# Accrufer (ferric maltol) Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

## POLICY REVIEW CYCLE

| Effective Date | Date of Origin |
|---|---|
| 9/1/2023 | 1/1/2022 |

## FDA APPROVED INDICATIONS AND DOSAGE

| Agent(s) | FDA Indication(s) | Notes | Ref# |
|---|---|---|---|
| Accrufer®<br><br>(ferric maltol)<br><br>Capsule | Treatment of iron deficiency in adults | | 1 |

*See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm*

## CLINICAL RATIONALE

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|---|---|
| Iron deficiency | Iron deficiency (ID) is the most common nutritional disorder worldwide and accounts for approximately one-half of anemia cases. ID is defined as the decrease of the total content of iron in the body. ID may be the result of excessive iron loss, or, less frequently, decreased absorption. In general, the iron absorbed daily equals the amount needed to compensate its loss, so that the overall iron pool remains stable. This fine balance is easily broken, because the capability to absorb iron orally is limited. When the inputs are less than necessary or, more frequently, when the outputs increase and cannot be compensated for, ID develops. Deficient intake is the most frequent etiology in ID.(2)<br><br>ID can be detected in an asymptomatic individual on a screening-analysis, or in a person with symptoms that include general weakness, fatigue, irritability, poor concentration, headache, and intolerance to exercise. These symptoms appear even in patients with ID and normal hemoglobin levels. Although the impact of ID on the quality of life of the subject is high, they often get used to their symptoms and these are assumed as normal. The patient becomes aware of an improvement only when the symptoms disappear. Some iron-deficient patients, with or without anemia, might have alopecia, atrophy of lingual papillae, or dry mouth due to loss of salivation. Pica, the eating disorder in which there is an irresistible desire to lick or eat non-nutritive and unusual substances, such as soil, chalk, gypsum, ice (pagophagia), or paper, might appear in some cases. Pagophagia is considered quite specific to ID and it responds quickly to treatment.(2)<br><br>Serum ferritin, in the absence of inflammation (usually defined as a normal C-reactive protein level), reflects total body iron deposits. Thus, a low serum ferritin (less than 30 ng/L) unequivocally means ID, whether accompanied by anemia or not. However, as serum ferritin is an acute phase reactant, a normal or even elevated ferritinemia does not exclude the presence of ID. ID could exist even with levels of ferritin up to 100 |

ng/mL in the presence of an inflammatory process. Another parameter of the normal "iron metabolism", especially useful when the determination of ferritin is equivocal, is the transferrin saturation index. This shows the percentage of transferrin that transports iron and thus a decrease (less than 20%) implies ID, either absolute or functional.(2)

In some cases, even taking into account all these determinations, ID can be difficult to diagnose. It generally occurs in situations where the anemia has a multifactorial origin.(2)

Oral iron supplementation is an inexpensive and effective option for treating ID in stable outpatients. Iron salts such as ferrous gluconate, ferrous sulfate, and ferrous fumarate remain the standard first-line therapy for treating ID. Other common iron formulations include ferrous ascorbate, ferrous succinate, carbonyl iron, ferric citrate, liposomal iron, heme iron peptide, and polysaccharide iron complexes. With consistent oral iron supplementation, reticulocytosis starts in 4-5 days, and hemoglobin (Hb) begins to improve by the second week. Oral iron therapy is often required for at least 3 to 6 months to replete iron stores and normalize ferritin levels, although more time may be required depending upon the severity and ongoing losses.(3)

Common elemental iron content of select available iron formulations in the United States and Canada(3)

| **Product** | **Dose per tablet (mg)** | **Elemental iron content per mg** |
|---|---|---|
| Ferrous gluconate | 240 | 27 |
| Ferrous gluconate | 325 | 38 |
| Ferrous sulfate | 325 | 65 |
| Ferrous fumarate | 325 | 106 |
| Heme iron polypeptide | 398 | 11 |
| Polysaccharide complex | 150 | 150 |
| Ferric citrate | 210 | 210 |

The list of examples in this table is not exhaustive. Liquid formulations are also available. Approximately 10% of elemental iron ingested is absorbed

Efficacy(1)

Accrufer delivers iron for uptake across the intestinal wall and transfer to transferrin and ferritin.

The safety and efficacy of Accrufer for the treatment of iron deficiency anemia was studied in two randomized, placebo-controlled tries (AEGIS 1 [NCT01252221] and AEGIS 2 [NCT01340872]). These trials enrolled 128 patients with quiescent inflammatory bowel disease (IBD) (58 patients with ulcerative colitis [UC] and 70 patients with Crohn's disease [CD]) and baseline ferritin less than 30 mcg/L and Hb concentrations between 9.5 g/dL and 12 g/dL for females and 9.5 g/dL and 13 g/dL for males. All patients had discontinued prior oral ferrous product treatment due to lack of efficacy or inability to tolerate oral iron replacement products.

The major efficacy outcome for AEGIS 1 and AEGIS 2 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 less than 0.0001).

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|---|---|
| | 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.<br><br>The safety and efficacy of Accrufer for the treatment of iron deficiency anemia was studied in AEGIS 3 (NCT02968368) that enrolled 167 patients with non-dialysis chronic kidney disease (CKD) and a baseline Hb concentrations between 8 g/dL and 11 g/dL with a transferrin saturation (TSAT) less than 15%.<br><br>The major efficacy outcome for AEGIS 3 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). |
| Safety(1) | Accrufer (ferric maltol) is contraindicated in:<br><br>• Patients with a hypersensitivity to the active substance or any excipient<br>• Hemochromatosis and other iron overload syndromes<br>• Patients receiving repeated blood transfusions<br><br>Advise patients that they should not use Accrufer if they are experiencing an IBD flare as there is potential risk of increased inflammation in the gastrointestinal tract. |

## REFERENCES


| Number | Reference |
|---|---|
| 1 | Accrufer Prescribing Information. Shield TX (UK). May 2022. |
| 2 | Camaschella C. Iron deficiency: new insights into diagnosis and treatment. Hematology AmSoc Hematol Educ Program (2015) 2015 (1):8-13. |
| 3 | Ning S, Zeller MP. Management of iron deficiency. Hematology Am Soc Hematol Educ Program. 2019;2019(1):315-322. doi:10.1182/hematology.2019000034. |

## POLICY AGENT SUMMARY PRIOR AUTHORIZATION

| Target Brand Agent(s) | Target Generic Agent(s) | Strength | Targeted MSC | Available MSC | Final Age Limit | Preferred Status |
|---|---|---|---|---|---|---|
| | | | | | | |
| Accrufer | ferric maltol cap | 30 MG | M ; N ; O ; Y | N | | |

## POLICY AGENT SUMMARY QUANTITY LIMIT

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | QL Amount | Dose Form | Day Supply | Duration | Addtl QL Info | Allowed Exceptions | Targeted NDCs When Exclusions Exist |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | |
| Accrufer | Ferric Maltol Cap | 30 MG | 60 | Capsules | 30 | DAYS | | | |

## CLIENT SUMMARY – PRIOR AUTHORIZATION

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | Client Formulary |
|---|---|---|---|
| Accrufer | ferric maltol cap | 30 MG | FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx |

## CLIENT SUMMARY – QUANTITY LIMITS

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## PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

| Module | Clinical Criteria for Approval |
|---|---|
| | **Initial Evaluation**<br><br>**Target Agent(s)** will be approved when ALL of the following are met:<br><br>1. ONE of the following:<br>A. The prescriber has provided information that ALL other forms of iron available over the counter (e.g., ferrous sulfate, ferrous gluconate, ferrous fumarate) are not clinically appropriate for the patient (medical records required) **OR**<br>B. BOTH of the following:<br>1. The prescriber has stated that the patient has tried other forms of iron available over the counter **AND**<br>2. Other forms of iron available over the counter were discontinued due to lack of effectiveness or an adverse event **OR**<br>C. The patient is currently being treated with the requested agent as indicated by ALL of the following: |

| Module | Clinical Criteria for Approval |
|---|---|
| | 1. A statement by the prescriber that the patient is currently taking the requested agent **AND**<br>2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND**<br>3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR**<br>D. The prescriber has provided documentation that ALL other forms of iron available over the counter (e.g., ferrous sulfate, ferrous gluconate, ferrous fumarate) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND**<br>2. If the patient has an FDA approved indication, then ONE of the following:<br>A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR**<br>B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND**<br>3. The patient does NOT have any FDA labeled contraindications to the requested agent<br><br>**Length of Approval:** 6 months<br><br>Note: If Quantity Limit applies, please refer to Quantity Limit Criteria<br><br>**Renewal Evaluation**<br><br>**Target Agent(s)** will be approved when ALL of the following are met:<br><br>1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND**<br>2. The patient has had clinical benefit with the requested agent (e.g., stable or improvement in hemoglobin) **AND**<br>3. The patient does NOT have any FDA labeled contraindications to the requested agent<br><br>**Length of Approval:** 12 months<br><br>NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria |

## QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

| Module | Clinical Criteria for Approval |
|---|---|
| | **Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met:<br><br>1. The requested quantity (dose) does NOT exceed the program quantity limit **OR**<br>2. ALL of the following:<br>A. The requested quantity (dose) is greater than the program quantity limit **AND**<br>B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND**<br>C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit<br><br>**Length of Approval:** Initial: 6 months, Renewal: 12 months |