Accrufer® (ferric maltol) Phase 3A Studies

AEGIS 1 & 2 IBD
Gasche C, Ahmad T, Zsolt T, et al

Ferric maltol is effective in correcting iron deficiency anemia in patients with inflammatory bowel disease: results from a phase-3 clinical trial program.

Inflammatory Bowel Diseases 2015

AEGIS 1 & 2 IBD—LONG-TERM EXTENSION
Schmidt C, Ahmad T, Tulassay Z, et al

Ferric maltol therapy for iron deficiency anaemia in patients with inflammatory bowel disease: long-term extension data from a phase 3 study.

Alimentary Pharmacology and Therapeutics 2016

AEGIS 3 CKD
Pergola PE, Kopyt NP

Oral ferric maltol for the treatment of iron-deficiency anemia in patients with CKD: a randomized trial and open-label extension.

American Journal of Kidney Diseases 2021

These clinical papers may present some information about Accrufer that is not contained in or is inconsistent with its FDA-approved Prescribing Information. Shield Therapeutics recommends use of Accrufer only in accordance with its approved Prescribing Information.

INDICATIONS & USAGE

Accrufer® (ferric maltol) is indicated for the treatment of iron deficiency in adults.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Accrufer is contraindicated in patients with a history of:

- Hypersensitivity to Accrufer or any of its inactive components.
- Hemochromatosis and other iron overload syndromes.
- Receiving repeated blood transfusions as this may result in iron overload.

Please see Important Safety Information throughout and accompanying full Prescribing Information.

ACCRUFeR®
(ferric maltol) 30 mg capsules

AEGIS 1 & 2 IBD
Gasche et al

IBD 12-week study

A short-term (12 weeks) phase 3 trial of patients with inflammatory bowel disease (IBD) who were treated for iron deficiency anemia (IDA) with Accrufer®

ABBREVIATED STUDY DESIGN:

AEGIS 1 & 2 studied adult patients with ulcerative colitis (UC) or Crohn's disease (CD), mild-to-moderate IDA (hemoglobin [Hb] 9.5-12.0 g/dL and 9.5-13.0 g/dL in females and males, respectively), and documented failure on previous oral ferrous products. Patients received oral ferric maltol capsules (Accrufer 30 mg twice a day) or identical placebo for 12 weeks according to a randomized, double-blind, placebo-controlled study design.

Primary endpoint: change in Hb from baseline to week 12. Secondary endpoints included changes in Hb concentration from baseline to weeks 4 and 8, serum ferritin concentration, and percentage transferrin saturation (TSAT).

SELECTED RESULTS:

- "Ferric maltol demonstrated a good tolerability profile, with a similar overall incidence of AEs [adverse events] compared with placebo."

Changes in hemoglobin, ferritin, and TSAT between baseline and week 12

		Ferric Maltol (n=64), Mean (SD)	Placebo (n=64), Mean (SD)
Hemoglobin, g/dL	Baseline	11.00 (1.03)	11.10 (0.85)
	Week 12	13.20 (1.04)	11.20 (0.98)
Ferritin, µg/L	Baseline	8.6 (6.8)	8.2 (6.5)
	Week 12	26.0 (30.6)	9.8 (9.6)
TSAT, %	Baseline	10.6 (11.7)	9.5 (7.5)
	Week 12	28.5 (17.2)	9.8 (8.1)

AUTHORS' CONCLUSIONS:

"In conclusion, this randomized controlled study demonstrated that the novel oral iron therapy, ferric maltol, provided rapid and clinically meaningful improvements in Hb concentration, normalized Hb in the majority of patients, and showed a favorable safety and tolerability profile."

Please scan the QR code for a complete presentation of study design, results, safety, and conclusions:
Gasche C, Ahmad T, Zsolt T, et al. Ferric maltol is effective in correcting iron deficiency anemia in patients with inflammatory bowel disease: results from a phase-3 clinical trial program. *Inflamm Bowel Dis*. 2015;21:579-588.

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WARNINGS AND PRECAUTIONS

Increased Risk of Inflammatory Bowel Disease (IBD) Flare

Avoid use of Accrufer in patients with an active IBD flare, as there is potential risk of increased inflammation in the gastrointestinal tract.

Iron Overload

Excessive therapy with iron products can lead to excess storage of iron with the possibility of iatrogenic hemosiderosis. Do not administer Accrufer to patients with evidence of iron overload or patients receiving intravenous iron. Assess iron parameters prior to initiating Accrufer and monitor iron parameters while on therapy.

Risk of Overdosage in Children Due to Accidental Ingestion

Accidental overdose of iron products is a leading cause of fatal poisoning in children under age 6. Keep out of reach of children.

ADVERSE REACTIONS

Most common adverse reactions (≥2%) reported with Accrufer during the double-blind, placebo-controlled portions of the pivotal trials were flatulence (4.6%), diarrhea (4%), constipation (4%), discolored feces (4%) and abdominal pain (2.9%).

To report adverse events, please contact Shield Therapeutics at 1-888-963-6267. You may also contact the FDA at www.fda.gov/medwatch or 1-800-FDA-1088.

Please see accompanying full Prescribing Information.

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AEGIS 1 & 2 IBD—Long-Term Extension
Schmidt et al

IBD 52-week open-label extension study

A long-term (64 weeks) phase 3 extension study to continue the evaluation of the efficacy of Accrufer in patients with IBD who had IDA

ABBREVIATED STUDY DESIGN:

After the 12 weeks of randomized, double-blind study (AEGIS 1 & 2 IBD), an open-label extension trial was conducted of Accrufer 30 mg twice daily for adult patients with UC or CD in whom previous oral ferrous therapies had failed to correct IDA. All patients who completed the initial 12-week period were able to continue into the 52-week open-label extension.

Primary endpoint: absolute change in Hb from baseline to week 64. Secondary endpoints included absolute serum ferritin concentration and TSAT.

SELECTED RESULTS:

- "The tolerability of this novel ferric iron formulation remained favourable throughout this long-term (64-week) study, with few patients withdrawing due to medication-related effects."
- "Median treatment compliance was very high (97%) during the long-term extension...."

Changes in hemoglobin between baseline and week 64

N=128		Group Continuing with Ferric Maltol Mean (SD)	Group Switched to Treatment with Ferric Maltol Mean (SD)
Hemoglobin, g/dL	Baseline	11.00 (1.03)	11.10 (0.85)
	Week 64	13.9 9 (1.26)	13.33 (1.46)

Changes in mean absolute ferritin and TSAT between baseline, week 16, and week 64
(including patients in both the randomized and long-term extension phases)

Ferritin, µg/L	Baseline	8.4 (6.6) N=128
	Week 16	25.5 (42.0) N=91
	Week 64	57.4 (77.4) N=72
TSAT, %	Baseline	10% (10%) N=128
	Week 16	26% (17%) N=91
	Week 64	29% (13%) N=72

AUTHORS' CONCLUSIONS:

"This long-term study demonstrated that, after significant improvements in haemoglobin during the initial 12 weeks of randomised ferric maltol treatment, continued treatment with this novel oral iron therapy maintained or further improved haemoglobin up to 64 weeks without substantial numbers of adverse events."

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Schmidt C, Ahmad T, Tulassay Z, et al. Ferric maltol therapy for iron deficiency anaemia in patients with inflammatory bowel disease: long-term extension data from a phase 3 study. *Aliment Pharmacol Ther*. 2016;44:259-270.

AEGIS 3 CKD
Pergola and Kopyt

CKD 16-week and 36-week open-label extension study

A randomized trial and long-term open-label extension of Accrufer in the treatment of IDA in patients with chronic kidney disease (CKD)

ABBREVIATED STUDY DESIGN:

AEGIS 3 CKD studied adult patients with moderate-to-severe CKD and anemia due to low blood iron levels. The trial consisted of a double-blind treatment phase in which patients were randomized into either Accrufer twice daily or matching placebo capsules for 16 weeks. All patients completing 16 weeks of double-blind treatment were offered treatment with Accrufer 30 mg twice daily for a further 36 weeks.

Primary endpoint: change in Hb from baseline to week 16. Secondary endpoints included changes in Hb, ferritin, TSAT, and serum iron measures.

SELECTED RESULTS:

- "Improvements in hemoglobin in patients receiving ferric maltol during double-blind treatment were maintained with continued open-label ferric maltol to week 52, with a total increase of 0.7 g/dL from baseline to Week 52."
- "...74% [of patients] completed the open-label treatment period."

Changes in hemoglobin and iron measures during double-blind treatment at end of trial
Hemoglobin and iron measures at the end of open-label treatment compared with baseline

Efficacy measure		Ferric Maltol (DB) to Ferric Maltol (OLE) (n=68)	Placebo (DB) to Ferric Maltol (OLE) (n=30)
Hemoglobin mean ± SD g/dL	Week 52	10.9 ± 1.5	10.9 ± 1.4
	Change from baseline	0.7 ± 1.7	0.5 ± 1.4
Ferritin mean ± SD ng/dL	Week 52	142.5 ± 106.0	146.3 ± 145.1
	Change from baseline	59.3 ± 65.9	43.3 ± 120.6
TSAT mean ± SD %	Week 52	23.5 ± 9.0	21.4 ± 11.1
	Change from baseline	7.1 ± 8.9	5.1 ± 11.1
Serum Iron mean ± SD µmol/L	Week 52	12.4 ± 4.1	12.0 ± 5.8
	Change from baseline	2.9 ± 4.7	2.5 ± 6.4

Note: Conversion factor for units: serum iron in µmol/L to mg/dL, x5.587.
DB, double-blind treatment phase; OLE, open-label extension phase; SD, standard deviation; TSAT, transferrin saturation.

AUTHORS' CONCLUSIONS:

"Our study shows that ferric maltol 30 mg twice daily, which provided 60 mg of elemental iron/day, can increase hemoglobin by 0.7 g/dL over 52 weeks of treatment and is well tolerated with extended use in patients with stage 3 or 4 CKD."

Please scan the QR code for a complete presentation of study design, results, safety, and conclusions:
Pergola PE, Kopyt NP. Oral ferric maltol for the treatment of iron-deficiency anemia in patients with CKD: a randomized trial and open-label extension [published online ahead of print, May 21, 2021]. *Am J Kidney Dis*. 2021;S0272-6386(21)00624-7.

See Inside to Learn More

Accrufer® (ferric maltol): Proven to be effective and well tolerated in multiple phase 3 trials

- Improved hemoglobin levels over 12 and 16 weeks and maintained them over 52 and 64 weeks
- Ferritin and TSAT levels were increased at weeks 12 and 16 with steady, in-range levels maintained over 52 and 64 weeks
- Shown to be safe and well tolerated across studies
- High proportions of patients on Accrufer treatment completed 12 and 16 weeks of treatment in both the IBD and CKD populations

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SHIELD THERAPEUTICS

Austin, Texas 78759
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