IRON THEY'LL ACTUALLY TAKE[1]

ACCRUFeR® (ferric maltol) has a unique "maltol shield" that protects the iron as it passes through the stomach, resulting in unprecedented GI tolerability and clinically proven efficacy.[2,3]

ACCRUFeR®
(ferric maltol) *30 mg capsules*

INDICATIONS AND 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.

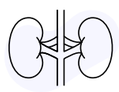
PATIENTS WITH ID/IDA NEED TOLERABLE AND EFFECTIVE TREATMENT

In the United States, about 10 million people have iron deficiency (ID) and about 5 million have iron deficiency anemia (IDA).[4]

Prevalence is highest in women of childbearing age and patients with inflammatory conditions.[5]

Women's health
- Menorrhagia
- Pregnancy
- Uterine Fibroids

Inflammatory bowel disease
- Crohn's disease
- Ulcerative colitis



Chronic kidney disease

Traditional oral iron treatments, such as ferrous salts (Fe^{2+}), often cause GI side effects because they dissociate in the stomach.

- When ferrous salts dissociate in the stomach, they can bind together, creating clumps that are hard to absorb. 90% of Fe^{2+} in ferrous salts goes unabsorbed.[12]
- Unabsorbed Fe^{2+} oxidizes, which can generate reactive oxygen species (ROS).[3,7,11]
- ROS can cause irritation and damage when they reach the intestinal lining, contributing to GI discomfort.[3,7,11]

Additionally, free iron in the colon can have adverse impacts on the gut microbiome, adding to the inflammation with which IBD patients are already dealing.[8]

Up to **60%** of patients will **discontinue treatment** with ferrous salts because of adverse reactions.[6]

More than two-thirds of people taking traditional oral iron report GI issues, such as:[9,10]

- Heartburn
- Loss of appetite
- Stomach cramps
- Nausea
- Diarrhea
- Discolored stool
- Flatulence
- Constipation

WHY ACCRUFeR?

ACCRUFeR is an FDA-approved treatment that delivers a low dose of elemental iron that can reverse IDA while minimizing risk for unmanageable GI side effects.[2]

Designed with a "maltol shield"

Uniquely formulated with a "maltol shield" that **protects the iron as it passes through the stomach**, reducing the likelihood of reactive oxygen species formation, which **minimizes GI side effects**.[2,12,14]

Unprecedented tolerability

In clinical studies, 4.6% of patients taking ACCRUFeR (n=175) discontinued treatment due to adverse reactions, compared with 2.5% of patients taking a placebo (n=120).[2,13]

Established safety and efficacy

FDA approval was achieved based on three pivotal studies in patients with ID/IDA associated with chronic inflammation and malabsorption, resulting in **significant improvement across iron indices**, including hemoglobin, ferritin, and TSAT.*[2,11,12]

**Not to be used by patients with an active IBD flare*

Committed to affordability

Eligible patients may **pay as little as $0** for ACCRUFeR.*

** Restrictions apply.*

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.

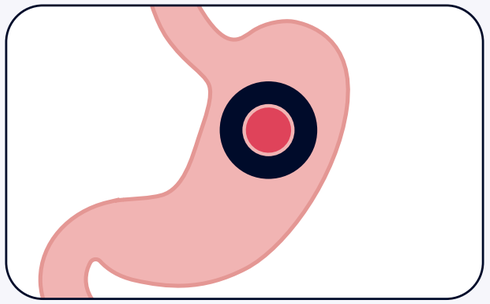
Please see Important Safety Information throughout and accompanying full Prescribing Information.

UNIQUELY FORMULATED WITH A "MALTOL SHIELD"

ACCRUFeR is a stable complex of ferric iron (Fe^{3+}) and maltol, a naturally occurring sugar derivative.[2,12] Unlike iron salts, this iron-sugar derivative complex stays intact in the stomach, dissociating when it reaches the duodenum for optimal iron absorption.[2]

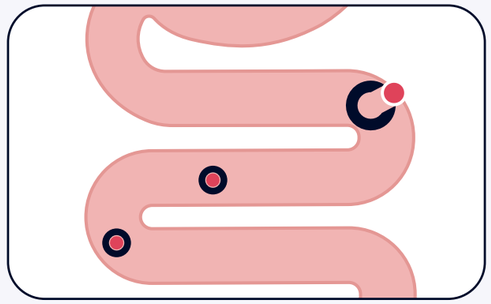
ACCRUFeR in Action

Tightly bound in the stomach



The "maltol shield" protects iron from the stomach, remaining tightly bound as it passes through.

Dissociates upon uptake in the duodenum



Iron remains bioavailable, chelated, and ready to replenish iron stores.

Excess iron is excreted in the stool.

Why the "maltol shield" matters:[12]

- It reduces the likelihood of reactive oxygen species (ROS) formation, **minimizing the risk** for GI side effects and irritation or damage to the intestinal lining.
- Since the iron and maltol remain chelated until absorption, there is **less free iron** in the gut, lessening the risk for added bowel inflammation.

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.

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

UNPRECEDENTED TOLERABILTY AND ESTABLISHED SAFETY

In clinical studies, GI adverse reactions were mild to moderate in nature, and less than 5% of patients reported individual GI adverse reactions.[2]

Pooled Results from AEGIS IBD and AEGIS CKD

Adverse reactions reported by ≥1% of patients treated with ACCRUFeR during the double-blind period of placebo-controlled studies[2]

Gastrointestinal Adverse Reactions	ACCRUFeR (n=175)	Placebo (n=120)
Flatulence	4.6%	0%
Diarrhea	4%	1.7%
Constipation	4%	0.8%
Discolored feces	4%	0.8%
Abdominal pain	2.9%	2.5%
Nausea	1.7%	0.8%
Vomiting	1.7%	0%
Abdominal discomfort	1.1%	0%
Abdominal distension	1.1%	0%

Excluding open-label extension period

In clinical trials, **4.6%** of patients (n=175) discontinued ACCRUFeR because of adverse reactions compared to 2.5% of patients (n=120) on placebo.[2,13]

Neither short- nor long-term treatment led to iron overload.[1,11,12]

ADVERSE REACTIONS

Most common adverse reactions (≥1%) reported with ACCRUFeR during the double-blind, placebo-controlled portions of the pivotal trials were flatulence, diarrhea, constipation, feces discolored, abdominal pain, nausea, vomiting, and abdominal discomfort/distension.

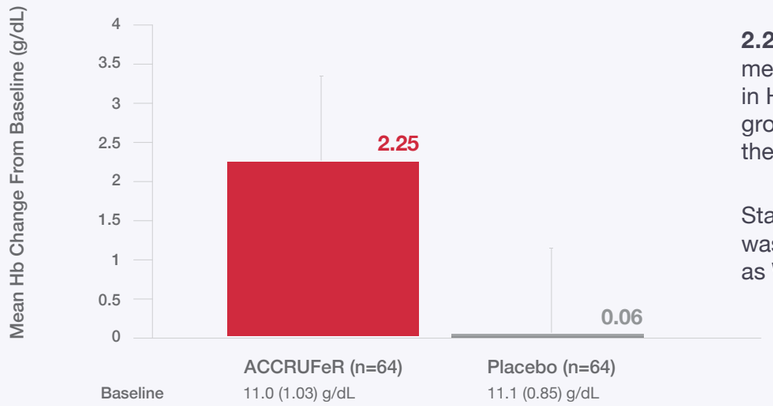
To report adverse events, please contact Shield Therapeutics at 1-888-963-6267. You may also contact the FDA at **www.fda.gov/medwatch** or **1-800-FDA-1088**.

SIGNIFICANT AND RAPID IMPROVEMENTS IN HEMOGLOBIN IN ADULTS WITH IBD

ACCRUFeR established safety and efficacy in patients with Crohn's disease and ulcerative colitis in two 12-week, phase 3A, randomized and placebo-controlled pivotal trials with a 52-week open label extension phase **in patients that had previously failed treatment with oral ferrous products.**[1,2,11]

Primary Endpoint: LS Mean (SE) Hb Concentration from Baseline to Week 12

One-sided 97.5% CI, 1.81; P<0.0001 based on ANCOVA



2.25 (0.12) g/dL LS mean (SE) improvement in Hb in the ACCRUFeR group vs 0.06 (0.13) in the placebo.[2]

Statistical significance was achieved as early as **Week 4**.

At Week 12 **78%** of patients (n=64) taking ACCRUFeR saw **a ≥1 g/dL increase in Hb** compared to 11% on placebo.[11]

**According to responder analysis*

Secondary Endpoints:
Mean (SD) Increase; ACCRUFeR increased ferritin levels and TSAT.[2,11]

	ACCRUFeR (n=64)	**Placebo** (n=64)
Ferritin (mcg/L)	**17.3** (28.30)	**1.2** (7.85)
TSAT (%)	**+18%** (20.2)	**-0.4%** (7.8)

DRUG INTERACTIONS

- Avoid concomitant use with dimercaprol
- Separate administration of ACCRUFeR from certain oral medications where interaction might occur. Monitor clinical responses as appropriate

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

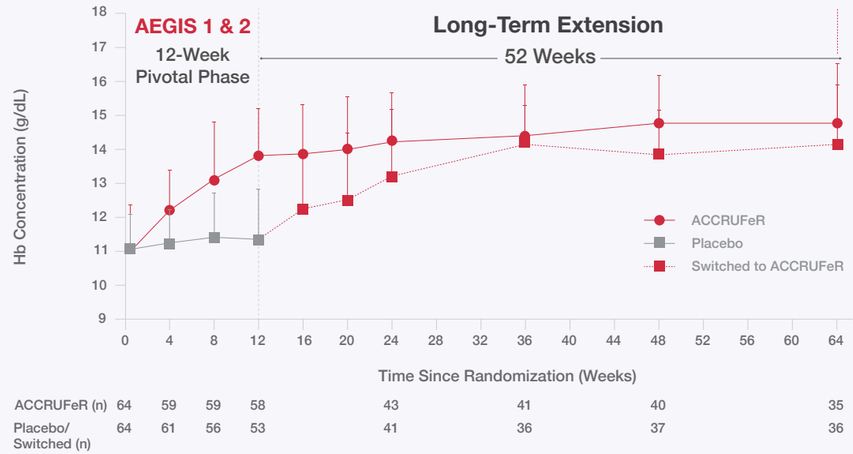
IMPROVEMENTS IN Hb WERE MAINTAINED UP TO 64 WEEKS

At Week 12, patients on placebo switched to ACCRUFeR, and patients already on treatment continued for an additional 52 weeks.[1,2]

Mean Improvement in Hb from Baseline to Week 64

Hb in patients on ACCRUFeR (n=35)	**Hb in patients on placebo who switched after Week 12** (n=36)
3.1 (1.46) g/dL	**2.2** (1.61) g/dL

Absolute Hb Concentrations from Baseline to Week 64



At Week 64 **86%** The cumulative proportion of patients (n=111) who **maintained normal Hb** was 86.1%.[1]

**According to responder analysis*

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

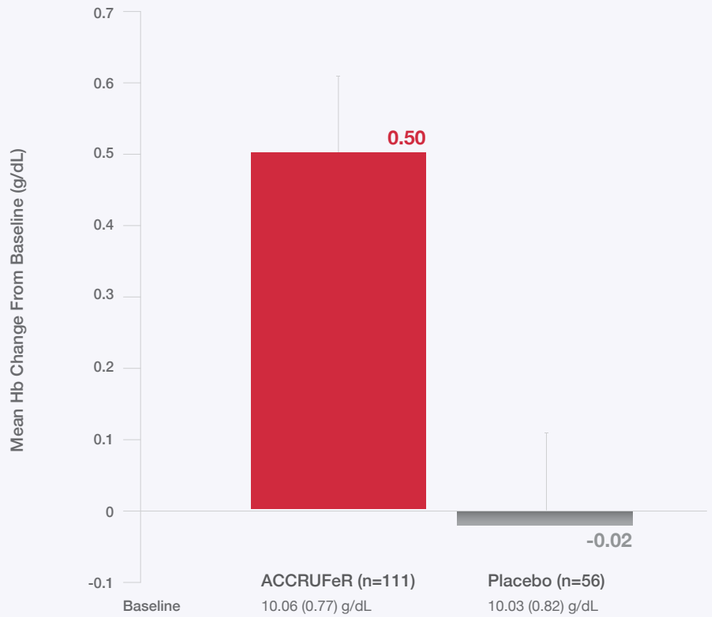
Excessive therapy with iron products can lead to excess storage of iron with the possibility of iatrogenic hemosiderosis. Do not administer ACCRUFeR to patients with evidence of iron overload or patients receiving intravenous iron. Assess iron parameters prior to initiating ACCRUFeR and monitor iron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

SIGNIFICANT IMPROVEMENTS IN HEMOGLOBIN IN ADULTS WITH CKD[2,12]

ACCRUFeR established safety and efficacy in patients with stage 3 or 4 chronic kidney disease (CKD), **excluding those on erythropoiesis-stimulating agents**, in a 16-week, phase 3A, randomized and placebo-controlled pivotal trial with a 36-week open label extension phase.

Primary Endpoint: LS Mean (SE) Change in Hb at Week 16

95% CI: 0.10, 0.93; P=0.0149



0.52 (0.21) g/dL improvement in Hb in patients taking ACCRUFeR vs placebo.

Secondary Endpoints:
Mean change from baseline to Week 16[2,13]

	ACCRUFeR (n=111)	Placebo (n=56)	Mean difference
Ferritin (mcg/L)	49.3	6.3	43.0
TSAT (%)	3.9	0.3	3.6

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.

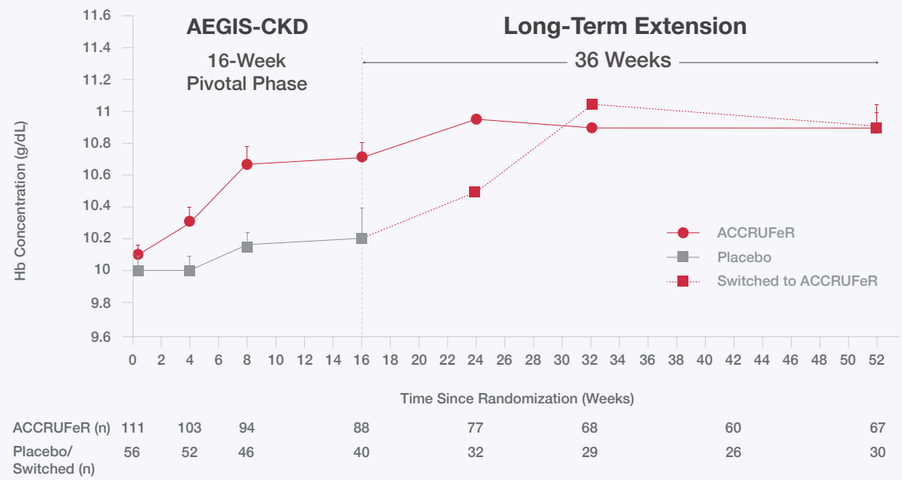
INCREASED Hb CONCENTRATIONS WERE MAINTAINED OVER 52 WEEKS

At Week 16, patients on placebo switched to ACCRUFeR, and patients already on treatment continued for an additional 36 weeks.[2,12] Increases in Hb for patients taking ACCRUFeR at Weeks 4,8, and 16 were consistent with changes seen in the AEGIS-IBD studies.[2,13]

Mean Improvement in Hb from Baseline to Week 52

Hb in patients on ACCRUFeR	Hb in patients on placebo who switched after Week 16
0.7 (1.7) **g/dL**	**0.5** (1.4) **g/dL**

Absolute (SE) Hb Concentrations in Patients Over 52 Weeks



No patients treated with ACCRUFeR in either long-term study **required IV iron intervention**[1,11,12]

ADVERSE REACTIONS

Most common adverse reactions (≥1%) reported with ACCRUFeR during the double-blind, placebo-controlled portions of the pivotal trials were flatulence, diarrhea, constipation, feces discolored, abdominal pain, nausea, vomiting, and abdominal discomfort/distension.

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**.

PATIENTS TAKE ONE 30-MG, GLUTEN-FREE CAPSULE BID[2]

Treatment considerations[2]

- Advise patients to take ACCRUFeR 1 hour before or 2 hours after a meal.
- Treatment duration depends on deficiency severity; at least 12 weeks of treatment is typically needed.
- Treatment with ACCRUFeR should be continued until ferritin levels are within normal ranges.
- Stool softener or other supplements, like vitamin C, are not required.

97%

median overall treatment compliance rate was seen across a 12-week and 52-week open label extension.[1]

START YOUR PATIENTS ON ACCRUFeR

We're committed to making ACCRUFeR affordable. **Scan the QR code below to learn more.**

About AEGIS IBD

STUDY DESCRIPTION The study enrolled 128 IBD patients (58 ulcerative colitis, 70 Crohn's disease) with IDA across 2 studies. Hb concentrations were between 9.5 g/dL and 12/13 g/dL for females/males and ferritin <30 mcg/L. A responder analysis was done defining treatment responders as patients who achieved increases in Hb of ≥ 1 g/dL or ≥ 2 g/dL, or Hb normalization by Week 12. Normalization of Hb was defined based on Hb values ≥12 g/dL for females or ≥ 13 g/dL for males. **STUDY ENDPOINTS** Primary endpoint: Mean difference in Hb concentration from baseline to Week 12 between ACCRUFeR and placebo. Secondary endpoints: Changes in Hb concentration from baseline to Weeks 4 and 8, serum ferritin concentration, and TSAT. **BASELINE CHARACTERISTICS** Mean age: 38.5 (placebo) to 40.1 (ACCRUFeR) years. Gender and ethnicity: 45 males and 83 females; 122 white and 6 others.

About AEGIS CKD

STUDY DESCRIPTION The study included 167 stage 3 or 4 CKD patients with IDA that were randomized 2:1 (ACCRUFeR to placebo).
STUDY ENDPOINTS Primary endpoint: The mean difference in Hb concentration from baseline to Week 16 between ACCRUFeR and placebo. Secondary endpoints: Proportions of patients with Hb increases of at least 1 g/dL and at least 2 g/dL at Week 16; the proportion of patients achieving a Hb concentration of at least 11.0 g/dL at Week 16; change in Hb concentration from baseline to Weeks 4 and 8; and changes in ferritin, TSAT, and serum iron measures at Weeks 4, 8, and 16. **BASELINE CHARACTERISTICS** Mean age: 65.2 (placebo) to 68.5 (ACCRUFeR) years, range 30-90 years. Gender and ethnicity: 50 males and 117 females; 123 White, 35 African American, and 9 other.

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ACCRUFeR®
(ferric maltol) 30 mg capsules

GIVE THEIR STOMACH A BREAK

Prescribe an iron they'll actually take.[1]

Visit ACCRUFeRHCP.com to learn more.

INDICATIONS AND USAGE

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

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