HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use FERRIPROX safely and effectively. See full prescribing information for FERRIPROX.

FERRIPROX® (deferiprone) tablets, for oral use
Initial U.S. Approval: 2011

WARNING: AGRANULOCYTOSIS/NEUTROPENIA
See full prescribing information for complete boxed warning.

- **FERRIPROX can cause agranulocytosis that can lead to serious infections and death. Neutropenia may precede the development of agranulocytosis. (5.1)**
- **Measure the absolute neutrophil count (ANC) before starting FERRIPROX and monitor weekly while on therapy. (5.1)**
- **Interrupt FERRIPROX if infection develops and monitor the ANC more frequently. (5.1)**
- **Advise patients taking FERRIPROX to report immediately any symptoms indicative of infection. (5.1)**

----------RECENT MAJOR CHANGES----------

Dosage and Administration, Dosing (2.1) 07/2019

----------INDICATIONS AND USAGE----------

FERRIPROX® (deferiprone) is an iron chelator indicated for the treatment of patients with transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate. (1)

Approval is based on a reduction in serum ferritin levels. There are no controlled trials demonstrating a direct treatment benefit, such as improvement in disease-related symptoms, functioning, or increased survival (1).

Limitations of Use

Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with other chronic anemias. (1)

----------DOSAGE AND ADMINISTRATION----------

- 25 mg/kg to 33 mg/kg body weight, orally, three times per day, for a total daily dose of 75 mg/kg to 99 mg/kg body weight. (2.1)

----------DOSAGE FORMS AND STRENGTHS----------

Tablets: 1,000 mg film-coated with functional scoring. (3)

----------CONTRAINDICATIONS----------

- Hypersensitivity to deferiprone or to any of the excipients in the formulation. (4)

----------WARNINGS AND PRECAUTIONS----------

- Embryofetal Toxicity: Advise women of the potential hazard to the fetus and to avoid pregnancy while on this drug. (5.2)
- Liver Enzyme Elevations: Monitor monthly and discontinue for persistent elevations. (5.3)
- Zinc Deficiency: Monitor during therapy and supplement for deficiency. (5.4)

----------ADVERSE REACTIONS----------

- The most common adverse reactions are (incidence ≥ 5%) nausea, vomiting and abdominal pain, alanine aminotransferase increased, arthralgia and neutropenia. (5.1, 6)

To report SUSPECTED ADVERSE REACTIONS, contact ApoPharma at: Telephone: 1-866-949-0995 or FDA at 1-800-FDA-1088
Email: medicalsafety@apopharma.com or www.fda.gov/medwatch

----------DRUG INTERACTIONS----------

- Avoid use with other drugs known to be associated with neutropenia or agranulocytosis; however, if this is not possible, closely monitor the absolute neutrophil count. (7.1)
- Avoid use of UGT1A6 inhibitors with FERRIPROX. (7.2)
- Allow at least a 4-hour interval between FERRIPROX and mineral supplements or antacids that contain polyvalent cations (e.g., iron, aluminum, or zinc). (7.3)

----------USE IN SPECIFIC POPULATIONS----------

- Lactation: Advise women not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 07/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: AGRANULOCYTOSIS/NEUTROPENIA
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Dosing
2.2 Interactions with Foods, Vitamins and Drugs
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Agranulocytosis/Neutropenia
5.2 Embryofetal Toxicity
5.3 Liver Enzyme Elevations
5.4 Zinc Deficiency
6 ADVERSE REACTIONS
6.1 Clinical Trial Experience
6.2 Postmarketing Experience
7 DRUG INTERACTIONS
7.1 Drugs Associated with Neutropenia or Agranulocytosis
7.2 UDP-Glucuronosyltransferases (UGTs)
7.3 Polyvalent Cations
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.3 Females and Males of Reproductive Potential
8.4 Pediatric Use
8.5 Geriatric Use
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14 CLINICAL STUDIES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: AGRANULOCYTOSIS/NEUTROPENIA

- **FERRIPROX can cause agranulocytosis that can lead to serious infections and death. Neutropenia may precede the development of agranulocytosis. *[see Warnings and Precautions (5.1)]***
- **Measure the absolute neutrophil count (ANC) before starting FERRIPROX therapy and monitor weekly while on therapy. Interrupt FERRIPROX therapy if neutropenia develops. *[see Warnings and Precautions (5.1)]***
- **Interrupt FERRIPROX if infection develops, and monitor the ANC more frequently. *[see Warnings and Precautions (5.1)]***
- **Advise patients taking FERRIPROX to report immediately any symptoms indicative of infection. *[see Warnings and Precautions (5.1)]***

1 INDICATIONS AND USAGE

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

Approval is based on a reduction in serum ferritin levels. There are no controlled trials demonstrating a direct treatment benefit, such as improvement in disease-related symptoms, functioning, or increased survival *[see Clinical Studies (14)]*.

Limitations of Use:

- Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with other chronic anemias.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing

Starting Dose

The recommended initial dose of FERRIPROX is 25 mg/kg, orally, three times per day for a total of 75 mg/kg/day. Round dose to the nearest 500 mg (half-tablet).

Table 1a: Tablet requirement to achieve a 25 mg/kg dose (rounded to the nearest half-tablet) for administration three times a day.

Body Weight (kg)	Number of 1,000 mg tablets		
	Morning	Midday	Evening
20	0.5	0.5	0.5
30	1	0.5	1
40	1	1	1
50	1.5	1	1.5
60	1.5	1.5	1.5
70	2	1.5	2
80	2	2	2
90	2.5	2	2.5

Dose Adjustments

Tailor dose adjustments to the individual patient's response and therapeutic goals (maintenance or reduction of body iron burden). The maximum dose is 33 mg/kg, three times per day for a total of 99 mg/kg/day.

Table 1b: Tablet requirement to achieve a 33 mg/kg dose (rounded to the nearest half-tablet) for administration three times a day.

Body Weight (kg)	Number of 1,000 mg tablets		
	Morning	Midday	Evening
20	0.5	0.5	1
30	1	1	1
40	1.5	1	1.5
50	1.5	1.5	2
60	2	2	2
70	2.5	2	2.5
80	2.5	2.5	3
90	3	3	3

Monitor serum ferritin concentration every two to three months to assess the effects of FERRIPROX on body iron stores. If the serum ferritin is consistently below 500 mcg/L, consider temporarily interrupting FERRIPROX therapy until serum ferritin rises above 500 mcg/L.

2.2 Interactions with Foods, Vitamins and Drugs

Allow at least a 4-hour interval between FERRIPROX and other medications or supplements containing polyvalent cations such as iron, aluminum, or zinc. Avoid use of UGT1A6 inhibitors (e.g. diclofenac, probenecid, or silymarin (milk thistle)) with FERRIPROX *[see Drug Interactions (7.2 and 7.3), Clinical Pharmacology (12.3)]*.

3 DOSAGE FORMS AND STRENGTHS

1,000 mg film-coated tablets with functional scoring.

4 CONTRAINDICATIONS

FERRIPROX is contraindicated in patients with known hypersensitivity to deferiprone or to any of the excipients in the formulation. The following reactions have been reported in association with the administration of deferiprone: Henoch-Schönlein purpura; urticaria; and periorbital edema with skin rash *[see Adverse Reactions (6.2)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Agranulocytosis/Neutropenia

Fatal agranulocytosis can occur with FERRIPROX use. FERRIPROX can also cause neutropenia, which may foreshadow agranulocytosis. Measure the absolute neutrophil count (ANC) before starting FERRIPROX therapy and monitor it weekly while on therapy.

Interrupt FERRIPROX therapy if neutropenia develops (ANC < 1.5 x 10^9/L).

Interrupt FERRIPROX if infection develops and monitor the ANC frequently.

Advise patients taking FERRIPROX to immediately interrupt therapy and report to their physician if they experience any symptoms indicative of infection.

In pooled clinical trials, the incidence of agranulocytosis was 1.7% of patients. The mechanism of FERRIPROX-associated agranulocytosis is unknown. Agranulocytosis and neutropenia usually resolve upon discontinuation of FERRIPROX, but there have been reports of agranulocytosis leading to death.

Implement a plan to monitor for and to manage agranulocytosis/neutropenia prior to initiating FERRIPROX treatment.

For neutropenia (ANC < 1.5 x 10^9/L and > 0.5 x 10^9/L):

Instruct the patient to immediately discontinue FERRIPROX and all other medications with a potential to cause neutropenia.

Obtain a complete blood cell (CBC) count, including a white blood cell (WBC) count corrected for the presence of nucleated red blood cells, an absolute neutrophil count (ANC), and a platelet count daily until recovery (ANC $\geq$ 1.5 x 10^9/L).

For agranulocytosis (ANC < 0.5 x 10^9/L):

Consider hospitalization and other management as clinically appropriate.

Do not resume FERRIPROX in patients who have developed agranulocytosis unless potential benefits outweigh potential risks. Do not rechallenge patients who develop neutropenia with FERRIPROX unless potential benefits outweigh potential risks.

5.2 Embryofetal Toxicity

Based on evidence of genotoxicity and developmental toxicity in animal studies, FERRIPROX can cause fetal harm when administered to a pregnant woman. The limited available data on the use of FERRIPROX in pregnant women are insufficient to inform risk. In animal studies, administration of deferiprone during the period of organogenesis resulted in embryofetal death and malformations at doses lower than equivalent human clinical doses.

Advise pregnant women of the potential risk to the fetus *[see Use in Specific Populations (8.1, 8.3)]*. Advise females of reproductive potential to use highly effective contraception during treatment with FERRIPROX. Six months of contraception is recommended after cessation of therapy. Advise males of reproductive potential to use effective contraception during treatment with FERRIPROX. Three months of contraception is recommended after cessation of therapy *[see Use in Specific Populations (8.1)]*.

5.3 Liver Enzyme Elevations

In clinical studies, 7.5% of 642 patients treated with FERRIPROX developed increased ALT values. Four (0.62%) FERRIPROX-treated subjects discontinued the drug due to increased serum ALT levels and 1 (0.16%) due to an increase in both ALT and AST.

Monitor serum ALT values monthly during therapy with FERRIPROX, and consider interruption of therapy if there is a persistent increase in the serum transaminase levels.

5.4 Zinc Deficiency

Decreased plasma zinc concentrations have been observed on FERRIPROX therapy. Monitor plasma zinc, and supplement in the event of a deficiency.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described below and elsewhere in the labeling:

- Agranulocytosis/Neutropenia *[see Warnings and Precautions (5.1)]*
- Liver Enzyme Elevations *[see Warnings and Precautions (5.3)]*
- Zinc Deficiency *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adverse reaction information for FERRIPROX represents the pooled data collected from 642 patients who participated in single arm or active-controlled clinical trials.

The most serious adverse reaction reported in clinical trials with FERRIPROX was agranulocytosis *[see Warnings and Precautions (5.1)]*.

The most common adverse reactions reported during clinical trials were nausea, vomiting, abdominal pain, alanine aminotransferase increased, arthralgia and neutropenia.

The table below lists the adverse drug reactions that occurred in at least 1% of patients treated with FERRIPROX in clinical trials.

Table 2:Adverse drug reactions occurring in ≥ 1% of FERRIPROX-treated patients

Body System Adverse Reaction	(N=642) % Subjects
BLOOD AND LYMPHATIC SYSTEM DISORDERS	
Neutropenia	6
Agranulocytosis	2
GASTROINTESTINAL DISORDERS	
Nausea	13
Abdominal pain/discomfort	10
Vomiting	10
Diarrhea	3
Dyspepsia	2
INVESTIGATIONS	
Alanine Aminotransferase increased	7
Weight increased	2
Aspartate Aminotransferase increased	1
METABOLISM AND NUTRITION DISORDERS	
Increased appetite	4
Decreased appetite	1
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	
Arthralgia	10
Back pain	2
Pain in extremity	2
Arthropathy	1
NERVOUS SYSTEM DISORDERS	
Headache	2

Gastrointestinal symptoms such as nausea, vomiting, and abdominal pain were the most frequent adverse reactions reported by patients participating in clinical trials and led to the discontinuation of FERRIPROX therapy in 1.6% of patients.

Chromaturia (reddish/brown discoloration of the urine) is a result of the excretion of iron in the urine.

6.2 Postmarketing Experience

The following additional adverse reactions have been reported in patients receiving FERRIPROX. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or to establish a causal relationship to drug exposure.

Blood and lymphatic system disorders: thrombocytosis, pancytopenia.

Cardiac disorders: atrial fibrillation, cardiac failure.

Congenital, familial and genetic disorders: hypospadias.

Eye disorders: diplopia, papilledema, retinal toxicity.

Gastrointestinal disorders: enterocolitis, rectal hemorrhage, gastric ulcer, pancreatitis, parotid gland enlargement.

General disorders and administration site conditions: chills, pyrexia, edema peripheral, multi-organ failure.

Hepatobiliary disorders: jaundice, hepatomegaly.

Immune system disorders: anaphylactic shock, hypersensitivity.

Infections and infestations: cryptococcal cutaneous infection, enteroviral encephalitis, pharyngitis, pneumonia, sepsis, furuncle, infectious hepatitis, rash pustular, subcutaneous abscess.

Investigations: blood bilirubin increased, blood creatinine phosphokinase increased.

Metabolism and nutrition disorders: metabolic acidosis, dehydration.

Musculoskeletal and connective tissue disorders: myositis, chondropathy, trismus.

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.