Package leaflet: Information for the patient

Ziremilon 200 mg/ml emulsion for infusion

soya-bean oil/ medium chain triglycerides/olive oil/fish oil

Read all of this leaflet carefully before you are given 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 Ziremilon is and what it is used for

Ziremilon contains four different lipids (fats): soya-bean oil, medium chain triglycerides, olive oil and fish oil which is rich in omega-3 fatty acids. The liquid is a mixture of fats and water which is called a 'lipid emulsion'.
- It works by providing energy and fatty acids for your body
- It is put into your blood by a drip or an infusion pump
- A health care professional will give you Ziremilonwhen other forms of feeding are not good enough or have not worked.

2. What you need to know before you are given Ziremilon

You should not be given Ziremilon:
- if you are allergic to soya-bean oil, medium-chain tryglycerides, olive oil, fish oil or any of the other ingredients of this medicine (listed in section 6).
- If you are allergic to any other products containing fish, egg, soy or peanut.
- If you have too much fat in the blood (called 'severe hyperlipemia').
- If you have serious kidney or liver problems.
- If you have severe blood clotting problems (called 'coagulation disorders').
- If you are in acute shock.
- If you have fluid in the lungs (called 'pulmonary oedema') , too much body fluid (called 'hyperhydration') or have heart failure (due to too much body fluid).
- If you are in an unstable condition, for example shortly after serious injury, heart attack, stroke, blood clot (thrombosis), metabolic acidosis (metabolic disturbance which results in high acid levels in the blood), or untreated diabetes, blood poisoning and dehydration.

Warnings and precautions
Talk to your doctor or nurse before you are given this medicine if you have a problem with high levels of lipids in the blood because your body cannot use fat properly (called 'impaired lipid metabolism').

When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed. Exposure of Ziremilon to ambient light, especially after admixtures with vitamins, generates peroxides and other degradation products that can be reduced by protection from light exposure.

Allergic reactions
If you have an allergic reaction while receiving Ziremilon, it needs to be stopped straight away. Tell the doctor or nurse straight away if you get any of the following while you are having the infusion:
- fever (high temperature)
- shivering
- rash
- difficulty breathing

Children
Talk to your doctor or nurse if this medicine is being given to your newborn child and they have:
- too much of a substance called "bilirubin" in their blood (hyperbilirubinemia)
- a high pressure in their lungs (pulmonary hypertension)

If your newborn child receives Ziremilon for a long time the doctor will take blood tests to see how it is working.

Other medicines and Ziremilon
Tell your doctor if you are taking, have recently taken or might take any other medicines.
In particular, tell your doctor if you are taking or have recently taken medicines used to stop blood clotting, such as warfarin and heparin.
- Ziremilon naturally contains vitamin K_1, which can affect warfarin. However, the vitamin K_1 content in Ziremilon is so low that such problems are unlikely.
- Heparin given in clinical doses may at first cause higher levels of fatty acids in the blood due to liberation of fatty acids from the tissues into the bloodstream and then less fatty acids are removed from your blood (decreased triglyceride clearance).

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before you are given this medicine.
It is not known whether it is safe to receive Ziremilon while you are pregnant or breast-feeding. If you need to have direct feeding into your vein during pregnancy or breast-feeding, your doctor will give you Ziremilon only after careful consideration.

Driving and using machines
Not relevant as the medicine is given at the hospital.

Ziremilon contains sodium
This medicine contains 50.2 mg sodium (main component of cooking/table salt) per 1000 ml. This is equivalent to 2.51% of the recommended maximum daily dietary intake of sodium for an adult.

3. How Ziremilon is given

Ziremilon is put into your blood by a drip or an infusion pump. Your doctor will decide your dose depending on your body weight and your ability to utilise the amount of fat infused.

When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed (see section 2).

For medical and health care professionals, please see "Method of administration" at the end of this leaflet for more details regarding dosage and administration.

If you are given more Ziremilon than you should
In case the dose Ziremilon given to you is too high, there is a risk of taking in more fat than your body can handle. This is called 'fat overload syndrome'. See section 4, Possible side effects, for more information.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

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

Fat overload syndrome
This might happen when your body has problems using fat, because of having too much Ziremilon. It may also happen because of a sudden change in your condition (such as kidney problems or infection). The fat overload syndrome is characterized by high levels of fat in the blood (hyperlipidemia), fever, more fat in your tissues than normal (fat infiltration) and disorders in various organs of the body and coma. All symptoms will usually disappear when you stop receiving the infusion.

Common (may affect up to 1 in 10 people)
- slight rise in body temperature

Uncommon (may affect up to 1 in 100 people)
- shivering
- loss of appetite
- feeling sick (nausea)
- being sick (vomiting)

Rare (may affect up to 1 in 1,000 people)
- allergic reactions (such as high temperature, swelling, lowering of blood pressure, skin rash, redness, headache)
- feelings of hot and cold
- paleness
- bluish discolouration of skin and mucous membranes (due to reduced oxygen content in the blood)
- pains in neck, back, bones, chest and lower back
- raised or lowered blood pressure
- shortness of breath

Very rare (may affect up to 1 in 10,000 people)
- prolonged and convulsive erection in men

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 HPRA Pharmacovigilance, Website: www. hpra.ie.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Ziremilon

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

Do not use this medicine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special temperature storage conditions. Do not freeze.
Store in the overpouch.

Do not use Ziremilon if you notice that the package is damaged. Use only if the solution is white and homogenous. For single use only. Any unused product should be thrown away. Do not re-use it.

When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed (see section 2).

6. Contents of the pack and other information

What Ziremilon contains

- The active substances are:

Refined soya-bean oil	60 mg/ml
Medium-chain triglycerides	60 mg/ml
Refined olive oil	50 mg/ml
Fish oil, rich in omega-3 fatty acids	30 mg/ml

- The other ingredients are: glycerol, egg phospholipids, all-rac-α-tocopherol (vitamin E), water for injections, sodium hydroxide (pH adjustment), sodium oleate

What Ziremilon looks like and contents of the pack
Ziremilon is a white, homogenous emulsion and is available in plastic bags.

Pack sizes
1 bag x 100 ml, 10 bags x 100 ml
1 bag x 250 ml, 10 bags x 250 ml
1 bag x 500 ml, 12 bags x 500 ml

Not all package sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorization Holder
Noridem Enterprises Ltd.
Evagorou & Makariou,
Mitsi Building 3, Office 115,
Nicosia 1065, Cyprus

Manufacturer
DEMO S.A. PHARMACEUTICAL INDUSTRY
21st Km National Road Athens–Lamia,
14568 Krioneri, Attiki, Greece
T: +30 210 8161802, **F:** +30 2108161587

This medicine is authorised in the Member States of the European Economic Area under the following names:

Sweden	Maxivalen
Austria	Ziremilon 200 mg/ml Emulsion zur Infusion
Belgium	Ziremilon 200 mg/ml émulsion pour perfusion/ emulsie voor infusie/ Emulsion zur Infusion
Czech Republic	Ziremilon
Denmark	Maxivalen
Finland	Maxivalen
France	ZIREMILON 200 mg/ml emulsion pour perfusion
Germany	Ziremilon 200 mg/ml Emulsion zur Infusion
Greece	Maxivalen
Ireland	Ziremilon 200 mg/ml emulsion for infusion
Hungary	Ziremilon 200 mg/ml emulziós infúzió
Italy	Ziremilon
Norway	Maxivalen

Poland	Maxivalen
Romania	Ziremilon 200 mg/ml emulsie perfuzabilă
Spain	Ziremilon 200 mg/ml emulsión para perfusión EFG
Slovakia	Ziremilon

This leaflet was last revised in month YYYY.

The following information is intended for healthcare professionals only:

Warnings and precautions
The concentration of triglycerides in serum should not exceed 3 mmol/l during infusion. An overdose may lead to fat overload syndrome. Special caution should be taken in patients with a marked risk for hyperlipidema (e.g. patients with high lipid dosage, severe sepsis and extremely low birth weight infants).

Administration of medium-chain fatty acids alone can result in metabolic acidosis. This risk is to a great extent eliminated by the simultaneous infusion of the long chain fatty acids included in Ziremilon. Concomitant administration of carbohydrates will further eliminate this risk.
Hence, simultaneous infusion of carbohydrate or a carbohydrate-containing amino acid solution is recommended. Laboratory test generally associated with monitoring of intravenous nutrition should be checked regularly. These include blood glucose levels, liver functions tests, acid base metabolism, fluid balance, full blood count and electrolytes.

This medicinal product contains soya-bean oil, fish oil and egg phospholipids, which may rarely cause allergic reactions. Cross allergic reaction has been observed between soya-bean and peanut.

Any sign or symptom of anaphylactic reaction (such as fever, shivering, rash or dyspnoea) should lead to immediate interruption of the infusion.

Lipid emulsions should be given with caution to neonates and premature neonates with hyperbilirubinemia and cases with pulmonary hypertension. In neonates, particularly premature neonates on long term parenteral nutrition, blood platelet counts, liver function tests and serum triglycerides should be monitored.

Posology and method of administration

Posology

The patient's ability to eliminate the fat infused, should govern the dose and infusion rate.

Adults
The standard dose is 1.0-2.0 g fat/kg body weight (b.w.)/day, corresponding to 5-10 ml/kg b.w./day. The recommended infusion rate is 0.125 g fat/kg b.w./hour, corresponding to 0.63 ml Ziremilon/kg b.w./hour, and should not exceed 0.15 g fat/kg b.w./hour, corresponding to 0.75 ml Ziremilon/kg b.w./hour.

Paediatric population

Neonates and infants
The initial dose should be 0.5-1.0 g fat/kg b.w./day followed by a successive increase by 0.5-1.0 g fat/kg b.w./day up to 3.0 g fat/kg b.w./day.
It is recommended not to exceed a daily dose of 3 g fat/kg b.w./d, corresponding to 15 ml Ziremilon /kg b.w./day.

The rate of infusion should not exceed 0.125 g fat/kg b.w./hour.
In premature and low birthweight neonates, Ziremilon should be infused continuously over about 24 hours.

Children
It is recommended not to exceed a daily dose of 3 g fat/kg b.w./d, corresponding to 15 ml Ziremilon /kg b.w./day.

The daily dose should be increased gradually during the first week of administration. The infusion rate should not exceed 0.15 g fat/kg b.w./hour.

Method of administration
Intravenous infusion into a peripheral or central vein.
When used in neonates and children below 2 years, the solution (in bags and administration sets) should be protected from light exposure until administration is completed.

Incompatibilities
This medicinal product must not be mixed with other medicinal products except those mentioned in section Instructions on handling.

Instructions on handling
Use only if the emulsion is homogeneous.
Inspect the emulsion visually for phase separation prior to administration. Ensure that the final emulsion for infusion does not show any evidence of phase separation.

When used in neonates and children below 2 years, protect from light exposure, until administration is completed. Exposure of Ziremilon to ambient light, especially after admixture with vitamins, generates peroxides and other degradation products that can be reduced by protection from light exposure.

For single use only. Any unused emulsion should be discarded.

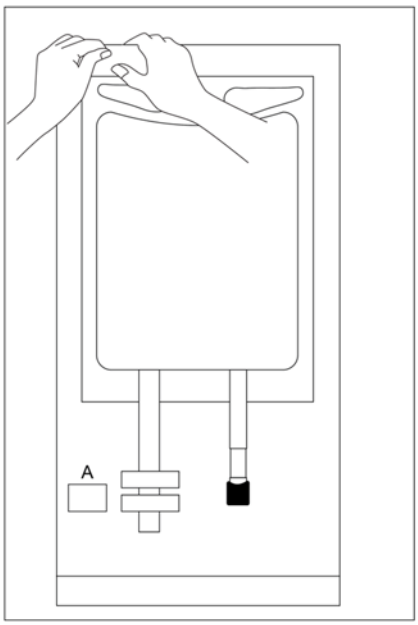
Additives
Ziremilon may be aseptically admixed with amino acid, glucose, and electrolyte solutions.

Compatibility for different additives and the storage time of the different admixtures will be available upon request from the marketing authorisation holder.

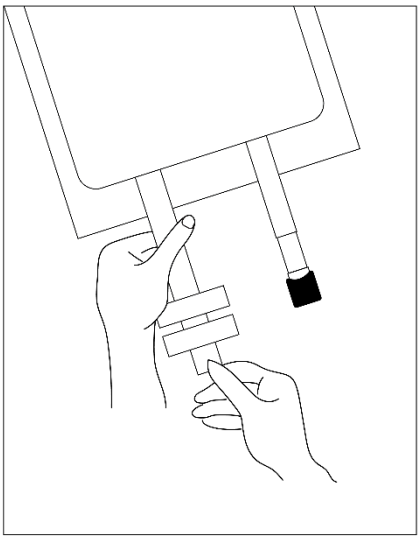
Additions should be made aseptically.

Storage after mixing
From a microbiological point of view if additions are made to Ziremilon, the admixtures should be used immediately. If admixtures are not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless additions have taken place in controlled and validated aseptic conditions.

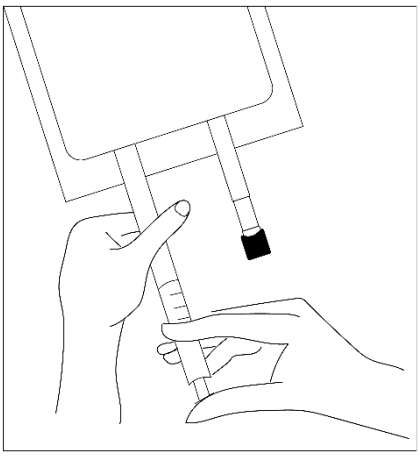
Instructions for use



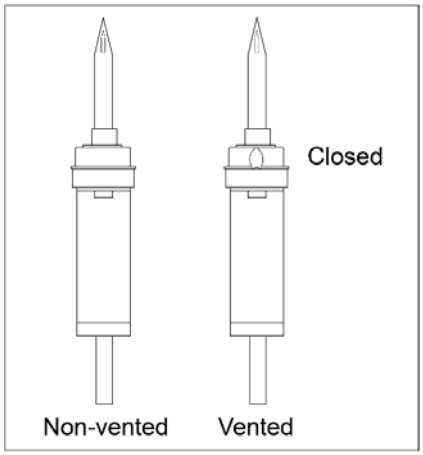
1. Remove the overwrap by tearing at the notch and pulling down along the container. The oxygen absorber (A) should be disposed.



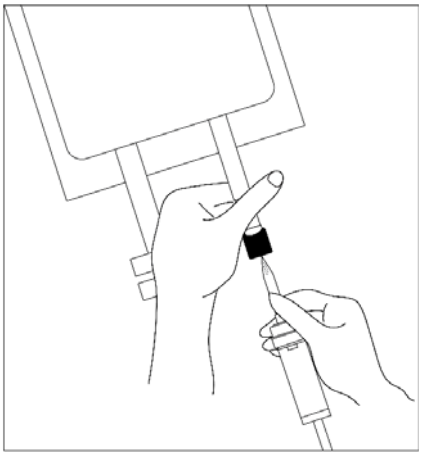
2. If no additives are to be used go to 4. If additives are to be used, break off the tamper-evident arrow flag from the white additive port.



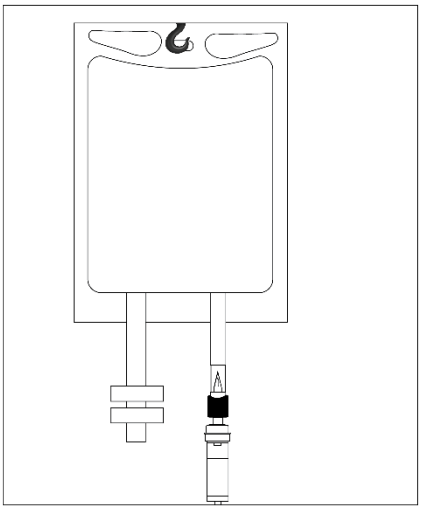
3. Take the syringe containing the additives. Hold the base of the additive port. Insert the needle horizontally through the centre of the septum of the additive port and inject the additives (with known compatibility). Use syringes with needles of 18 – 23 gauge and length of max. 40 mm



4. Use a non-vented infusion set or close the air vent on a vented set. Follow the instructions for use for the infusion set. Use a spike with diameter as specified in ISO 8536-4, 5.6 +/- 0.1 mm.



5. Hold the base of the infusion port. Insert the spike through the infusion port, by rotating your wrist slightly until the spike is inserted.



6. Hang the bag in the hanger cut and start infusion.