NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

MultipleTechnology Appraisal

Desferrioxamine, deferiprone and deferasirox for the treatment of chronic iron overload in people with thalassaemia

Scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of desferrioxamine, deferiprone and deferasirox for the treatment of chronic iron overload in people with thalassaemia.

Background

Iron overload occurs when excess iron collects in the body. As the body has very limited capacity for removing iron, iron gradually accumulates. Excess unbound (free) iron deposits in the tissues of the liver, endocrine organs and heart. This can lead to liver cirrhosis, endocrine complications such as diabetes, impaired growth in children, sterility, and heart failure. Chronic iron overload therefore increases mortality risk. Iron overload can be caused by excessive absorption of iron from diet or more commonly through frequent blood transfusions.

Blood transfusions represent lifesaving therapy for patients with chronic anaemia, such as those suffering from thalassaemia. Thalassaemia is the name given to a group of inherited blood disorders that cause the body to make fewer healthy red blood cells and less haemoglobin. There are two basic groups of thalassaemia disorders: alpha-thalassaemia and beta-thalassaemia. These conditions cause varying degrees of anaemia, which can range from insignificant to life threatening. The most severe forms are known as alpha- or beta-thalassaemia major and the least severe forms as alpha- or beta-thalassaemia minor. Both forms of thalassaemia minor do not usually require any specific treatment whilst alpha-thalassaemia major usually results in intrauterine death. Beta-thalassaemia major involves frequent blood transfusions (possibly twelve or more each year). In addition, thalassaemia intermedia is associated with significant iron overload due to either increased oral iron absorption or intermittent blood transfusions. Some people with thalassaemia intermedia require regular blood transfusions but in general this is fewer than seven episodes per year.

The prevalence of thalassaemia varies considerably across different ethnic communities. For example, the estimated prevalence is 16% in people from Cyprus and 3-8% in populations from Bangladesh, China, India, Malaysia and Pakistan. A very low prevalence has been reported among people of Northern European origin (0.1%).

People with thalassaemia are at risk of collecting excess iron in their bodies both from the disease itself and from the multiple blood transfusions that they receive. Total body iron stores are usually within the range of 3 – 4 grams. Each unit of transfused blood contains 200-250 mg of iron, all of which cannot be excreted. The risk of iron overload increases once patients have received approximately 10 transfusions. An adult patient with a high transfusion requirement, defined as 3-4 units of blood per month (such as given in beta-thalassaemia major), will need iron chelation therapy after 6 months. The timing for children will depend on the transfusion frequency and amount of blood being transfused. Data provided by the UK thalassaemia register, which ceased recording in 2003, suggested there were 624 beta thalassaemia major patients at risk of iron overload at that time, plus *"a small proportion"* of the 162 patients registered with other beta thalassaemias.

In the UK the current treatment options for patients with thalassaemia presenting with transfusion-related iron overload are three iron chelating agents as outlined below.

The technologies

Desferrioxamine

Desferrioxamine mesilate (Desferal, Novartis; Desferrioxamine mesilate, Hospira) has a UK marketing authorisation for the treatment of chronic iron overload, including acute iron poisoning; primary and secondary haemochromatosis including thalassaemia and transfusional haemosiderosis; in patients in whom concomitant disorders (for example, severe anaemia, hypoproteinaemia, renal or cardiac failure) preclude phlebotomy; and for the diagnosis of iron storage disease and sideroblastic anaemia, auto-immune haemolytic anaemia and other chronic anaemias. The summary of product characteristics (SPC) for Desferal (Novartis) states that it is administered parenterally. The SPC for desferrioxamine mesilate (Hospira) states that it is administered intramuscularly, intravenously, or subcutaneously.

Deferasirox

Deferasirox (Exjade, Novartis pharmaceuticals) is an iron-chelating agent that is given as dispersible tablets once daily and taken as a suspension (usually in water or fruit juice). It has a UK marketing authorisation for the treatment of chronic iron overload due to frequent blood transfusions (≥ 7 ml/kg/month of packed red blood cells) in patients with beta thalassaemia major aged 6 years and older.

Deferasirox also has UK marketing authorisation for the treatment of chronic iron overload due to blood transfusions when desferrioxamine therapy is contraindicated or inadequate in the following patient groups:

- in patients with other anaemias,

- in patients aged 2 to 5 years,

- in patients with beta thalassaemia major with iron overload due to infrequent blood transfusions (<7 ml/kg/month of packed red blood cells).

Deferiprone

Deferiprone (Ferriprox, Apotex) is an iron chelator that is usually given 3 times daily as film coated tablets or as an oral solution. It has a UK marketing authorisation for the treatment of iron overload in patients with thalassaemia major when desferrioxamine therapy is contraindicated or inadequate.

Intervention(s)	Desferrioxamine Deferasirox Deferiprone
Population(s)	People with thalassaemia who have developed chronic iron overload following blood transfusions
Comparators	Deferasirox, deferiprone and desferrioxamine will be compared with each other as appropriate
Outcomes	The outcome measures to be considered include: • liver iron content and liver pathology • total body iron excretion • cardiac iron content and cardiac function • effects on iron balance • mortality • adverse effects of treatment • health related quality of life
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.

Other considerations	Where the evidence allows, combinations of the different iron chelators will be considered. Where appropriate, treatment of children and adults will be considered separately. Where the evidence allows, patients with significant cardiac iron overload will be considered as a subgroup. If the evidence allows, the effect of adherence to treatment on outcomes will be considered.
Related NICE recommendations	None