## Drug Monograph

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| Drug/Drug Class: | **Ferriprox® (deferiprone) Tablet / Chelating Agent** |
| Prepared for: | MO HealthNet |
| Prepared by: | ACS, A Xerox Company |

☒ **New Criteria** ☐ **Revision of Existing Criteria**

## Executive Summary

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| **Purpose:** | The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, or require prior authorization for use. |
| **Dosage Forms & Manufacturer:** | Each Ferriprox® tablet contains 500 mg of deferiprone. Manufactured by ApoPharma USA, Inc., Rockville, MD 20850. |
| **Summary of Findings:** | Ferriprox® is an oral iron chelator that has demonstrated efficacy for the treatment of patients with transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate. Patients with thalassemia have excess iron in the body from frequent blood transfusions (transfusional iron overload), a condition that is serious and can be fatal. These patients also have a risk of developing liver disease, diabetes, arthritis, heart failure, or an abnormal heart rhythm. Ferriprox® is the first new FDA-approved treatment for this disorder since 2005, and was approved under the FDA's accelerated approval program as an orphan drug. |
| **Status Recommendation:** | ☐ Prior Authorization (PA) Required ☒ Open Access<br>☐ Clinical Edit ☐ PDL |
| **Type of PA Criteria:** | ☐ Increased Risk of ADE ☐ Non-Preferred Agent<br>☐ Appropriate Indications ☒ No PA Required |

## Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug or not (open access). While prescription expenditures are increasing at double-digit rates, payors are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

## Introduction[1]

Patients with thalassemia have excess iron in the body from frequent blood transfusions (transfusional iron overload), a condition that is serious and can be fatal. These patients also have a risk of developing liver disease, diabetes, arthritis, heart failure, or an abnormal heart rhythm.

## Dosage Form(s)[1]

Ferriprox® is supplied in 500 mg tablets containing 500 mg of deferiprone.

## Manufacturer

ApoPharma USA Inc., Rockville, MD 20850.

## Indication(s)[1]

Ferriprox® is indicated for the treatment of patients with transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate.

## Clinical Efficacy[1-11] (mechanism of action/pharmacology, comparative efficacy)

Deferiprone is a chelating agent with an affinity for ferric ion (iron III). It binds with ferric ions to form neutral 3:1 (deferiprone:iron) complexes that are stable over a wide range of pH values. Deferiprone has a lower binding affinity for other metals such as copper, aluminum, and zinc compared with iron.

**Pharmacokinetics**

| | **FERRIPROX** |
|---|---|
| **Protein binding** | < 10% |
| **Volume of distribution** | 1.6 L/kg (thalassemia patients)<br>1 L/kg (healthy volunteers) |
| **Metabolism** | Hepatic via UGT 1A6 to 3-O-glucuronide (inactive). |
| **Excretion** | Urine |
| **Half-life** | 1.9 hours |

The approval of Ferriprox® was primarily based upon a pooled analysis of data from 12 clinical trials involving 236 patients. In this retrospective analysis, the efficacy of Ferriprox® was assessed in transfusion-dependent iron overload patients in whom previous iron chelation therapy had failed or was considered inadequate due to poor tolerance. The main criterion for chelation failure was a serum ferritin > 2500 mcg/L before treatment with

Ferriprox®. Ferriprox® therapy (35 to 99 mg/kg/day) was considered successful if patients experienced a >= 20% decline in serum ferritin within one year of starting therapy. Of the 224 patients with thalassemia who received Ferriprox® monotherapy and were eligible for serum ferritin analysis, 105 (47%) were male, 119 (53%) were female, and the mean age was 18.2 years. A 20% or greater reduction in serum ferritin was achieved by 50% of the patients (n=236; 95% confidence interval, 43% to 57%). There are no controlled trials with Ferriprox demonstrating a direct treatment benefit, such as improvement in disease-related symptoms, functioning, or increased survival.

## Warnings[1]

- Fatal agranulocytosis and neutropenia can occur; monitor absolute neutrophil count prior to and weekly during therapy; interrupt therapy for an infection.
- Caution advised for patients at risk for QT prolongation; one patient with previous history of QT prolongation developed Torsades de pointes.
- Ferriprox® can cause fetal harm; advise women of potential hazard to fetus and to avoid pregnancy.
- Serum ALT levels may increase; monitor serum ALT monthly during therapy; consider interruption of therapy with persistent increase in serum transaminases.
- Plasma zinc levels may decrease; monitor zinc levels and add supplements for deficiency.

## Adverse Effects[1]

| **Most common, >= 1%** | **Ferriprox®** |
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| ▪ Chromaturia | 14.6% |
| ▪ Nausea | 12.6% |
| ▪ Abdominal pain/discomfort | 10.4% |
| ▪ Arthralgia | 9.8% |
| ▪ Vomiting | 9.8% |
| ▪ Alanine aminotransferase increased | 7.5% |
| ▪ Neutrophil count decreased | 7.3% |
| ▪ Neutropenia | 6.2% |
| ▪ Increased appetite | 4.0% |
| ▪ Diarrhea | 3.0% |
| ▪ Headache | 2.5% |
| ▪ Back pain | 2.0% |
| ▪ Dyspepsia | 2.0% |
| ▪ Pain in extremity | 1.9% |
| ▪ Weight increased | 1.9% |
| ▪ Agranulocytosis | 1.7% |
| ▪ Arthropathy | 1.4% |
| ▪ Aspartate aminotransferase increased | 1.2% |
| ▪ Decreased appetite | 1.1% |

## Drug Interactions[1]

- Aluminum
- Calcium
- Copper

- Magnesium
- Silymarin (milk thistle; UGT 1A6 inhibitor)
- Zinc

## Dosage and Administration[1]

The recommended initial oral dose is 25 mg/kg 3 times daily (total, 75 mg/kg/day). Adjust dose based on patient response to a maximum of 33 mg/kg 3 times daily (total, 99 mg/kg/day).

Additional information for preparation of solution can be found in the product package insert.

## Cost Comparison[2] (at commonly used dosages)

| GENERIC NAME | BRAND NAME | MANUFACTURER | STRENGTH | DOSE** | COST/ MONTH* |
|---|---|---|---|---|---|
| Deferiprone | Ferriprox® | ApoPharma | 500 mg tablets | 3 tablets TID | $ 8553.60 |

*WAC (Wholesale Acquisition Cost)
** Patient weighing 60 Kg

## Conclusion

Ferriprox® is the first new FDA-approved treatment for transfusional iron overload due to thalassemia syndromes since 2005, and was approved under the FDA's accelerated approval program as an orphan drug. The manufacturer has agreed to several post-marketing requirements and commitments, including further study of its use in patients with sickle cell disease who have transfusional iron overload, a pharmacovigilance study of agranulocytosis, a study to assess the potential for QT interval prolongation, and pharmacokinetic studies in subjects with hepatic or renal impairment. A liquid formulation is also being investigated for use in young children.

## Recommendation

MO HealthNet recommends Open Access status for this product.

## References


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