PACKAGE LEAFLET: INFORMATION FOR THE USER

Primacor 1mg/ml Solution for Injection

Milrinone

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Is this leaflet hard to see or read? Phone 0800 035 2525 for help

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

What is in this leaflet

1. What Primacor is and what it is used for

The name of your medicine is Primacor 1mg/ml Solution for Injection (called Primacor in this leaflet). Primacor contains a medicine called milrinone. This belongs to a group of medicines called phosphodiesterase inhibitors. It works by making your heart muscle contract more strongly and your blood vessels become wider. This means blood can flow more easily making your heart pump blood more successfully.

Primacor can be used for:

- Short-term treatment of severe congestive heart failure (where the heart cannot pump enough blood to the rest of the body) when other medicines have not worked.
- Treatment after a heart operation for when your heart is having difficulty pumping blood around your body.

Primacor can be used in children for:

- Short term treatment (up to 35 hours) of severe congestive heart failure (where the heart cannot pump enough blood to the rest of the body) when other medicines have not worked.
- Short term treatment (up to 35 hours) of acute heart failure after a heart operation i.e. when your heart is having difficulty pumping blood around your body.

2. What you need to know before you use Primacor

Do not use Primacor if:

× You are allergic (hypersensitive) to milrinone or any of the other ingredients of Primacor (listed in section 6)
Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue.

× You have lost body fluids and are severely dehydrated.

Do not use this medicine if any of the above apply to you. If you are not sure, talk to your doctor, nurse or pharmacist before using Primacor.

Warnings and precautions

Talk to your doctor, nurse or pharmacist before using Primacor if:

- You are having or have just had a heart attack.
- You have severe heart valve problems such as narrowing, thickening or blockage of your heart valves.
- You have uneven or uncontrolled fast heartbeats. You may also be experiencing pounding in your chest, light-headedness, fainting and shortness of breath.
- You have low blood pressure which may make you feel dizzy, light-headed or faint.
- You have previously taken water tablets (diuretics) which caused you to have heart problems.
- You have low levels of potassium in your blood. Your doctor may do blood tests to check this.
- You have kidney problems.

If you are not sure if any of the above apply to you, talk to your doctor, nurse or pharmacist before using Primacor.

Children and adolescents

The following should be considered in addition to warnings and precautions described for adults:

Before giving Primacor infusion, your doctor will check a lot of parameters such as heart rhythm and blood pressure. He/she will order blood tests as well.

The infusion will not start if your child's heart rhythm and blood pressure is not stable.

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The following information is intended for healthcare professionals only:

Practical information on preparation and administration of Primacor 1mg/ml Solution for Injection (*see also Section 3*).

Posology and method of administration

For intravenous administration.

Adults

Primacor Injection should be given as a loading dose of 50 µg/kg administered over a period of 10 minutes usually followed by a continuous infusion at a dosage titrated between 0.375 µg/kg/min and 0.75 µg/kg/min according to haemodynamic and clinical response, but should not exceed 1.13 mg/kg/day total dose.

The following provides a guide to maintenance infusion delivery rate based upon a solution containing milrinone 200 µg/ml prepared by adding 40 ml diluent per 10 ml ampoule (400 ml diluent per 100 ml Primacor Injection). 0.45% saline, 0.9% saline or 5% glucose may be used as diluents.

Primacor Injection Dose (µg/kg/min)	Infusion Delivery Rate (ml/kg/hr)
0.375	0.11
0.400	0.12
0.500	0.15
0.600	0.18
0.700	0.21
0.750	0.22

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Please tell your doctor if:

- Your child has kidney problems.
- Your child is a preterm infant or has a low birth weight.
- Your child has a certain heart problem named Patent Ductus Arteriosus – a connection between 2 major blood vessels (aorta and pulmonary artery) which persists though it should be closed.

In these cases, your doctor will decide if your child will be treated with Primacor.

Other medicines and Primacor

Tell your doctor, nurse or pharmacist if you are taking or have recently taken any other medicines. This includes medicines you buy without a prescription, including herbal medicines. This is because Primacor can affect the way some other medicines work. Also some medicines can affect the way Primacor works.

In particular, tell your doctor, nurse or pharmacist if you are taking:

- Digoxin – used for heart problems.
- Water tablets (diuretics).
- Medicines used to treat high blood pressure or angina (chest pain) such as amlodipine, nifedipine or felodipine.

Pregnancy and breast-feeding

Talk to your doctor, nurse or pharmacist before having this medicine if you are pregnant, might become pregnant, or think you may be pregnant.

If you are breast-feeding or planning to breast-feed, talk to your doctor or pharmacist before taking any medicine.

3. How to use Primacor

Primacor will normally be given by your doctor or nurse. This is because it needs to be given as an injection.

Using this medicine

- This medicine is usually given in a 'drip' after being diluted using either a sugar or salt solution.
- If you feel the effect of your medicine is too weak or too strong, tell your doctor or nurse.

How much will be given to you

- Your doctor will decide how much medicine you should have based on your body weight.
- If you have problems with your kidneys, you may be given a lower dose.

Adults (including the elderly)

- Your doctor should give you a first dose of 50 micrograms for every kilogram of your weight over 10 minutes.
- This is then followed by a smaller dose between 0.375 and 0.75 micrograms for every kilogram of body weight per minute as needed.
- The medicine is usually given for 2-3 days, but it may be given for up to 5 days.
- If you are using this medicine after a heart operation, it will usually only be given for up to 12 hours.

Children and adolescents

- Your doctor should give your child a first dose ranging between 50 and 75 micrograms for every kilogram of his/her weight, over a period of 30-60 minutes.
- This is then followed by a dose ranging from 0.25-0.75 micrograms for every kilogram of his/her weight per minute according to your child's response to the treatment and occurrence of side effects. Primacor can be given for up to 35 hours.

During infusion, your child will be closely monitored. Your doctor will check a lot of parameters such as heart rhythm and blood pressure, and blood will be taken to evaluate the response to therapy and occurrence of side effects.

If you use more Primacor than you should

It is unlikely that your doctor or nurse will give you too much of this medicine. Your doctor and nurse will check your progress and the medicine that you are given. Always ask if you are not sure why you are getting a dose of medicine.

The following effects may happen if you use too much Primacor: feeling dizzy, light-headedness and fainting (due to low blood pressure) and an uneven heartbeat.

If you forget to use Primacor

Your doctor or nurse will have instructions on when to give you this medicine. It is unlikely that you will not be given the medicine as it has been prescribed. However, if you do think you have missed a dose, tell your doctor or nurse.

If you stop using Primacor

Keep using Primacor until your doctor tells you to stop. Do not stop using Primacor just because you feel better. If you stop, your illness may get worse.

Tests

Your doctor or nurse will use an electrocardiogram (ECG) to check how well your heart works. They will also carry out blood tests and check your blood pressure and pulse rate.

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

Solutions of different concentrations may be used according to patient fluid requirements. The duration of therapy should depend upon the patient's response. In congestive cardiac failure, patients have been maintained on the infusion for up to 5 days, although the usual period is 48 – 72 hours. In acute states following cardiac surgery, it is unlikely that treatment need be maintained for more than 12 hours.

Renal impairment

Dosage adjustment required. Data obtained from patients with severe renal impairment but without heart failure have demonstrated that the presence of renal impairment significantly increases the terminal elimination half-life of milrinone.

For patients with clinical evidence of renal impairment, the loading dose is not affected, but the following maintenance infusion rates are recommended using the infusion solution described above.

Creatinine Clearance (ml/min/1.73m²)	Primacor Injection Dose (µg/kg/min)	Maintenance Infusion Delivery Rate (ml/kg/hr)
5	0.20	0.06
10	0.23	0.07
20	0.28	0.08
30	0.33	0.10
40	0.38	0.11
50	0.43	0.13

The infusion rate should be adjusted according to haemodynamic response.

Elderly

Experience so far suggests that no special dosage recommendations are necessary.

4. Possible side effects

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

Stop using Primacor and tell you doctor straight away if:

- You have an **allergic reaction**. The signs may include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue, fainting or losing consciousness. The chances of this happening are very rare.

Tell a doctor or nurse straight away if you notice any of the following side effects:

Common (affects less than 1 in 10 people)

- Uneven, increased or fast heartbeats. You may also experience pounding in your chest, feel light-headed, faint or short of breath.

Uncommon (affects less than 1 in 100 people)

- Ventricular fibrillation – a serious heart rhythm problem. Signs of this include very fast, uneven or forceful heartbeat (palpitations), dizziness and loss of consciousness. You may also feel sick, have cold sweats, shortness of breath and chest pain.
- Thrombocytopenia – a blood problem. Signs of this are that you may bruise more easily than usual.
- Chest pain.

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

- Torsades de Pointes – a serious heart rhythm problem. Signs of this include very fast, uneven or forceful heartbeat (palpitations), dizziness and loss of consciousness. You may also feel sick, have cold sweats, shortness of breath, unusual pale complexion and chest pain.
- Difficulty breathing, wheezing or tightness in the chest.

Tell a doctor or nurse as soon as possible if you notice any of the following side effects:

Common (affects less than 1 in 10 people)

- Low blood pressure. Signs of this include feeling dizzy, lightheaded or fainting. If you also notice signs like a fast or uneven heartbeat or chest pain this could be a more serious side effect (see above).
- Headache.

Uncommon (affects less than 1 in 100 people)

- Feeling shaky.
- Low levels of potassium in your blood. Signs of this are tiredness, confusion, muscle weakness and muscle cramps. This may be due to low levels of potassium in your body.

Tell a doctor or nurse if any of the following side effects gets serious or lasts longer than a few days:

Uncommon (affects less than 1 in 100 people)

- A blood test may show changes in the way the liver is working.

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

- Skin rashes including at the site of the injection.

Talk to your doctor, nurse or pharmacist if any of the side effects gets serious or lasts longer than a few days, or if you notice any side effects not listed in this leaflet.

Additional side effects in children and adolescents:

Not known (frequency cannot be estimated from the available data)

- Bleeding into the fluid-filled areas (ventricles) surrounded by the brain (intraventricular haemorrhage).
- A heart problem known as Patent Ductus Arteriosus – a connection between 2 major blood vessels (aorta and pulmonary artery) which persists though it should be closed. This can cause excess fluid in the lungs, bleedings, destruction of the bowel or part of the bowel and possibly be fatal.
- Changes in the way the kidneys are working if you already have low blood pressure.

Moreover, compared to adults, decrease in the number of platelets in the blood seems to occur more often in children and the risk of this side effect is increased with the duration of the Primacor infusion. Heart rhythm troubles seem to occur less often in children than in adults.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist 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 at: 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 Primacor

This medicine will be kept by your doctor or pharmacist in a safe place where children cannot see or reach it.

Do not use Primacor after the expiry date, which is stated on the ampoule and the carton. The expiry date refers to the last day of the month.

Primacor should be stored below 25°C. Do not freeze.

Do not throw away any medicines via wastewater or household waste. Your doctor or nurse will throw away medicines you no longer use. These measures will help protect the environment.

Paediatric population

In published studies selected doses for infants and children were:

- *Intravenous loading dose:* 50 – 75 µg/kg administered over 30 – 60 minutes.
- *Intravenous continuous infusion:* To be initiated on the basis of haemodynamic response and the possible onset of undesirable effects between 0.25 – 0.75 µg/kg/min for a period up to 35 hours.

In clinical studies on low cardiac output syndrome in infants and children under 6 years of age after corrective surgery for congenital heart disease 75 µg/kg loading dose over 60 minutes followed by a 0.75 µg/kg/min infusion for 35 hours significantly reduced the risk of development of low cardiac output syndrome.

Results of pharmacokinetic studies have to be taken into consideration.

Renal impairment:

Due to lack of data the use of milrinone is not recommended in paediatric population with renal impairment.

Patent ductus arteriosus:

If the use of milrinone is desirable in preterm or term infants at risk of/with patent ductus arteriosus, the therapeutic need must be weighed against potential risks.

Overdose

Overdose of intravenous Primacor may produce hypotension (because of its vasodilatory effect) and cardiac arrhythmia. If this occurs, Primacor Injection administration should be reduced or temporarily discontinued until the patient's condition stabilises. No specific antidote is known, but general measures for circulatory support should be taken.

6. Contents of the pack and other information

What Primacor contains

- Each 1 ml of injection contains 1 mg of the active substance, milrinone.
- The other ingredients are lactic acid, glucose anhydrous, water for injection and sodium hydroxide (for pH adjustment).

What Primacor looks like and contents of the pack

Primacor is a clear, colourless to pale yellow liquid and is available as 10 ml or 20 ml glass ampoules in boxes of 10.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK.

Tel: 0800 035 2525

email: uk-medicalinformation@sanofi.com

Manufacturer

Delpharm Dijon, 6 Boulevard de l'Europe, 21800 Quetigny, France

This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist.

This leaflet was last revised in July 2020

Incompatibilities

Furosemide or bumetanide should not be administered in intravenous lines containing Primacor Injection since precipitation occurs on admixture. Sodium Bicarbonate Intravenous infusion should not be used for dilution.

Other drugs should not be mixed with Primacor Injection until further compatibility data are available.

Shelf life

36 months when unopened. A diluted solution of Primacor Injection should be used within 24 hours.

Special precautions for storage

Store below 25°C. Do not freeze.

Special precautions for disposal

Infusion solutions diluted as recommended with 0.45% saline, 0.9% saline or 5% glucose should be freshly prepared before use. Parenteral drug products should be examined visually and should not be used if particulate matter or discolouration are present.