NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Technology Appraisal

Deferasirox and deferiprone for the treatment of chronic iron overload

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of deferasirox and deferiprone, within their licensed indications, for the treatment of chronic iron overload.

Background

Iron overload occurs when excess iron collects in the body. As there are no natural means of removing excess iron, iron gradually accumulates. This results in abdominal discomfort and fatigue and can lead to major damage of the heart and liver with increased mortality. Iron overload can be caused by a malabsorption of iron from the ingestion of food or more commonly through frequent blood transfusions. Blood transfusions represent lifesaving therapy for patients with chronic anaemia, such as those suffering from thalassaemia and sickle cell disease. Total body iron stores are usually within the range of 200-1500 mg and with each unit of transfused blood, 200-250 mg of iron is transferred, all of which cannot be excreted. The risk of iron overload increases once patients have received approximately 20 transfusions.

Currently in the UK, patients presenting with transfusion-related iron overload are treated with deferoxamine (DFO), also known as desferrioxamine. Patients receive DFO via nightly infusions (5–7 times a week) from as early as 2 years of age. Patients over the age of 6 years who are suffering from beta-thalassaemia major also have the option to try deferiprone when deferoxamine therapy is contraindicated or inadequate. Deferiprone is an oral tablet given three times a day.

The technologies

Deferasirox

Deferasirox (Exjade, Novartis pharmaceuticals) is an orally active iron-chelating agent that is given once daily as a suspension (usually in water or fruit juice). It has 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 orally active iron chelator and has a UK marketing authorisation for the treatment of iron overload in patients with thalassaemia major when deferoxamine therapy is contraindicated or inadequate.

Intervention(s)	Deferasirox Deferiprone
Population(s)	People with chronic iron overload under the conditions as specified in the marketing authorisations of deferasirox and deferiprone.
Comparators	For people with thalassaemia major: • Deferoxamine, also known as desferrioxamine When desferrioxamine is contraindicated or inadequate: • Deferasirox and deferiprone will be compared with each other • Treatment without desferrioxamine

Outcomes	The outcome measures to be considered include:
	• absolute and relative change of liver iron content
	• total body iron excretion
	• changes in serum ferritin levels, including:
	  ○ maintenance of iron balance
	  ○ induction of negative iron balance
	• 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	Guidance will only be issued in accordance with marketing authorisation.
Related NICE recommendations	None

How is chronic iron overload defined? What is the expected incidence and prevalence in England and Wales?

Are there specific populations that should be considered in the appraisal?

What constitutes treatment without desferrioxamine in clinical practice in the NHS in England and Wales?

Have the most appropriate comparators for the treatment of chronic iron overload been included in the scope? Are the comparators listed routinely used in clinical practice?

Are there any subgroups of patients in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

NICE intends to appraise this technology through its Multiple Technology Appraisal (MTA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)