SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Milrinone 1 mg/ml Solution for Injection/Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml solution for injection/infusion contains 1 mg milrinone.

Each ampoule of 10 ml solution for injection/infusion contains 10 mg milrinone.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection/infusion.

Clear, colourless to pale yellow liquid with a pH of 3.2-4.0.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Adults

Milrinone Injection is indicated for the short-term treatment (48 hours) of severe congestive heart failure unresponsive to conventional maintenance therapy (glycosides, diuretics, vasodilators and/or angiotensin converting enzyme (ACE) inhibitors).

Children

In paediatric population Milrinone Injection is indicated for the short-term treatment (up to 35 hours) of severe congestive heart failure unresponsive to conventional maintenance therapy (glycosides, diuretics, vasodilators and/or angiotensin converting enzyme (ACE) inhibitors), and for the short-term treatment (up to 35 hours) of paediatric patients with acute heart failure, including low output states following cardiac surgery.

4.2 Posology and method of administration

Posology

Careful monitoring should be maintained during milrinone therapy including blood pressure, heart rate, clinical state, electro-cardiogram, fluid balance, electrolytes and renal function (i.e. serum creatinine)(see section 4.4).

Facilities must be available for immediate treatment of potential adverse cardiac effects (e.g. life-threatening ventricular arrhythmias).

The infusion rate should be adjusted according to haemodynamic response.

Adults: Milrinone 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 (standard 0.5 µg/kg/min) according to haemodynamic and clinical response and the possible onset of undesirable effects such as hypotension and arrhythmias.

The total does should not exceed 1.13 mg/kg/day total dose which corresponds to an infusion rate of 45.0 µg/kg/hr.

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. 0.9% saline or 5% glucose may be used as diluents.

Milrinone Injection Dose (µg/kg/min)	Maintenance Infusion (µg/kg/hr)	Infusion Delivery Rate (ml/kg/hr)
0.375	22.5	0.11
0.400	24.0	0.12
0.500	30.0	0.15
0.600	36.0	0.18
0.700	42.0	0.21
0.750	45.0	0.22

Solutions of different concentrations may be used according to patient fluid requirements. The duration of therapy should depend upon the patient´s response.

Elderly

Experience so far suggests that no special dosage recommendations are necessary in patients with normal renal function. Renal clearance may be reduced in elderly patients, lower Milrinone Injection doses may be required in such cases.

Renal Impairment

Dosage adjustment required. Dosage adjustment in patients with renal impairment is based on data obtained from patients with common renal impairment but without congestive heart failure, who show significant increases to the terminal elimination half-life of milrinone. The loading dose is not affected, but a reduction in the

maintenance infusion rates may be necessary depending on the severity (creatinine clearance) of the renal impairment (see table below):

Creatinine Clearance (ml/min/1.73m^2)	Milrinone Injection Dose (µg/kg/min)	Maintenance Infusion Delivery Rate (for a solution containing 200 µg milrinone per ml) (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

Paediatric population

In published studies selected doses for infants and children were:

- Intravenous loading dose: 50 to 75 µg/kg administered over 30 to 60 minutes.
- Intravenous continuous infusion: To be initiated on the basis of hemodynamic response and the possible onset of undesirable effects between 0.25 to 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 (see section 5.2) 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 (for further information please see section 4.4).

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 (see section 4.4, 4.8, 5.2, and 5.3).

Method of administration

For slow intravenous administration. To avoid local irritation, as large a vein as possible should be punctured. Extravascular injection must be avoided.

Milrinone Injection may not be mixed with other diluents as stated above (see section 6.2). Solutions of different concentrations may be used according to patient fluid requirements. After dilution the solution is a clear, colourless to pale yellow liquid.

The duration of therapy should depend upon the patient's response but should not exceed 48 hours due to a lack of evidence of safety and efficay in long-term treatment of congestive heart failure (see section 4.4).

4.3 Contraindications

Hypersensitivity to milrinone (active substance) or to any of the excipients of Milrinon Injection (see section 6.1).

Severe hypovolaemia.

4.4 Special warnings and precautions for use

Careful monitoring should be maintained during therapy with Milrinone Injection, including blood pressure, heart rate, clinical state, electrocardiogram, fluid balance, electrolytes and renal function (i.e. serum creatinine). Facilities must be available for immediate treatment of potential adverse cardiac effect (e.g. life threatening ventricular arrhythmias).

In patients with severe obstructive aortic or pulmonary valvular disease, or hypertrophic subaortic stenosis (KMP), milrinone should not be used in lieu of surgical relief of the obstruction. As with other drugs with inotropic / vasodilator properties, it may aggravate outflow obstruction in these conditions.

Milrinone is not recommended immediately following acute myocardial infarction until safety and efficacy have been established in this situation. Use of positive inotropic such as milrinone in the acute phase of post myocardial infarction may lead to an undesirable increase in myocardial oxygen consumption (MVO2). Heightened caution is needed in patients in the acute phase of myocardial infarction in spite of milrinone does not increase MVO2 in patients with chronic heart failure.

There is a possibility of an increased ventricular response rate in patients with atrial flutter or fibrillation. In these patients, prior digitalisation or treatment with other agents to prolong atrio-ventricular node conduction time should be considered, as milrinone produces a slight enhancement in A-V node conduction.

Supraventricular and ventricular arrhythmias have been observed in the high-risk population treated with milrinone. In some patients, an increase in ventricular ectopy including non-sustained ventricular tachycardia has been observed.

Patients, especially those with complex ventricular arrhythmias, should therefore be kept under continuous ECG and clinical monitoring during Milrinone Injection therapy and the dosage should be carefully adjusted.

If prior vigorous diuretic therapy is suspected of having caused significant decreases in cardiac filling pressure, Milrinone Injection should be cautiously administered while monitoring blood pressure, heart rate and clinical symptomatology.

Fluid and electrolyte changes, as well as serum creatinine levels should be carefully monitored during treatment. Improvement in cardiac output with resultant diuresis may necessitate a reduction in the dose of diuretic.

Potassium loss due to excessive diuresis may predispose digitalised patients to arrhythmias. Therefore, hypokalaemia should be corrected by potassium supplementation in advance of, or during, the use of Milrinone Injection.

Milrinone may induce hypotension as a consequence of its vasodilatory activity; caution should therefore be exercised when Milrinone Injection is administered to patients who are hypotensive prior to treatment. In patients showing excessive decreases in blood pressure after milrinone administration, the treatment should be discontinued until the hypotensive effect has been resolved and then resumed, if necessary, at a lower rate of infusion.

Decrease in haemoglobin, including anaemia, often takes place in the setting of cardiac failure. Due to the risk of thrombocytopenia or anaemia, careful monitoring of the corresponding laboratory parameters is required in patients with decreased platelet count or decreased haemoglobin.

There is no experience in controlled trials with infusions of milrinone for periods exceeding 48 hours.

Cases of infusion site reaction have been reported with Milrinone Injection (see section 4.8). Consequently, careful monitoring of the infusion site should be maintained to avoid possible extravasation.

Milrinone Injection should not be given to patients with rare glucose-galactose malabsorption.

Paediatric population

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

In neonates, monitoring should include heart rate and rhythm, systemic arterial blood pressure via umbilical artery catheter or peripheral catheter, central venous pressure, cardiac index, cardiac output, systemic vascular resistance, pulmonary artery pressure, and atrial pressure. Laboratory values that should be followed are platelet count, serum potassium, liver function, and renal function.

Frequency of assessment is determined by baseline values, and it is necessary to evaluate the neonate´s response to changes in therapy.

Literature revealed that in paediatric patients with impaired renal function, there were marked impairment of milrinone clearance and clinically significant side effects, but the specific creatinine clearance at which doses must be adjusted in paediatric patients is still not clear. Therefore, the use of milrinone is not recommended in this population (see section 4.2).

In paediatric patients milrinone should be initiated only if the patient is hemodynamically stable.

Caution should be exercised in neonates with risk factors of intraventricular haemorrhage (i.e. preterm infant, low birth weight) since milrinone may induce thrombocytopenia. In clinical studies in paediatric patients, risk of thrombocytopenia increased significantly with duration of infusion. Clinical data suggest that milrinone-related thrombocytopenia is more common in children than in adults (see section 4.8).

In clinical studies milrinone appeared to slow the closure of the ductus arteriosus in paediatric population. Therefore, 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 (see section 4.2, 4.8, 5.2 and 5.3).

Use in the elderly

There are no special recommendations for elderly patients. No age-related effects on the incidence of adverse reactions have been observed. Controlled pharmacokinetic studies have not shown changes in the pharmacokinetic profile of milrinone in the elderly.

Use in patients with renal impairment

In patients with severe renal impairment, dosage adjustment is required (see section 4.2).

This medicine contains less than 1 mmol sodium (23 mg) per ampoule, that is to say essentially 'sodium free'.

4.5 Interaction with other medicinal products and other forms of interaction

Fluid and electrolyte changes, as well as serum creatinine levels, should be carefully monitored during treatment with milrinone. The effect of milrinone and diuretics may be mutually potentiated. Additive, diuretic and hypokalaemic effects have been observed. Improvement in cardiac output and consequently, diuresis, may require reduction in the dose of a diuretic agent. Potassium loss due to excessive diuresis may predispose digitalised patients to arrhythmias. Therefore, hypokalaemia should be corrected by potassium supplementation in advance of, or during milrinone use.

If inotropic agents (e.g. dobutamine) are co-administered, the positive inotropic effects may be potentiated.

For incompatibilities, reference is made to section 6.2.

4.6 Fertility, Pregnancy and lactation

Pregnancy:

Although animal studies have not revealed evidence of drug-induced foetal damage or other deleterious effects on reproductive function, the safety of milrinone in human pregnancy has not yet been established. It should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Breast-feeding:

There is insufficient information on the excretion of milrinone in human milk. A decision must be made whether to discontinue breast-feeding or to discontinue Milrinone Injection therapy taking into account the benefit of breast feeding for the child and the benefit of therapy from the woman.

Fertility:

See section 5.3.

4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Adverse reactions have been ranked under heading of system-organ class and frequency using the following convention:

- very common (≥1/10),
- common (≥1/100 to <1/10),
- uncommon (≥1/1,000 to <1/100),
- rare (≥1/10,000 to <1/1,000),
- very rare (<1/10,000),
- not known (cannot be estimated from the available data).

Blood and lymphatic system disorders:

- *Uncommon:* Thrombocytopenia
- *Not known:* Reduction of red blood count and/or haemoglobin concentration

Immune system disorders:

- *Very rare*: Anaphylactic shock

Metabolism and nutrition disorders:

- *Uncommon*: Hypokalaemia

Nervous system disorders:

- *Common:* Headaches, usually mild to moderate in severity
- *Uncommon:* Tremor

Cardiac disorders:

- *Common:* Ventricular ectopic activity, non-sustained or sustained ventricular tachycardia, supraventricular arrhythmias [1], hypotension

[1] The incidence of arrhythmias has not been related to dose or plasma levels of milrinone. Life threatening arrhythmias are often found to be associated with underlying risk factors such as pre-existing arrhythmias, metabolic abnormalities (e.g. hypokalaemia), elevated serum digoxin levels or catheter insertion. Clinical data suggest that milrinone-related arrhythmias are less common in children than in adults.

- *Uncommon:* Ventricular fibrillation, angina/chest pain
- *Very rare:* Torsades de pointes

Respiratory, thoracic and mediastinal disorders:

- *Very rare:* Bronchospasm

Hepatobiliary disorders:

- *Uncommon:* Liver function tests abnormal

Skin and subcutaneous tissue disorders:

- *Very rare*: Skin reactions such as rash

General disorders and administration site conditions:

- *Not known:* Infusion site reaction

Paediatric population:

Nervous system disorders:

- *Not known:* Intraventricular haemorrhage (see section 4.4).

Congenital, familial, and genetic disorders:

- *Not known:* Patent ductus arteriosus (see section 4.2, 4.4, 5.2 and 5.3).

  The critical consequences of the patent ductus arteriosus are related to a combination of pulmonary overcirculation with consecutive pulmonary oedema and haemorrhage and of reduced organ perfusion with consecutive intraventricular haemorrhage and necrotizing enterocolitis with possible fatal outcome as described in literature.

Long-term safety data for paediatric population are not yet available.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Overdose of intravenous Milrinone Injection may produce hypotension (because of its vasodilatory effect) and cardiac arrhythmia. If this occurs, Milrinone 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: phosphodiesterase inhibitor

ATC code: C01CE02

Mechanism of action

Milrinone is a positive inotropic and vasodilator substance with little chronotropic, bathmotropic and dromotropic activity.

It differs from both digitalis glycosides and catecholamines in terms of its structure and mode of action.

Pharmacodynamic effects

At inotropic and vasorelaxant concentrations, milrinone is a selective inhibitor of the peak III cAMP phosphodiesterase isoenzyme in cardiovascular muscles. In the myocardial cell, this inhibitory effect leads to a cAMP-mediated increase in intracellular ionised calcium and myocardial contractility, as well as a cAMP-dependent phosphorylation of contractile proteins. In the vascular muscle cell, there is a cAMP-mediated decrease in intracellular ionised calcium and hence a relaxation of vascular muscles. Further experimental findings indicate that milrinone is not a beta-receptor agonist and, unlike digitalis glycosides, it does not inhibit Na+/Ka+-ATPase activity.

Clinical efficacy and safety

Clinical studies in patients with heart failure have shown that milrinone, depending on the dose and its plasma concentration, leads to an increase in the maximum rate of increase of left-ventricular pressure. Studies in healthy subjects have shown that the slope of the left-ventricular pressure/volume relationship increases during milrinone therapy. This indicates a direct inotropic effect of the substance. In patients with heart failure, milrinone also led to a dose-related and plasma concentration-related increase in forearm blood flow, indicating a direct vasodilator effect on the arteries.

In addition to the increase in myocardial contractility, milrinone improves diastolic function, as demonstrated by improvements in left-ventricular diastolic relaxation.

In patients with impaired myocardial function, injection of milrinone within the usual dosage range led to a rise in the cardiac index and a reduction in pulmonary capillary pressure and vascular resistance. The heart rate increased by 3% to 10%, depending on the dose. Mean arterial blood pressure fell dose-dependently by 5% to 17%. The haemodynamic improvements correlated with the dose and milrinone plasma concentration and were accompanied by an improvement in clinical symptoms. The vast majority of patients showed improvements in haemodynamic parameters within five to fifteen minutes after the start of treatment.

Milrinone also shows a positive inotropic effect in digitalised patients. There are no indications that milrinone increases the toxicity of glycosides. Close to maximum effects of milrinone on cardiac output and pulmonary capillary pressure are seen at milrinone plasma concentrations within the range of 150 ng/ml to 250 ng/ml.

Paediatric population

Literature review identified clinical studies with patients treated for low cardiac output syndrome following cardiac surgery, septic shock or pulmonary hypertension.

The usual dosages were a loading dose of 50 to 75 µg/kg administered over 30 to 60 minutes followed by an intravenous continuous infusion of 0.25 to 0.75 µg/kg/min for a period up to 35 hours. In these studies, milrinone demonstrated an increase of cardiac output, a decrease in cardiac filling pressure, a decrease in systemic and pulmonary vascular resistance, with minimal changes in heart rate and in myocardial oxygen consumption.

Studies of a longer use of milrinone are not sufficient to recommend an administration of milrinone during a period of more than 35 hours.

5.2 Pharmacokinetic properties

Distribution

In vitro protein binding assays revealed that milrinone, depending on the assay method used, is 70–91% protein-bound at therapeutically relevant plasma concentrations. Six to twelve hours after a constant maintenance infusion of 0.50 micrograms/kg BW/min, steady-state plasma concentrations of milrinone are approximately 200 ng/ml.

Following intravenous injections of 12.5 micrograms/kg BW to 125 micrograms/kg BW in patients with heart failure, milrinone had a volume of distribution of 0.38 l/kg BW, a mean terminal elimination half-life of 2.3 hours and a clearance of 0.13 l/kg BW/h.

Following intravenous infusions of 0.20 micrograms/kg BW/min to 0.7 micrograms/kg BW/min in patients with heart failure, the substance had a volume of distribution of approximately 0.45 l/kg BW, the mean terminal elimination half-life was 2.4 hours and clearance was 0.14 l/kg BW/h. These pharmacokinetic parameters were not dose-dependent. Conversely, the area under the plasma concentration-time curve after the injections was significantly dose-dependent. Via ultracentrifugation, milrinone was shown to be up to 70% bound to human plasma proteins at plasma concentrations between 70 and 400 nanograms/ml.

Both clearance and half-life were prolonged in patients with heart failure in relation to their degree of renal impairment compared to healthy subjects. Data from patients with severe renal insufficiency (creatinine clearance less than 30 ml/min) showed that the terminal elimination half-life is prolonged in cases of renal insufficiency.

Biotransformation and elimination

In humans, milrinone is mainly excreted in the urine. The main excretory products in humans are milrinone (83%) and its O-glucuronide metabolite (12%). In healthy subjects, excretion in the urine is rapid; approximately 60% is recovered in the urine within the first two hours after administration and approximately 90% of the dose within the first eight hours after administration. Mean renal clearance of milrinone IV is approximately 0.3 l/min; this is indicative of active secretion.

Paediatric population

Milrinone is cleared more rapidly in children than in adults, but infants have significantly lower clearance than children, and preterm infants have even lower clearance. As a consequence of this more rapid clearance compared to adults, steady-state plasma concentrations of milrinone were lower in children than in adults. In paediatric population with normal renal function steady-state milrinone plasma

concentrations after 6 to 12 hours continuous infusion of 0.5 to 0.75 µg/kg/min were about of 100 to 300 ng/ml.

Following intravenous infusion of 0.5 to 0.75 µg/kg/min to neonates, infants and children after open heart surgery, milrinone has a volume of distribution ranging from 0.35 to 0.9 litres/kg with no significant difference across age groups. Following intravenous infusion of 0.5 µg/kg/min to very preterm infants to prevent systemic outflow after birth, milrinone has a volume distribution of about 0.5 litres/kg.

Several pharmacokinetic studies showed that, in paediatric population, clearance increases with increasing age. Infants have significantly lower clearance than children (3.4 to 3.8 ml/kg/min versus 5.9 to 6.7 ml/kg/min). In neonates milrinone clearance was about 1.64 ml/kg/min and preterm infants have even lower clearance (0.64 ml/kg/min).

Milrinone has a mean terminal half-life of 2 to 4 hours in infants and children and a mean terminal elimination half-life of 10 hours in preterm infants.

It was concluded that the optimal dose of milrinone in paediatric patients in order to obtain plasma levels above the threshold of pharmacodynamic efficacy appeared higher than in adults, but that optimal dose in preterms in order to obtain plasma levels above the threshold of pharmcodynamic efficacy appeared lower than in children.

Patent ductus arteriosus

Milrinone is cleared by renal excretion and has a volume of distribution that is restricted to extracellular space which suggests that the fluid overload and hemodynamic changes associated with patent ductus arteriosus may have an effect of distribution and excretion of milrinone (see section 4.2, 4.4, 4.8 and 5.3).

5.3 Preclinical safety data

Acute toxicity

After oral administration, the LD_{50} for male mice is 137 mg/kg and for female mice 170 mg/kg, while the LD_{50} for male rats is 91 mg/kg and for female rats 153 mg/kg.

After intravenous administration of milrinone, focal epicardial and endocardial haemorrhages and focal myocardial fibroses (particularly in the papillary muscle and in the endocardial areas) occur in rabbits.

Subacute toxicity

Subacute toxicity was examined in rats and dogs. In dogs, endocardial haemorrhages and myocardial fibroses occurred in all treated groups after cumulative and fractioned administration of milrinone in quantities just above the therapeutic dose.

Subchronic and chronic toxicity

Oral and intravenous application of milrinone to rats, dogs and monkeys lead in therapeutic doses, or in doses just above the therapeutic dose, to myocardial degenerations, fibroses and, particularly in the region of the papillary muscles of the left ventricle, to subendocardial haemorrhages.

Lesions of the coronary vessels, characterised by a periarterial oedema and inflammation, were only observed in dogs.

Carcinogenicity

In long-term trials, no tumour-producing potential was detected in rats and mice. Endocardial haemorrhages and myocardial necroses and fibroses occurred in rats. At the highest dosage, myocardial degenerations and fibroses were detected in mice. In the stomachs of mice, necroses and ulcers were detected.

Mutagenicity

A detailed in vitro and in vivo test on mutagenicity produced negative results.

Fertility/reproductive toxicology

Milrinone, at oral doses of up to 40 times the usual human therapy dose, did not have an effect on the fertility of male and female rats.

Studies of the reproductive toxicology in rats and rabbits did not produce any evidence of a teratogenic action at doses of up to 10 times (oral) and 2.5 times (i.v.) of the usual human therapy dose.

In a study spanning 3 generations (P, F1, F2 generation) of rats treated orally with milrinone, no effect on the development of the animals and their reproductive capacity was detected in the mothers or the descendents, even at the highest dose (40 times the usual human therapy dose).

Embryonic/foetal dose in relation to the mother's serum concentration:

A diaplacental transmission of milrinone to the foetus is documented in a study of pregnant monkeys which had human therapy doses administered intravenously. The ratio of maternal serum values to foetal serum levels was 4:1.

Juvenile animals:

A preclinical study was performed to clarify the ductus-dilating effects of PDE 3 inhibitors in near-term rat pups and their differential effects in near-term and preterm foetal rats. Postnatal ductus arteriosus dilatation by milrinone was studied with three doses (10, 1 and 0.1mg/kg). The dilating effects of milrinone in the foetal ductus constricted by indomethacin were studied by simultaneous administration of milrinone (10, 1 and 0.1mg/kg) and indomethacin (10 mg/kg) to the mother rat at D21 (near-term) and D19 (preterm). This in vivo study has shown that milrinone induces dose-dependent dilation of the foetal and the postnatal constricted ductus arteriosus. Dilating effects were more potent with injection immediately after birth than at 1 hour after birth. In addition, study showed that the premature ductus arteriosus is more sensitive to milrinone than the mature ductus arteriosus (see section 4.2, 4.4, 4.8, and 5.2).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactic acid, glucose anhydrous, sodium hydroxide, water for injections

6.2 Incompatibilities

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

6.3 Shelf life

3 years

After opening or after dilution with isotonic sodium chloride or glucose 5 % solution the chemical and physical in-use stability has been demonstrated for 24 h at 25°C. From a microbiological point of view, unless the method of opening and dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

10 ml solution in an ampoule (glass type I) in pack sizes of 5 or 10.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Milrinone Injection as well as any dilution is a clear, colourless to pale yellow liquid. The drug product should be examined visually and should not be used if particulate matter or discolouration are present (see also section 4.2).

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

MACURE PHARMA UK LTD
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138-142 Holborn, London
EC1N 2 SW

8 MARKETING AUTHORISATION NUMBER(S)

PL 54594/0002

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