Patient package insert according to Pharmacists' Regulations (Preparations) – 1986

This medicine can be sold with a physician's prescription only

Defirox 125, 250, 500 mg

Dispersible Tablets

Each dispersible tablet contains deferasirox in a dosage of 125, 250 or 500 mg respectively.
Inactive ingredients and allergens in the medicine – see section 6 "Additional information" and in section 2 "Important information about some of the ingredients of this medicine".

Read this entire leaflet carefully before using this medicine. This leaflet contains concise information about the medicine. If you have further questions, ask the doctor or pharmacist.
This medicine has been prescribed to treat your illness or to treat your child's illness. Do not pass it on to others. It may harm them, even if you think that their illness is the same as yours.

1. What is the medicine intended for?

- To treat chronic iron overload caused by blood transfusions, in adults and children (aged 2 years and above).
- To treat chronic iron overload that is not blood transfusion-dependent in thalassemia patients from 10 years of age and older.

Therapeutic group: Iron chelating agent.

Repeated blood transfusions are sometimes necessary in patients suffering from certain types of anemia such as thalassemia, sickle-cell anemia and myelodysplastic syndromes (MDS). However, repeated blood transfusions may cause a build-up of excess iron. This is because blood contains iron and the body does not have a natural way to remove the excess iron received with the blood transfusions.
In thalassemia patients that are not blood transfusion-dependent, iron overload may develop over time mainly due to increased absorption of iron from food in response to low blood cell counts.
Over time, the excess iron can cause damage to vital organs such as the liver and heart.
Iron chelator medicines are used to remove the excess iron and reduce the risk of causing damage to the body's organs.
Defirox traps and removes excess iron which is then excreted mainly in the stools.

2. Before using the medicine

Do not use the medicine if:

- You are hypersensitive (allergic) to the active ingredient (deferasirox), or to any of the other ingredients this medicine contains (see section 6). If this is relevant to you, **tell the doctor before taking Defirox.** If you think you are allergic, consult the doctor.
- You have moderate or severe kidney disease.
- You are currently taking other iron chelator medicine.

Defirox is not recommended if:

- You have advanced stage myelodysplastic syndrome (MDS; decreased production of blood cells by the bone marrow), or advanced cancer.

Special warnings regarding the use of the medicine
Before the treatment with Defirox, tell the doctor if:

- You have a liver or kidney problem.
- You have a cardiac problem caused by iron overload.
- You notice a marked decrease in urine output (sign of a kidney problem).
- You have a severe rash or breathing difficulties and dizziness or swelling mainly of the face and throat (signs of a severe allergic reaction, also see section 4 "Side effects").
- You have a combination of any of the following symptoms: rash, red skin, blisters on the lips, eyes or mouth, skin peeling, high fever, flu-like symptoms, enlarged lymph nodes (signs of a severe skin reaction, also see section 4 "Side effects").
- You experience a combination of drowsiness, upper right abdominal pain, yellowing or increased yellowing of the skin or eyes and dark urine (signs of liver problems).
- You experience difficulty thinking, remembering information or solving problems, feel less alert or aware of the surroundings or feel very sleepy with low energy (signs of a high level of ammonia in the blood, which may be associated with liver or kidney problems, also see section 4 "Side effects").
- You vomit blood and/or have black stools.
- You frequently have abdominal pain, particularly after eating or taking **Defirox.**
- You have frequent heartburn.
- You have a low platelet or white blood cell count in blood tests.
- You have blurred vision.
- You have diarrhea or vomiting.

If any of these conditions apply to you, tell the doctor immediately.

Children and adolescents
Defirox can be used in children and adolescents aged 2 years and above to treat chronic iron overload caused by blood transfusions and aged 10 and above to treat non-blood transfusion-dependent chronic iron overload in thalassemia patients.
The doctor will adjust the dosage according to the child's growth.
Defirox is not intended for use in children under 2 years of age.

Tests and follow-up
During the treatment you need to undergo regular blood and urine tests. These tests will monitor the amount of iron in your body (blood ferritin levels) to check whether **Defirox** is having the desired effect. These tests will also monitor kidney function (blood creatinine levels, presence of protein in the urine) and liver functions (levels of transaminases, bilirubin and alkaline phosphatase in the blood). The doctor may ask you to undergo a kidney biopsy, if he/she suspect significant kidney damage. You may also have MRI (magnetic resonance imaging) tests to determine the amount of iron in your liver. The doctor will take these tests into consideration when deciding which dosage of **Defirox** is best for you and will also use these tests to decide when you should stop taking **Defirox.**
You must undergo hearing and vision tests before beginning treatment and once a year during the treatment as a precaution.

Drug interactions
If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

- Do not combine the administration of **Defirox** with other iron chelating products.
- Do not take antacids (medicines used to treat heartburn) containing aluminum at the same time of day as **Defirox**.

In particular inform the doctor or pharmacist if you are taking:

- Ciclosporin (used to prevent the rejection of a transplanted organ or for other conditions, such as rheumatoid arthritis or skin asthma).
- Simvastatin (used to lower cholesterol).
- Certain painkillers or anti-inflammatory medicines (e.g., aspirin, ibuprofen, corticosteroids).
- Oral bisphosphonates (used to treat osteoporosis).
- Anticoagulant medicines (used to prevent or treat formation of blood clots).
- Hormonal contraceptives (birth control products).
- Bepridil, ergotamine (used to treat heart problems and migraines).
- Repaglinide (used to treat diabetes).
- Rifampicin (used to treat tuberculosis).
- Phenytoin, phenobarbital, carbamazepine (used to treat epilepsy).
- Ritonavir (used to treat HIV infection).
- Paclitaxel (used to treat cancer).
- Theophylline (used to treat respiratory diseases such as asthma).
- Clozapine (used to treat psychiatric disorders such as schizophrenia).
- Tizanidine (used as a muscle relaxant).
- Cholestyramine (used to lower cholesterol levels in the blood).
- Busulfan (used as treatment prior to the transplantation in order to destroy the original bone marrow before the transplant).
- Midazolam (used to ease anxiety and/or sleeping difficulties).

Additional tests may be required to monitor the levels of some of the medicines in your blood.

Use of this medicine and food
Take **Defirox** on an empty stomach and wait at least 30 minutes before eating any food, preferably at the same time each day.
Dissolve the tablets in a glass of water, apple juice or orange juice. Do not dissolve the tablets in fizzy drinks or milk (also see section 3 "How to take **Defirox**").

Use in the elderly (adults aged 65 and above)
Elderly people aged 65 and above can use the same dose of **Defirox** as other adults. Elderly patients may experience more side effects (mainly diarrhea) than younger patients. They need to be monitored closely by the doctor for detection of side effects that may require a dosage adjustment.

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you may be pregnant or planning to become pregnant, consult the doctor before using this medicine.
Defirox is not recommended during pregnancy unless clearly necessary. If you are using hormonal contraceptives, you should use an additional or different type of contraceptive (e.g., a condom), as **Defirox** may reduce the effectiveness of hormonal contraceptives.
Breastfeeding is not recommended during treatment with **Defirox**.

Driving and using machines
If you feel dizzy after taking **Defirox**, do not drive a vehicle or operate tools or machinery until you feel normal again.
As for children, they should be cautioned against riding a bicycle or playing near the road, and the like.

Important information about some of the ingredients of this medicine
Defirox contains lactose. If you have been told in the past by a doctor that you have an intolerance to certain sugars, consult the doctor before taking this medicine.
Each **Defirox 125 mg** dispersible tablet contains approximately 104 mg lactose.
Each **Defirox 250 mg** dispersible tablet contains approximately 209 mg lactose.
Each **Defirox 500 mg** dispersible tablet contains approximately 417 mg lactose.
This should be taken into consideration in patients with diabetes.
This medicine contains less than 1 millimole sodium (23 mg) per dispersible tablet, that is to say essentially "sodium-free".

3. How to use this medicine

Always use this medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the medicine.
Treatment with **Defirox** will be overseen by a doctor who is experienced in the treatment of iron overload.
The dosage and the treatment regimen will be determined by the doctor only. The dosage of **Defirox** is related to the body weight in all patients. The doctor will calculate the dosage you need and tell you how many tablets to take each day.
The usual daily dosage at the beginning of treatment is generally:

- For patients regularly receiving blood transfusions – 20 mg per kg body weight. The doctor may recommend a higher or lower starting dosage based on your individual treatment needs.
- For patients who do not regularly receive blood transfusions – 10 mg per kg body weight.
- Depending on your response to the treatment, the doctor may later adjust your treatment to a higher or lower dose.

The maximum daily dosage is:

- 40 mg per kg body weight for patients regularly receiving blood transfusions.
- 20 mg per kg body weight for adult patients not regularly receiving blood transfusions.
- 10 mg per kg body weight for children up to the age of 18 not regularly receiving blood transfusions.

Do not exceed the recommended dose.

Duration of treatment:
Continue taking Defirox each day, as long as the doctor instructs you to do so. This treatment is long-term treatment, and it may last for months or years. The doctor will regularly monitor your condition to make sure the treatment is having the desired effect (also see in section 2 "Tests and follow-up").
If you have questions regarding the duration of treatment, refer to the doctor.

Method of administration:
When to take Defirox

- Take **Defirox** once a day, every day, at about the same time.
- Take the tablets on an empty stomach.
- Then wait at least 30 minutes before eating any food.

Taking **Defirox** at the same time each day will help you remember when to take the tablets.

How to take Defirox

Place the tablet(s) into a glass of water, apple juice or orange juice (100-200 ml).

Stir until the tablet(s) dissolve(s) completely. The liquid in the glass will look cloudy.

Drink all the contents of the glass, and then add a little water or juice to what remains in the glass, stir and drink that as well.

Do not dissolve the tablets in fizzy drinks or milk.
Do not chew, break or crush the tablets. Do not swallow the tablets whole.

For any question regarding how **Defirox** works or why it has been prescribed for you, refer to the doctor or pharmacist.

If you have accidentally taken a higher dose
If you have taken an overdose or if a child or someone else has accidentally swallowed the medicine, proceed immediately to a doctor or a hospital emergency room and bring the package of the medicine with you. Urgent medical treatment may be necessary.
You may experience effects such as abdominal pain, diarrhea, nausea and vomiting and kidney or liver problems that could be serious.

If you forgot to take the medicine
If you forgot to take this medicine at the designated time, take the dose as soon as you remember on the same day. Take the next dose at the usual time. Do not take a double dose the following day to compensate for forgotten tablet(s).
Adhere to the treatment as recommended by the doctor.
Even if there is an improvement in your health, do not stop taking the medicine without consulting the doctor.

If you stop taking the medicine
Do not stop the treatment with **Defirox** without explicit instruction from the doctor.
If you stop taking **Defirox**, the excess iron will no longer be removed from your body (also see above "Duration of treatment").

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.
If you have further questions on the use of this medicine, consult the doctor or pharmacist.

4. Side effects

Like any medicine, the use of **Defirox** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them. Most of the side effects are mild to moderate and will usually pass after a few days to a few weeks of treatment.

Some side effects may be severe and require immediate medical treatment.
These side effects are uncommon side effects (effects that appear in 1-10 out of 1,000 users) or rare side effects (effects that appear in 1-10 out of 10,000 users).

Stop taking the medicine and refer to the doctor immediately if any of the following cases applies to you or your child:

- Severe rash or breathing difficulties and dizziness or swelling mainly of the face and throat (signs of a severe allergic reaction).
- A combination of any of the following symptoms: rash, red skin, blisters on the lips, eyes or mouth, skin peeling, high fever, flu-like symptoms, enlarged lymph nodes (signs of severe skin reaction).
- A marked decrease in urine output (sign of a kidney problem).
- A combination of drowsiness, upper right abdominal pain, yellowing or increased yellowing of the skin or eyes and dark urine (signs of liver problems).
- Difficulty thinking, remembering information or solving problems, reduced alertness or awareness or sleepiness with low energy (signs of a high level of ammonia in the blood, which may be related to liver or renal problems and lead to a change in brain function).
- Bloody vomit and/or black stools.
- Frequent abdominal pains, especially after eating or taking **Defirox.**
- Frequent heartburn.
- Partial loss of vision.
- Severe upper abdominal pain (pancreatitis).

Certain side effects may become serious.
These side effects are uncommon.

Refer to a doctor as soon as possible if:

- You suffer from blurred or cloudy vision
- You suffer from reduced hearing

Additional side effects:

Very common side effects (effects that appear in more than 1 in 10 users):

- Abnormal tests related to kidney function

Common side effects (effects that appear in 1-10 out of 100 users):

- Gastrointestinal disorders such as nausea, vomiting, diarrhea, abdominal pain, swelling, constipation, indigestion
- Rash
- Headache
- Abnormal tests related to liver function
- Itching
- Abnormal urine tests (protein in the urine)

If any of the above effects affects you severely, refer to a doctor.

Uncommon side effects (effects that appear in 1-10 out of 1,000 users):

- Dizziness
- Fever
- Sore throat
- Swelling of arms or legs
- Change in the color of the skin
- Anxiety
- Sleeping disorders
- Tiredness

If any of the above effects affects you severely, refer to a doctor.

Side effects with unknown frequency (effects for which a frequency has not yet been determined):

- A decrease in the number of blood cells involved in blood clotting (thrombocytopenia), in the number of red blood cells (anemia aggravated), in the number of white blood cells (neutropenia) or in the number of all kinds of blood cells (pancytopenia)
- Hair loss
- Kidney stones
- Low urine output
- A tear in the stomach or intestine wall that may cause pain and nausea
- Severe upper abdominal pain (pancreatitis)
- Abnormal level of acid in the blood

If a side effect appears, if one of the side effects worsens, or if you suffer from a side effect which is not mentioned in this leaflet, consult the doctor.
Side effects can be reported to the Ministry of Health via the link "דיווח על תופעות לוואי עקב טיפול תרופתי" that can be found on the home page of the Ministry of Health website (www.health.gov.il) directing to the online form of adverse events reporting or via the following link: https://sideeffects.health.gov.il

5. How to store the medicine

- Avoid poisoning! This medicine and any other medicine must be stored in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (EXP) stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** store below 25°C. Store in the original package to protect from moisture.
- Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:
Lactose monohydrate, crospovidone, microcrystalline cellulose, povidone, magnesium stearate, sodium laurilsulfate, silica colloidal anhydrous, purified water

What the medicine looks like and what the package contains:
Defirox 125 mg: cream-colored tablets, round and flat with beveled edges, embossed with "D" on the top and "125" on the bottom on one side and no embossment on the other side.
Defirox 250 mg: cream-colored tablets, round and flat with beveled edges, embossed with "D" on the top and "250" on the bottom on one side and no embossment on the other side.
Defirox 500 mg: cream-colored tablets, round and flat with beveled edges, embossed with "D" on the top and "500" on the bottom on one side and no embossment on the other side.
Each package contains 28 dispersible tablets.

Manufacturer's name and address:
Pharmascience Inc., Montreal, Canada

Revised in April 2022 according to MOH guidelines.

Drug registration number at the national drug registry of the Ministry of Health:
Defirox 125 mg: 167-88-35880-00
Defirox 250 mg: 167-89-35881-00
Defirox 500 mg: 167-90-35882-00

Defirox 125 250 500 mg PIL PB0622-07

Registration holder:
Dexcel® Ltd.
1 Dexcel St., Or Akiva 3060000, Israel