PACKAGE LEAFLET

Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- This medicinal product has been prescribed for you personally. Never give it to anyone else. It may harm them, even if their symptoms are the same as yours.

In this leaflet:

1. What Ferriprox® is and what it is used for
2. Before you take Ferriprox®
3. How to take Ferriprox®
4. Possible side effects
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Ferriprox® 500 mg film-coated tablets

Deferiprone

The active substance is deferiprone 500 mg/tablet.

The other ingredients are:
Core tablet: Microcrystalline cellulose, Magnesium stearate, Colloidal silicon dioxide
Coating: Hypromellose, Macrogol, Titanium dioxide

1. WHAT FERRIPROX® IS AND WHAT IT IS USED FOR

Deferiprone is a medicine that removes iron from the body.
Ferriprox® tablets are white, capsule-shaped, film-coated tablets imprinted "APO" bisect "500" on one side, plain on the other. The tablet is scored and breakable in half. Ferriprox® is packaged in bottles of 100 tablets.

Ferriprox® is indicated for the treatment of iron overload in patients with thalassemia major when deferoxamine therapy is contra-indicated or inadequate.

Pharmacotherapeutic group: Iron Chelator, ATC code: V03AC02

The active substance is deferiprone (3-hydroxy-1 ,2-dimethylpyridin-4(1 H)-one), a bidentate ligand, which binds to iron in a 3:1 molar ratio. Clinical studies have demonstrated that Ferriprox® is effective in promoting iron excretion and that a dose of 25 mg/kg three times per day can prevent the progression of iron accumulation as assessed by serum ferritin, in transfusion-dependent thalassemia patients.

Deferiprone is rapidly absorbed from the upper part of the gastro-intestinal tract. Peak serum concentration is reported to occur 45 to 60 minutes following a single dose in fasted patients. This may be extended to 2 hours in fed patients. Deferiprone is metabolised predominantly to a glucuronide conjugate. This metabolite lacks iron-binding capacity due to inactivation of the 3-hydroxy group of deferiprone. In humans, deferiprone is eliminated mainly via the kidneys with reports of 75% to 90% of the ingested dose being recovered in the urine in the first 24 hours, in the form of free deferiprone, the glucuronide metabolite and the iron-deferiprone complex.

2. BEFORE YOU TAKE FERRIPROX®

Ferriprox® is unable to be taken if:
- you have a history of hypersensitivity (an allergy) to the active substance or any of the other ingredients (see above)
- you have a history of repeated episodes of neutropenia (low white blood cell count)
- you have a history of agranulocytosis (very low white blood cell count $< 0.5 \times 10^9$/L)
- you are currently taking medication known to cause neutropenia
- you are pregnant or breast-feeding

The way deferiprone causes neutropenia is not known. Patients should not take medicinal products known to be associated with neutropenia or those which can cause agranulocytosis.

Special warnings for taking Ferriprox®:
The most serious undesirable effect of deferiprone is the occurrence of a very low white blood cell count. This condition, known as severe neutropenia or agranulocytosis, has occurred in about 1 out of 100 patients who have taken deferiprone in clinical studies. Because white blood cells help to fight infection, a low white blood cell count may place you at risk to develop a serious infection. If an infection of this nature is not discovered and treated early, it could cause death. Your doctor will ask you to have a blood test (to check your white blood cell count) performed regularly, as frequently as every week. It is very important for you to keep all of these appointments. Report immediately to your doctor any symptoms of infection such as: fever, sore throat or flu-like symptoms.

Your doctor may monitor your serum ALT level at regular intervals during therapy with Ferriprox®, and interruption of therapy may be considered if a persistent increase in serum ALT levels occurs.

Ferriprox® should be prescribed by a Hematologist, Pediatrician or other Medical Physician.

Your doctor will also ask you to come in for tests to monitor body iron load. In addition, he or she also might ask you to undergo liver biopsies.

Patients with iron overload are at increased risk of cancer. In these circumstances, the impact of deferiprone is not known.

The positive and negative effects of iron chelation can only be demonstrated after many years. Therefore, further studies are ongoing. In addition, cancer-predicting studies are underway.

Use during pregnancy and breast-feeding: Do not take this medication if you are breast-feeding, if you are pregnant, or if you are trying to become pregnant. This medication could seriously harm your baby. You must use effective contraception while you are taking Ferriprox®. Ask your doctor which method is best for you. If you become pregnant while taking Ferriprox®, stop taking the medicine immediately and tell your doctor.

Driving and using machines:
There is no evidence that Ferriprox® affects your ability to drive or use machinery.

Taking Ferriprox® with other products:
Tell your doctor about all other medications that you are taking, even ones that you can buy without a prescription. Your doctor can tell you which medications you can safely take with Ferriprox®.

Since this compound binds to metallic cations, the potential exists for interactions between deferiprone and trivalent cation-dependent medicinal products such as aluminium-based antacids.

Based on the reported adverse interaction that can occur between deferoxamine and vitamin C, caution should be used when administering concurrent deferiprone and vitamin C.

3. HOW TO TAKE FERRIPROX®

It is important to follow the directions that your doctor has given to you. The amount of deferiprone that you take will depend on your weight. Ferriprox® is usually prescribed as 25 mg/kg body weight, calculated to the nearest half tablet, to be taken three (3) times

per day for a total daily dose of 75 mg/kg body weight. Take your first dose in the morning. Take your second dose midday. Take your third dose in the evening. It is not necessary to take Ferriprox® with food. However, you may find it easier to remember to take your medication, if you take it with your meals. Ferriprox® will be most effective if you do not miss any doses. If you do miss one dose take it as soon as you remember and take your next dose at its regularly scheduled time. If you miss more than one dose, do not take the missed tablets, just continue with your normal schedule. Do not change your daily dose without first consulting with your doctor.

Very limited data are available on Ferriprox® use in children under 6 years of age; therefore, the use of Ferriprox® in this group should not be recommended unless the potential benefits outweigh the potential risks.

There are no reports of overdose with deferiprone.

4. POSSIBLE SIDE EFFECTS

Like all medicines, deferiprone can have side effects.

The most serious undesirable effect of deferiprone is the occurrence of a very low white blood cell count. This condition, known as severe neutropenia or agranulocytosis, has occurred in about 1 out of 100 patients who have taken deferiprone in clinical studies. A low white blood cell count can also be associated with an infection. Report immediately to your doctor any symptoms of infection such as: fever, sore throat or flu-like symptoms.

Some of the patients enrolled in clinical studies with deferiprone developed joint pain and swelling. In most patients, the pain disappeared while still taking Ferriprox®.

Some patients treated with Ferriprox® have experienced some or all of the following symptoms: increase in liver enzymes, abdominal pain, nausea, vomiting, diarrhea and increase in appetite. Most patients find that these undesirable effects disappear after a few days to a few weeks of continued treatment. If you experience nausea or vomiting, it may help to take your Ferriprox® with some food.

Your urine may become reddish/brown in colour. This is the most common undesirable effect of deferiprone and it is not harmful.

If you notice any side effects, please inform your doctor, pharmacist or the local distributing company immediately, who will in turn communicate it to the Medical Information Division at Apotex (Canada) by calling: +1 (416) 401-7780.

5. STORING FERRIPROX®

Do not store above 30°C.
Do not use Ferriprox® after the expiry date stated on the container. Keep out of the reach and sight of children.

Thai Reg. No.1C 25/51 (NC)

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