Ferriprox® (deferiprone)

Oral Solution

Prescribing Information

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) oral solution, 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 the ANC weekly 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)**

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)

Limitation 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

- Oral Solution: 100 mg/mL (50 g/500 mL) (3)

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

- If infection occurs while on FERRIPROX, interrupt therapy and monitor the ANC more frequently. (5.1)
- FERRIPROX can cause fetal harm. Advise women of the potential hazard to the fetus and to avoid pregnancy while on this drug. (5.2)

ADVERSE REACTIONS

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

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

DRUG INTERACTIONS

- Avoid concomitant 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 concomitant use of UGT1A6 inhibitors with FERRIPROX. (7.2)
- Allow at least a 4-hour interval between FERRIPROX and mineral supplements, and antacids that contain polyvalent cations (e.g., iron, aluminum, and zinc). (7.3)

USE IN SPECIFIC POPULATIONS

- Nursing mothers: Discontinue the use of FERRIPROX or discontinue nursing. (8.3)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 05/2017

FULL PRESCRIBING INFORMATION: CONTENTS*

* 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 the ANC weekly 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)].*

Limitation 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.

Table 1a: Volume of oral solution (rounded to the nearest 2.5 mL) required to achieve a 25 mg/kg dose for administration three times a day.

Body Weight (kg)	Dose (mg)	mL of oral solution
20	500	5
30	750	7.5
40	1,000	10
50	1,250	12.5
60	1,500	15
70	1,750	17.5
80	2,000	20
90	2,250	22.5

Dose Adjustments

Dose adjustments should be tailored 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. The dose should be rounded by the prescriber to the nearest 2.5 mL.

Table 1b: Volume of oral solution (rounded to the nearest 2.5 mL) required to achieve a 33 mg/kg dose for administration three times a day.

Body Weight (kg)	Dose (mg)	mL of oral solution
20	660	7.5
30	990	10
40	1,320	12.5
50	1,650	17.5
60	1,980	20
70	2,310	22.5
80	2,640	27.5
90	2,970	30

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.

After first opening of the bottle, use within 35 days. Store the bottle in the original carton to protect from light. Store FERRIPROX only in the original container. After 35 days, discard the contents of the bottle. Store at 20º to 25ºC (68º to 77ºF); excursions permitted to 15º to 30ºC (59º to 86ºF) *[see USP Controlled Room Temperature]*.

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, and zinc. Avoid concomitant 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

Oral Solution: 100 mg/mL (50 g/500 mL)

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 the ANC weekly 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 ≥ 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. 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. If FERRIPROX is used during pregnancy or if the patient becomes pregnant while taking FERRIPROX, the patient should be apprised of the potential hazard to the fetus. Women of reproductive potential should be advised to avoid pregnancy when taking FERRIPROX *[see Use in Specific Populations (8.1) and Nonclinical Toxicology (13.1)]*.

5.3 Liver Enzyme Elevations

In clinical studies, 7.5% of 642 subjects 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

6.1 Clinical Trial Experience

The following 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)]*

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 chromaturia, 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% FERRIPROX-treated patients

Body System Preferred Term	(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
Neutrophil count decreased	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
URINARY DISORDERS	
Chromaturia	15

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 the 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.

Nervous system disorders: cerebellar syndrome, cerebral hemorrhage, convulsion, gait disturbance, intracranial pressure increased, psychomotor skills impaired, pyramidal tract syndrome, somnolence.

Psychiatric disorders: bruxism, depression, obsessive-compulsive disorder.

Renal disorders: glycosuria, hemoglobinuria.

Respiratory, thoracic and mediastinal disorders: acute respiratory distress syndrome, epistaxis, hemoptysis, pulmonary embolism.

Skin, subcutaneous tissue disorders: hyperhidrosis, periorbital edema, photosensitivity reaction, pruritis, urticaria, rash, Henoch-Schönlein purpura.

Vascular disorders: hypotension, hypertension.

7 DRUG INTERACTIONS

7.1 Drugs Associated with Neutropenia or Agranulocytosis

Avoid concomitant use of FERRIPROX with other drugs known to be associated with neutropenia or agranulocytosis; however, if this is not possible, monitor the absolute neutrophil count more frequently *[see Warnings and Precautions (5.1)]*.

7.2 UDP-Glucuronosyltransferases (UGTs)

A clinical study to evaluate the effect of coadministration of UGT1A6 inhibitors with FERRIPROX on the systemic exposure of deferiprone has not been conducted. However, in the presence of the UDP glucuronosyltransferase (UGT) 1A6 inhibitor, phenylbutazone, the *in vitro* glucuronidation of deferiprone is reduced by 78%. Therefore, avoid concomitant use of UGT1A6 inhibitors (e.g. diclofenac, probenecid, or silymarin (milk thistle)) with FERRIPROX *[see Dosage and Administration (2.2), Adverse Reactions (6.1), Clinical Pharmacology (12.3)]*.

7.3 Polyvalent Cations

Concurrent use of FERRIPROX with foods, mineral supplements, and antacids that contain polyvalent cations has not been studied. However, since deferiprone has the potential to bind polyvalent cations (e.g., iron, aluminum, and zinc), allow at least a 4-hour interval between FERRIPROX and other medications (e.g., antacids), or supplements containing these polyvalent cations *[see Dosage and Administration (2)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category D *[see Warnings and Precautions (5.2), Nonclinical Toxicology (13.1)]*

Risk Summary

Based on evidence of genotoxicity and developmental toxicity in animal studies, FERRIPROX can cause fetal harm when administered to a pregnant woman. 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. There are no studies in pregnant women, and available human data are limited. If FERRIPROX is used during pregnancy or if the patient becomes pregnant while taking FERRIPROX, the patient should be apprised of the potential hazard to the fetus.

Animal Data

Skeletal and soft tissue malformations occurred in offspring of rats and rabbits that received deferiprone orally during organogenesis at the lowest doses tested (25 mg/kg per day in rats; 10 mg/kg per day in rabbits). These doses were equivalent to 3% to 4% of the maximum recommended human dose (MRHD) based on body surface area. No maternal toxicity was evident at these doses.

Embryofetal lethality and maternal toxicity occurred in pregnant rabbits given 100 mg/kg/day deferiprone orally during the period of organogenesis. This dose is equivalent to 32% of the MRHD based on body surface area.

8.3 Nursing Mothers

It is not known whether deferiprone is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for adverse reactions in nursing infants from FERRIPROX, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

The safety and effectiveness of FERRIPROX in pediatric patients have not been established.

8.5 Geriatric Use

Safety and effectiveness in elderly individuals have not been established. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

8.6 Renal Impairment

An open-label, non-randomized, parallel group clinical study was conducted to evaluate the effect of impaired renal function on the safety, tolerability, and pharmacokinetics of a single 33 mg/kg oral dose of FERRIPROX. Subjects were categorized into 4 groups based on estimated glomerular filtration rate (eGFR): healthy volunteers (eGFR ≥ 90 mL/min/1.73 m^2), mild renal impairment (eGFR 60 - 89 mL/min/1.73 m^2), moderate renal impairment (eGFR 30 - 59 mL/min/1.73 m^2), and severe renal impairment (eGFR 15 - 29 mL/min/1.73 m^2). Renal function does not influence the pharmacokinetics of deferiprone and deferiprone 3-*O*-glucuronide.

8.7 Hepatic Impairment

An open-label, non-randomized, parallel group clinical study was conducted to evaluate the effect of impaired hepatic function on the pharmacokinetics of a single 33 mg/kg oral dose of FERRIPROX. Subjects were categorized into 3 groups based on the Child-Pugh classification score: healthy volunteers, mild hepatic impairment (Class A: 5– 6 points), and moderate hepatic impairment (Class B: 7– 9 points). Mild and moderate hepatic impairment do not influence the pharmacokinetics of deferiprone and deferiprone 3-*O*-glucuronide. One subject with moderate hepatic impairment experienced a serious adverse event of acute liver and renal injury. The pharmacokinetics of deferiprone and deferiprone 3-*O*-glucuronide have not been evaluated in patients with severe hepatic impairment (Child Pugh Class C: 10-15 points).

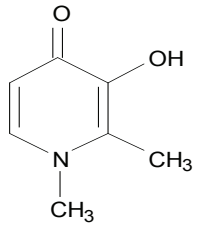
10 OVERDOSAGE

No cases of acute overdose have been reported. There is no specific antidote to FERRIPROX overdose.

Neurological disorders such as cerebellar symptoms, diplopia, lateral nystagmus, psychomotor slowdown, hand movements and axial hypotonia have been observed in children treated with 2.5 to 3 times the recommended dose for more than one year. The neurological disorders progressively regressed after deferiprone discontinuation.

11 DESCRIPTION

FERRIPROX (deferiprone) oral solution contains 100 mg/mL deferiprone (3-hydroxy-1,2-dimethylpyridin-4-one), a synthetic, orally active, iron-chelating agent. The molecular formula for deferiprone is $C_7H_9NO_2$ and its molecular weight is 139.15 g/mol. Deferiprone has the following structural formula:



Deferiprone is a white to pinkish-white powder. It is sparingly soluble in deionized water and has a melting point range of 272°C - 278°C.

FERRIPROX oral solution is a clear, reddish orange colored solution. Each mL of oral solution contains 100 mg deferiprone and the following inactive ingredients: purified water, hydroxyethylcellulose, glycerin, hydrochloric acid, artificial cherry flavor, peppermint oil, FD&C Yellow No. 6 and sucralose.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Deferiprone is a chelating agent with an affinity for ferric ion (iron III). Deferiprone 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 than for iron.

12.2 Pharmacodynamics

No clinical studies were performed to assess the relationship between the dose of FERRIPROX and the amount of iron eliminated from the body.

Cardiac Electrophysiology

At a dose 1.5 times the maximum recommended dose, FERRIPROX does not prolong the QT interval to any clinically relevant extent.

12.3 Pharmacokinetics

Deferiprone is rapidly absorbed from the upper part of the gastrointestinal tract, appearing in the blood within 5 to 10 minutes of oral administration. Peak serum concentrations occur approximately 1 hour after a single dose in fasted healthy subjects and patients, and up to 2 hours after a single dose in the fed state. Administration with food decreased the maximum concentration (C_{max}) of deferiprone by 38% and the area under the concentration-time curve (AUC) by 10%. The magnitude of the exposure change does not warrant dose adjustment.

In healthy subjects, the mean C_{max} of deferiprone in serum was about 20 mcg/mL, and the mean AUC was about 50 mcg·h/mL following oral administration of a 1,500 mg dose of FERRIPROX tablets or oral solution in the fasting state. Dose proportionality over the labeled dosage range of 25 to 33 mg/kg three times per day (75 to 99 mg/kg per day) has not been studied.

The elimination half-life of deferiprone is approximately 2 hours. Following oral administration, 75% to 90% of the administered dose is recovered in the urine in the first 24 hours, primarily as metabolite. In humans, the majority of the deferiprone is metabolized, primarily by UGT1A6. The contribution of extrahepatic (e.g., renal) UGT1A6 is unknown. The major metabolite of deferiprone is the 3-*O*-glucuronide, which lacks iron binding capability.

In a bioequivalence study, the rate (C_{max}) and the extent (AUC) of drug absorption of the solution and tablet formulations were shown to be equivalent.

Specific Populations

The pharmacokinetics of deferiprone has not been studied in geriatric or pediatric populations, and the influence of race, gender, or obesity has not been established.

Drug Interactions

Deferiprone is primarily eliminated via metabolism to the 3-*O*-glucuronide. *In vitro* UGT1A6 is primarily responsible for the glucuronidation of deferiprone which can be reduced up to 78% in the presence of the UGT1A6 inhibitor phenylbutazone.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies have not been conducted with deferiprone. However, in view of the genotoxicity results, and the findings of mammary gland hyperplasia and mammary gland tumors in rats treated with deferiprone in the 52-week toxicology study, tumor formation in carcinogenicity studies must be regarded as likely.

Deferiprone was positive in a mouse lymphoma cell assay *in vitro*. Deferiprone was clastogenic in an *in vitro* chromosomal aberration test in mice and in a chromosomal aberration test in Chinese Hamster Ovary cells. Deferiprone given orally or intraperitoneally was clastogenic in a bone marrow micronucleus assay in non-iron-loaded mice. A micronucleus test was also positive when mice predosed with iron dextran were treated with deferprone. Deferiprone was not mutagenic in the Ames bacterial reverse mutation test.

A fertility and early embryonic development study of deferiprone was conducted in rats. Sperm counts, motility and morphology were unaffected by treatment with deferiprone. There were no effects observed on male or female fertility or reproductive function at the highest dose which was 25% of the MRHD based on body surface area.

14 CLINICAL STUDIES

In a prospective, planned, pooled analysis of patients from several studies, 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 serum ferritin > 2,500 mcg/L before treatment with FERRIPROX. FERRIPROX therapy (35-99 mg/kg/day) was considered successful in individual patients who experienced a ≥ 20% decline in serum ferritin within one year of starting therapy.

Data from a total of 236 patients were analyzed. Of the 224 patients with thalassemia who received deferiprone monotherapy and were eligible for serum ferritin analysis, 105 (47%) were male and 119 (53%) were female. The mean age of these patients was 18.2 years.

For the patients in the analysis, the endpoint of at least a 20% reduction in serum ferritin was met in 50% (of 236 subjects), with a 95% confidence interval of 43% to 57%.

A small number of patients with thalassemia and iron overload were assessed by measuring the change in the number of milliseconds (ms) in the cardiac MRI T2* value before and after treatment with deferiprone for one year. There was an increase in cardiac MRI T2* from a mean at baseline of 11.8 ± 4.9 ms to a mean of 15.1 ± 7.0 ms after approximately one year of treatment. The clinical significance of this observation is not known.

16 HOW SUPPLIED/STORAGE AND HANDLING

FERRIPROX® (deferiprone) oral solution is provided in amber polyethylene terephthalate (PET) bottles with child resistant closures (polypropylene). Each pack contains one bottle of 500 mL oral solution and a graduated measuring cup (polypropylene).

Oral solution, 100 mg/mL (50 g/500 mL), NDC 52609-4502-7

Store at 20º to 25ºC (68º to 77ºF); excursions permitted to 15º to 30ºC (59º to 86ºF) [see USP Controlled Room Temperature].

Store in the original package in order to protect from light.

17 PATIENT COUNSELING INFORMATION

See FDA-Approved Patient Labeling (Medication Guide, Instructions for Use)

- Instruct patients and their caregivers that FERRIPROX is light sensitive and to store FERRIPROX in the originally supplied bottle and carton. Store FERRIPROX at 20º to 25ºC (68º to 77ºF); excursions permitted to 15º to 30ºC (59º to 86ºF) [see USP Controlled Room Temperature]. Instruct patients and their caregivers to store FERRIPROX out of the sight and reach of children.
- Inform patients of the risks of developing agranulocytosis and instruct them to immediately interrupt therapy and report to their physician if they experience any symptoms of infection such as fever, sore throat or flu-like symptoms.
- Advise patients that the amount of FERRIPROX prescribed is based on body weight and on the therapeutic goal (reduction or stabilization of the body iron load). Advise patients to use the measuring cup provided with FERRIPROX to measure the volume prescribed. Instruct patients to add about 10-15 mL of water to the measuring cup and swirl it around to mix the water with any remaining medicine in the cup and drink the mixture. The measuring cup should be hand-washed with water after use.
- Advise patients to take the first dose of FERRIPROX in the morning, the second dose at midday, and the third dose in the evening. Clinical experience suggests that taking FERRIPROX with meals may reduce nausea. If a dose of this medicine has been missed, take as soon as possible. However, if it is almost time for the next dose, skip the missed dose and go back to the regular dosing schedule. Do not catch-up or double doses.
- Advise patients to contact their physician in the event of overdose.
- Inform patients that their urine might show a reddish/brown discoloration due to the excretion of the iron-deferiprone complex. This is a very common sign of the desired effect of FERRIPROX, and it is not harmful.
- Counsel women of reproductive potential to avoid pregnancy while taking FERRIPROX. Advise patients to immediately notify their physician if they become pregnant, or if they plan to become pregnant during therapy.
- Inform patients that they should not breast feed while taking FERRIPROX.

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