Mid and South Essex Health and Care Partnership

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Mid and South Essex Medicines Optimisation Committee (MSEMOC)

FERRIC MALTOL (FERACCRU®) FOR THE TREATMENT OF IRON DEFICIENCY IN ADULTS with INFLAMMATORY BOWEL DISEASE

RED: RECOMMENDED FOR RESTRICTED USE in Secondary Care by Gastroenterology Specialists

Name: generic (trade)	What it is	Licensed indications	Decision status	NICE/SMC guidance
Ferric maltol (Feraccru®)	Iron in a stable ferric state complex with a trimaltol ligand	Treatment of iron deficiency in adults	Final	NICE – no guidance SMC- not recommended

MSEMOC recommendation:

Ferric maltol (Feraccru®) is RECOMMENDED FOR RESTRICTED USE for IRON DEFICIENCY ANAEMIA (IDA) in ADULTS with INFLAMMATORY BOWEL DISEASE (IBD):

- **For initiation and continuation in secondary care by gastroenterology specialists only**
- **Restricted for use as a third line oral treatment option where:**
  - **The patient has a diagnosis of IBD and a haemoglobin >95g/L but less than normal range (120g/L in women, 130g/L in men) AND**
  - **Two or more different oral iron salts have been trialled for an adequate period of time but are not tolerated AND**
  - **The next step in treatment would otherwise be intravenous iron**
- **Formulary status will be reviewed after the first 12 months (February 2022) and continued provided demonstration of expected outcomes by presentation of audit (refer to implementation section for further details)**

Providers commissioned to provide services on behalf of Mid and South Essex CCGs are reminded that they are required to follow the local joint formulary and prescribing guidance, as detailed in the medicines management service specification of their contract.

Background information:

- Feraccru® is licenced in adults for the treatment of iron deficiency anaemia. The recommended dose of ferric maltol is 30mg twice daily, morning and evening, taken whole on an empty stomach with half a glass of water. Treatment duration will depend on the severity of the IDA, but generally 12 weeks' treatment is required. Treatment should be continued until tests demonstrate that iron stores have been replenished.
- Between 20-76% of patients with inflammatory bowel diseases (IBD) experience Iron Deficiency Anaemia (IDA) which impairs quality of life causing symptoms such as headache and fatigue.
- Feraccru® (oral ferric maltol), is an iron complex consisting of a single ferric iron ion (Fe^{3+}) chelated, with high affinity, to three maltol molecules. Maltol is a naturally occurring sugar derivative which is formed during when sugar caramelises and it is often used as a flavour enhancer in food products. The maltol moiety ensures that the ferric iron remains tightly bound to maltol at the higher pH of the gut where most iron absorption occurs. This purported high comparative bioavailability means that greater amounts of elemental iron can be delivered more easily. Also, the gastrointestinal mucosa is not exposed to high levels of free iron so it is hypothesised that the potential for tolerability problems is minimised.
- NICE recommend iron salts should be given by mouth unless there are good reasons for using another route, however, ferric maltol has not been included. Oral iron preparations listed in the NICE guidance include ferrous sulphate, ferrous fumarate and ferrous gluconate. However, adverse effects from taking an iron supplement are commonly experienced.
- Iron can be administered parenterally as iron dextran, iron sucrose, ferric carboxymaltose, or iron isomaltoside 1000. Parenteral iron is generally reserved for use when oral therapy is unsuccessful because the patient cannot tolerate oral iron, or does not take it reliably, or if there is continuing blood loss, or in malabsorption.
- Feraccru® should not be used in patients with inflammatory bowel disease (IBD) flare or in IBD- patients with haemoglobin (Hb) <95 g/L.

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ASSESSMENT AGAINST THE ETHICAL FRAMEWORK

Evidence of Clinical Effectiveness:

Comparison of the efficacy of Feraccru® with placebo

The safety and efficacy of Feraccru® for the treatment of iron deficiency anaemia was studied in 128 patients with inactive to mildly active IBD. Patients were enrolled in one combined randomised, placebo-controlled clinical study. All patients had discontinued from prior oral ferrous product (OFP) treatment: more than 60 % of the subjects stopped taking prior OFP due to adverse events. Subjects were randomised to receive either 30 mg Feraccru® twice daily or a matched placebo control for 12 weeks. The difference between the change from baseline for Feraccru® compared to placebo at week 12 was 2.25 g/dL ($p<0.0001$) [(2)].

Comparison of the efficacy of Feraccru® with other oral iron preparations

A meta-analysis was conducted including data from study ST10-01-301/302 and 21 published studies. The median duration of supplementation with ferrous sulphate (200mg three times a day) for these 21 trials was 6 weeks (range 4-20 weeks) and the reported mean Hb increase was 2.2 g/dL (SD 1.2). The mean increase with Feraccru® (30mg twice a day) at 4, 8 and 12 weeks was 1.08, 1.79 and 2.26 g/dL, respectively. In the meta-analysis, there was no significant difference for the comparison of change in Hb increase between ferrous sulphate and Feraccru® [(3)].

Comparison of the efficacy of Feraccru® with intravenous iron preparations

A 52-week AEGIS–H2H Phase 3b study compared the efficacy of oral ferric maltol to ferric carboxymaltose (FCM) in the treatment and maintenance of iron deficiency anaemia in subjects with inactive IBD in whom other oral iron therapies had failed. This was a multi-national Phase IIIb randomised, active-controlled trial in 242 patients across USA and Europe. Change in Hb concentration from baseline to week 12: 2.66g/dL ferric maltol compared to 3.00g/dL for ferric carboxymaltose [(4)].

SAFETY

- Ferric maltol is contraindicated in patients with hypersensitivity to the active substance or any excipients, haemachromatosis or other iron overload syndromes and in patients receiving repeated blood transfusions.
- There is limited data on the use of ferric maltol in patient with severe IDA ((haemoglobin <95g/L) or active IBD, and its use is cautioned in these patients.
- The most commonly reported adverse effects were were gastrointestinal symptoms (abdominal pain [8%], flatulence [4%], constipation [4%], abdominal discomfort [2%]/distension [2%] and diarrhoea [3%]) and these were mainly mild to moderate in severity. Reported severe adverse reactions were abdominal pain [4%], constipation [0.9%] and diarrhoea [0.9%].
- There is no evidence that ferric maltol exacerbates symptoms of IBD.

Cost of treatment and Cost Effectiveness:

- The Scottish Medicines Consortium and the All Wales Medicines Strategy Group have advised that ferric maltol is not recommended for use since the cost-effectiveness data was insufficient to demonstrate an economic case.
- Comparative price of typical iron correction course:
  - Ferrous sulphate 200mg tablets, two or three times daily x 12 weeks = **£5.40 - £8.10**
  - Ferrous fumarate 210mg two or three times daily x 12 weeks = **£7.98 - £11.97**
  - Feraccru® 30mg capsules twice daily x 12 weeks (minimum) = **£142.80**
  - Cosmofer®: Dose for a patient weighing 70kg would be **1175mg-2000mg** depending on the haemoglobin level = **£159.40****
  - Venofer®: Dose for a patient weighing 70kg would be **125mg - 200mg** over several injections (maximum 20mg per administration) = **£71.68 - £102.40****
  - Ferinject®: Dose for a patient weighing 70kg would be **500mg – 2000mg** (depending on Hb) over 1 – 2 injections / infusions = **£95.50 - £308.46****
  - Cost of administration of IV iron has not been considered.

** Patients at the higher end of the dosing schedules for IV iron administration may be contraindicated for ferric maltol if they have IBD with a haemoglobin level of <95 g/L and therefore direct cost comparison at the higher dose range should be used with caution.

The needs of the population:

- The needs of the population may be low as there are alternative iron replacement therapies available.
- There is no evidence to demonstrate clinical advantage of ferric maltol over IV iron, and correction of iron deficiency via this route would not be as rapid, however, it may be a more acceptable therapy route for patients.

The needs of the community:

- The needs of the community may be low as the estimated patient numbers for treatment are low, the submitting consultant has estimated using this for approximately 10 patients in the first year, it is not known whether similar patient numbers would be expected from other sites in the HCP and therefore this assessment may be considered uncertain.
- If ferric maltol were added to the formulary as a yellow drug, this would present a cost pressure in primary care prescribing since IV iron is currently administered by acute trusts.
- If ferric maltol were added to the formulary as a red drug, there may be a small cost and capacity efficiency opportunity for the acute trusts in avoiding IV administration of iron

Equity and Equality:
No impact anticipated. Guidance applies to all relevant patients where indicated. There is no differential impact expected on one or more equality groups differently to others Age, Disability; Gender reassignment; Marriage & Civil Partnership; Pregnancy & Maternity; Race; Religion & Belief; Sex; Sexual orientation.

Policy drivers:

- **NICE Clinical Knowledge Summary: Iron deficiency anaemia**
  Includes only the oral iron preparations (ferrous sulphate, ferrous fumerate and ferrous gluconate). A lack of response or a patient unable to tolerate 2 or more different oral iron preparations are reasons to refer for specialist assessment.
- **The Northern Treatment Advisory Group (NTAG)**
  In September 2016 NTAG recommended the use of ferric maltol as an alternative option in patients with mild to moderate IDA with IBD who have tried at least two oral ferrous salts and have a reported intolerance to oral ferrous salts due to adverse effects after an adequate trial. Initiation and prescribing of ferric maltol should be carried out by an IBD specialist.
- **The Scottish Medicines Consortium**
  In December 2016, The Scottish Medicines Consortium has advised that ferric maltol is not recommended for use within NHS Scotland for the treatment of iron deficiency anaemia in adults with inflammatory bowel disease as the economic case was not demonstrated.
- **All Wales Medicines Strategy Group (AWMSG)**
  Ferric maltol is not recommended for use within NHS Wales for the treatment of iron deficiency anaemia in adults with inflammatory bowel disease. The cost-effectiveness data presented in the submission were insufficient for AWMSG to recommend its use.

EoE CCG decisions:

- **Cambridge and Peterborough CCG (Sept 17):**
  Feraccru® for mild to moderate iron deficiency anaemia in patients with inflammatory bowel disease. Feraccru® (oral ferric maltol) is recommended as an alternative to intravenous iron where two or more first line oral ferrous salts have failed or there is reported intolerance (RECOMMENDED Specialist advice)
  Feraccru® will only be recommended within its product licence 'mild to moderate iron deficiency anaemia in patients with inflammatory bowel disease' as a 12-week treatment course. (12-week treatment course = £142.80) Budget impact model: 485 patients potentially per annum would be eligible across C&PCCG (population 998K). Activity associated with IV iron administration is billed as SA04K and SA04L (Best Practice Tariffs): £323.30 and £289.55; average of £307.68 used in calculations based on actual split in billing data M1-M5 1718. (Data provided by CUHFT)

Treatment	Cost of treatment course (per patient)	Cost of treatment (485 patients)	Additional cost for 13% failure rate	Total Cost
Feraccru® (oral)	£142.80	£69,258	£19,383	£88,641
IV iron	£307.68	£149,224		£149,224
Total Savings				**£60,583**

  Savings will be seen by a reduction in secondary care activity.

- **Norfolk and Waveney Drug and Therapeutics Committee (March 19):**
  Due to concerns that use of Ferric maltol (Feraccru®) would become widespread in primary care as a general treatment for iron deficiency anaemia, the D&TC recommended a revised classification of Red (Hospital/Specialist use only), where the specialist provides the complete treatment course.
- **West Essex CCG (Jan 18):**
  Not recommended for prescribing in primary or secondary care. MOPB January 2018 (On the RED list).
- **Ipswich and East Suffolk CCG:** Non-formulary

Other:

- **London Medicines Evaluation Network Review**
  Ferric Maltol (oral Feraccru®) for the treatment of iron deficiency anaemia in adults with inflammatory bowel disease:
  The review concluded that Feraccru® may be a useful treatment option in patients with mild to moderate IDA with either CD or UC who have reported intolerance to oral ferrous salts. In these patients, it should be considered as an alternative to IV iron products if there is no urgent need to raise Hb levels (e.g. prior to surgery), i.e. second line to other oral ferrous iron products and an alternative to IV iron products. It is expected that at least 12 weeks of treatment with Feraccru® would be required to raise Hb levels to target, after which it should be used for 1-3 months afterwards as is the current practice with other orally administered iron products in IBD. Data for use of Feraccru® for up to 12 months is available to support safe use in patients who require continued use for a longer period of time

Implementability:

- No issues identified
- Secondary care providers must:
  - Implement the use of an internal proforma (i.e. a hospital use only) for gastroenterology specialists to submit to the hospital pharmacy team
  - Submit an audit report in 6 to 12 months' time (from the date of publication of the decision document) to MSEMOC on use of ferric maltol (with at least 10 patients), it must include:
    - Total number of patients treated with ferric maltol
    - Whether use was in line with the recommendation
    - The baseline number of intravenous iron infusions being carried out per year prior to the introduction of ferric maltol
    - The proportion of patients going onto require intravenous iron infusions in 1 year despite treatment with ferric maltol and the reasons for this (e.g. adverse effects, nonresponse)
    - The number of intravenous iron infusions avoided in 1 year through use of ferric maltol
    - Impact on patient related outcomes, such as (i) adverse effects (ii) compliance (iii) normalisation of Hb/resolution of anaemia
    - The number of patients discontinuing treatment with ferric maltol and reasons for stopping
    - This recommendation will be reviewed, if necessary, on receipt of the report

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Acknowledgements	Mid and South Essex CCGs Medicines Management Teams
Version	1.0
Author	HCPMSEMOC working group
Approved by	MSEMOC; MSE Joint Committee
Date Approved	December 2020; January 2021
Review Date	December 2025 or sooner if subject to any new updates nationally