologist)
- Dr Andrew Robins (paediatric lead)
- Dr Janine Younis (paediatric deputy lead)
- Red Cell specialist registrar doctors
- Haemoglobinopathy nurse specialists
  (Emma Prescott, Niamh Malone-Cooke, Matty Asante-Owusu, Edith Aimiwu, Sarah Cullen and Olivia Kudom)

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

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.whitthealthPALS@nhs.net

If you need a large print, audio or translated copy of this leaflet please contact us on 020 7288 3182. We will try our best to meet your needs.