Chiesi TOTAL care℠

Lesa, Chiesi Total Care pharmacist

FERRIPROX® (DEFERIPRONE) STARTER KIT

Indication

Ferriprox® (deferiprone) is an iron chelator indicated for the treatment of transfusional iron overload in patients with:

- thalassemia syndromes
- sickle cell disease or other anemias

Ferriprox Tablets are indicated in adult and pediatric patients ≥8 years of age; Ferriprox Oral Solution is indicated in patients ≥3 years of age.

Limitations of Use:

Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

Important Safety Information

WARNING: AGRANULOCYTOSIS AND NEUTROPENIA

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

Please see full Prescribing Information, including boxed WARNING and Medication Guide inside.

Ferriprox TWICE-A-DAY deferiprone 1000 mg tablets

Ferriprox deferiprone
1000 mg tablets
500 mg tablets
Oral solution 100 mg/mL

Chiesi TOTAL care℠

Getting Started Guide

To get a patient started on Ferriprox® (deferiprone) follow **2 steps** outlined in this guide.


Pranav, actual Ferriprox patient

Visit chiesitotalcare.com or call

1-866-758-7071 – we're ready to help!

Indication

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- **Interrupt Ferriprox therapy if neutropenia develops.**
- **Interrupt Ferriprox if infection develops, and monitor the ANC more frequently.**
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Please see full Prescribing Information, including boxed WARNING and Medication Guide inside.

Ferriprox TWICE-A-DAY deferiprone 1000 mg tablets

Ferriprox® deferiprone
1000 mg tablets
500 mg tablets
Oral solution 100 mg/mL

Step 1:

Fill out the Physician Order/Prescription & Statement of Medical Necessity Form

Chiesi TOTAL Care℠

Physician Prescription/Order & Statement of Medical Necessity

Ferriprox® TWICE-A-DAY deferiprone 1000 mg tablets

Ferriprox® deferiprone 1000 mg tablets, 500 mg tablets, Oral solution 100 mg/mL

1. First prescription for the patient: Fax completed form to 1-866-565-7794
2. Subsequent prescription: May be e-script via EVERSANA Life Science Services Specialty Pharmacy in your EMR/HMR system
Call 1-866-758-7071 if you have questions regarding this form or contact Chiesi Total Care℠

PATIENT INFORMATION

Patient Name (Last, First) _____ Email _____

Social Security # _____-_____-_____ Sex: ☐ Male ☐ Female Date of Birth _____ (mm/dd/yyyy)

Address _____ City _____ State _____ Zip _____

Primary Phone (Required) _____ Cell Phone _____ Language: ☐ English ☐ Other _____

Please attach copies of patient insurance and prescription cards – front and back.

MEDICAL INFORMATION

A

Diagnosis: ☐ Transfusional Iron Overload E83.111

Due to: ☐ Beta Thalassemia D56.1 ☐ Other Thalassemias D56.8 ☐ Other Anemias _____
☐ Sickle Cell Disease D57.1 ☐ Other Sickle Cell Disease D57.8 ☐ Other _____

Height_____ inches or _____cm Weight _____ lb or _____ kg Allergies: ☐ None or Specify_____

Lab test	Results	Date (mm/dd/yyyy)
Most recent serum ferritin level (acceptable level <500 ng/mL)		

If available please provide the following	Results	Date (mm/dd/yyyy)
Most recent liver iron concentration value (acceptable level <3,000 μg/g dry weight)		
Most recent cardiac MRI T2* value (acceptable level >20 ms)		

Prior Chelation Therapy _____ **Current Chelation Therapy** _____

Approximate number of blood units/month	
Approximate interval between transfusions (weeks)	

FERRIPROX® (DEFERIPRONE) PRESCRIPTION/ORDER

B

TWICE-A-DAY FORMULATION

☐ **Ferriprox (deferiprone) Twice-A-Day tablets 1000 mg†**
Sig: Take _____tablets po BID

THREE-TIMES-A-DAY FORMULATION†

☐ Ferriprox (deferiprone) oral solution 100 mg/mL
Sig: Take _____mL po TID or see Rx attached

† 500 mg and 1000 mg Three-Times-A-Day tablets are still available. Talk to your pharmacist for more information.

(Standard dose is 75-99 mg/kg/day divided into 2 doses/day for Twice-A-Day tablets or 3 doses/day for oral solution.) **Dispense 30-day supply.**
Number of Refills _____

PHYSICIAN/OFFICE INFORMATION

Prescriber's Name (print) _____ Office Phone _____

Practice/Group Name _____ Office Fax _____

Address _____ Suite_____ License # _____

City _____ State _____ Zip _____

Office Contact Person _____ NPI #_____

By signing below, I certify that I am part of the Chiesi Total Care Program, that the therapy described above is medically necessary, and that the information provided is accurate to the best of my knowledge. I also attest that I have obtained the patient's authorization to release the above information and such other personal information as may be necessary to the Chiesi Total Care Program and/or their agents. If the patient is 18 years old or younger, I attest that I have obtained permission from the patient's legal guardian.

C

Prescriber's Signature _____ _____ Date _____
Substitution Permitted Dispense as Written

Ferriprox Twice-A-Day is available as 1000 mg BID tablets.
Ferriprox is available as 1000 mg and 500 mg (immediate release) Three-Times-A-Day tablets and as 100 mg/mL oral solution.
Please see Important Safety Information, including boxed WARNING, on the back.

Scan for digital RX form.

Important Safety Information

Ferriprox can cause fetal harm. Advise females of reproductive potential to use an effective method of contraception during treatment with Ferriprox and for at least six months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with Ferriprox and for at least three months after the last dose. Advise females not to breastfeed during treatment with Ferriprox and for at least 2 weeks after the last dose.

A Specify appropriate ICD-10 diagnosis code(s) for secondary diagnosis.

If patient has transfusional iron overload, both the **DIAGNOSIS** (primary diagnosis) and **DUE** to (secondary diagnosis) sections must be completed.

ICD-10 Diagnosis Codes

Diagnosis	Current indication
D55.8	Other anemias due to enzyme disorders
D56.1	Beta Thalassemia
D56.8	Other Thalassemia
D57.1	Sickle Cell Disease
D57.8	Other Sickle Cell Disease
D58.1	Hereditary elliptocytosis
D58.9	Hereditary hemolytic anemia, unspecified
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]
D61.2	Aplastic anemia due to other external agents

Diagnosis	Current indication
D61.89	Other plastic anemias and other bone marrow failure syndromes
D61.9	Aplastic anemia, unspecified
D63.8	Anemia in other chronic diseases classified elsewhere
D64.1	Secondary sideroblastic anemia due to disease
D64.3	Other sideroblastic anemias
D64.4	Congenital dyserythropoietic anemia
D64.9	Anemia, unspecified
E83.111	Hemochromatosis due to repeated red blood cell transfusions
E87.71	Transfusion associated circulatory overload

Intended as a reference for coding and billing for product and associated services. Not intended to be a directive, nor does the use of the recommended codes guarantee reimbursement. Providers are responsible for ensuring the accuracy and validity of all billing and claims for appropriate reimbursement.

B Specify formulation and titration schedule.

THERAPEUTIC DOSE

75 mg/kg/day ▶ 99 mg/kg/day

ADJUST FOR OPTIMAL CHELATION

Increasing the dose of Ferriprox from 75 mg/kg/day up to 99 mg/kg/day may improve efficacy in iron chelation.[1,2]

Sample dosing assuming 60 kg patient @ 99 mg/kg/day (when no titration is required):

TWICE-A-DAY FORMULATION

☑ **Ferriprox (deferiprone) Twice-A-Day tablets 1000 mg†**

Sig: Take 3 tablets po BID

Titration schedule if needed:

Help to minimize gastrointestinal (GI) upset

WEEK 1	WEEK 2
45 mg/kg/day	60 mg/kg/day

Titrate Ferriprox by 15 mg/kg/day weekly.

Sample titration assuming 60 kg patient titrating from 45 up to 60 mg/kg/day (with adjustment):

TWICE-A-DAY FORMULATION

☑ **Ferriprox (deferiprone) Twice-A-Day tablets 1000 mg†**

Sig: Take Week one: 1.5 tablets / Week 2: 2 tablets po BID

You may also attach separate instructions for titration schedule.

C Write "Dispense as written" on prescriptions.

Important Safety Information

Avoid co-administration of Ferriprox with other drugs known to be associated with neutropenia or agranulocytosis; however, if this is unavoidable, closely monitor the absolute neutrophil count. Avoid co-administration with UGT1A6 inhibitors. Allow at least a 4-hour interval between administration of Ferriprox and drugs or supplements containing polyvalent cations (e.g., iron, aluminum, or zinc).

Please see full Prescribing Information, including boxed WARNING and Medication Guide inside.

Step 2:

Once you have completed the form:

1. Attach copies of patient insurance and prescription cards – front and back.

2. **First prescription for the patient:**

   THE FIRST COPY OF THE FORM MUST BE FAXED FOR EACH PATIENT. Fax completed form to Chiesi Total Care℠ at 1-866-565-7794. **Please complete one form per patient.**

3. **Subsequent prescriptions:**

   If you wish to send subsequent forms via e-script please search for "Eversana Life Science Services Specialty Pharmacy" in your EMR/HMR's e-prescribing software

The fillable pdf can be downloaded and saved for future use.
Scan the QR code to download a copy.

Indication

Ferriprox® (deferiprone) is an iron chelator indicated for the treatment of transfusional iron overload in patients with:

- thalassemia syndromes
- sickle cell disease or other anemias

Ferriprox Tablets are indicated in adult and pediatric patients ≥8 years of age; Ferriprox Oral Solution is indicated in patients ≥3 years of age.

Limitations of Use:

Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

Important Safety Information

WARNING: AGRANULOCYTOSIS AND NEUTROPENIA

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

Ferriprox is contraindicated in patients with known hypersensitivity to deferiprone or to any of the excipients in the formulations.

In pooled clinical trials, 7.5% of 642 patients with thalassemia syndromes 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. In pooled clinical trials, 7.7% of 196 patients with sickle cell disease or other anemias treated with Ferriprox developed increased ALT values. 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. Decreased plasma zinc concentrations have been observed on deferiprone therapy. Monitor plasma zinc annually, and supplement in the event of a deficiency.

Ferriprox can cause fetal harm. Advise females of reproductive potential to use an effective method of contraception during treatment with Ferriprox and for at least six months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with Ferriprox and for at least three months after the last dose. Advise females not to breastfeed during treatment with Ferriprox and for at least 2 weeks after the last dose.

Avoid co-administration of Ferriprox with other drugs known to be associated with neutropenia or agranulocytosis; however, if this is unavoidable, closely monitor the absolute neutrophil count. Avoid co-administration with UGT1A6 inhibitors. Allow at least a 4-hour interval between administration of Ferriprox and drugs or supplements containing polyvalent cations (e.g., iron, aluminum, or zinc).

The most common adverse reactions in patients with thalassemia (incidence ≥6%) are nausea, vomiting, abdominal pain, arthralgia, ALT increased and neutropenia. The most common adverse reactions in patients with sickle cell disease or other anemias (incidence ≥6%) are pyrexia, abdominal pain, bone pain, headache, vomiting, pain in extremity, sickle cell anemia with crisis, back pain, ALT increased, AST increased, arthralgia, oropharyngeal pain, nasopharyngitis, neutrophil count decreased, cough and nausea.

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, and it is not harmful.

Advise patients to avoid alcohol while taking Ferriprox tablets (twice-a-day). Consumption of alcohol while taking Ferriprox tablets (twice-a-day) may result in more rapid release of deferiprone.

Please see full Prescribing Information, including boxed WARNING and Medication Guide inside.

References: **1.** Ferriprox® (deferiprone) Prescribing Information. Chiesi, November 2021. **2.** Binding A, et al. Deferiprone exerts a dose-dependent reduction of liver iron in adults with iron overload. *Eur J Haematol* 2019;103(2):80-87.

For more information, visit ferriprox.com.
Chiesi Total Care℠ Program offered through EVERSANA Life Science Services Specialty Pharmacy

PP-F-0312 V2.0 2022

Ferriprox® TWICE-A-DAY deferiprone 1000 mg tablets

Ferriprox® deferiprone
1000 mg tablets
500 mg tablets
Oral solution 100 mg/mL

Chiesi TOTAL care℠

Physician Prescription/Order & Statement of Medical Necessity

Ferriprox TWICE-A-DAY deferiprone 1000 mg tablets

Ferriprox deferiprone
1000 mg tablets
500 mg tablets
Oral solution 100 mg/mL

1. First prescription for the patient: Fax completed form to 1-866-565-7794
2. Subsequent prescription: May be e-script via EVERSANA Life Science Services Specialty Pharmacy in your EMR/HMR system
Call 1-866-758-7071 if you have questions regarding this form or contact Chiesi Total Care℠

PATIENT INFORMATION

Patient Name (Last, First) _____ Email _____

Social Security # _____-_____-_____ Sex: ☐ Male ☐ Female Date of Birth _____ (mm/dd/yyyy)

Address _____ City _____ State _____ Zip _____

Primary Phone (Required) _____ Cell Phone _____ Language: ☐ English ☐ Other _____

Please attach copies of patient insurance and prescription cards – front and back.

MEDICAL INFORMATION

Diagnosis: ☐ Transfusional Iron Overload E83.111

Due to: ☐ Beta Thalassemia D56.1 ☐ Other Thalassemias D56.8 ☐ Other Anemias _____
☐ Sickle Cell Disease D57.1 ☐ Other Sickle Cell Disease D57.8 ☐ Other _____

Height_____ inches or _____cm Weight _____ lb or _____ kg Allergies: ☐ None or Specify_____

Lab test	Results	Date (mm/dd/yyyy)
Most recent serum ferritin level (acceptable level <500 ng/mL)		
If available please provide the following	Results	Date (mm/dd/yyyy)
Most recent liver iron concentration value (acceptable level <3,000 μg/g dry weight)		
Most recent cardiac MRI T2* value (acceptable level >20 ms)		

Prior Chelation Therapy _____ **Current Chelation Therapy** _____

Transfusion History

Approximate number of blood units/month	
Approximate interval between transfusions (weeks)	

FERRIPROX® (DEFERIPRONE) PRESCRIPTION/ORDER

TWICE-A-DAY FORMULATION

☐ **Ferriprox (deferiprone) Twice-A-Day tablets 1000 mg†**
Sig: Take _____tablets po BID

THREE-TIMES-A-DAY FORMULATION†

☐ Ferriprox (deferiprone) oral solution 100 mg/mL
Sig: Take _____mL po TID or see Rx attached

† 500 mg and 1000 mg Three-Times-A-Day tablets are still available. Talk to your pharmacist for more information.

(Standard dose is 75-99 mg/kg/day divided into 2 doses/day for Twice-A-Day tablets or 3 doses/day for oral solution.) **Dispense 30-day supply.**
Number of Refills _____

PHYSICIAN/OFFICE INFORMATION

Prescriber's Name (print) _____ Office Phone _____

Practice/Group Name _____ Office Fax _____

Address _____ Suite_____ License # _____

City _____ State _____ Zip _____

Office Contact Person _____ NPI #_____

By signing below, I certify that I am part of the Chiesi Total Care Program, that the therapy described above is medically necessary, and that the information provided is accurate to the best of my knowledge. I also attest that I have obtained the patient's authorization to release the above information and such other personal information as may be necessary to the Chiesi Total Care Program and/or their agents. If the patient is 18 years old or younger, I attest that I have obtained permission from the patient's legal guardian.

Prescriber's Signature _____ _____ Date _____

Substitution Permitted **Dispense as Written**

Ferriprox Twice-A-Day is available as 1000 mg BID tablets.
Ferriprox is available as 1000 mg and 500 mg (immediate release) Three-Times-A-Day tablets and as 100 mg/mL oral solution.
Please see Important Safety Information, including boxed WARNING, on the back.

Scan for digital RX form.

Indication

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- thalassemia syndromes
- sickle cell disease or other anemias

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Limitations of Use

Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

Important Safety Information

WARNING: AGRANULOCYTOSIS AND NEUTROPENIA

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

Ferriprox is contraindicated in patients with known hypersensitivity to deferiprone or to any of the excipients in the formulations.

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Ferriprox can cause fetal harm. Advise females of reproductive potential to use an effective method of contraception during treatment with Ferriprox and for at least six months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with Ferriprox and for at least three months after the last dose. Advise females not to breastfeed during treatment with Ferriprox and for at least 2 weeks after the last dose.

Avoid co-administration of Ferriprox with other drugs known to be associated with neutropenia or agranulocytosis; however, if this is unavoidable, closely monitor the absolute neutrophil count. Avoid co-administration with UGT1A6 inhibitors. Allow at least a 4-hour interval between administration of Ferriprox and drugs or supplements containing polyvalent cations (e.g., iron, aluminum, or zinc).

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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, and it is not harmful.

Advise patients to avoid alcohol while taking Ferriprox tablets (twice-a-day). Consumption of alcohol while taking Ferriprox tablets (twice-a-day) may result in more rapid release of deferiprone.

Please see full Prescribing Information, including boxed WARNING and Medication Guide.

Chiesi Total Care Program offered through EVERSANA Life Science Services Specialty Pharmacy.

CHIESI TOTAL CARE

PHONE
1-866-758-7071

HOURS OF OPERATION
Monday to Friday
7:00am - 6:00pm (Central Time)

FAX
1-866-565-7794

WEBSITE
chiesitotalcare.com

For more information, visit ferriprox.com.

PP-F-0131 V6.0 2023

Ferriprox TWICE-A-DAY deferiprone 1000 mg tablets

Ferriprox® deferiprone
1000 mg tablets
500 mg tablets
Oral solution 100 mg/mL

PATIENT ENROLLMENTFORM

Fax completed form to Chiesi Total Care at 866-565-7794| Phone: 866-758-7071

Copay Assistance Programs

Nursing Support Services

Dedicated Total Care Team

Chiesi Total Care (the "Program") provides product support to eligible patients who have been prescribed a Chiesi USA, Inc. product. Program support may include: (1) reimbursement and financial support (such as investigating insurance coverage, confirming out-of-pocket costs, and reviewing eligibility for financial assistance and copay programs); (2) working with patients and pharmacies to fill prescriptions; (3) home infusion support (if applicable); and (4) providing disease, medication, and adherence-related educational resources and communications.

Patient Name:_____ **Date of Birth:** _____(mm/dd/yy)

ENROLLMENT INTO CHIESI TOTAL CARE

By signing this authorization form ("Authorization"), I confirm I would like to enroll in the Program and authorize Chiesi USA, Inc., and its affiliates, service providers, agents, and successors (together, "Chiesi") to provide me with Program support. I authorize Chiesi, my healthcare providers and their staff, my health plan, patient assistance programs, and my pharmacies to process and share my personal health information (such as information about my diagnosis and treatment), personal identifying information (such as contact information and program preferences), and insurance information (such as prescriptions and plans) (together my "Information") in order to enroll me in the Program, provide Program support, administer the Program, meet legal obligations, conduct other business activities, and complete government reporting activities. For example, Chiesi may use my Information to communicate with me (such as by mail, phone, e-mail, and text message*), tailor Program-related communications and services to my needs, and share my Information with my healthcare providers to dispense Chiesi products to me. Chiesi may also de-identify my Information, combine it with information about other patients, and use the results for Chiesi USA, Inc.'s and its affiliate's business purposes. I understand that once my Information is disclosed, my Information may no longer be protected by federal privacy laws and could be re-disclosed. However, Chiesi will only process and disclose my Information as described in this Authorization. Additional information on Chiesi's privacy practices can be found at https://www.chiesiusa.com/privacy-policy/.

I understand that this Program is optional. I can refuse to sign this Authorization and refusing to sign will not affect my treatment, insurance coverage, or eligibility for benefits or Chiesi products. However, I understand that I need to sign this form to participate in the Program.

I understand that I may cancel this Authorization at any time or receive a copy of this Authorization by mailing a letter requesting cancellation to Chiesi Total Care, 17877 Chesterfield Airport Rd, Chesterfield, MO 63005. I may also revoke my authorization to receive automated calls or text messages by replying STOP to any text from Chiesi Total Care or by contacting Chiesi Total Care in writing at the address above. Upon cancellation, to the extent required by applicable law and personal data rights, Chiesi will no longer process my Information. I understand my cancellation will not apply to any of my Information already used or disclosed based on this Authorization prior to receipt of the cancellation. Unless cancelled earlier, this Authorization expires ten (10) years from the date signed below, or as otherwise required by state or local law.

By signing below, I acknowledge that my pharmacy will receive payment from Chiesi for disclosing my Information to Chiesi. I acknowledge that if I am enrolled in a government-funded healthcare program, I am not eligible for and will not accept any co-pay assistance from Chiesi Total Care. I understand and agree that if my insurance information changes at any time while I am participating in the Chiesi Total Care Program, I will notify Chiesi Total Care as soon as possible, and any such change may affect my eligibility for such assistance programs.

By signing below, I also acknowledge that I have read and agree to the terms and conditions of the Chiesi Total Care support programs on page 2 of this document.

Feed Back: We greatly appreciate your feedback. Please indicate whether you would like to be contacted by Chiesi about opportunities for you to provide feedback to us (such as Program feedback surveys or market research):

☐ YES, I would like to be contacted to provide feedback.

☐ NO, I would not like to be contacted to provide feedback.

TEXT: Please indicate whether you authorize Chiesi to send text messages to the number(s) you provide. Your consent to receiving text messages is not a condition of receiving medication or services from Chiesi.

☐ YES, I consent to receive text messages.

☐ NO, I do not consent to receive text messages.

Patient or Legal Guardian Signature: _____ **Signature date:** _____ (mm/dd/yy)

Please specify any additional contacts with whom Chiesi Total Care is allowed to discuss your Information:

Additional Contact Name:_____ **Relationship to Patient:** _____

*Additional charges may apply. I understand that my telephone provider may charge me fees for calls or texts I receive, and I agree that Chiesi Total Care will not pay those fees.

PP-G-0606 V1.0

PATIENT ENROLLMENTFORM

Fax completed form to Chiesi Total Care at 866-565-7794| Phone: 866-758-7071

CHIESI TOTAL CARE Terms and Conditions

Chiesi Total Care Patient Support Services Program Terms and Conditions

To enroll in Chiesi Total Care (the "Program") and to assess eligibility for patient support services of the Program, patient must complete the Program Enrollment and Authorization Form and have a valid prescription for an eligible product of the Program. Additional documentation may be required. The patient must be a resident of the US or one of its territories. If the patient is incapable of acting on their own behalf or if the patient is under 18 years old, enrollment into the Program may be completed by another person acting on their behalf (such as a caregiver).

A patient who receives health care benefits under any plan or program funded in whole or in part by federal or state governments including Medicare, Medicaid, TRICARE, Veterans Affairs (VA), State Prescription Assistance Plans (SPAPs) (other than health insurance for federal government employees) or any state health care program such as Medicaid, Children's Health Insurance Program, programs funded under Maternal and Child Health Program or programs funded under Social Services Block Grant (collectively, "Government-funded Plans") are not eligible for the financial patient support services of the Program. A patient covered under a commercial health plan purchased through a health insurance marketplace or exchange is not a Government-funded Plan beneficiary even if the costs of such coverage are subsidized by the federal government. If a change in prescription drug coverage should occur, the patient must notify the Program; such change may affect eligibility for the support services provided in the Program. Patients who have prescribed a product for an indication that is not consistent with the US Food and Drug Administration-approved labeling will not be eligible for financial patient support services offered through the Program.

Patients residing in or receiving treatment in certain states may not be eligible for certain patient support services of the Program. Patients may not seek reimbursement for value received from the Program. The Program does not obligate the use of any specific medication or health care provider.

Program benefits may not be sold, purchased, traded, or offered for sale, purchase, or trade. The Chiesi Total Care patient support services are not valid where prohibited by law, taxed, or otherwise restricted. Offer subject to change or discontinuance without notice. Restrictions, including monthly maximums, may apply. This is not health insurance.

This is a voluntary program. Patients who choose not to enroll in the Program will be able to receive medication. Patients may participate in Chiesi Total Care without participating in a patient support services program of Chiesi Total Care. After enrolling in Chiesi Total Care, participants may opt out by contacting the Program, as outlined in the Chiesi Total Care Enrollment and Authorization Form. Patients must renew their eligibility by December 31 of each year to continue to receive support under the Program.

By participating in the Program, participants acknowledge that they understand and agree to comply with the Program Terms and Conditions.

Chiesi TOTAL care℠

Ferriprox® (deferiprone) Prior Authorization and Access Guide

Visit chiesitotalcare.com or call

1-866-758-7071 – we're ready to help!

Indication

Ferriprox® (deferiprone) is an iron chelator indicated for the treatment of transfusional iron overload in patients with:

- thalassemia syndromes
- sickle cell disease or other anemias

Ferriprox Tablets are indicated in adult and pediatric patients ≥8 years of age; Ferriprox Oral Solution is indicated in patients ≥3 years of age.

Limitations of Use:

Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

Important Safety Information

WARNING: AGRANULOCYTOSIS AND NEUTROPENIA

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

Please see full Prescribing Information, including boxed WARNING and Medication Guide inside.

Ferriprox® TWICE-A-DAY deferiprone 1000 mg tablets

Ferriprox® deferiprone
1000 mg tablets
500 mg tablets
Oral solution 100 mg/mL

Chiesi Total Care℠ will submit for insurance reimbursement and help you navigate prior authorization (PA).

HERE'S A STEP-BY-STEP LOOK AT THE PROCESS

1

SUBMISSION

Your Chiesi Total Care Team starts the process when a new Rx form has been submitted.

The Chiesi Total Care team helps you submit PA.

2

MONITORING PA

Chiesi Total Care monitors and tracks PA submission until an outcome is determined by payor.

3

PA IS APPROVED

- Your office and/or patient is notified

PA IS DENIED

- Send denial documentation to Chiesi Total Care
- Chiesi Total Care can help in denial situations with a high success rate

APPEAL

Based on the letter, Chiesi Total Care can submit a patient level appeal with signed patient consent.

OR

Your office can submit a physician level appeal. Chiesi Total Care can assist and coach on best practices.*

*Chiesi Total Care assistance is neither medical guidance nor a suggestion that you submit an appeal. The resources and information provided in this guide is general in nature and is not intended to be conclusive or exhaustive. As the patient's healthcare provider, you are responsible for applying your clinical judgment regarding appropriate care and treatment of each patient.

4

PA OR APPEAL IS APPROVED

Pharmacy fills Rx and medication is dispensed to the patient

Contact your dedicated Chiesi Total Care program specialist with any questions you may have about your case.

PA denied? Chiesi Total Care is here to help.

It's not uncommon for the first PA submission to be denied. With a long track record of success in gaining PA and appeal approvals, Chiesi Total Care is here to provide assistance with the appeal process. Chiesi Total Care will assist in providing additional resources and/or publications depending on the reasons for denial. To request a copy of an additional resource or publication, please reach out directly to us.medical@chiesi.com.

Visit chiesitotalcare.com or call
1-866-758-7071

Chiesi Total Care can help improve compliance and adherence.

Chiesi TOTAL care℠

We provide updates on your patient's therapy and alert the office should there be an issue with compliance. We also help patients stay compliant by helping them cope with side effects and answering questions.

We can help by:

- Alerting when to refill or when refills are being missed
- Counseling patients on managing side effects
- Providing 24/7 pharmacist access
- Enrolling patients in the Ferriprox Copay Program – patients may pay as little as $0 if eligible†

Lesa, Chiesi Total Care Pharmacist

† Please refer to the full Terms and Conditions in the back pocket for additional eligibility requirements.

Here is a checklist of best practices for Prior Authorization submission:

- ☐ Write "Dispense as written" on prescription Rx form
- ☐ Include pertinent clinical notes, dates, and laboratory findings
- ☐ Include prescribing practitioner NPI number and contact information
- ☐ Include medical rationale for why the patient cannot use generic or preferred formulary drugs
- ☐ Include therapeutic alternatives that were tried in the past, include documentation as to why it was inadequate

Important Safety Information

Avoid co-administration of Ferriprox with other drugs known to be associated with neutropenia or agranulocytosis; however, if this is unavoidable, closely monitor the absolute neutrophil count. Avoid co-administration with UGT1A6 inhibitors. Allow at least a 4-hour interval between administration of Ferriprox and drugs or supplements containing polyvalent cations (e.g., iron, aluminum, or zinc).

Please see full Prescribing Information, including boxed WARNING and Medication Guide, in the folder.

Important Safety Information

Indication

Ferriprox® (deferiprone) is an iron chelator indicated for the treatment of transfusional iron overload in patients with:

- thalassemia syndromes
- sickle cell disease or other anemias

Ferriprox Tablets are indicated in adult and pediatric patients ≥8 years of age; Ferriprox Oral Solution is indicated in patients ≥3 years of age.

Limitations of Use:

Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

Important Safety Information

WARNING: AGRANULOCYTOSIS AND NEUTROPENIA

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

Ferriprox is contraindicated in patients with known hypersensitivity to deferiprone or to any of the excipients in the formulations.

In pooled clinical trials, 7.5% of 642 patients with thalassemia syndromes 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. In pooled clinical trials, 7.7% of 196 patients with sickle cell disease or other anemias treated with Ferriprox developed increased ALT values. 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. Decreased plasma zinc concentrations have been observed on deferiprone therapy. Monitor plasma zinc annually, and supplement in the event of a deficiency.

Ferriprox can cause fetal harm. Advise females of reproductive potential to use an effective method of contraception during treatment with Ferriprox and for at least six months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with Ferriprox and for at least three months after the last dose. Advise females not to breastfeed during treatment with Ferriprox and for at least 2 weeks after the last dose.

Avoid co-administration of Ferriprox with other drugs known to be associated with neutropenia or agranulocytosis; however, if this is unavoidable, closely monitor the absolute neutrophil count. Avoid co-administration with UGT1A6 inhibitors. Allow at least a 4-hour interval between administration of Ferriprox and drugs or supplements containing polyvalent cations (e.g., iron, aluminum, or zinc).

The most common adverse reactions in patients with thalassemia (incidence ≥6%) are nausea, vomiting, abdominal pain, arthralgia, ALT increased and neutropenia. The most common adverse reactions in patients with sickle cell disease or other anemias (incidence ≥6%) are pyrexia, abdominal pain, bone pain, headache, vomiting, pain in extremity, sickle cell anemia with crisis, back pain, ALT increased, AST increased, arthralgia, oropharyngeal pain, nasopharyngitis, neutrophil count decreased, cough and nausea.

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, and it is not harmful.

Advise patients to avoid alcohol while taking Ferriprox tablets (twice-a-day). Consumption of alcohol while taking Ferriprox tablets (twice-a-day) may result in more rapid release of deferiprone.

Please see full Prescribing Information, including boxed WARNING and Medication Guide inside.

For more information, visit ferriprox.com.
Chiesi Total Care℠ Program offered through EVERSANA Life Science Services Specialty Pharmacy

PP-F-0313 V2.0

Sample Letter of Medical Necessity

Using this template:

- ☐ Fill in the template using the instructions highlighted in blue.
- ☐ Once you have filled in the information, remove any remaining instructions in blue.
- ☐ Select all the text and change the font to black so the whole document appears as one letter.

Use the steps above as a checklist to make sure you have completed these steps prior to sending. **It is important to follow these steps to ensure the letter is clear and concise.**

[Insurance Company]
[Address]
[City, State, Zip]

Re: **[Patient Name]**
[Policy #]
[DOB]
[Address]
[City, State, Zip]

To Whom It May Concern:

I am writing this letter of medical necessity on behalf of **[Patient Name, ID#, Group #]** to request coverage for **[Product name (generic name)].** Included in this letter of medical necessity is information on the treatment rationale, medical records, medical necessity data and medical studies confirming currently prescribed product as an effective treatment for the diagnosis associated with **[ICD10 Code]**.

Treatment Rationale:
[Provide information on patient response and history to past treatments and anticipated prognosis and rationale for the currently prescribed product].

Outline of Medical Studies:
[Outline a brief overview of the studies evaluating the use of the currently prescribed product in this condition and/or patient population. Remember to include the FDA approved indications and usage].

Medical Record Information:
[Highlight key dates and entries of the medical record how the currently prescribed product is used].

Per the included medical information, it is my professional opinion that the currently prescribed product is medically necessary in treating the patient and the denials for the patient's use of the drug should be reversed. Please call my office at **[Office Phone Number]** if I can provide further information.

Sincerely,
[Physician Name and Signature]
[Phone Number]
Enclosure: [As required]

Sample Letter of Appeal

Please Note: By downloading materials from this link, you agree to all the following. These materials are available for download and public personal use. These materials have no value and are not to be re-sold or repurposed. They are solely for your personal use. No purchase from or relationship with Chiesi Total Care℠ is required to download or use these materials. Chiesi Total Care℠ makes no representations or warranties about these materials or their fitness for any specific use. Chiesi Total Care℠ is not responsible for any changes made to these template documents. All billing and coding decisions are the responsibility of the relevant physician. Chiesi Total Care℠ does not guarantee any specific reimbursement or favorable results.

Using this template:

- ☐ Fill in the template using the instructions highlighted in blue.
- ☐ Once you have filled in the information, remove any remaining instructions in blue.
- ☐ Select all the text and change the font to black so the whole document appears as one letter.

Use the list above as a checklist to make sure you have completed these steps prior to sending. **It is important to follow these steps to ensure the letter is clear and concise.**

[Insurance Company]
[Address]
[City, State, Zip]

Re: **[Patient Name]**
[Policy #]
[DOB]
[Address]
[City, State, Zip]

To Whom It May Concern:

I am writing to appeal the denial of benefits for the use of **[Product name (generic name)]** for services requested for **[Patient Name, ID#, Group #]**. Included in this letter of appeal are information on the treatment rationale, medical records, medical necessity data and medical studies confirming currently prescribed product as an effective treatment for the diagnosis associated with **[ICD10 Code]**.

Treatment Rationale:
[Provide information on patient response and history to past treatments and anticipated prognosis and rationale for the currently prescribed product].

Outline of Medical Studies:
[Outline a brief overview of the studies evaluating the use of the currently prescribed product in this condition and/or patient population. Remember to include the FDA approved indications and usage].

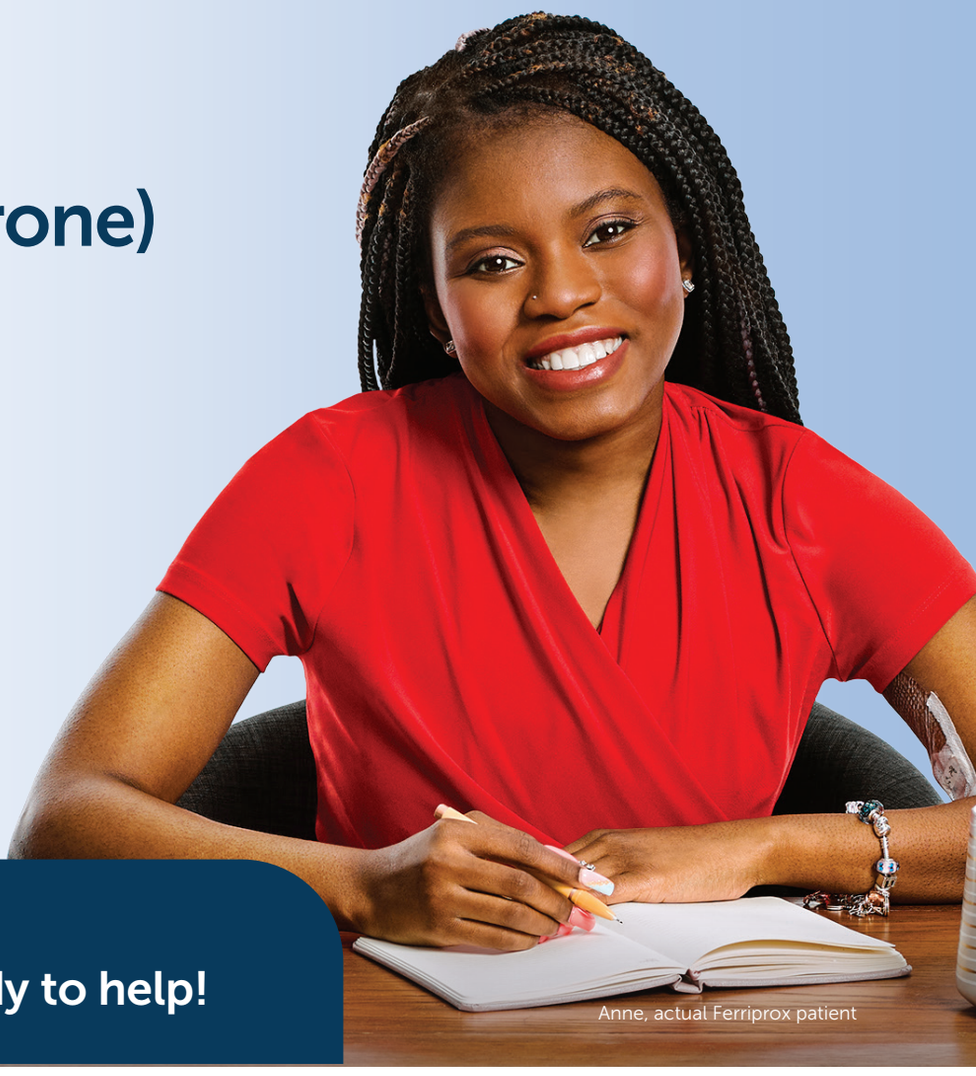
Medical Record Information:
[Highlight key dates and entries of the medical record how the currently prescribed product is used].

Per the included medical information, it is my professional opinion that the currently prescribed product is medically necessary in treating the patient and the denials for the patient's use of the drug should be reversed. Please call my office at **[Office Phone Number]** if I can provide further information or speak with a review board to appeal the denial of coverage decision. I look forward to reaching resolution of overturning the denied status of the currently prescribed product for this patient.

Sincerely,
[Physician Name and Signature]
[Phone Number]
Enclosure: [Original denial notification copy]

Chiesi TOTAL care℠

Ferriprox® (deferiprone) Dosing and Administration


Anne, actual Ferriprox patient

Visit chiesitotalcare.com or call

1-866-758-7071 – we're ready to help!

Indication

Ferriprox® (deferiprone) is an iron chelator indicated for the treatment of transfusional iron overload in patients with:

- thalassemia syndromes
- sickle cell disease or other anemias

Ferriprox Tablets are indicated in adult and pediatric patients ≥8 years of age; Ferriprox Oral Solution is indicated in patients ≥3 years of age.

Limitations of Use:

Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

Important Safety Information

WARNING: AGRANULOCYTOSIS AND NEUTROPENIA

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

Please see full Prescribing Information, including boxed WARNING and Medication Guide inside.

Ferriprox® TWICE-A-DAY deferiprone 1000 mg tablets

Ferriprox® deferiprone

1000 mg tablets
500 mg tablets
Oral solution 100 mg/mL

Ferriprox® dosing optimization

Ferriprox dosing is adjustable

Administration with food may reduce the incidence of nausea and vomiting.[1]

THERAPEUTIC DOSE

75 mg/kg/day ▶ **99** mg/kg/day

TITRATION SCHEDULE IF NEEDED:

Help to minimize gastrointestinal (GI) upset

WEEK 1	WEEK 2
45 mg/kg/day	**60** mg/kg/day

Titrate Ferriprox by 15 mg/kg/day weekly.

ADJUST FOR OPTIMAL CHELATION

Increasing the dose of Ferriprox from 75 mg/kg/day up to 99 mg/kg/day may improve efficacy in iron chelation.[1,2]

The incidence of neutropenia and agranulocytosis is not dose related within the therapeutic range.[3]

Important Safety Information

Avoid co-administration of Ferriprox with other drugs known to be associated with neutropenia or agranulocytosis; however, if this is unavoidable, closely monitor the absolute neutrophil count. Avoid co-administration with UGT1A6 inhibitors. Allow at least a 4-hour interval between administration of Ferriprox and drugs or supplements containing polyvalent cations (e.g., iron, aluminum, or zinc).

Monitoring your patients on Ferriprox is straightforward:[1]

Absolute neutrophil count (ANC)

† For patients whose Ferriprox has not been interrupted due to any decrease in the neutrophil count the frequency of ANC monitoring may be extended.
‡ After one year of therapy: Monitor ANC every two to four weeks (or at the patient's blood transfusion interval) in patients that have not experienced an interruption due to any decrease in ANC.

Reduction in the frequency of ANC monitoring should be considered on an individual patient basis, according to the healthcare provider's assessment of the patient's understanding of the risk minimization measures required during therapy.

Serum liver enzymes

Monthly, on therapy

Increased ALT levels were observed in clinical trials. Consider interruption of therapy if there is a **persistent** increase in serum transaminase levels.

Plasma zinc concentration

Annually, on therapy

Decreased plasma zinc concentrations have been observed in patients on Ferriprox.

Important Safety Information

The most common adverse reactions in patients with thalassemia (incidence ≥6%) are nausea, vomiting, abdominal pain, arthralgia, ALT increased and neutropenia. The most common adverse reactions in patients with sickle cell disease or other anemias (incidence ≥6%) are pyrexia, abdominal pain, bone pain, headache, vomiting, pain in extremity, sickle cell anemia with crisis, back pain, ALT increased, AST increased, arthralgia, oropharyngeal pain, nasopharyngitis, neutrophil count decreased, cough and nausea.

Please see Important Safety Information on reverse. Please see full Prescribing Information, including boxed WARNING and Medication Guide, in the folder.

Choice of formulations

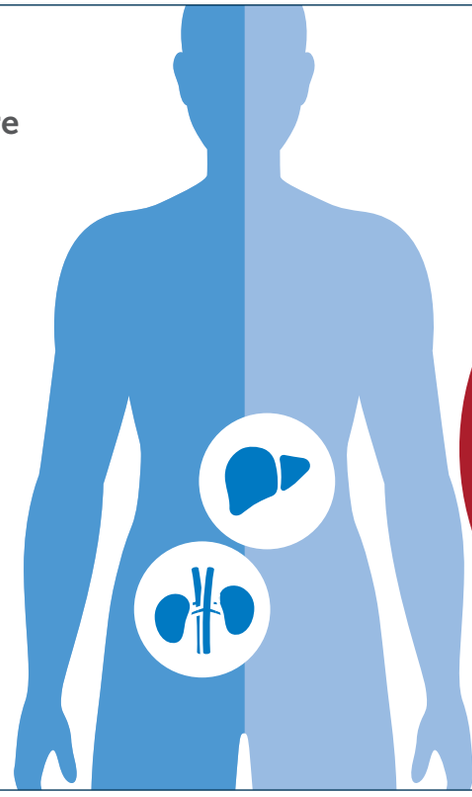
Ferriprox offers a choice of oral formulations for optimal chelation[1§]

		
Strength	1000 mg	100 mg/mL
NDC#	10122-104-01	10122-101-50
Frequency	Twice-A-Day	Three-Times-A-Day
Formulation	Tablets	Oral solution

§ 500 mg and 1000 mg Three-Times-A-Day tablets are still available. Talk to a Chiesi Total Care pharmacist for more information: 1-866-758-7071.

No dosage adjustment required for patients with renal or hepatic impairment[1]

Ferriprox is suitable for patients with mild to severe renal or mild to moderate hepatic impairment.[1¶]



In clinical studies, renal or hepatic impairment had no significant effect on systemic exposure to Ferriprox[1]

¶ Ferriprox was not studied in patients with end-stage renal disease (ESRD) or severe hepatic impairment.

Chiesi

TOTAL care℠

Pranav and Anne, actual Ferriprox patients

Indication and Important Safety Information

Indication

Ferriprox® (deferiprone) is an iron chelator indicated for the treatment of transfusional iron overload in patients with:

- thalassemia syndromes
- sickle cell disease or other anemias

Ferriprox Tablets are indicated in adult and pediatric patients ≥8 years of age; Ferriprox Oral Solution is indicated in patients ≥3 years of age.

Limitations of Use:

Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

Important Safety Information

WARNING: AGRANULOCYTOSIS AND NEUTROPENIA

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

Ferriprox is contraindicated in patients with known hypersensitivity to deferiprone or to any of the excipients in the formulations.

In pooled clinical trials, 7.5% of 642 patients with thalassemia syndromes 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. In pooled clinical trials, 7.7% of 196 patients with sickle cell disease or other anemias treated with Ferriprox developed increased ALT values. 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. Decreased plasma zinc concentrations have been observed on deferiprone therapy. Monitor plasma zinc annually, and supplement in the event of a deficiency.

Ferriprox can cause fetal harm. Advise females of reproductive potential to use an effective method of contraception during treatment with Ferriprox and for at least six months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with Ferriprox and for at least three months after the last dose. Advise females not to breastfeed during treatment with Ferriprox and for at least 2 weeks after the last dose.

Avoid co-administration of Ferriprox with other drugs known to be associated with neutropenia or agranulocytosis; however, if this is unavoidable, closely monitor the absolute neutrophil count. Avoid co-administration with UGT1A6 inhibitors. Allow at least a 4-hour interval between administration of Ferriprox and drugs or supplements containing polyvalent cations (e.g., iron, aluminum, or zinc).

The most common adverse reactions in patients with thalassemia (incidence ≥6%) are nausea, vomiting, abdominal pain, arthralgia, ALT increased and neutropenia. The most common adverse reactions in patients with sickle cell disease or other anemias (incidence ≥6%) are pyrexia, abdominal pain, bone pain, headache, vomiting, pain in extremity, sickle cell anemia with crisis, back pain, ALT increased, AST increased, arthralgia, oropharyngeal pain, nasopharyngitis, neutrophil count decreased, cough and nausea.

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, and it is not harmful.

Advise patients to avoid alcohol while taking Ferriprox tablets (twice-a-day). Consumption of alcohol while taking Ferriprox tablets (twice-a-day) may result in more rapid release of deferiprone.

Please see full Prescribing Information, including boxed WARNING and Medication Guide.

References: **1.** Ferriprox® (deferiprone) Prescribing Information. Chiesi, November 2021. **2.** Binding A, et al. Deferiprone exerts a dose-dependent reduction of liver iron in adults with iron overload. *Eur J Haematol* 2019;103(2):80-87. **3.** Tricta F, et al. Deferiprone-inducted agranulocytosis: 20 years of clinical observations. *Am J Haematol* 2016;91(10):1026-1031.

For more information, visit ferriprox.com.
Chiesi Total Care℠ Program offered through EVERSANA Life Science Services Specialty Pharmacy

PP-F-0314 V1.0 2022

Ferriprox® TWICE-A-DAY deferiprone 1000 mg tablets

Ferriprox® deferiprone
1000 mg tablets
500 mg tablets
Oral solution 100 mg/mL

Chiesi Total Care℠ Copay Assistance Program Terms and Conditions

The Chiesi Total Care Copay Assistance Program (the "Copay Program") may pay for eligible out-of-pocket medication, up to $10,000 per calendar year. After reaching the maximum Copay Program benefit, the patient will be responsible for any remaining out-of-pocket costs incurred during that calendar year.

The Copay Program is valid only for patients with commercial insurance who have a valid prescription for a US Food and Drug Administration-approved indication for the product. A patient who receives health care benefits under any plan or program funded in whole or in part by federal or state governments including Medicare, Medicaid, TRICARE, Veterans Affairs (VA), State Prescription Assistance Plans (SPAPs) (other than health insurance for federal government employees) or any state health care program such as Medicaid, Children's Health Insurance Program, programs funded under Maternal and Child Health Program or programs funded under Social Services Block Grant are not eligible for the Copay Program. A patient covered under a commercial health plan purchased through a health insurance marketplace or exchange is not a Government Program Beneficiary even if the costs of such coverage are subsidized by the federal government.

To enroll in the Copay Program, the patient must also enroll in Chiesi Total Care, a patient support services program offered by Chiesi. The patient must also be a resident of the US or one of its territories. **If the Patient is incapable of acting on their own behalf or if the Patient is under 18 years old, enrollment into Chiesi Total Care may be completed by another person acting on their behalf (such as a caregiver).**

If at any time a patient begins receiving prescription drug coverage under any such federal, state, or government-funded healthcare program, patient will no longer be able to participate in the Copay Program and patient must notify Chiesi Total Care to stop participation.

Patients residing in or receiving treatment in certain states may not be eligible for the Copay Program. Copay Program not available in California or Massachusetts when an AB-rated equivalent to the product is commercially available. Patients may not seek reimbursement for value received from Chiesi Total Care or from the Copay Program. The Copay Program does not obligate the use of any specific medication or health care provider. Participation in the Copay Program is not conditioned on any past, present, or future purchase.

The Copay Program benefits may not be sold, purchased, traded, or offered for sale, purchase, or trade. The Copay Program is not valid where prohibited by law, taxed, or otherwise restricted. Offer subject to change or discontinuance without notice. Restrictions, including monthly maximums, may apply. This is not health insurance.

This is a voluntary program. Patients who choose not to enroll in the Copay Program will still be able to receive medication. Patients may participate in Chiesi Total Care without participating in the Copay Program. After enrolling in the Copay Program or in Chiesi Total Care, participants may opt out by contacting Chiesi Total Care, as outlined in the Chiesi Total Care Enrollment and Authorization Form. Patients must renew their eligibility by December 31 of each year to continue to receive support under the Copay Program.

By participating in the Copay Program, participants acknowledge that they understand and agree to comply with these Terms and Conditions.

PP-G-0583 V1.0 2021

Chiesi
TOTAL care℠

SCAN THE QR CODE
FOR THE DIGITAL RX FORM

BY PHONE
1-866-758-7071

BY FAX
1-866-565-7794

HOURS OF OPERATION
Monday to Friday 7:00am – 6:00pm
(Central Time)

For more information, visit chiesitotalcare.com

Chiesi Total Care Program offered through EVERSANA Life Science Services Specialty Pharmacy.

PP-F-0325 V1.0 2022

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use FERRIPROX Tablets safely and effectively. See full prescribing information for FERRIPROX Tablets.
FERRIPROX® (deferiprone) tablets, for oral use
Initial U.S. Approval: 2011

WARNING: AGRANULOCYTOSIS AND 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 regularly while on therapy. (5.1)**
- **Interrupt FERRIPROX therapy if neutropenia develops. (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----------

Indications and Usage (1)	04/2021
Dosage and Administration, Important Dosage and Administration Information (2.1)	11/2021
Warnings and Precautions, Agranulocytosis and Neutropenia (5.1)	11/2021

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

FERRIPROX Tablets are an iron chelator indicated for the treatment of transfusional iron overload in adult and pediatric patients 8 years of age and older with thalassemia syndromes, sickle cell disease or other anemias. (1)

Limitations of Use

Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

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

- FERRIPROX Tablets are available in three formulations. Two different 1,000 mg formulations, and a 500 mg formulation, which have different dosing regimens to achieve the same total daily dosage. (2.1)
- To prevent medication errors, before prescribing and dispensing, ensure that the tablet formulation is appropriate for the dosing regimen. Each tablet has distinct identifying characteristics. (2.1, 3)
- FERRIPROX Tablets (twice a day), 1,000 mg:
  - Starting oral dosage: 75 mg/kg/day (actual body weight) in two divided doses (2.2)
  - Maximum oral dosage: 99 mg/kg/day (actual body weight) in two divided doses (2.2)
- FERRIPROX Tablets (three times a day), 1,000 mg:
  - Starting oral dosage: 75 mg/kg/day (actual body weight) in three divided doses (2.2)
  - Maximum oral dosage: 99 mg/kg/day (actual body weight) in three divided doses (2.2)
- FERRIPROX Tablets (three times a day), 500 mg:
  - Starting oral dosage: 75 mg/kg/day (actual body weight) in three divided doses (2.2)
  - Maximum oral dosage: 99 mg/kg/day (actual body weight) in three divided doses (2.2)

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

- Tablets (twice a day): 1,000 mg with functional scoring (3)
- Tablets (three times a day): 1,000 mg with functional scoring (3)
- Tablets (three times a day): 500 mg with functional scoring (3)

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

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

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

- Liver Enzyme Elevations: Monitor monthly and discontinue for persistent elevations. (5.2)
- Zinc Deficiency: Monitor during therapy and supplement for deficiency. (5.3)
- Embryo-Fetal Toxicity: Can cause fetal harm. (5.4)

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

- The most common adverse reactions in patients with thalassemia (incidence ≥ 6%) are nausea, vomiting, abdominal pain, arthralgia, ALT increased and neutropenia. (6)
- The most common adverse reactions in patients with sickle cell disease or other anemias (incidence ≥6%) are pyrexia, abdominal pain, bone pain, headache, vomiting, pain in extremity, sickle cell anemia with crisis, back pain, ALT increased, AST increased, arthralgia, oropharyngeal pain, nasopharyngitis, neutrophil count decreased, cough and nausea. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Chiesi USA, Inc. at 1-888-661-9260 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

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

- Drugs Associated with Neutropenia or Agranulocytosis: Avoid co-administration. If co-administration is unavoidable, closely monitor the absolute neutrophil count. (7.1)
- UGT1A6 Inhibitors: Avoid co-administration. (7.2)
- Polyvalent Cations: Allow at least a 4-hour interval between administration of FERRIPROX and drugs or supplements containing polyvalent cations (e.g., iron, aluminum, or zinc). (2.2, 7.2)

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

Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 11/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

WARNING: AGRANULOCYTOSIS AND 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 regularly 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 Tablets are indicated for the treatment of transfusional iron overload in adult and pediatric patients 8 years of age and older with thalassemia syndromes, sickle cell disease or other anemias.

Limitations of Use

- Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosage and Administration Information

FERRIPROX Tablets are available in two different 1,000 mg formulations and a 500 mg formulation, which have different oral dosing regimens to achieve the same total daily dosage.

- FERRIPROX Tablets (twice a day) - 1,000 mg - given two times a day *[see Dosage and Administration (2.2)]*
- FERRIPROX Tablets (three times a day) - 1,000 mg - given three times a day *[see Dosage and Administration (2.3)]*
- FERRIPROX Tablets - 500 mg - given three times a day *[see Dosage and Administration (2.4)]*

To prevent medication errors, before prescribing and dispensing, ensure that the tablet formulation is appropriate for the dosing regimen. Each tablet has distinct identifying characteristics *[see Dosage Forms and Strengths (3)]*.

For patients who have trouble swallowing tablets, consider the use of FERRIPROX Oral Solution (see the prescribing information for FERRIPROX Oral Solution).

Monitoring for Safety

Due to the risk of agranulocytosis, monitor ANC before and during FERRIPROX therapy.

Test ANC prior to start of FERRIPROX therapy and monitor on the following schedule during treatment:

- First six months of therapy: Monitor ANC weekly;
- Next six months of therapy: Monitor ANC once every two weeks;
- After one year of therapy: Monitor ANC every two to four weeks (or at the patient's blood transfusion interval in patients that have not experienced an interruption due to any decrease in ANC *[see Warnings and Precautions (5.1)]*.

Due to the risk of hepatic transaminase elevations, monitor ALT before and monthly during FERRIPROX therapy *[see Warnings and Precautions (5.2)]*.

Due to the risk of zinc deficiency, monitor zinc levels before and regularly during FERRIPROX therapy *[see Warnings and Precautions (5.3)]*.

2.2 Recommended Dosage for 1,000 mg FERRIPROX Tablets (twice a day) for Adult and Pediatric Patients with Transfusional Iron Overload due to Thalassemia Syndromes, Sickle Cell Disease or Other Anemias

Starting Dosage for Twice a Day Tablets

The recommended starting oral dosage of FERRIPROX Tablets (twice a day) is 75 mg/kg/day (actual body weight) in two divided doses per day (taken approximately 12 hours apart), with food. Round the total daily dose to the nearest 500 mg (half-tablet). Table 1 describes the number of FERRIPROX Tablets (twice a day) needed to achieve the 75 mg/kg/day total starting daily dosage.

Table 1: Number of FERRIPROX 1,000 mg Tablets (twice a day) Needed to Achieve the Total Starting Daily Dosage of 75 mg/kg (rounded to the nearest half-tablet)		
Body Weight (kg)	**Morning**	**Evening**
20	0.5	1
30	1	1.5
40	1.5	1.5
50	2	2
60	2	2.5
70	2.5	3
80	3	3
90	3.5	3.5

To minimize gastrointestinal upset when first starting therapy, dosing can start at 45 mg/kg/day and increase weekly by 15 mg/kg/day increments until the full prescribed dose is achieved.

Dosage Adjustments for Twice a Day Tablets

Tailor dosage adjustments of FERRIPROX Tablets (twice a day) to the individual patient's response and therapeutic goals (maintenance or reduction of body iron burden). The maximum total daily oral dosage is 99 mg/kg (actual body weight) divided into two doses taken approximately 12 hours apart with food. Table 2 describes the number of FERRIPROX Tablets (twice a day) needed to achieve the 99 mg/day total maximum daily dosage.

Table 2: Number of FERRIPROX 1,000 mg Tablets (twice a day) Needed to Achieve a Total Maximum Recommended Daily Dosage of 99 mg/kg (rounded to the nearest half-tablet)		
Body Weight (kg)	**Morning**	**Evening**
20	1	1
30	1.5	1.5
40	2	2
50	2.5	2.5
60	3	3
70	3.5	3.5
80	4	4
90	4.5	4.5

2.3 Recommended Dosage for 1,000 mg FERRIPROX Tablets (three times a day) for Adult and Pediatric Patients with Transfusional Iron Overload due to Thalassemia Syndromes, Sickle Cell Disease or Other Anemias

Starting Dosage for Three Times a Day Tablets

The recommended starting oral dosage of FERRIPROX Tablets (three times a day) is 75 mg/kg/day (actual body weight), in three divided doses per day. Table 3 describes the number of FERRIPROX Tablets (three times a day) needed to achieve the 75 mg/kg/day total starting dosage). Round dose to the nearest 500 mg (half-tablet).

Table 3: Number of FERRIPROX 1,000 mg Tablets (three times a day) Needed to Achieve the Total Starting Daily Dosage of 75 mg/kg (rounded to the nearest half-tablet)			
Body Weight (kg)	**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

To minimize gastrointestinal upset when first starting therapy, dosing can start at 45 mg/kg/day and increase weekly by 15 mg/kg/day increments until the full prescribed dose is achieved.

Dosage Adjustments for Three Times Daily Tablets

Tailor dosage adjustments for FERRIPROX Tablets (three times a day) to the individual patient's response and therapeutic goals (maintenance or reduction of body iron burden). The maximum oral dosage is 99 mg/kg/day (actual body weight), in three divided doses per day. Table 4 describes the number of FERRIPROX Tablets (three times a day) needed to achieve the 99 mg/day total maximum daily dosage.

Table 4: Number of FERRIPROX 1,000 mg Tablets (three times a day) Needed to Achieve the Maximum Total Daily Dosage of 99 mg/kg (rounded to the nearest half-tablet)

Body Weight (kg)	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

2.4 Recommended Dosage for 500 mg FERRIPROX Tablets (three times a day) for Adult and Pediatric Patients with Transfusional Iron Overload due to Thalassemia Syndromes, Sickle Cell Disease or Other Anemias

Starting Dosage for Three Times a Day Tablets

The recommended starting oral dosage of FERRIPROX Tablets (three times a day) is is 75 mg/kg/day (actual body weight), in three divided doses per day. Table 5 describes the number of FERRIPROX Tablets (three times a day) needed to achieve the 75 mg/kg/day total starting dosage. Round dose to the nearest 250 mg (half-tablet).

Table 5: Number of FERRIPROX 500 mg Tablets (three times a day) Needed to Achieve the Total Starting Daily Dosage of 75 mg/kg dose (rounded to the nearest half-tablet)

Body Weight (kg)	Morning	Midday	Evening
20	1	1	1
30	1.5	1.5	1.5
40	2	2	2
50	2.5	2.5	2.5
60	3	3	3
70	3.5	3.5	3.5
80	4	4	4
90	4.5	4.5	4.5

To minimize gastrointestinal upset when first starting therapy, dosing can start at 45 mg/kg/day and increase weekly by 15 mg/kg/day increments until the full prescribed dose is achieved.

Dosage Adjustments

Tailor dosage adjustments for FERRIPROX Tablets (three times a day) to the individual patient's response and therapeutic goals (maintenance or reduction of body iron burden). The maximum oral dosagee is 99 mg/kg/day (actual body weight), in three divided

doses per day. Table 6 describes the number of FERRIPROX Tablets (three times a day) needed to achieve the 99 mg/day total maximum daily dosage.

Table 6:	**Number of FERRIPROX 500 mg Tablets (three times a day) Needed to Achieve the Maximum Total Daily Dosage of 99 mg/kg dose (rounded to the nearest half-tablet)**		
Body Weight (kg)	**Morning**	**Midday**	**Evening**
20	1.5	1	1.5
30	2	2	2
40	3	2	3
50	3.5	3	3.5
60	4	4	4
70	5	4.5	4.5
80	5.5	5	5.5
90	6	6	6

2.5 Monitoring Ferritin Levels to Assess Efficacy

Monitor serum ferritin concentration every two to three months to assess the effect 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.

2.6 Dosage Modification for Drug Interactions

Allow at least a 4-hour interval between administration of FERRIPROX and other drugs or supplements containing polyvalent cations such as iron, aluminum, or zinc *[see Drug Interactions (7.2), Clinical Pharmacology (12.3)]*.

3 DOSAGE FORMS AND STRENGTHS

- Tablets (twice a day): 1,000 mg, capsule-shaped, white to off-white tablets with functional scoring, engraved “FPX” bisect “DR” on one side, “APO” bisect “1000” on the other”.
- Tablets (three times a day): 1,000 mg film-coated, capsule-shaped, white to off-white tablets with functional scoring, and imprinted with “APO” score “1000” on one side and plain on the other.
- Tablets: 500 mg film-coated, capsule-shaped, white to off-white tablets with functional scoring, and imprinted with “APO” score “500” on one side and plain on the other.

4 CONTRAINDICATIONS

FERRIPROX is contraindicated in patients with known hypersensitivity to deferiprone or to any of the excipients in the formulations. 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 and 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 regularly while on therapy *[see Dosage and Administration (2.1)]*.

Reduction in the frequency of ANC monitoring should be considered on an individual patient basis, according to the health care provider’s assessment of the patient’s understanding of the risk minimization measures required during 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.

The incidence of agranulocytosis was 1.7% of patients in pooled clinical trials of 642 patients with thalassemia syndromes and 1.5% of patients in pooled clinical trials of 196 patients with sickle cell disease or other anemias. 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 and neutropenia prior to initiating FERRIPROX treatment.

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 have developed neutropenia with FERRIPROX unless potential benefits outweigh potential risks.

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).

5.2 Liver Enzyme Elevations

In pooled clinical trials, 7.5% of 642 patients with thalassemia syndromes 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. In pooled clinical trials, 7.7% of 196 patients with sickle cell disease or other anemias treated with FERRIPROX developed increased ALT values.

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 *[see Dosage and Administration (2.1)]*.

5.3 Zinc Deficiency

Decreased plasma zinc concentrations have been observed on FERRIPROX therapy. Monitor plasma zinc annually, and supplement in the event of a deficiency *[see Dosage and Administration (2.1)]*.

5.4 Embryo-Fetal Toxicity

Based on findings from animal reproduction studies and evidence of genotoxicity, FERRIPROX can cause fetal harm when administered to a pregnant woman. The 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 embryo-fetal death and malformations at doses lower than equivalent human clinical doses. Advise pregnant women and females of reproductive potential of the potential risk to the fetus *[see Use in Specific Populations (8.1)]*.

Advise females of reproductive potential to use an effective method of contraception during treatment with FERRIPROX and for at least six months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with FERRIPROX and for at least three months after the last dose *[see Use in Specific Populations (8.1, 8.3)]*.

6 ADVERSE REACTIONS

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

- Agranulocytosis and Neutropenia *[see Warnings and Precautions (5.1)]*
- Liver Enzyme Elevations *[see Warnings and Precautions (5.2)]*
- Zinc Deficiency *[see Warnings and Precautions (5.3)]*

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.

FERRIPROX Tablets (twice a day) were evaluated in trials in healthy subjects. FERRIPROX Tablets (twice a day) contain deferiprone, the same active ingredient as FERRIPROX Tablets (deferiprone) (three times a day) and FERRIPROX Oral Solution (deferiprone).

The following adverse reaction information represents the pooled data collected from single arm or active-controlled clinical trials with FERRIPROX Tablets (deferiprone) (three times a day) or FERRIPROX Oral Solution (deferiprone).

Thalassemia Syndromes

The safety of FERRIPROX was evaluated in the pooled clinical trial database *[see Clinical Studies (14.1)]*. Patients received FERRIPROX Tablets (three times a day) or FERRIPROX Oral Solution . FERRIPROX was administered orally three times a day

(total daily dose either 50, 75, or 99 mg/kg), N=642. Among 642 patients receiving FERRIPROX, 492 (76.6%) were exposed for 6 months or longer and 365 (56.9%) were exposed for greater than one year.

The median age of patients who received FERRIPROX was 19 years (range 1, 77 years); 50.2% female; 71.2% White, 17.8% Asian, 9.2% Unknown, 1.2% Multi-racial and 0.6% Black.

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

The most common adverse reactions (≥6%) reported during clinical trials were nausea, vomiting, abdominal pain, arthralgia, alanine aminotransferase increased and neutropenia.

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

Table 7:Adverse reactions occurring in ≥ 1% of FERRIPROX-treated patients with thalassemia syndromes

Body System **Adverse Reaction**	**(N=642)** **% Patients**
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.

Sickle Cell Disease or Other Anemias

The safety of FERRIPROX compared to deferoxamine was evaluated in LA38-0411 *[see Clinical Studies (14.2)]*. Patients received FERRIPROX Tablets or FERRIPROX Oral Solution orally three times a day (total daily dose 75-99 mg/kg/day) n=152) or the control arm, deferoxamine, 20-40 mg/kg/day (children) or 40-50 mg/kg/day (adults), by subcutaneous infusion for 5 – 7 days per week, n=76. Among 152 patients receiving FERRIPROX, 120 (78.9%) were exposed for 6 months or longer and 17 (11.2%) were exposed for greater than one year.

The median age of patients who received FERRIPROX was 15 years (range 3, 59 years); 54.6% male; 78.9% White, 15.1% Black and 5.9% Multi-racial.

The most common adverse reactions (≥6%) reported during clinical trials in patients with SCD or other anemias were pyrexia, abdominal pain, bone pain, headache, vomiting, pain in extremity, sickle cell anemia with crisis, back pain, alanine aminotransferase (ALT) increased, aspartate aminotransferase (AST) increased, arthralgia, oropharyngeal pain, nasopharyngitis, neutrophil count decreased, cough and nausea.

The table below lists the adverse reactions (irrespective of a causal assessment; adverse events) of interest that occurred in patients treated with FERRIPROX in clinical trials in subjects with sickle cell disease or other anemias.

Table 8:Adverse reactions occurring in ≥5% of FERRIPROX-treated patients with sickle cell disease or other anemias

Body System **Adverse Reaction**	**FERRIPROX (N=152)** **% Patients**	**DEFEROXAMINE (N=76)** **% Patients**
BLOOD AND LYMPHATIC SYSTEM DISORDERS		
Sickle cell anemia with crisis	17	13
GASTROINTESTINAL DISORDERS		
Abdominal pain*	26	13
Vomiting	19	11
Nausea	7	9
Diarrhea	5	8
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS		
Pyrexia	28	33
Pain	5	4
INFECTIONS AND INFESTATIONS		
Nasopharyngitis	9	12
Upper respiratory tract infection	5	3
INVESTIGATIONS		
Alanine aminotransferase increased	12	0
Aspartate aminotransferase increased	11	0
Neutrophil count decreased	8	4
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS		
Bone pain	25	34
Pain in extremity	18	15
Back pain	13	18
Arthralgia	10	8
NERVOUS SYSTEM DISORDERS		
Headache	20	13
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS		
Oropharyngeal pain	10	15
Cough	8	15

*Grouped term

Clinically relevant adverse reactions in <5% of patients include neutropenia and agranulocytosis.

Pediatric Patients

FERRIPROX has been studied in 86 pediatric patients with sickle cell disease or other anemias. Pediatric patients (<17 years) had an increase in the following adverse reactions as compared to adults: abdominal pain, neutrophil count decreased, bone pain and oropharyngeal pain.

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, 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 co-administration of FERRIPROX with other drugs known to be associated with neutropenia or agranulocytosis. If co-administration is unavoidable, closely monitor the absolute neutrophil count *[see Warnings and Precautions (5.1)]*.

7.2 Effect of Other Drugs on FERRIPROX

UDP-Glucuronosyltransferases (UGT)

Avoid 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)]*.

Polyvalent Cations

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 (2.2)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

In animal reproduction studies, oral administration of deferiprone to pregnant rats and rabbits during organogenesis at doses 33% and 49%, respectively, of the maximum recommended human dose (MRHD) resulted in structural abnormalities, embryo-fetal mortality and alterations to growth *(see Data)*. The limited available data from deferiprone use in pregnant women are insufficient to inform a drug-associated risk of major birth defects and miscarriage. Based on evidence and developmental toxicity in animal studies, FERRIPROX can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and of miscarriage is 2-4% and 15-20%, respectively.

Data

Human Data

Post-marketing data available from 39 pregnancies of deferiprone-treated patients and 10 pregnancies of partners of deferiprone-treated patients are as follows:

Of the 39 pregnancies in deferiprone-treated patients, 23 resulted in healthy newborns, 6 ended in spontaneous abortion, 9 had unknown outcomes, and 1 infant was born with anal atresia, nephroptosis, ventricular septal defect, hemivertebra and urethral fistula.

Of the 10 pregnancies in partners of deferiprone-treated patients, 5 resulted in healthy newborns, 1 resulted in a healthy newborn with slight hypospadias, 1 was electively terminated, 1 resulted in the intrauterine death of twins, and 2 had unknown outcomes.

Animal Data

During organogenesis, pregnant rats and rabbits received deferiprone at oral doses of 0, 30, 80 or 200 mg/kg/day, and 0, 10, 50, or 150 mg/kg/day, respectively. The daily dose was administered as two equal divided doses approximately 7 hours apart. Doses of 200 mg/kg/day in rats and 150 mg/kg/day in rabbits, approximately 33% and 49% of the MRHD, respectively, resulted in increased post-implantation loss and reduced fetal weights in the presence of maternal toxicity (reduced maternal body weight and body weight gain in both rats and rabbits; abnormal large placenta at low incidence in rats). The 200 mg/kg/day dose in rats resulted in external, visceral and skeletal fetal malformations such as cranial malformations, cleft palate, limb malrotation, anal atresia, internal hydrocephaly, anophthalmia and fused bones. The dose of 150 mg/kg/day in rabbits resulted in external fetal malformations (partially opened eyes) and minor blood vessel and skeletal variations.

In rats, malformations including micrognathia and persistent ductus arteriosus could be observed in the absence of maternal toxicity at doses equal to or greater than 30 and 80 mg/kg/day, approximately 5% and 13% of the MHRD, respectively.

8.2 Lactation

Risk Summary

There is no information regarding the presence of deferiprone in human milk, the effects on the breastfed child, or the effects on milk production.

Because of the potential for serious adverse reactions in the breastfed child, including the potential for tumorigenicity shown for deferiprone in animal studies, advise patients that breastfeeding is not recommended during treatment with FERRIPROX, and for at least 2 weeks after the last dose.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Pregnancy testing is recommended for females of reproductive potential prior to initiating FERRIPROX.

Contraception

Females

FERRIPROX can cause embryo-fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]*. Advise female patients of reproductive potential to use effective contraception during treatment with FERRIPROX and for at least 6 months after the last dose.

Males

Based on genotoxicity findings, advise males with female partners of reproductive potential to use effective contraception during treatment with FERRIPROX and for at least 3 months after the last dose *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

The safety and effectiveness of FERRIPROX for the treatment of transfusional iron overload due to thalassemia syndromes have been established in pediatric patients 8 years of age and older. Use of FERRIPROX for this indication is supported by evidence of efficacy from clinical trials in adult patients with thalassemia and evidence of safety in pediatric patients with sickle cell disease.

The safety and effectiveness of FERRIPROX for the treatment of transfusional iron overload due to sickle cell disease or other anemias have been established in 86 pediatric patients 3 to 16 years of age, among the 152 patients treated with FERRIPROX Tablets or Oral Solution in an adequate and well-controlled study *[see Adverse Reactions (6.1) and Clinical Studies (14.2)]*. The study included 56 patients 3 to <12 years of age and 30 patients 12 to 16 years of age. Seventy-six percent of these patients had sickle cell disease. The recommended starting dose and dose-modifications are the same for children and adults *[see Indications and Usage (1), Dosage and Administration (2.1), and Clinical Studies (14)]*.

Fourteen patients with spherocytosis (including hereditary) (ages 3-15), two patients with pyruvate kinase deficiency (ages 4 and 6), two patients with dyserythropoietic anemia (ages 10-12) and two patients with hemolytic anemia (ages 8 and 10 years old) were treated with FERRIPROX in the clinical trial, LA38-0411.

A US registry established from December 2011 through December 2019, contains 125 patients from 4 to < 17 years old who have received FERRIPROX and have sickle cell disease. The adverse reactions, including agranulocytosis, seen in the 8 year period of the registry are similar to those seen in the most recent clinical studies.

Safety and effectiveness of FERRIPROX Tablets have not been established in pediatric patients with chronic iron overload due to blood transfusions who are less than 8 years of age.

8.5 Geriatric Use

Clinical studies of deferiprone did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

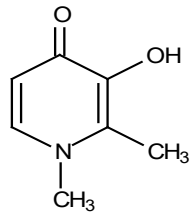
10 OVERDOSAGE

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 Tablets (deferiprone) contain 1,000 mg or 500 mg 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 (14.3 mg/mL) and has a melting point range of 272 °C - 278 °C.

FERRIPROX Tablets (twice a day), 1,000 mg

White to off-white, capsule-shaped tablets, and imprinted with “FPX” score “DR” on one side and “APO” score “1000” on the other. The tablets can be broken in half along the score line. Each tablet contains 1,000 mg deferiprone and the following inactive ingredients: Tablet core - hypromellose acetate succinate, magnesium oxide, colloidal silicon dioxide and magnesium stearate; Coating - triethyl citrate, talc, titanium dioxide, and methacrylic acid and ethyl acrylate copolymer.

FERRIPROX Tablets (three times a day), 1,000 mg

White to off-white, capsule-shaped tablets, and imprinted with “APO” score “1000” on one side and plain on the other. The tablets can be broken in half along the score line. Each tablet contains 1,000 mg deferiprone and the following inactive ingredients: Tablet core - methylcellulose, crospovidone, and magnesium stearate; Coating - hypromellose, hydroxypropyl cellulose, macrogol, and titanium dioxide.

FERRIPROX Tablets, 500 mg

White to off-white, capsule-shaped tablets, and imprinted with “APO” score “500” on one side and plain on the other. The tablets can be broken in half along the score line. Each tablet contains 500 mg deferiprone and the following inactive ingredients: Tablet core - microcrystalline cellulose, magnesium stearate, colloidal silicon dioxide; Coating - hypromellose, polyethylene glycol, titanium dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Deferiprone is a chelating agent with an affinity for ferric ions (iron III). Deferiprone binds with ferric ions to form neutral 3:1 (deferiprone:iron) complexes that are stable at physiological pH.

12.2 Pharmacodynamics

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

Cardiac Electrophysiology

At the maximum approved recommended dose, deferiprone does not prolong the QT interval to any clinically relevant extent.

12.3 Pharmacokinetics

FERRIPROX Tablets (twice a day), 1,000 mg

In healthy subjects, the mean ± SD C_{max} of deferiprone in serum was 6 ± 2 mcg/mL, and the mean ± SD AUC was 28 ± 7 mcg·h/mL following oral administration of a 1,000 mg dose of FERRIPROX Tablets (twice a day) with food.

Absorption

Peak serum concentrations of deferiprone occur approximately 2 hours after a single dose of FERRIPROX Tablets (twice a day) in fasted healthy subjects.

Effect of Food

Following the administration of FERRIPROX Tablets (twice a day) to healthy volunteers, the C_{max} and the AUC of deferiprone remain unchanged after a high-fat meal (approximately 1,000 calories, 53% fat, 33% carbohydrates, and 14% protein) compared to fasted conditions.

Effect of Alcohol

At 40% (v/v) alcohol concentration *in vitro* dissolution studies, there was 88% release of deferiprone from a 1,000 mg FERRIPROX tablet (twice a day) within two hours compared to 4% release of deferiprone within 2 hours in the absence of alcohol.

Distribution

The apparent mean ± SD volume of distribution (V/F) of deferiprone was 97 ± 28 L following oral administration of a 1,000 mg dose of FERRIPROX Tablets (twice a day) with food.

Elimination

The mean ± SD elimination half-life of deferiprone is 1.8 ± 0.3 hours following the administration of FERRIPROX Tablets (twice a day).

Metabolism

Deferiprone is metabolized primarily by UGT1A6. The major metabolite of deferiprone is the 3-*O*-glucuronide, which lacks iron-binding capability.

Excretion

Following oral administration, 75% to 90% of the administered dose was recovered in urine (primarily as metabolite) in the first 24 hours.

FERRIPROX Tablets (three times a day), 1,000 mg and 500 mg

The mean C_{max} and AUC of deferiprone was 20 mcg/mL and 50 mcg·h/mL, respectively, in healthy subjects. The dose proportionality of deferiprone over the approved recommended dosage range is unknown.

Absorption

Deferiprone appeared in the blood within 5 to 10 minutes after oral administration. Peak serum concentration of deferiprone was reached approximately 1 to 2 hours after a single dose.

Effect of Food

No clinically significant differences in the pharmacokinetics of deferiprone were observed following administration with food.

Elimination

The elimination half-life of deferiprone is approximately 2 hours.

Metabolism

Deferiprone is metabolized primarily by UGT1A6. The major metabolite of deferiprone is the 3-*O*-glucuronide, which lacks iron binding capability.

Excretion

Following oral administration, 75% to 90% of the administered dose was recovered in urine (primarily as metabolite) in the first 24 hours.

Specific Populations

No clinically significant differences in the pharmacokinetics of deferiprone were observed based on sex, race/ethnicity, body weight, mild to severe (eGFR 15 to 89 mL/min/1.73 m^2) renal impairment, or mild (Child Pugh Class A) to moderate (Child Pugh Class B) hepatic impairment. The effect of age, including geriatric or pediatric populations, end stage renal disease or severe (Child Pugh Class C) hepatic impairment on the pharmacokinetics of deferiprone is unknown.

Drug Interaction Studies

In Vitro Studies

UGTIA6 Inhibitors: Phenylbutazone (UGT1A6 inhibitor) decreased glucuronidation of deferiprone by up to 78%.

Polyvalent Cations: Deferiprone has the potential to bind polyvalent cations (e.g., iron, aluminum, and zinc).

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 deferiprone. 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.

14 CLINICAL STUDIES

FERRIPROX Tablets (twice a day) were evaluated in trials in healthy subjects. FERRIPROX Tablets (twice a day) contain deferiprone, the same active ingredient as FERRIPROX Tablets and FERRIPROX Oral Solution. The following information is based on studies with FERRIPROX Tablets (deferiprone) (three times a day) and FERRIPROX Oral Solution (deferiprone).

14.1 Transfusional Iron Overload in Patients with Thalassemia Syndromes

In a prospective, planned, pooled analysis of patients with thalassemia syndromes from several studies, the efficacy of deferiprone 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 deferiprone. Deferiprone 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 (range 2 to 62; 91 patients were <17).

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.

14.2 Transfusional Iron Overload in Patients with Sickle Cell Disease and other Anemias

Study LA38-0411, an actively-controlled non-inferiority study compared the efficacy of FERRIPROX to that of deferoxamine in patients with sickle cell disease and other transfusion-dependent anemias by evaluating liver iron concentration (LIC). The efficacy of FERRIPROX was established based upon the change in LIC from baseline after 12 months of FERRIPROX (75 or 99 mg/kg/day) compared to deferoxamine (20 or 40 mg/kg (pediatric patients); 40 or 50 mg/kg (adult patients)). Patient enrollment was stopped following an interim analysis. After adjusting for the type I (alpha) error, the non-inferiority criterion was established as the upper limit of the 96.01% confidence interval for the difference between treatments being ≤2 mg/g dry weight (dw).

Data from 185 patients (122 on FERRIPROX and 63 on deferoxamine) were available. Among the 122 FERRIPROX treated patients, the mean age was 15.9 years (range 3-46); 57.4% were male; 75.4% were White, 17.2% were Black and 7.4% were Multi-racial; 85% were diagnosed with Sickle Cell Disease and 15% with other anemias. Over 12 months, the Least Squares estimate of mean decrease from baseline in LIC was 4.13 ± 0.50 mg/g dw for FERRIPROX and 4.38 ± 0.59 mg/g dw for deferoxamine, and the non-inferiority criterion was met.

Upon completion of the first year of therapy in the non inferiority study, 89 patients from the ferriprox group opted to continue with treatment and 45 from the deferoxamine group opted to switch to ferriprox treatment. This group continued for up to an additional 2 years. LIC continued to decrease over time, with the mean value dropping from 14.93 mg/g dw at baseline to 12.30 mg/g dw after one year of treatment, to 11.19 mg/g dw after two years of treatment, and to 10.45 mg/g dw after three years of treatment.

16 HOW SUPPLIED/STORAGE AND HANDLING

FERRIPROX Tablets (twice a day), 1,000 mg

FERRIPROX® Tablets (deferiprone) (twice a day) are white to off-white capsule-shaped, beveled edge, biconvex coated tablets, and have a functional score engraved “FPX” bisect “DR” on one side, “APO” bisect “1000” on the other. They are supplied in child-resistant blister packs or HDPE bottles.

1,000 mg tablets, carton of 5 x 10-count blister packs NDC 10122-104-01

1,000 mg tablets, bottle of 50 tablets NDC 10122-104-05

1,000 mg tablets, bottle of 500 tablets NDC 10122-104-50

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

FERRIPROX Tablets (three times a day), 1,000 mg

FERRIPROX® Tablets (deferiprone) (three times a day) are white to off-white capsule-shaped tablets, film-coated, and have a functional score imprinted with “APO” score “1000” on one side and are plain on the other. They are provided in HDPE bottles.

1,000 mg film-coated tablets, 50 tablets NDC 10122-103-05

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Keep the bottle tightly closed to protect from moisture.

FERRIPROX Tablets, 500 mg

FERRIPROX® Tablets (deferiprone) are white to off-white capsule-shaped tablets, film-coated, and have a functional score imprinted with “APO” score “500” on one side and are plain on the other. They are provided in HDPE bottles.

500 mg film-coated tablets, 100 tablets NDC 10122-100-10

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

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide)

- Instruct patients and their caregivers to store FERRIPROX at 68°F to 77°F (20°C to 25°C); excursions permitted to 59°F to 86°F (15°C to 30°C) [see USP Controlled Room Temperature].
- FERRIPROX Tablets (twice a day), 1,000 mg:

  Advise patients to take the first dose of FERRIPROX Tablets (twice a day) in the morning and the second in the evening.

Advise patients to take FERRIPROX Tablets (twice a day) with food to reduce the risk of nausea and vomiting.

Advise patients to avoid alcohol while taking FERRIPROX Tablets (twice a day). Consumption of alcohol while taking FERRIPROX Tablets (twice a day) may result in more rapid release of deferiprone.

- FERRIPROX Tablets (three times a day), 1,000 mg:

  Store in the originally supplied bottle, closed tightly to protect from moisture.

  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.

- FERRIPROX Tablets, 500 mg:

  Store in the originally supplied bottle, closed tightly to protect from moisture.

  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 it 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.
- Inform patients of the risks of developing agranulocytosis and the need for regular blood testing before and during their treatment to monitor for decreases in their ANC. 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 *[see Dosage and Administration (2.1) and Warnings and Precautions (5.1)]* in order to check their ANC within 24 hours. Advise them if they are unable to reach their physician, seek care from another provider so as not to delay medical care.
- Inform patients of the risk of abnormal liver transaminases and the need for regular blood testing before and during their treatment to monitor for increases in ALT *[see Dosage and Administration (2.1) and Warnings and Precautions (5.2)]*.
- Inform patients of the risk of zinc deficiency and the need for regular blood testing before and during their treatment to monitor for reductions in zinc *[see Dosage and Administration (2.1) and Warnings and Precautions (5.3)]*.
- 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, and it is not harmful.

Embryo-Fetal toxicity

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions (5.4) and Use in Specific Populations (8.1)]*. Advise female patients of reproductive potential to use effective contraception during treatment with FERRIPROX and for at least six months after the last dose *[see Use in Specific Populations (8.1, 8.3)]*. Advise males with female partners of reproductive potential to use effective contraception during treatment with FERRIPROX and for at least three months after the last dose *[see Use in Specific Populations (8.3) and Nonclinical Toxicology (13.1)]*.

Lactation

Advise females not to breastfeed during treatment with FERRIPROX and for at least 2 weeks after the last dose *[see Use in Specific Populations (8.2)]*.

Distributed by Chiesi USA, Inc., Cary, NC 27518. Manufactured by Apotex Inc., Toronto, Ontario, Canada, M9L 1T9.

CTFD-032-0521-00-W

Medication Guide
FERRIPROX (Feh ri prox) Tablets
(deferiprone)

What is the most important information I should know about FERRIPROX Tablets?

FERRIPROX Tablets can cause serious side effects, including a very low white blood cell count. One type of white blood cell that is important for fighting infections is called a neutrophil. If your neutrophil count is low (neutropenia), you may be at risk of developing a serious infection that can lead to death. Neutropenia is common with FERRIPROX Tablets and can become severe in some people. Severe neutropenia is known as agranulocytosis. If you develop agranulocytosis, you will be at risk of developing serious infections that can lead to death.

Your healthcare provider will do a blood test before you start FERRIPROX Tablets and regularly during treatment to check your neutrophil count. If you develop neutropenia, your healthcare provider should check your blood counts every day until your white blood cell count improves. Your healthcare provider may temporarily stop treatment with FERRIPROX Tablets if you develop neutropenia or infection.

Stop taking FERRIPROX Tablets and call your healthcare provider or get medical help right away if you develop any of these symptoms of infection:

- fever
- sore throat or mouth sores
- flu-like symptoms
- chills and severe shaking

It is important for you to have your white blood cell count checked within 24 hours of developing symptoms of an infection to see if you have severe neutropenia (agranulocytosis). Do not delay getting medical care if you are unable to reach your healthcare provider.

See **"What are the possible side effects of FERRIPROX Tablets?"** for more information about side effects.

What is FERRIPROX Tablets?

FERRIPROX Tablets is a prescription medicine used to treat iron overload from blood transfusions in adults and children 8 years of age and older with:

- thalassemia syndromes.
- sickle cell disease or other anemias.

It is not known if FERRIPROX Tablets is safe and effective to treat iron overload due to blood transfusions:

- in people with myelodysplastic syndrome or Diamond Blackfan anemia
- in children less than 8 years of age

Do not take FERRIPROX Tablets if you are allergic to deferiprone or any of the ingredients in FERRIPROX Tablets. See the end of this Medication Guide for a complete list of ingredients in FERRIPROX Tablets.

Before taking FERRIPROX Tablets, tell your healthcare provider about all of your medical conditions, including if you:

- have liver problems
- are pregnant or plan to become pregnant. FERRIPROX Tablets can harm your unborn baby. You should avoid becoming pregnant during treatment with FERRIPROX Tablets. Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with FERRIPROX Tablets.
  Females who are able to become pregnant:
  - Your healthcare provider should do a pregnancy test before you start treatment with FERRIPROX Tablets.
  - You should use effective birth control during treatment with FERRIPROX Tablets and for at least 6 months after the last dose.

  Males with female partners who are able to become pregnant:
  - You should use effective birth control during treatment with FERRIPROX Tablets and for at least 3 months after the last dose.
- are breastfeeding or plan to breastfeed. It is not known if FERRIPROX Tablets passes into your breast milk. Do not breastfeed during treatment with FERRIPROX Tablets and for at least 2 weeks after the last dose.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

How should I take FERRIPROX Tablets?

- Take FERRIPROX Tablets exactly as your healthcare provider tells you.
- Your healthcare provider will prescribe FERRIPROX Tablets based on your body weight.
- Your healthcare provider will check your body iron level during treatment with FERRIPROX Tablets and may change your dose if needed. Your healthcare provider may also change your dose of FERRIPROX Tablets if you have certain side effects. Do not change your dose of FERRIPROX Tablets unless your healthcare provider tells you to.
- **There are 3 types of FERRIPROX Tablets that are taken on different schedules. Be sure you are taking the correct tablet and ask your healthcare provider if unsure.**

FERRIPROX Tablets 1,000 mg Twice-a-Day 2 times each day with food	**FERRIPROX Tablets 1,000 mg 3 times each day**	**FERRIPROX Tablets 500 mg 3 times each day**
Take your first dose in the morning and the second dose in the evening, about 12 hours apart.	Take your first dose in the morning, the second dose at mid-day, and the third dose in the evening.	Take your first dose in the morning, the second dose at mid-day, and the third dose in the evening.

- Taking FERRIPROX Tablets with meals may help reduce nausea.
- **If you must take a medicine to treat indigestion (antacid), or supplements that contain iron, aluminum, or zinc during treatment with FERRIPROX Tablets, allow at least 4 hours between taking FERRIPROX Tablets and these products.**
- If you take too much FERRIPROX Tablets, call your healthcare provider.
- If you miss a dose, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose and then continue with your regular schedule. Do not try to catch-up or take 2 doses at the same time to make up for a missed dose.

What should I avoid during treatment with FERRIPROX Tablets?

- Avoid drinking alcohol during treatment with FERRIPROX Tablets 1,000 mg (2 times a day). This may cause a faster release of the medicine.

What are the possible side effects of FERRIPROX Tablets?

FERRIPROX Tablets can cause serious side effects, including:

- **See "What is the most important information I should know about FERRIPROX Tablets?"**
- **Increased liver enzyme levels in your blood.** Your healthcare provider should do blood tests to check your liver function before you start and then monthly during treatment with FERRIPROX Tablets. Your healthcare provider may temporarily stop treatment with FERRIPROX Tablets if you develop increased liver enzyme levels and they continue to be increased.
- **Decreased levels of zinc in your blood.** Your healthcare provider will do blood tests to check your zinc levels before you start and during treatment with FERRIPROX Tablets, and may prescribe a zinc supplement for you if your zinc levels are low.

The most common side effects of FERRIPROX Tablets in people with thalassemia include:

- nausea
- vomiting
- stomach-area (abdominal) pain
- joint pain
- abnormal liver function tests
- low white blood cells

The most common side effects of FERRIPROX Tablets in people with sickle cell disease or other anemias include:

- fever
- stomach-area (abdominal) pain
- bone pain
- headache
- vomiting
- pain in arms or legs
- sickle cell anemia with crisis
- back pain
- abnormal liver function tests
- joint pain
- mouth and throat pain
- common cold
- low white blood cells
- cough
- nausea

FERRIPROX Tablets may cause a change in urine color to reddish-brown. This is not harmful and is expected during treatment with FERRIPROX Tablets.

These are not all of the possible side effects of FERRIPROX Tablets.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store FERRIPROX Tablets?

FERRIPROX Tablets 1,000 mg Twice-a-Day 2 times each day with food	FERRIPROX Tablets 1,000 mg 3 times each day	FERRIPROX Tablets 500 mg 3 times each day
• Store at room temperature between 68°F to 77°F (20°C to 25°C).	• Store at room temperature between 68°F to 77°F (20°C to 25°C). • Store in the original bottle and tightly closed to protect from moisture.	• Store at room temperature between 68°F to 77°F (20°C to 25°C).

Keep FERRIPROX Tablets and all medicines out of the reach of children.

General information about the safe and effective use of FERRIPROX Tablets.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use FERRIPROX Tablets for a condition for which it was not prescribed. Do not give FERRIPROX Tablets to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about FERRIPROX Tablets that is written for health professionals.

What are the ingredients in FERRIPROX Tablets?

FERRIPROX Tablets 1,000 mg Twice-a-Day 2 times each day with food	FERRIPROX Tablets 1,000 mg 3 times each day	FERRIPROX Tablets 500 mg 3 times each day
Active ingredient: deferiprone **Inactive ingredients:** Tablet core: hypromellose acetate succinate, magnesium oxide, colloidal silicon dioxide and magnesium stearate. Coating: triethyl citrate, talc, titanium dioxide, and methacrylic acid and ethyl acrylate copolymer.	**Active ingredient:** deferiprone **Inactive ingredients:** Tablet core: methylcellulose, crospovidone, and magnesium stearate. Coating: hypromellose, hydroxypropyl cellulose, macrogol, and titanium dioxide.	**Active ingredient:** deferiprone **Inactive ingredients:** Tablet core: microcrystalline cellulose, magnesium stearate, colloidal silicon dioxide. Coating: hypromellose, polyethylene glycol, and titanium dioxide.

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CTFD-033-0521-00-W

For more information, call 1-888-661-9260.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 11/2021

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use FERRIPROX Oral Solution safely and effectively. See full prescribing information for FERRIPROX Oral Solution.
FERRIPROX® (deferiprone) oral solution, for oral use
Initial U.S. Approval: 2011

WARNING: AGRANULOCYTOSIS AND 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 regularly while on therapy. (5.1)**
- **Interrupt FERRIPROX therapy if neutropenia develops. (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----------

Indications and Usage (1)	04/2021
Dosage and Administration, Important Dosage and Administration Information (2.1)	11/2021
Warnings and Precautions, Agranulocytosis and Neutropenia (5.1)	11/2021

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

FERRIPROX Oral Solution is an iron chelator indicated for the treatment of transfusional iron overload in adult and pediatric patients 3 years of age and older with thalassemia syndromes, sickle cell disease or other anemias. (1)

Limitations of Use

Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

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

25 mg/kg to 33 mg/kg actual 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----------

- Liver Enzyme Elevations: Monitor monthly and discontinue for persistent elevations. (5.2)
- Zinc Deficiency: Monitor during therapy and supplement for deficiency. (5.3)
- Embryo-Fetal Toxicity: Can cause fetal harm. (5.4)

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

- The most common adverse reactions in patients with thalassemia (incidence ≥ 6%) are nausea, vomiting, abdominal pain, arthralgia, ALT increased and neutropenia. (6)
- The most common adverse reactions in patients with sickle cell disease or other anemias (incidence ≥6%) are pyrexia, abdominal pain, bone pain, headache, vomiting, pain in extremity, sickle cell anemia with crisis, back pain, ALT increased, AST increased, arthralgia, oropharyngeal pain, nasopharyngitis, neutrophil count decreased, cough and nausea. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Chiesi USA, Inc. at 1-888-661-9260 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

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

- Drugs Associated with Neutropenia or Agranulocytosis: Avoid co-administration. If co-administration is unavoidable, closely monitor the absolute neutrophil count. (7.1)
- UGT1A6 Inhibitors: Avoid co-administration. (7.2)
- Polyvalent Cations: Allow at least a 4-hour interval between administration of FERRIPROX and drugs or supplements containing polyvalent cations (e.g., iron, aluminum, or zinc). (2.2, 7.2)

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

Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 11/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

WARNING: AGRANULOCYTOSIS AND 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 regularly while on therapy.** ***[see Warnings and Precautions (5.1)]***
- **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 Oral Solution is indicated for the treatment of transfusional iron overload in adult and pediatric patients 3 years of age and older with thalassemia syndromes, sickle cell disease or other anemias.

Limitations of Use

- Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosage and Administration Information

Monitoring for Safety

Due to the risk of agranulocytosis, monitor ANC before and during FERRIPROX therapy.

Test ANC prior to start of FERRIPROX therapy and monitor on the following schedule during treatment:

- First six months of therapy: Monitor ANC weekly;
- Next six months of therapy: Monitor ANC once every two weeks;
- After one year of therapy: Monitor ANC every two to four weeks (or at the patient's blood transfusion interval in patients that have not experienced an interruption due to any decrease in ANC *[see Warnings and Precautions (5.1)]*.

Due to the risk of hepatic transaminase elevations, monitor ALT before and monthly during FERRIPROX therapy *[see Warnings and Precautions (5.2)]*.

Due to the risk of zinc deficiency, monitor zinc levels before and regularly during FERRIPROX therapy *[see Warnings and Precautions (5.3)]*.

2.2 Recommended Dosage for FERRIPROX Oral Solution for Adult and Pediatric Patients with Transfusional Iron Overload due to Thalassemia Syndromes, Sickle Cell Disease or Other Anemias

Starting Dosage

The recommended starting oral dosage of FERRIPROX Oral Solution is 25 mg/kg (actual body weight), three times per day for a total of 75 mg/kg/day. Round dose to the nearest 2.5 mL.

Table 1: Volume of FERRIPROX Oral Solution in mL Needed to Achieve the Total Starting Daily Dosage of 75 mg/kg (rounded to the nearest 2.5 mL)

Body Weight (kg)	Morning	Midday	Evening
20	5	5	5
30	7.5	7.5	7.5
40	10	10	10
50	12.5	12.5	12.5
60	15	15	15
70	17.5	17.5	17.5

80	20	20	20
90	22.5	22.5	22.5

To minimize gastrointestinal upset when first starting therapy, dosing can start at 45 mg/kg/day and increase weekly by 15 mg/kg/day increments until the full prescribed dose is achieved.

Dosage Adjustments

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

Table 2: Volume of FERRIPROX Oral Solution in mL Needed to Achieve the Maximum Total Daily Dosage of 99 mg/kg (rouded to the nearest 2.5 mL)

Body Weight (kg)	Morning	Midday	Evening
20	7.5	5	7.5
30	10	10	10
40	15	10	15
50	17.5	15	17.5
60	20	20	20
70	25	22.5	22.5
80	27.5	25	27.5
90	30	30	30

2.3 Monitoring Ferritin Levels to Assess Efficacy

Monitor serum ferritin concentration every two to three months to assess the effect 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.

2.4 Dosage Modification for Drug Interactions

Allow at least a 4-hour interval between administration of FERRIPROX and other drugs or supplements containing polyvalent cations such as iron, aluminum, or zinc *[see Drug Interactions (7.2), Clinical Pharmacology (12.3)]*.

3 DOSAGE FORMS AND STRENGTHS

Oral Solution: 100 mg/mL (50 g/500 mL), clear, reddish orange colored solution.

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 and 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 regularly while on therapy.

Reduction in the frequency of ANC monitoring should be considered on an individual patient basis, according to the health care provider's assessment of the patient's understanding of the risk minimization measures required during 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.

The incidence of agranulocytosis was 1.7% of patients in pooled clinical trials of 642 patients with thalassemia syndromes and 1.5% of patients in pooled clinical trials of 196 patients with sickle cell disease or other anemias. 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 and neutropenia prior to initiating FERRIPROX treatment.

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 have developed neutropenia with FERRIPROX unless potential benefits outweigh potential risks.

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).

5.2 Liver Enzyme Elevations

In pooled clinical trials, 7.5% of 642 patients with thalassemia syndromes 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. In pooled clinical trials, 7.7% of 196 patients with sickle cell disease or other anemias treated with FERRIPROX developed increased ALT values.

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 *[see Dosage and Administration (2.1)]*.

5.3 Zinc Deficiency

Decreased plasma zinc concentrations have been observed on FERRIPROX therapy. Monitor plasma zinc annually, and supplement in the event of a deficiency *[see Dosage and Administration (2.1)]*.

5.4 Embryo-Fetal Toxicity

Based on findings from animal reproduction studies and evidence of genotoxicity, FERRIPROX can cause fetal harm when administered to a pregnant woman. The 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 embryo-fetal death and malformations at doses lower than equivalent human clinical doses. Advise pregnant women and females of reproductive potential of the potential risk to the fetus *[see Use in Specific Populations (8.1)]*.

Advise females of reproductive potential to use an effective method of contraception during treatment with FERRIPROX and for at least six months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with FERRIPROX and for at least three months after the last dose *[see Use in Specific Populations (8.1, 8.3)].*

6 ADVERSE REACTIONS

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

- Agranulocytosis and Neutropenia *[see Warnings and Precautions (5.1)]*
- Liver Enzyme Elevations *[see Warnings and Precautions (5.2)]*
- Zinc Deficiency *[see Warnings and Precautions (5.3)]*

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.

The following adverse reaction information represents the pooled data collected from single arm or active-controlled clinical trials with FERRIPROX Tablets (deferiprone) (three times a day) or FERRIPROX Oral Solution (deferiprone).

Thalassemia Syndromes

The safety of FERRIPROX was evaluated in the pooled clinical trial database *[see Clinical Studies (14.1)]*. Patients received FERRIPROX Tablets (three times a day) or FERRIPROX Oral Solution. FERRIPROX was administered orally three times a day

(total daily dose either 50, 75, or 99 mg/kg), N=642. Among 642 patients receiving FERRIPROX, 492 (76.6%) were exposed for 6 months or longer and 365 (56.9%) were exposed for greater than one year.

The median age of patients who received FERRIPROX was 19 years (range 1, 77 years); 50.2% female; 71.2% White, 17.8% Asian, 9.2% Unknown, 1.2% Multi-racial and 0.6% Black.

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

The most common adverse reactions (≥6%) reported during clinical trials were nausea, vomiting, abdominal pain, arthralgia, alanine aminotransferase increased and neutropenia.

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

Table 3:Adverse reactions occurring in ≥ 1% of FERRIPROX-treated patients with thalassemia syndromes

Body System **Adverse Reaction**	**(N=642)** **% Patients**
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.

Sickle Cell Disease or Other Anemias

The safety of FERRIPROX compared to deferoxamine was evaluated in LA38-0411 *[see Clinical Studies (14.2)]*. Patients received FERRIPROX Tablets or FERRIPROX Oral Solution orally three times a day (total daily dose 75-99 mg/kg/day) n=152) or the control arm, deferoxamine, 20-40 mg/kg/day (children) or 40-50 mg/kg/day (adults), by subcutaneous infusion for 5 – 7 days per week, n=76. Among 152 patients receiving FERRIPROX, 120 (78.9%) were exposed for 6 months or longer and 17 (11.2%) were exposed for greater than one year.

The median age of patients who received FERRIPROX was 15 years (range 3, 59 years); 54.6% male; 78.9% White, 15.1% Black and 5.9% Multi-racial.

The most common adverse reactions (≥6%) reported during clinical trials in patients with SCD or other anemias were pyrexia, abdominal pain, bone pain, headache, vomiting, pain in extremity, sickle cell anemia with crisis, back pain, alanine aminotransferase (ALT) increased, aspartate aminotransferase (AST) increased, arthralgia, oropharyngeal pain, nasopharyngitis, neutrophil count decreased, cough and nausea.

The table below lists the adverse reactions (irrespective of a causal assessment; adverse events) of interest that occurred in patients treated with FERRIPROX in clinical trials in subjects with sickle cell disease or other anemias.

Table 4:Adverse reactions occurring in ≥5% of FERRIPROX-treated patients with sickle cell disease or other anemias

Body System **Adverse Reaction**	**FERRIPROX (N=152) % Patients**	**DEFEROXAMINE (N=76) % Patients**
BLOOD AND LYMPHATIC SYSTEM DISORDERS		
Sickle cell anemia with crisis	17	13
GASTROINTESTINAL DISORDERS		
Abdominal pain*	26	13
Vomiting	19	11
Nausea	7	9
Diarrhea	5	8
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS		
Pyrexia	28	33
Pain	5	4
INFECTIONS AND INFESTATIONS		
Nasopharyngitis	9	12
Upper respiratory tract infection	5	3
INVESTIGATIONS		
Alanine aminotransferase increased	12	0
Aspartate aminotransferase increased	11	0
Neutrophil count decreased	8	4
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS		
Bone pain	25	34
Pain in extremity	18	15
Back pain	13	18
Arthralgia	10	8
NERVOUS SYSTEM DISORDERS		
Headache	20	13
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS		
Oropharyngeal pain	10	15
Cough	8	15

*Grouped term

Clinically relevant adverse reactions in <5% of patients include neutropenia and agranulocytosis.

Pediatric Patients

FERRIPROX has been studied in 86 pediatric patients with sickle cell disease or other anemias. Pediatric patients (<17 years) had an increase in the following adverse reactions as compared to adults: abdominal pain, neutrophil count decreased, bone pain and oropharyngeal pain.

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, 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 co-administration of FERRIPROX with other drugs known to be associated with neutropenia or agranulocytosis. If co-administration is unavoidable, closely monitor the absolute neutrophil count *[see Warnings and Precautions (5.1)]*.

7.2 Effect of Other Drugs on FERRIPROX

UDP-Glucuronosyltransferases (UGT)

Avoid 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)]*.

Polyvalent Cations

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 (2.2)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

In animal reproduction studies, oral administration of deferiprone to pregnant rats and rabbits during organogenesis at doses 33% and 49%, respectively, of the maximum recommended human dose (MRHD) resulted in structural abnormalities, embryo-fetal mortality and alterations to growth *(see Data)*. The limited available data from deferiprone use in pregnant women are insufficient to inform a drug-associated risk of major birth defects and miscarriage. Based on evidence and developmental toxicity in animal studies, FERRIPROX can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and of miscarriage is 2-4% and 15-20%, respectively.

Data

Human Data

Post-marketing data available from 39 pregnancies of deferiprone-treated patients and 10 pregnancies of partners of deferiprone-treated patients are as follows:

Of the 39 pregnancies in deferiprone-treated patients, 23 resulted in healthy newborns, 6 ended in spontaneous abortion, 9 had unknown outcomes, and 1 infant was born with anal atresia, nephroptosis, ventricular septal defect, hemivertebra and urethral fistula.

Of the 10 pregnancies in partners of deferiprone-treated patients, 5 resulted in healthy newborns, 1 resulted in a healthy newborn with slight hypospadias, 1 was electively terminated, 1 resulted in the intrauterine death of twins, and 2 had unknown outcomes.

Animal Data

During organogenesis, pregnant rats and rabbits received deferiprone at oral doses of 0, 30, 80 or 200 mg/kg/day, and 0, 10, 50, or 150 mg/kg/day, respectively. The daily dose was administered as two equal divided doses approximately 7 hours apart. Doses of 200 mg/kg/day in rats and 150 mg/kg/day in rabbits, approximately 33% and 49% of the MRHD, respectively, resulted in increased post-implantation loss and reduced fetal weights in the presence of maternal toxicity (reduced maternal body weight and body weight gain in both rats and rabbits; abnormal large placenta at low incidence in rats). The 200 mg/kg/day dose in rats resulted in external, visceral and skeletal fetal malformations such as cranial malformations, cleft palate, limb malrotation, anal atresia, internal hydrocephaly, anophthalmia and fused bones. The dose of 150 mg/kg/day in rabbits resulted in external fetal malformations (partially opened eyes) and minor blood vessel and skeletal variations.

In rats, malformations including micrognathia and persistent ductus arteriosus could be observed in the absence of maternal toxicity at doses equal to or greater than 30 and 80 mg/kg/day, approximately 5% and 13% of the MHRD, respectively.

8.2 Lactation

Risk Summary

There is no information regarding the presence of deferiprone in human milk, the effects on the breastfed child, or the effects on milk production.

Because of the potential for serious adverse reactions in the breastfed child, including the potential for tumorigenicity shown for deferiprone in animal studies, advise patients that breastfeeding is not recommended during treatment with FERRIPROX, and for at least 2 weeks after the last dose.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Pregnancy testing is recommended for females of reproductive potential prior to initiating FERRIPROX.

Contraception

Females

FERRIPROX can cause embryo-fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]*. Advise female patients of reproductive potential to use effective contraception during treatment with FERRIPROX and for at least 6 months after the last dose.

Males

Based on genotoxicity findings, advise males with female partners of reproductive potential to use effective contraception during treatment with FERRIPROX and for at least 3 months after the last dose *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

The safety and effectiveness of FERRIPROX for the treatment of transfusional iron overload due to thalassemia syndromes have been established in pediatric patients 3 years of age and older. Use of FERRIPROX for this indication is supported by evidence of efficacy from clinical trials in adult patients with thalassemia and evidence of safety in pediatric patients with sickle cell disease.

The safety and effectiveness of FERRIPROX for the treatment of transfusional iron overload due to sickle cell disease or other anemias have been established in 86 pediatric patients 3 to 16 years of age, among the 152 patients treated with FERRIPROX Tablets or Oral Solution in an adequate and well-controlled study *[see Adverse Reactions (6.1) and Clinical Studies (14.2)]*. The study included 56 patients 3 to <12 years of age and 30 patients 12 to 16 years of age. Seventy-six percent of these patients had sickle cell disease. The recommended starting dose and dose-modifications are the same for children and adults *[see Indications and Usage (1), Dosage and Administration (2.1), and Clinical Studies (14)]*.

Fourteen patients with spherocytosis (including hereditary) (ages 3-15), two patients with pyruvate kinase deficiency (ages 4 and 6), two patients with dyserythropoietic anemia (ages 10-12) and two patients with hemolytic anemia (ages 8 and 10 years old) were treated with FERRIPROX in the clinical trial, LA38-0411.

A US registry established from December 2011 through December 2019, contains 125 patients from 4 to < 17 years old who have received FERRIPROX and have sickle cell disease. The adverse reactions, including agranulocytosis, seen in the 8 year period of the registry are similar to those seen in the most recent clinical studies.

Safety and effectiveness of FERRIPROX Oral Solution has not been established in pediatric patients with chronic iron overload due to blood transfusions who are less than 3 years of age.

8.5 Geriatric Use

Clinical studies of deferiprone did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

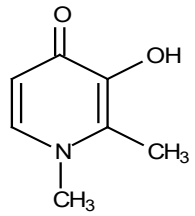
10 OVERDOSAGE

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 Oral Solution (deferiprone) 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 (14.3 mg/mL) 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 ions (iron III). Deferiprone binds with ferric ions to form neutral 3:1 (deferiprone:iron) complexes that are stable at physiological pH.

12.2 Pharmacodynamics

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

Cardiac Electrophysiology

At the maximum approved recommended dose, deferiprone does not prolong the QT interval to any clinically relevant extent.

12.3 Pharmacokinetics

The mean C_{max} and AUC of deferiprone was 20 mcg/mL and 50 mcg·h/mL, respectively, in healthy subjects. The dose proportionality of deferiprone over the approved recommended dosage range is unknown.

Absorption

Deferiprone appeared in the blood within 5 to 10 minutes after oral administration. Peak serum concentration of deferiprone was reached approximately 1 to 2 hours after a single dose.

Effect of Food

No clinically significant differences in the pharmacokinetics of deferiprone were observed following administration with food.

Elimination

The elimination half-life of deferiprone is approximately 2 hours.

Metabolism

Deferiprone is metabolized primarily by UGT1A6. The major metabolite of deferiprone is the 3-*O*-glucuronide, which lacks iron binding capability.

Excretion

Following oral administration, 75% to 90% of the administered dose was recovered in urine (primarily as metabolite) in the first 24 hours.

Specific Populations

No clinically significant differences in the pharmacokinetics of deferiprone were observed based on sex, race/ethnicity, body weight, mild to severe (eGFR 15 to 89 mL/min/1.73 m^2) renal impairment, or mild (Child Pugh Class A) to moderate (Child Pugh Class B) hepatic impairment. The effect of age, including geriatric or pediatric populations, end stage renal disease or severe (Child Pugh Class C) hepatic impairment on the pharmacokinetics of deferiprone is unknown.

Drug Interaction Studies

In Vitro Studies

UGTIA6 Inhibitors: Phenylbutazone (UGT1A6 inhibitor) decreased glucuronidation of deferiprone by up to 78%.

Polyvalent Cations: Deferiprone has the potential to bind polyvalent cations (e.g., iron, aluminum, and zinc).

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 deferiprone. 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.

14 CLINICAL STUDIES

14.1 Transfusional Iron Overload in Patients with Thalassemia Syndromes

In a prospective, planned, pooled analysis of patients with thalassemia syndromes from several studies, the efficacy of deferiprone 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 deferiprone. Deferiprone 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 (range 2 to 62; 91 patients were <17).

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.

14.2 Transfusional Iron Overload in Patients with Sickle Cell Disease and other Anemias

Study LA38-0411, an actively-controlled non-inferiority study compared the efficacy of FERRIPROX to that of deferoxamine in patients with sickle cell disease and other transfusion-dependent anemias by evaluating liver iron concentration (LIC). The efficacy of FERRIPROX was established based upon the change in LIC from baseline after 12 months of FERRIPROX (75 or 99 mg/kg/day) compared to deferoxamine (20 or 40 mg/kg (pediatric patients); 40 or 50 mg/kg (adult patients)). Patient enrollment was stopped following an interim analysis. After adjusting for the type I (alpha) error, the non-inferiority criterion was established as the upper limit of the 96.01% confidence interval for the difference between treatments being ≤2 mg/g dry weight (dw).

Data from 185 patients (122 on FERRIPROX and 63 on deferoxamine) were available. Among the 122 FERRIPROX treated patients, the mean age was 15.9 years (range 3-46); 57.4% were male; 75.4% were White, 17.2% were Black and 7.4% were Multi-racial; 85% were diagnosed with Sickle Cell Disease and 15% with other anemias. Over 12 months, the Least Squares estimate of mean decrease from baseline in LIC was 4.13 ± 0.50 mg/g dw for FERRIPROX and 4.38 ± 0.59 mg/g dw for deferoxamine, and the non-inferiority criterion was met.

Upon completion of the first year of therapy in the non inferiority study, 89 patients from the ferriprox group opted to continue with treatment and 45 from the deferoxamine group opted to switch to ferriprox treatment. This group continued for up to an additional 2 years. LIC continued to decrease over time, with the mean value dropping from 14.93 mg/g dw at baseline to 12.30 mg/g dw after one year of treatment, to 11.19 mg/g dw after two years of treatment, and to 10.45 mg/g dw after three years of treatment.

16 HOW SUPPLIED/STORAGE AND HANDLING

FERRIPROX® Oral Solution (deferiprone) 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 10122-101-50

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

Store in the original bottle and carton to protect from light.

After first opening of the bottle, discard any unused portion after 35 days.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide *and Instructions for Use*)

- Instruct patients and their caregivers to store FERRIPROX Oral Solution at 68°F to 77°F (20°C to 25°C); excursions permitted to 59°F to 86°F (15°C to 30°C) [see USP Controlled Room Temperature]. Store in the originally supplied bottle and carton to protect from light.
- Advise patients to use the measuring cup provided with FERRIPROX Oral Solution 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 Oral Solution in the morning, the second dose at midday, and the third dose in the evening. Clinical experience suggests that taking FERRIPROX Oral Solution with meals may reduce nausea.If a dose of this medicine has been missed, take it 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.
- Inform patients of the risks of developing agranulocytosis and the need for regular blood testing before and during their treatment to monitor for decreases in their ANC. 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 *[see Dosage and Administration (2.1) and*

Warnings and Precautions (5.1)] in order to check their ANC within 24 hours. Advise them if they are unable to reach their physician, seek care from another provider so as not to delay medical care.

- Inform patients of the risk of abnormal liver transaminases and the need for regular blood testing before and during their treatment to monitor for increases in ALT *[see Dosage and Administration (2.1) and Warnings and Precautions (5.2)]*.
- Inform patients of the risk of zinc deficiency and the need for regular blood testing before and during their treatment to monitor for reductions in zinc *[see Dosage and Administration (2.1) and Warnings and Precautions (5.3)]*.
- 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, and it is not harmful.

Embryo-Fetal toxicity

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions (5.4) and Use in Specific Populations (8.1)]*. Advise female patients of reproductive potential to use effective contraception during treatment with FERRIPROX and for at least six months after the last dose *[see Use in Specific Populations (8.1, 8.3)]*. Advise males with female partners of reproductive potential to use effective contraception during treatment with FERRIPROX and for at least three months after the last dose *[see Use in Specific Populations (8.3) and Nonclinical Toxicology (13.1)]*.

Lactation

Advise females not to breastfeed during treatment with FERRIPROX and for at least 2 weeks after the last dose *[see Use in Specific Populations (8.2)]*.

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CTFD-015-0521-02-W

Medication Guide
FERRIPROX (Feh ri prox) Oral Solution
(deferiprone)
oral solution, for oral use
100 mg/mL

What is the most important information I should know about FERRIPROX Oral Solution?

FERRIPROX Oral Solution can cause serious side effects, including a very low white blood cell count. One type of white blood cell that is important for fighting infections is called a neutrophil. If your neutrophil count is low (neutropenia), you may be at risk of developing a serious infection that can lead to death. Neutropenia is common with FERRIPROX Oral Solution and can become severe in some people. Severe neutropenia is known as agranulocytosis. If you develop agranulocytosis, you will be at risk of developing serious infections that can lead to death.

Your healthcare provider will do a blood test before you start FERRIPROX Oral Solution and regularly during treatment to check your neutrophil count. If you develop neutropenia, your healthcare provider should check your blood counts every day until your white blood cell count improves. Your healthcare provider may temporarily stop treatment with FERRIPROX Oral Solution if you develop neutropenia or infection.

Stop taking FERRIPROX Oral Solution and call your healthcare provider or get medical help right away if you develop any of these symptoms of infection:

- fever
- sore throat or mouth sores
- flu-like symptoms
- chills and severe shaking

It is important for you to have your white blood cell count checked within 24 hours of developing symptoms of an infection to see if you have severe neutropenia (agranulocytosis). Do not delay getting medical care if you are unable to reach your healthcare provider.

See **"What are the possible side effects of FERRIPROX Oral Solution?"** for more information about side effects.

What is FERRIPROX Oral Solution?

FERRIPROX Oral Solution is a prescription medicine used to treat iron overload from blood transfusions in adults and children 3 years of age and older with:

- thalassemia syndromes.
- sickle cell disease or other anemias.

It is not known if FERRIPROX Oral Solution is safe and effective to treat iron overload due to blood transfusions:

- in people with myelodysplastic syndrome or Diamond Blackfan anemia
- in children less than 3 years of age

Do not take FERRIPROX Oral Solution if you are allergic to deferiprone or any of the ingredients in FERRIPROX Oral Solution. See the end of this Medication Guide for a complete list of ingredients in FERRIPROX Oral Solution.

Before taking FERRIPROX Oral Solution, tell your healthcare provider about all of your medical conditions, including if you:

- have liver problems
- are pregnant or plan to become pregnant. FERRIPROX Oral Solution can harm your unborn baby. You should avoid becoming pregnant during treatment with FERRIPROX Oral Solution. Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with FERRIPROX Oral Solution.
  Females who are able to become pregnant:
  - Your healthcare provider should do a pregnancy test before you start treatment with FERRIPROX Oral Solution.
  - You should use effective birth control during treatment with FERRIPROX Oral Solution and for at least 6 months after the last dose.

  Males with female partners who are able to become pregnant:
  - You should use effective birth control during treatment with FERRIPROX Oral Solution and for at least 3 months after the last dose.
- are breastfeeding or plan to breastfeed. It is not known if FERRIPROX Oral Solution passes into your breast milk. Do not breastfeed during treatment with FERRIPROX Oral Solution and for at least 2 weeks after the last dose.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

How should I take FERRIPROX Oral Solution?

Read the Instructions for Use for detailed instructions about how to measure and take a dose of FERRIPROX Oral Solution.

- Take FERRIPROX Oral Solution exactly as your healthcare provider tells you.
- Your healthcare provider will prescribe FERRIPROX Oral Solution based on your body weight.
- Your healthcare provider will check your body iron level during treatment with FERRIPROX Oral Solution and may change your dose if needed. Your healthcare provider may also change your dose of FERRIPROX Oral Solution if you have certain side effects. Do not change your dose of FERRIPROX Oral Solution unless your healthcare provider tells you to.
- Use the measuring cup that comes with FERRIPROX Oral Solution to measure your prescribed dose.
- **Take FERRIPROX Oral Solution 3 times each day.** Take your first dose in the morning, the second dose at mid-day, and the third dose in the evening.
- Taking FERRIPROX Oral Solution with meals may help reduce nausea.
- **If you must take a medicine to treat indigestion (antacid), or supplements that contain iron, aluminum, or zinc during treatment with FERRIPROX Oral Solution, allow at least 4 hours between taking FERRIPROX Oral Solution and these products.**
- If you take too much FERRIPROX Oral Solution, call your healthcare provider.
- If you miss a dose, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose and then continue with your regular schedule. Do not try to catch-up or take 2 doses at the same time to make up for a missed dose.

What are the possible side effects of FERRIPROX Oral Solution?

FERRIPROX Oral Solution can cause serious side effects, including:

- **See "What is the most important information I should know about FERRIPROX Oral Solution?"**
- **Increased liver enzyme levels in your blood.** Your healthcare provider should do blood tests to check your liver function before you start and then monthly during treatment with FERRIPROX Oral Solution. Your healthcare provider may temporarily stop treatment with FERRIPROX Oral Solution if you develop increased liver enzyme levels and they continue to be increased.
- **Decreased levels of zinc in your blood.** Your healthcare provider will do blood tests to check your zinc levels before you start and during treatment with FERRIPROX Oral Solution, and may prescribe a zinc supplement for you if your zinc levels are low.

The most common side effects of FERRIPROX Oral Solution in people with thalassemia include:

- nausea
- vomiting
- stomach-area (abdominal) pain
- joint pain
- abnormal liver function tests
- low white blood cells

The most common side effects of FERRIPROX Oral Solution in people with sickle cell disease or other anemias include:

- fever
- stomach-area (abdominal) pain
- bone pain
- headache
- vomiting
- pain in arms or legs
- sickle cell anemia with crisis
- back pain
- abnormal liver function tests
- joint pain
- mouth and throat pain
- common cold
- low white blood cells
- cough
- nausea

FERRIPROX Oral Solution may cause a change in urine color to reddish-brown. This is not harmful and is expected during treatment with FERRIPROX Oral Solution.

These are not all of the possible side effects of FERRIPROX Oral Solution.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store FERRIPROX Oral Solution?

- Store FERRIPROX Oral Solution at room temperature between 68°F to 77°F (20°C to 25°C).
- Store FERRIPROX Oral Solution in the original bottle and carton to protect from light.
- After first opening, use a bottle of FERRIPROX Oral Solution within 35 days. After 35 days, discard the bottle and any unused FERRIPROX Oral Solution.

Keep FERRIPROX Oral Solution and all medicines out of the reach of children.

General information about the safe and effective use of FERRIPROX Oral Solution.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use FERRIPROX Oral Solution for a condition for which it was not prescribed. Do not give FERRIPROX Oral Solution to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about FERRIPROX Oral Solution that is written for health professionals.

What are the ingredients in FERRIPROX Oral Solution?

Active ingredient: deferiprone
Inactive ingredients: purified water, hydroxyethylcellulose, glycerin, hydrochloric acid, artificial cherry flavor, peppermint oil, FD&C Yellow No. 6, and sucralose.

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Manufactured by: Apotex Inc., Toronto, Ontario, Canada, M9L 1T9.
CTFD-016-0521-02-W

For more information, call 1-888-661-9260.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 11/2021

Instructions for Use
FERRIPROX (Feh' ri prox) Oral Solution
(deferiprone)
oral solution, for oral use
100 mg/mL

Read this Instructions for Use before taking FERRIPROX Oral Solution or giving FERRIPROX Oral Solution to your child and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your or your child's medical condition or treatment.

Important information:

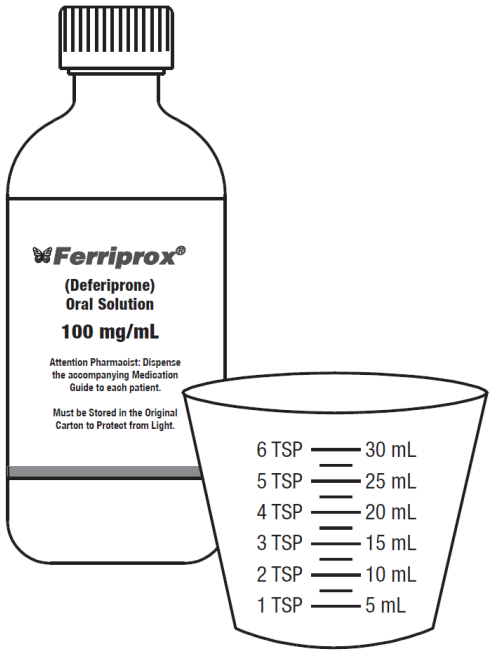
- Store FERRIPROX Oral Solution at room temperature between 68°F to 77°F (20°C to 25°C).
- Store FERRIPROX Oral Solution in the original bottle and carton to protect from light.
- After first opening, use a bottle of FERRIPROX Oral Solution within 35 days. After 35 days, discard the bottle and any unused FERRIPROX Oral Solution.

Keep FERRIPROX Oral Solution and all medicines out of the reach of children.

Supplies needed to measure and take a dose of FERRIPROX Oral Solution **(See Figure A)**:

- 1 bottle of FERRIPROX Oral Solution
- 1 measuring cup (supplied with each bottle of FERRIPROX Oral Solution). The measuring cup has markings for teaspoons (TSP) and milliliters (mL). **Note:** 1 TSP is equal to 5 mL.

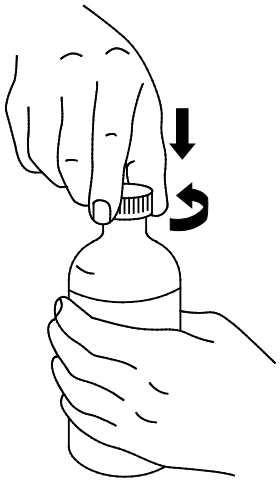
Figure A



If you do not receive a measuring cup with your FERRIPROX Oral Solution, ask your pharmacist. Only use the measuring cup that comes with FERRIPROX Oral Solution to make sure that you measure the right amount of medicine.

Step 1: To open the bottle of FERRIPROX Oral Solution, remove the outer plastic wrapper from the child-resistant cap. Push down on the child-resistant cap and turn the cap in the direction of the arrow **(See Figure B)**.

Figure B

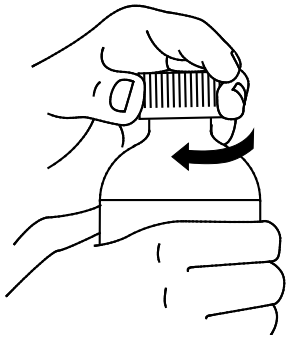


Step 2: Pour the prescribed dose of FERRIPROX Oral Solution into the measuring cup **(See Figure C)**.

Figure C

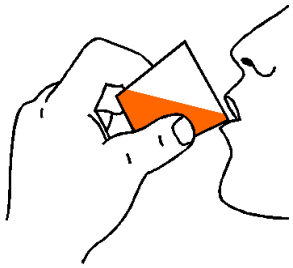
Step 3: Put the child-resistant cap back on the FERRIPROX Oral Solution bottle and turn it in the direction of the arrow. (**See Figure D**)

Figure D



Step 4: Swallow the prescribed dose of FERRIPROX Oral Solution (**See Figure E**).

Figure E



Step 5: Add about 10 to 15 mL of water to the measuring cup (**See Figure F**). Gently swirl the measuring cup to mix the water and any FERRIPROX Oral Solution left in the measuring cup (**See Figure G**). Drink all the mixture in the measuring cup (**See Figure H**).

Figure F

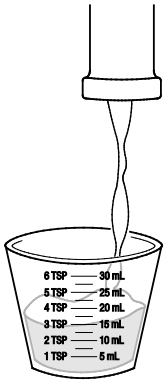


Figure G

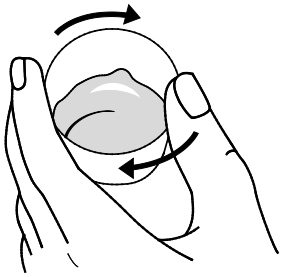
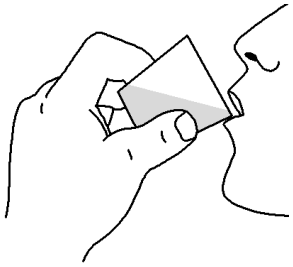


Figure H



Step 6: Hand-wash the measuring cup with water.

Step 7: Keep the measuring cup with the bottle of FERRIPROX Oral Solution.

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