Package leaflet: Information for the user

CosmoFer®, 50 mg/ml solution for injection and for infusion Iron(III)

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or nurse.

What is in this leaflet

1. What CosmoFer is and what it is used for

CosmoFer contains a combination of iron and dextran (a long chain of sugar molecules).
The type of iron in CosmoFer is the same as that found naturally in the body called 'ferritin'.
This means that you can have CosmoFer by injection in high doses.
CosmoFer is used for low levels of iron (sometimes called 'iron deficiency') if:

- you cannot take iron by mouth, for example you cannot tolerate it
- you have taken iron by mouth and it has not worked
- your doctor decides you need iron very quickly to build up your iron stores.

2. What you need to know before you receive CosmoFer

You must not receive CosmoFer:

- if you are allergic (hypersensitive) to the product or any of the other ingredients of this medicine (listed in section 6)
- if you have experienced serious allergic (hypersensitive) reactions to other injectable iron preparations
- if you have anaemia that is not caused by low levels of iron (deficiency), such as 'haemolytic' anaemia
- if you have too much iron (overload) or a problem in the way your body uses iron
- if you have liver problems such as 'cirrhosis' or 'hepatitis'
- if you have a bacterial or viral infection
- if you have kidney problems, such as acute kidney failure.

Warnings and precautions

Talk to your doctor or nurse before receiving CosmoFer:

- if you have a history of medicine allergy
- if you have systemic lupus erythematosus
- if you have rheumatoid arthritis
- if you have severe asthma, eczema or allergies

Children

CosmoFer is for adults only. Children under 14 should not have this medicine.

Other medicines and CosmoFer

Please tell your doctor or nurse if you are taking or have recently taken any other medicines. This includes medicines obtained without a prescription and herbal medicines. This is because CosmoFer can affect the way some medicines work. Also some other medicines can affect the way CosmoFer works.
In particular tell your doctor or nurse if you are taking any of the following medicines:

- vitamins and minerals
- iron containing medicines you take by mouth. You should not take iron by mouth until at least 5 days after finishing CosmoFer.

Pregnancy and breast-feeding

CosmoFer has not been tested in pregnant women. It is important to tell your doctor if you are pregnant, think you may be pregnant, or are planning to have a baby. If you become pregnant during treatment, you must ask your doctor for advice. Your doctor will decide whether or not you should be given this medicine.
If you are breast-feeding, ask your doctor for advice before you are given CosmoFer.

Driving and using machines

Ask your doctor if you can drive or operate machines after having CosmoFer.

Having blood tests while you are having CosmoFer

CosmoFer may affect the results of some blood tests to measure 'bilirubin' and calcium. Tell your doctor if you have any blood test while you are having CosmoFer.

3. How CosmoFer is given

Your doctor or nurse will administer CosmoFer by injection or infusion into your vein or you may have it injected into your muscle; the CosmoFer will be administered in a structure where immunoallergic events can receive appropriate and prompt treatment.
You will be observed for at least 30 minutes by your doctor or nurse after each administration.
The dose depends on your blood iron (haemoglobin) level and your weight. Your doctor will calculate the dose for you. It is usually given to you two or three times each week.

If you get more CosmoFer than you should

A trained and qualified person will give you CosmoFer. It is unlikely that you will have too much. They will monitor your dose so that an iron build up does not happen in your body. If you think you have been given too much, tell your doctor or nurse straight away.

4. Possible side effects

Like all medicines CosmoFer can cause side effects, although not everybody gets them.
The following side effects may happen with this medicine:
Allergic reactions (affecting less than 1 in 100 people)
If you have an allergic reaction to CosmoFer tell your doctor or nurse straight away so that they can stop it if necessary. The signs of this may include:

- shortness of breath
- nettle rash or hives, flushing, rashes, itching
- nausea and shivering.

More serious allergic reactions, may happen in the first few minutes of having CosmoFer (affecting less than 1 in 10,000 people). The signs may include:

- sudden onset of difficulty breathing (respiratory difficulty)
- serious problems with your heart and circulation (cardiovascular collapse)
- fatalities have been reported.

Also, there have been reports of delayed allergic reactions, that may happen a few hours or up to four days after being given CosmoFer. The signs may include:

- pain in your joints or muscles
- sometimes a high temperature (fever).

Please contact your doctor if you have any of these signs.

Other side effects include

Uncommon (affecting less than 1 in 100 people):

- pain in and around the stomach (abdominal pain), being sick (vomiting)
- blurred vision
- feeling hot
- cramps
- numbness

Rare (affecting less than 1 in 1,000 people):

- loss of consciousness
- altered mental status
- seizure (fits)
- dizziness, restlessness, fatigue
- low blood pressure
- angioedema, a type of severe allergic reaction, signs may include swelling
- uneven (irregular) heart beat, high pulse rate, chest pain
- diarrhoea, sweating and tremor.

Very rare (affecting less than 1 in 10,000 people):

- lower red blood cells than usual (this would show up in some blood tests)
- headache
- unusual feeling on the surface of your body
- raised blood pressure
- temporary deafness
- palpitations
- in pregnancy, the baby's heart rate may slow.

Some other side effects have been reported. People with 'rheumatoid' arthritis may have worsening of joint pain.

Possible side effects after an injection into your vein

If you have CosmoFer into a vein, there may be reactions, such as soreness and swelling (inflammation) around the vein. There have also been reports of inflammation of the vein.

Possible side effects after an injection into your muscle

If you have CosmoFer into a muscle, there may be reactions, such as staining of the skin, bleeding, formation of boils, tissue damage (necrosis or atrophy) and pain.
If any of the side effects gets serious or if you notice any side effects not listed in this leaflet, please tell your doctor or nurse.

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly:
Ireland: via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie
United Kingdom: via Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store CosmoFer

This medicinal product does not require any special storage conditions. Do not freeze. Inspect ampoules visually for sediment and damage before use. Use only those containing sediment-free, homogeneous solution. Hospital staff will make sure that the product is stored and disposed of correctly. CosmoFer should not be used after the expiry date which is stated on the ampoule. Exp. is the abbreviation used for expiry date. The expiry date refers to the last day of that month.
Keep out of the reach and sight of children.

6. Contents of the pack and other information

What CosmoFer contains

- The active substance in CosmoFer is an Iron(III)-hydroxide dextran complex.
  A 2 ml ampoule contains 100 mg iron(III), a 5 ml ampoule contains 250 mg iron(III) and a 10 ml ampoule contains 500 mg iron(III)
- The other ingredients are Water for injections, Sodium hydroxide (pH adjuster) and Hydrochloric acid (pH adjuster).

What CosmoFer looks like and contents of the pack

CosmoFer is contained in clear glass ampoules. The pack sizes are the following:
Packing containing 5 x 2 ml, packing containing 10 x 2 ml, packing containing 10 x 5 ml, packing containing 2 x 10 ml and packing containing 5 x 10 ml.

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and Manufacturer
Pharmacosmos A/S
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The following information is intended for healthcare professionals only:

Monitor carefully patients for signs and symptoms of hypersensitivity reactions during and following each administration of CosmoFer.
CosmoFer should only be administered when staff trained to evaluate and manage anaphylactic reactions is immediately available, in an environment where full resuscitation facilities can be assured. The patient should be observed for adverse effects for at least 30 minutes following each CosmoFer injection (see section 4.4).

Administration:
CosmoFer solution for infusion and injection can be administered by an intravenous drip infusion or by a slow intravenous injection of which the intravenous drip infusion is the preferred route of administration, as this may help to reduce the risk of hypotensive episodes. However, CosmoFer may also be administered as undiluted solution intramuscularly.

Adults and elderly
The total cumulative dose of CosmoFer is determined by haemoglobin level and body weight. The dose and dosage schedule for CosmoFer must be individually estimated for each patient based on a calculation of the total iron deficit.

Children (under 14 years)
CosmoFer should not be used for children. There is no documentation for efficacy and safety.

Dosage:
The normal recommended dosage schedule is 100-200 mg iron corresponding to 2-4 ml, two or three times a week depending on the haemoglobin level. However, if clinical circumstances require rapid delivery of iron to the body iron stores CosmoFer may be administered as a total dose infusion up to a total replacement dose corresponding to 20 mg iron/kg body weight.
The CosmoFer injection should not be administered concomitantly with oral iron preparations as the absorption of oral iron will be reduced (please refer to section 4.5).

Intravenous drip infusion:
CosmoFer must be diluted only in 0.9% sodium chloride solution (normal saline) or in 5% glucose solution. CosmoFer in a dose of 100-200 mg iron (2-4ml) may be diluted in 100 ml. On each occasion the first 25 mg of iron should be infused over a period of 15 minutes. If no adverse reactions occur during this time the remaining portion of the infusion should be given at an infusion rate of not more than 100 ml in 30 minutes.

Intravenous injection:
CosmoFer may be administered in a dose of 100 – 200 mg iron (2-4 ml) by slow intravenous injection (0.2 ml/min) preferably diluted in 10 – 20 ml 0.9% sodium chloride or 5% glucose solution. On each occasion before administering a slow intravenous injection, 25 mg of iron should be injected slowly over a period of 1 to 2 minutes. If no adverse reactions occur within 15 minutes, the remaining portion of the injection may be given.

Total dose infusion:
Immediately before administration the total amount of CosmoFer required, determined from the dosage table or by calculation, is added aseptically to the required volume, usually 500 ml of sterile normal sodium chloride or 5% glucose solutions. The total amount of CosmoFer, up to 20 mg/kg bodyweight, is infused intravenously over 4 – 6 hours. The first 25 mg of iron should be infused over a period of 15 minutes. The patient must be kept under close medical observation during this period. If no adverse reactions occur during this time, then the remaining portion of the infusion should be given. The rate of infusion may be increased progressively to 45 – 60 drops per minute. Patients should be observed carefully during the infusion and for at least 30 minutes after completion.
Total Dose Infusion (TDI) has been associated with an increased incidence of adverse reactions, in particular delayed hypersensitivity–like reactions. The intravenous administration of CosmoFer by the total dose infusion method should be restricted to hospital use only.

Injection into dialyser:
CosmoFer may be administered during a haemodialysis session directly into the venous limb of the dialyser under the same procedures as outlined for intravenous administration.

Intramuscular injection:
The total amount of CosmoFer required is determined either from the dosage table or by calculation. It is administered as a series of undiluted injections of up to 100 mg iron (2.0 ml) each determined by the patient's body weight. If the patient is moderately active, injections may be given daily into alternate buttocks. In inactive or bedridden patients, the frequency of injections should be reduced to once or twice weekly.
CosmoFer must be given by deep intramuscular injection to minimise the risk of subcutaneous staining. It should be injected only into the muscle mass of the upper outer quadrant of the buttock - never into the arm or other exposed areas. A 20 - 21 gauge needle at least 50 mm long should be used for normal adults. For obese patients the length should be 80 - 100 mm whereas for small adults a shorter and smaller needle (23 gauge x 32 mm) is used. The patient should be lying in the lateral position with the injection site uppermost, or standing bearing their weight on the leg opposite the injection site. To avoid injection or leakage into the subcutaneous tissue, a Z-track technique (displacement of the skin laterally prior to injection) is recommended.
CosmoFer is injected slowly and smoothly. It is important to wait for a few seconds before withdrawing the needle to allow the muscle mass to accommodate the injection volume.
To minimise leakage up the injection track, the patient should be encouraged not to rub the injection site.

Calculation of dose:

a) Iron replacement in patients with iron deficiency anaemia:
Factors contributing to the formula are shown below. The required dose has to be individually adapted according to the total iron deficit calculated by the following formula – haemoglobin in g/l or mmol/l.

Total dose (mg Fe) – Hb in g/l:

(Body weight (kg) x (target Hb - actual Hb) (g/l) x 0.24) + mg iron for iron stores

The factor 0.24 is derived from the following assumptions:
a) Blood volume 70 ml/kg of body weight ≈ 7% of body weight
b) Iron content of haemoglobin 0.34%
Factor 0.24 = 0.0034 x 0.07 x 1000 (conversion from g to mg).

Total dose (mg Fe) – Hb in mmol/l:

Body weight in kg x (target Hb in mmol/l – actual Hb in mmol/l) x 3.84 + mg iron for iron stores.

The factor 3.84 is derived from the following assumptions:
a) Blood volume 70 ml/kg of body weight ≈ 7% body weight
b) Iron content of haemoglobin 0.34%
c) Factor for conversion from haemoglobin g/l to mmol/l is 0.06205
Factor 3.84 = 0.0034 x 0.07 x 1000 / 0.06205

b) Iron replacement for blood loss:
Iron therapy in patients with blood loss should be directed toward replacement of an amount of iron equivalent to the amount of iron represented in the blood loss. The table and formula described are not applicable for simple iron replacement values. Quantitative estimates of the individual’s periodic blood loss and hematocrit during the bleeding episode provide a convenient method of calculation of the required iron dose.
The required CosmoFer dose to compensate the iron deficit is calculated according to the following formulas:

- If the volume of blood lost is known: The administration of 200 mg i.v. iron (4 ml CosmoFer) results in an increase of haemoglobin which is equivalent to 1 unit blood (= 400 ml with 150 g/l Hb content or 9.3 mmol Hb/l – equivalent to 0.34% of 0.4 x 150 or 204 mg iron).
  Iron to be replaced [mg] = number of blood units lost x 200.
  Millilitres of CosmoFer needed = number of blood units lost x 4.

- If the Hb level is reduced: Use the previous formula considering that the depot iron does not need to be restored.