NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Technology Appraisal

Deferasirox and deferiprone for the treatment of chronic iron overload in people with thalassaemia

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 in people with thalassaemia.

Background

Iron overload occurs when excess iron collects in the body. As there are no natural means of removing excess iron, iron gradually accumulates. Excess unbound (free) iron deposits in the tissues of the liver, endocrine organs and heart. The complications are liver cirrhosis, endocrine complications such as diabetes, impaired growth in children, sterility etc, and cardiomyopathy (heart failure). All these conditions lead to early morbidity and mortality. Iron overload can be caused by a malabsorption of iron from excessive absorption of iron from diet or more commonly through frequent blood transfusions (transfusion to replace blood loss from trauma would not carry the same risk of iron overload).

Blood transfusions represent lifesaving therapy for patients with chronic anaemia, such as those suffering from thalassaemia. 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 20 transfusions. A patient with a high transfusion requirement, defined as 3-4 units of blood per month (such as beta-thalassaemia major), will need iron chelation therapy after 6 months. 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.

Currently in the UK, patients presenting with transfusion-related iron overload are treated with desferrioxamine (DFO), also known as deferoxamine. Patients receive desferrioxamine 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 desferrioxamine therapy is contraindicated or inadequate.

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, i.e. ≥ 2 transfusions/month) 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 desferrioxamine therapy is contraindicated or inadequate. Deferiprone is available an oral tablet given three times a day and as oral solution

Intervention(s)	Deferasirox Deferiprone
Population(s)	People with thalassaemia who have developed chronic iron overload following blood transfusions
Comparators	For people with thalassaemia major: • Desferrioxamine, also known as deferoxamine 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
	• overall survival
	• adherence to treatment
	• 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 the marketing authorisations.
Related NICE recommendations	None

How is chronic iron overload defined in people with thalassaemia? What is the expected incidence and prevalence in England and Wales in this patient population?

To what extent in clinical practice are deferiprone and deferasirox used in combination with desferrioxamine? Should deferiprone and deferasirox be appraised as monotherapies or in combination with desferrioxamine?

Is the population defined appropriately?

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

Have the most appropriate comparators for deferiprone and deferasirox for the treatment of chronic iron overload in people with thalassaemia been included in the scope? Are the comparators listed routinely used in clinical practice?

Are there any subgroups of people 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?

What do you consider to be the relevant clinical outcomes and other potential health related benefits of eribulin in the treatment of breast cancer, particularly when compared with currently used treatment options?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

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)