

Accrufer[®] (ferric maltol)

Policy # 00839

Original Effective Date: 07/10/2023

Current Effective Date: 06/01/2026

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Accrufer^{®†} (ferric maltol) for the treatment of iron deficiency to be **eligible for coverage**.^{**}

Patient Selection Criteria

Coverage eligibility will be considered for Accrufer (ferric maltol) for the treatment of iron deficiency when ALL of the following criteria are met:

- Patient has a diagnosis of iron deficiency anemia; AND
- Patient's underlying cause of iron deficiency has been treated (e.g., gastrointestinal bleed, abnormal uterine bleeding, diet, etc.); AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient is 10 years of age or older; AND
- Patient has had an inadequate response to TWO over-the-counter oral iron supplementation products after at least 3 months of therapy with EACH product.
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Accrufer (ferric maltol) when the patient's underlying cause of iron deficiency has not been treated to be **not medically necessary**.^{**}

Based on review of available data, the Company considers the use of Accrufer (ferric maltol) when the patient has not had an inadequate response to TWO over-the-counter oral iron therapies after at least 3 months of therapy EACH to be **not medically necessary**.^{**}

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Accrufer (ferric maltol) when the patient selection criteria are not met (with the exception of those denoted above as **not medically necessary.** **) to be **investigational.***

Background/Overview

Accrufer is an iron replacement product indicated for the treatment of iron deficiency in adults and pediatric patients 10 years of age and older. It is available as 30 mg capsules. Accrufer is to be taken twice daily on an empty stomach. The active ingredient in Accrufer, ferric maltol, is a stable, non-salt form of oral iron replacement. The ferric form of iron must be taken on an empty stomach because it is not as easily absorbed as the ferrous version which can be taken with food. Though Accrufer may have a lower risk of gastrointestinal upset than others in its class, this can be decreased by taking the other formulations with food.

Iron deficiency is a lack of iron content in the body. This can be due to decreased absorption or a loss of iron. Iron deficiency anemia (IDA) occurs when red blood cell production, or erythropoiesis, is decreased. Iron deficiency can develop due to a number of causes including, insufficient oral intake of iron, blood loss due to menstruation or childbirth, and digestive diseases. IDA is more prevalent in women of childbearing age. The World Health Organization (WHO) defines anemia as hemoglobin less than 12 g/dL in women and less than 13 g/dL in men. A diagnosis of IDA must be confirmed by iron studies (for example, serum ferritin, transferrin, and/or total iron-binding capacity) in addition to a complete blood count. For patients with chronic kidney disease (CKD), kidney disease: Improving Global Outcomes (KDIGO), recommends using serum ferritin and transferrin saturation (TSAT) to assess a patient's iron stores because ferritin is likely elevated in these patients due to systemic inflammation. The cause of a patient's IDA should be assessed to determine if there is an underlying cause that needs to be treated. For patients who have uncomplicated IDA, oral iron supplementation is recommended as first line therapy. There are numerous over the counter oral iron formulations that are available including ferrous fumarate, ferrous gluconate, and ferrous sulfate. Patients with a history of gastric bypass surgery, malabsorption syndromes, CKD, or who are unable to tolerate oral iron products may require IV iron therapy. Selection of an iron product usually depends on content of elemental iron and patient tolerability.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Accrufer is an iron replacement product indicated for the treatment of iron deficiency in adults and pediatric patients 10 years of age and older.

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Inflammatory Bowel Disease

The safety and efficacy of Accrufer for the treatment of iron deficiency anemia was studied in two randomized, placebo-controlled trials: AEGIS 1 and AEGIS 2. These trials enrolled 128 patients (45 males and 83 females) with quiescent inflammatory bowel disease (IBD) (58 patients with Ulcerative Colitis [UC] and 70 patients with Crohn's disease [CD]) and baseline Hb concentrations between 9.5 g/dL and 12 /13 g/dL for females / males and ferritin < 30 mcg/L. All patients had discontinued prior oral ferrous product treatment due to lack of efficacy or inability to tolerate oral iron replacement products. Subjects were randomized 1:1 to receive either 30 mg Accrufer twice daily or a matched placebo control for 12 weeks. The major efficacy outcome was the mean difference in Hb concentration from baseline to week 12 between Accrufer and placebo. The Least Square [LS] mean difference from baseline was 2.18 g/dL ($p < 0.0001$). The LS mean difference in change from baseline Hb to Week 4 and 8 between Accrufer and placebo were 1.04 g/dl and 1.73 g/dl, respectively. The mean ferritin (mcg/L) levels in Accrufer subjects at baseline were 8.6 mcg/L [SD 6.77] and the mean ferritin (mcg/L) levels at Week 12 were 26.0 mcg/L [SD 30.57] with a mean overall improvement of 17.3 mcg/L.

Following completion of the 12-week placebo-controlled phase of the studies, eligible patients transitioned to Accrufer 30 mg twice daily open-label treatment for an additional 52 weeks. During the open-label phase with Accrufer, the mean change in Hb concentration from baseline to Week 64 was 3.1 g/dL [SD 1.46 g/dL] and the ferritin value demonstrated a mean of 68.9 mcg/L [SD 96.24] at 64 weeks, with a mean overall improvement of 60.4 mcg/L.

Chronic Kidney Disease

The safety and efficacy of Accrufer for the treatment of iron deficiency anemia was studied in AEGIS 3, a trial that enrolled 167 patients (50 males and 117 females) with non-dialysis dependent chronic kidney disease (CKD) and baseline hemoglobin (Hb) concentrations between 8g/dL and 11 g/dL and ferritin < 250 mcg/L with a Transferrin saturation (TSAT) < 25% or ferritin < 500 mcg/L with a TSAT < 15%. Accrufer was administered at a dose of 30 mg twice daily. Subjects were randomized 2:1 to receive either 30 mg Accrufer twice daily or a matched placebo control for 16 weeks. The major efficacy outcome was the mean difference in Hb concentration from baseline to Week 16 between Accrufer and placebo. The LS mean difference was 0.52 g/dL ($p = 0.0149$). The LS mean difference in change from baseline Hb to Week 4 and 8 between Accrufer and placebo were 0.13 g/dl and 0.46 g/dl, respectively. The mean change in ferritin concentration from baseline to Week 16 was 49.3 mcg/L for the Accrufer group and 6.3 mcg/L for the placebo group. The mean difference for Accrufer versus placebo was 43.0 mcg/L.

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Pediatric Patients with Iron Deficiency Anemia

The efficacy of Accrufer for the treatment of iron deficiency was evaluated in 24 patients aged 10 to < 18 years with iron deficiency anemia who received age-based dosing of Accrufer twice daily in the FORTIS study. Patients aged 10–11 years received 15 mg twice daily, while patients aged 12 to < 18 years received 30 mg twice daily. Efficacy was assessed based on the mean change from baseline to Week 12 in hemoglobin (Hb, g/dL) using descriptive statistics. A clinically significant increase in Hb was observed in children aged 10 years and above who received oral Accrufer twice daily for 12 weeks. The 15 mg twice daily dose is not approved and is not recommended for use. The mean change in Hb at Week 12 in the subgroup (N = 21) that received the recommended dose of Accrufer 30 mg orally twice daily was 1.23 g/dL (SD: 1.00).

References

1. Accrufer [package insert]. Shield Therapeutics, Inc. Austin, Texas. Updated December 2025.
2. Accrufer (ferric maltol). New Drug Review. IPD Analytics. July 2021.

Policy History

Original Effective Date: 07/10/2023

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06/01/2023 Medical Policy Committee review

06/14/2023 Medical Policy Implementation Committee approval. New policy.

06/06/2024 Medical Policy Committee review

06/12/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

06/05/2025 Medical Policy Committee review

06/11/2025 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

05/07/2026 Medical Policy Committee review

05/13/2026 Medical Policy Implementation Committee approval. Updated age requirement in eligibility criteria to align with FDA label update (now approved in pediatric patients 10 years of age and older).

Next Scheduled Review Date: 05/2027

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

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1. Consultation with technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan’s authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan’s pharmacy benefit.