NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
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Ferric maltol for treating iron deficiency anaemia in children and adolescents aged 1 month to 17 years

Company/Developer	Norgine Pharmaceuticals Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 34393	NICE ID: Not available	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase lll clinical development.

Summary

Ferric maltol is in clinical development for the treatment of children and adolescents with iron deficiency anaemia. Iron deficiency anaemia is diminished red blood cell production due to low iron stores in the body, and can develop because of malnutrition, malabsorption, or blood loss. Iron deficiency, with or without anaemia, adversely affects overall health and well-being, daily activities, productivity, and quality of life. Traditional iron replacement therapies have been associated with poor absorption of elemental iron; adverse effects which have limited their efficacy and reduced compliance, or requiring hospital attendance for intravenous iron administration which may be difficult or inconvenient for patients. There is need for more treatment options that provide adequate absorption of iron, produce a faster response, and are better tolerated than the currently available treatment options.

Ferric maltol is a complex of ferric iron and a trimaltol ligand (a novel, stable complex, formed between ferric iron (FeH) and maltol (3-hydroxy-2-methyl-4 pyrone)) designed to optimise iron absorption while reducing the gastrointestinal adverse events associated with unabsorbed free iron. Ferric maltol is administered orally and is absorbed by the cells of the gut; ferric iron is then absorbed after disassociation from the maltol complex and transported and stored in the body, helping to restore normal levels in patients with iron deficiency. Ferric maltol is approved for the treatment of iron deficiency in adults. If licensed, ferric maltol would offer an additional and better tolerated treatment option for children and adolescents with iron deficiency anaemia.

Proposed Indication

Treatment of iron deficiency anaemia in children and adolescents aged 1 month to 17 years. [1]

Technology

Description

Ferric maltol (Feraccru; ST10) contains iron in a stable ferric state as a complex with a trimaltol ligand. The maltol complex is designed to provide, in a controlled way, utilisable iron for uptake across the intestinal wall and transfer to the iron transport and storage proteins in the body (transferrin and ferritin, respectively). The complex dissociates on uptake from the gastro-intestinal tract and the complex itself does not enter the systemic circulation. [2]

Ferric maltol is currently in clinical development for the treatment of iron deficiency anaemia in children and adolescents aged 1 month to 17 years. In the phase III clinical trial (FORTIS, NCT05126901), children aged from 1 month up to less than 2 years were administered ferric maltol oral suspension at a dose of 0.1 ml/kg twice daily and continued for 7-10 days. Children and adolescents aged 2 to 17 years were administered ferric maltol oral suspension at a dose of 6 mg/kg to the maximum of 4 ml twice daily. [1]

Key Innovation

Ferric maltol has high bioavailability and is designed to be better tolerated than the currently available oral ferrous (Fe2+) products. [2] There are other oral iron preparations in salt form which are efficacious at correcting iron deficiency, however iron salts are often poorly tolerated because of gastrointestinal (GI) toxicity. Prior to the approval of ferric maltol for the treatment of iron deficiency in adults, the second-line treatment recommended for patients who cannot tolerate oral iron salts included intravenous (IV) iron. Although effective, parenteral iron products carry risks such as anaphylaxis, high cost, and the need for administration in a facility that is equipped to respond to severe reactions.. [3]

If licensed, ferric maltol will offer an effective oral alternative for the treatment of children and adolescents with iron deficiency anaemia who are unable to tolerate other oral iron formulations or fail to achieve adequate haematological response.

Regulatory & Development Status

Ferric maltol currently has Marketing Authorisation in the EU/UK for the treatment of iron deficiency in adults.[2]

Ferric maltol is also in the phase III/II clinical development for the following indications: [4]

- iron deficiency anaemia in subjects with chronic kidney disease
- iron deficiency anaemia in patients with inflammatory bowel disease
- as a perioperative for colorectal cancer

Patient Group

Disease Area and Clinical Need

Iron deficiency refers to any situation in which there is insufficient iron available in the body to meet physiologic needs. [5] Iron deficiency anaemia is diminished red blood cell production due to low iron stores in the body. Anaemia is defined as a haemoglobin (Hb) level two standard deviations below the normal for age and sex, in which for children aged 12 to 14 years, it is Hb below 120g/L. The cause of iron deficiency

anaemia is often multifactorial and may be broadly attributed to dietary deficiency, malabsorption, menstrual blood loss in females, or increased requirements. [6,7] The most common causes of iron deficiency in children include insufficient intake together with rapid growth, low birth weight and gastrointestinal losses related to excessive intake of cow's milk.[8] Iron deficiency adversely affects overall health and well-being, even before the development of anaemia. Iron deficiency, with or without anaemia, is associated with fatigue, impaired physical and cognitive function, headache, tachycardia, and dyspnoea, with resulting adverse impacts on daily activities, productivity, quality of life, and any additional underlying illnesses.[5]

In the UK, it is estimated that 3% of men and 8% of women have iron deficiency anaemia. Iron deficiency anaemia is the reason for at least 10% of gastroenterology referrals.[10] In England in 2022-2023, there were 192,237 finished consultant episodes (FCE) and 173,227 hospital admissions for iron deficiency anaemia (ICD-10 code D50) which resulted in 112,646 FCE bed days and 129, 683 day cases.[11]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommends the following regimen for the treatment of iron deficiency anaemia from age 12 years onwards: [12]

- a dose of 65 mg elemental iron (ferrous sulfate 200 mg) once daily (on an empty stomach)
- for people with significant intolerance to oral iron replacement therapy options, include alternate day dosing, oral ferric maltol, or parenteral iron preparations

The following regimen is also recommended for the treatment of iron deficiency anaemia in infants: [13]

- prophylaxis with an iron preparation may be appropriate in those with a poor diet, malabsorption, menorrhagia, pregnancy, in haemodialysis patients, and in the management of low birth-weight infants such as preterm neonates.
- iron salts should be given by mouth unless there are good reasons for using another route.
- iron supplementation is required to produce an optimum response to erythropoietin in iron-deficient children with chronic renal failure or in preterm neonates.

Clinical Trial Information

Trial	**FORTIS**; NCT05126901; Randomised, Open-label, Active-controlled, Multicentre, Comparative Study to Evaluate the Safety and Efficacy of Ferric Maltol (Iron (III)-Maltol Complex) (ST10) Oral Suspension Compared to Ferrous Sulfate Oral Liquid in Children and Adolescents Aged 2 to 17 Years With Iron-deficiency Anaemia, Incorporating a Single Arm Study in Infants Aged 1 Month to Less Than 2 Years **Phase III –** Recruiting **Location(s):** UK, USA, and Puerto Rico **Primary completion date:** May 2023
Trial Design	Randomised, parallel assignment, open label, active-controlled, multicentre
Population	N=110 (estimated); all sexes; Subjects aged 1 month to 17 years with iron deficiency anaemia
Intervention(s)	• Ferric maltol oral suspension for aged 1 month to < 2 years at a dose of 0.1 ml/kg twice daily (BID) for 7 to 10 days

	• Ferric maltol oral suspension for aged 2 to 17 years at a dose of 6 mg/kg to the maximum of 4 ml BID, that is, 2 to 11 years: 2.5 ml BID, 12-17 years: 5 ml BID
Comparator(s)	Ferrous sulphate oral liquid for aged 2 years to 17 years at a dose of 6 mg/kg to the maximum of 4 ml BID
Outcome(s)	Primary outcome measure: • Safety and gastrointestinal tolerability will be compared between ferric maltol oral suspension and ferrous sulfate oral liquid via summaries of treatment emergent adverse events (TEAEs), treatment emergent serious AEs (TESAEs) and treatment-emergent AEs [Time Frame: 12 weeks] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Ferric maltol is already marketed in the UK; a pack of 56 x 30mg capsules costs £47.60.[14]

Relevant Guidance

NICE Guidance

No guidance found

NHS England (Policy/Commissioning) Guidance

NHS England. 2013/14 NHS Standard Contract for Specialised Services for Haemoglobinopathy care (All Ages). B08/S/a.

Other Guidance

- NHS England. Adult Therapeutic Handbook. Iron Deficiency Anaemia in Acute Care. September 2023. [15]
- NHSGGC Guideline. Anaemia in children with chronic kidney disease. April 2022. [16]
- British Society of Gastroenterology. Guidelines for the Management of Iron Deficiency Anaemia in Adults. September 2021.[17]
- World Health Organization Guideline. daily iron supplementation in infants and children. March 2016. [18]

Additional Information

Norgine Pharmaceuticals Limiteddid not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective

decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

References

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