Source : MEDICINES ORG UK

**Monofer® 100 mg/ml solution for injection/infusion**

ferric derisomaltose

▼ 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 you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

**What is in this leaflet**

1. What Monofer is and what it is used for
2. What you need to know before you receive Monofer
3. How to use Monofer
4. Possible side effects
5. How to store Monofer
6. Contents of the pack and other information.

## 1. What Monofer is and what it is used for

Monofer contains a combination of iron and derisomaltose (a chain of sugar molecules). The type of iron in Monofer is the same as that found naturally in the body called 'ferritin'. This means that you can have Monofer by injection in high doses.

Monofer is used for low levels of iron (sometimes called 'iron deficiency' and 'iron deficiency anaemia') if:

- Oral iron does not work or you cannot tolerate it
- Your doctor decides you need iron very quickly to build up your iron stores

## 2. What you need to know before you receive Monofer

**You must not receive Monofer if you:**

- are allergic (hypersensitive) to the product or any of the other ingredients of this medicine (listed in section 6)
- have experienced serious allergic (hypersensitive) reactions to other injectable iron preparations.
- have anaemia **not** caused by iron deficiency
- have too much iron (overload) or a problem in the way your body uses iron
- have liver problems such as 'cirrhosis'

**Warnings and precautions**

Talk to your doctor or nurse before receiving Monofer if you:

- have a history of medicine allergy
- have systemic lupus erythematosus
- have rheumatoid arthritis
- have severe asthma, eczema or other allergies
- have an ongoing bacterial infection in your blood
- have reduced liver function

Incorrect administration of Monofer may cause leakage of the product at the injection site, which may lead to irritation of the skin and potentially long lasting brown discolouration at the site of injection. The administration must be stopped immediately when this occurs.

**Children and adolescents**
Monofer is for adults only. Children and adolescents should not have this medicine.

**Other medicines and Monofer**
Tell your doctor if you are using, have recently used or might use any other medicines.
Monofer given together with oral iron preparations can reduce the absorption of oral iron.

**Pregnancy and breast-feeding**
Monofer 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 Monofer. It is unlikely that Monofer represents a risk to the nursing child.

**Driving and using machines**
Ask your doctor if you can drive or operate machines after having Monofer.

## 3. How Monofer is administered

Before administration, your doctor will perform a blood test to determine the dose of Monofer you require.

Your doctor or nurse will administer Monofer by injection or infusion into your vein.
- Monofer may be administered as an intravenous injection up to 500 mg up to three times a week.
- Monofer may be administered during a dialysis session.
- Monofer may be administered as an intravenous infusion in a dose up to 20 mg iron/kg body weight or as weekly infusions until the total dose has been administered.

Monofer 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.

**If you receive more Monofer than you should**
A qualified health care professional will give you Monofer. It is unlikely that you will have too much. They will monitor your dose and blood to avoid iron building up in your body.

## 4. Possible side effects

Like all medicines, Monofer can cause side effects, although not everybody gets them.

**Allergic reactions**

Severe allergic reactions may occur, however they are in general rare.
Tell your doctor or nurse immediately if you experience any of the following signs and symptoms that may indicate a serious allergic reaction: swollen face, tongue or pharynx, difficulty to swallow, hives and difficulties to breath, and chest pain which can be a sign of a potentially serious allergic reaction called Kounis syndrome.

**Common** (may affect up to 1 in 10 people):

- Nausea
- Skin reactions at or near injection site including redness of the skin, swelling, burning, pain, bruising, discolouration, leakage to the tissue around the site of infusion, irritation
- Rash

**Uncommon** (may affect up to 1 in 100 people):
- Hypersensitivity reactions with potential shortness of breath and bronchospasm
- Headache
- Numbness
- Distortion of the sense of taste
- Blurred vision
- Loss of consciousness
- Dizziness
- Fatigue
- Increased heart rate
- Low or high blood pressure
- Chest pain, back pain, pain in your muscles or joints, muscle spasms
- Stomach pain, vomiting, impaired digestion, constipation, diarrhoea
- Itching, hives, skin inflammation
- Flushing, sweating, fever, feeling cold, shivering
- Low level of phosphate in the blood
- Infection
- Liver enzymes increased
- Local inflammation of a vein
- Skin exfoliation

**Rare** (may affect up to 1 in 1,000 people):
Irregular heart beat
- Hoarseness
- Seizure
- Tremor
- Altered mental status
- Malaise

Flu-like illness (may affect up to 1 in 1,000 people) may occur a few hours to several days after injection and is typically characterised by symptoms such as high temperature, and aches and pains in the muscles and joints.

**Not known**
- Skin discoloration at other areas of the body than the injection site

**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 via the Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store Monofer

Keep this medicine out of the sight and reach of children.

Do not use Monofer after the expiry date which is stated on the ampoule or vial label. EXP is the abbreviation used for expiry date. The expiry date refers to the last day of that month.

Inspect vials/ampoules visually for sediment and damage before use. Use only those containing sediment-free, homogeneous solution.

The reconstituted solution for injection should be visually inspected prior to use. Use only clear solutions without sediment.

This medicinal product does not require any special storage conditions. Hospital staff will make sure that the product is stored and disposed of correctly.

## 6. Contents of the pack and other information

### What Monofer contains

The active substance is iron (as ferric derisomaltose, an iron carbohydrate compound). The concentration of iron present in the product is 100 mg per millilitre. The other ingredients are sodium hydroxide (for pH adjustment), hydrochloric acid (for pH adjustment), and water for injection.

### What Monofer looks like and contents of the pack

Monofer is a dark brown, non-transparent solution for injection/infusion.

Monofer is supplied in glass ampoules or glass vials containing:
- 1 ml solution corresponding to 100 mg iron as ferric derisomaltose
- 2 ml solution corresponding to 200 mg iron as ferric derisomaltose
- 5 ml solution corresponding to 500 mg iron as ferric derisomaltose
- 10 ml solution corresponding to 1,000 mg iron as ferric derisomaltose

The pack sizes are the following:
Ampoule pack sizes: 5 x 1 ml, 10 x 1 ml, 5 x 2 ml, 10 x 2 ml, 2 x 5 ml, 5 x 5 ml, 2 x 10 ml, 5 x 10 ml
Vial pack sizes: 1 x 1 ml, 5 x 1 ml, 10 x 1 ml, 5 x 2 ml, 10 x 2 ml, 1 x 5 ml, 2 x 5 ml, 5 x 5 ml, 1 x 10 ml, 2 x 10 ml, 5 x 10 ml

Not all pack sizes may be marketed.

### Marketing Authorisation Holder and Manufacturer

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**This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:**

Austria, Bulgaria, Croatia, Denmark, Finland, Estonia, Germany, Iceland, Latvia, Lithuania, Netherlands, Norway, Romania, Slovenia, Sweden, United Kingdom (Northern Ireland): Monofer®
Belgium, Italy: Monoferric®
Ireland, Luxemburg, Poland: Monover®
Portugal: Monofar®

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The following information is intended for medical or healthcare professionals only:

Monitor carefully patients for signs and symptoms of hypersensitivity reactions during and following each administration of Monofer. Monofer 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 Monofer injection.

Each IV iron administration is associated with a risk of a hypersensitivity reaction. Thus, to minimise risk the number of single IV iron administrations should be kept to a minimum.

Posology

The posology of Monofer follows a stepwise approach: [1] determination of the individual iron need and [2] calculation and administration of the iron dose(s). The steps can be repeated after [3] post-iron repletion assessments.

*Step 1: Determination of the iron need:*

The iron need can be determined using either the Simplified Table (i) or the Ganzoni formula below (ii).

The iron need is expressed in mg elemental iron.

i. Simplified Table:

Table 1. Simplified Table

| Hb (g/dl) | Hb (mmol/l) | Patients with bodyweight <50 kg | Patients with bodyweight 50 kg to <70 kg | Patients with bodyweight ≥70 kg |
|---|---|---|---|---|
| ≥10 | ≥6.2 | 500 mg | 1000 mg | 1500 mg |
| <10 | <6.2 | 500 mg | 1500 mg | 2000 mg |

ii. Ganzoni formula:

Table 2. Ganzoni formula

$$\underset{[\text{mg iron}]}{\text{Iron need}} = \underset{[\text{kg}]}{\text{Body weight}^{(A)}} \times (\underset{[\text{g/dl}]}{\text{Target Hb}^{(D)}} - \text{Actual Hb})^{(B)} \times 2.4 + \underset{[\text{mg iron}]}{\text{Iron for iron stores}^{(C)}}$$

(A) It is recommended to use the patient's ideal body weight for obese patients or pre-pregnancy weight for pregnant women. For all other patients use actual body weight.
Ideal body weight may be calculated in a number of ways e.g. by calculating weight at BMI 25 i.e. ideal body weight = 25 * (height in m)$^2$

(B) To convert Hb [mM] to Hb [g/dl] you should multiply Hb [mM] by factor 1.61145

(C) For a person with a body weight above 35 kg, the iron stores are 500 mg or above. Iron stores of 500 mg are at the lower limit normal for small women. Some guidelines suggest using 10-15 mg iron /kg body weight.

(D) Default Hb target is 15 g/dl in the Ganzoni formula. In special cases such as pregnancy consider using a lower haemoglobin target.

iii. Fixed iron need:

A fixed dose of 1000 mg is given and the patient is re-evaluated for further iron need according to "Step 3: Post-iron repletion assessments". For patients weighing less than 50 kg use the Simplified table or Ganzoni formula for iron need calculation.

*Step 2: Calculation and administration of the maximum individual iron dose(s):*

Based on the iron need determined above the appropriate dose(s) of Monofer should be administered taking into consideration the following:

The total dose per week should not exceed 20 mg iron/kg bodyweight.
A single Monofer infusion should not exceed 20 mg iron/kg body weight.
A single Monofer bolus injection should not exceed 500 mg iron.

*Step 3: Post-iron repletion assessments:*

Re-assessment including blood tests should be performed by the clinician based on the individual patient's condition. To evaluate the effect of IV iron treatment the Hb level should be re-assessed no earlier than 4 weeks post final Monofer administration to allow adequate time for erythropoiesis and iron utilisation. In the event the patient requires further iron repletion, the iron need should be recalculated.

*Children and adolescents:*

Monofer is not recommended for use in children and adolescents < 18 years due to insufficient data on safety and efficacy.

Method of administration:

Monofer must be administered by the intravenous route either by injection or by infusion.

Monofer should not be administered concomitantly with oral iron preparations, since the absorption of oral iron might be decreased.

*Intravenous bolus injection:*

Monofer may be administered as an intravenous bolus injection up to 500 mg up to three times a week at an administration rate of up to 250 mg iron/minute. It may be administered undiluted or diluted in maximum 20 ml sterile 0.9% sodium chloride.

Table 3: Administration rates for intravenous bolus injection

| Volume of Monofer | Equivalent iron dose | Administration rate/ Minimum administration time | Frequency |
|---|---|---|---|
| ≤5 ml | ≤500 mg | 250 mg iron/minute | 1-3 times a week |

*Intravenous infusion:*

The iron need required may be administered in a single Monofer infusion up to 20 mg iron/kg body weight or as weekly infusions until the cumulative iron need has been administered.

If the iron need exceeds 20 mg iron/kg body weight, the dose must be split in two administrations with an interval of at least one week. It is recommended whenever possible to give 20 mg iron/kg body weight in the first administration. Dependent on clinical judgement the second administration could await follow-up laboratory tests.

Table 4: Administration rates for intravenous infusion

| Iron dose | Minimum administration time |
|---|---|
| ≤1000 mg | More than 15 minutes |
| >1000 mg | 30 minutes or more |

Monofer should be infused undiluted or diluted in sterile 0.9% sodium chloride.
For stability reasons, Monofer should not be diluted to concentrations less than 1 mg iron/ml (not including the volume of the ferric derisomaltose solution) and never diluted in more than 500 ml.

*Injection into dialyser:*

Monofer may be administered during a haemodialysis session directly into the venous limb of the dialyser under the same procedures as outlined for intravenous bolus injection.

Please refer to the SPC for further information on Monofer.