

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Perfan 5mg/ml Concentrate for Solution for Injection or Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of the concentrate contains 5 mg enoximone.

Each 20 ml ampoule contains 100 mg enoximone.

When diluted as recommended, the resulting diluted solution contains 2.5 mg of enoximone per ml.

Also includes: ethanol, sodium and propylene glycol.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Concentrate for solution for injection or infusion.

Clear, yellow solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Perfan 5 mg/ml concentrate for solution for injection or infusion is indicated for the treatment of congestive cardiac failure.

4.2 Posology and method of administration

Perfan 5 mg/ml concentrate for solution for injection or infusion must be diluted 1:1 with either 0.9% sodium chloride injection or water for injections before administration.

Loading Dose:

0.5 mg/kg initially at a rate not greater than 12.5 mg/min. This dose may be repeated in 30 minutes. A loading dose of 0.5 mg/kg often produces an increase in cardiac index of at least 25%. Peak response is usually noted by 30 minutes. Some patients may benefit from a third bolus given after 60 minutes.

Maintenance Dose:

Infusion: 2.5-5 micrograms/kg/min following loading dose. Most patients respond satisfactorily to 2.5-5.0 micrograms/kg/min. Maintaining and readjusting the infusion rate to the lowest effective dose is advisable. Accumulation of enoximone and enoximone sulfoxide has been observed at infusion rates of 10 micrograms/kg/min. Continued response to enoximone has been observed in studies using continuous 48-hour infusions in doses of 2.5-10 micrograms/kg/min. In clinical use, some patients have received up to 20 micrograms/kg/min for variable durations; the benefit of higher doses must be weighed against the potential increase in side effects.

Intermittent Bolus:

0.5 mg/kg every 4 to 8 hours after the initial dose. This dose may be repeated in 30 and 60 minutes dependent on patient response. In studies using intermittent boluses over a 24 hour period patients responding well to the initial bolus series maintain their response throughout therapy.

Patients with Renal Dysfunction

In patients with creatinine clearance below 40 ml/min, enoximone clearance is significantly reduced and the ratio of enoximone sulfoxide (a metabolite which has shown activity in animal studies) to enoximone plasma concentrations is significantly increased. Therefore, the clinical benefits of enoximone must be carefully weighed against the potential risk of drug and metabolite accumulation. Continuous ECG and frequent blood pressure monitoring are recommended as a precaution against significant changes in cardiac rhythm or blood pressure. Enoximone should be given by intermittent bolus rather than continuous infusion. The initial loading dose is given at standard doses and may be repeated in 30 minutes if there has been no response. Based on reductions in enoximone clearance, the maintenance dose is reduced.

4.3 Contraindications

Perfan 5 mg/ml concentrate for solution for injection or infusion is contra-indicated in patients with a known hypersensitivity to enoximone or any of the components of the medicinal product.

4.4 Special warnings and precautions for use

Enoximone therapy has been associated with reductions in platelet counts to below $100 \times 10^6/L$. Platelet counts should be monitored.

Enoximone should be used with caution in patients with congestive cardiac failure associated with blood platelet counts below $100 \times 10^6/L$.

Transient and variable changes in liver function tests have been observed, the patients should be carefully and regularly monitored with reference to hepatic and renal function.

In patients with fast atrial fibrillation or flutter, the enhanced atrioventricular conduction is not affected by enoximone and concomitant administration of digitalis should be considered. In such cases or in those with multifocal or runs of premature ventricular contractions, careful dose titration and close ECG monitoring is advisable, especially during intravenous therapy.

Blood pressure and heart rate should be monitored during intravenous therapy. Significant increases in heart rate are rare but the rate of infusion may have to be slowed or stopped in patients showing a tendency to hypotension and, if severe, supportive measures and intravenous fluid administration instituted.

Improvement in cardiac output is often followed by increased renal perfusion with resultant diuresis and fluid and electrolyte changes may require correction.

Care should be taken during intravenous therapy to avoid extravascular leakage of enoximone since this may cause irritation.

The safety and efficacy of enoximone injection for use in children has not been established.

4.5 Interaction with other medicinal products and other forms of interaction

No clinical manifestations of untoward drug interaction were observed in patients receiving Perfán 5 mg/ml concentrate for solution for injection or infusion most of whom concomitantly received one or more of the following: diuretics (amiloride, triamterene, frusemide and spironolactone), digitalis glycosides (digoxin), potassium supplements, antiarrhythmics (diltiazem, propranolol, lignocaine, nifedipine, procainamide and quinidine), vasodilators (captopril, hydralazine, nitroprusside and nitrates), anticoagulants (warfarin and heparin), analgesics (acetylsalicylic acid, paracetamol and codeine), sedatives (chloral hydrate, diazepam and lorazepam) and positive inotropic agents (dobutamine and dopamine).

4.6 Fertility, pregnancy and lactation

There are no adequate and well-controlled studies in pregnant women. Perfan 5 mg/ml concentrate for solution for injection or infusion should be used during pregnancy only if the potential benefit justifies the potential risk.

It is not known whether this drug is excreted in human milk. Use in women breast feeding infants is not recommended.

4.7 Effects on ability to drive and use machines

Not applicable as the product is used on hospitalised patients.

4.8 Undesirable effects

Side effects include ectopic beats, ventricular tachyarrhythmias, supra-ventricular and other arrhythmias, hypotension, headache, insomnia, nausea and/or vomiting or diarrhoea. Chills, oliguria, urinary retention, upper and lower extremity pain and fever.

4.9 Overdose

Intravenous administration of Perfan 5 mg/ml concentrate for solution for injection or infusion has been shown to produce reductions in blood pressure with occasional instances of hypotensive symptoms. If symptomatic hypotension is observed, administration of Perfan 5 mg/ml concentrate for solution for injection should be reduced or discontinued. No specific antidote is known, but general measures for circulatory support should be taken.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Enoximone, an imidazolone, has both positive inotropic and vasodilator properties, inhibiting cardiac phosphodiesterase III with an increase in cAMP.

5.2 Pharmacokinetic properties

Enoximone half-life ranged from 3 to 8 hours for enoximone and 6-11 hours for the sulphoxide. 0.45% of the intact drug was recovered from the urine and 74% of the metabolite, which is pharmacologically active.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethanol, anhydrous
Sodium hydroxide
Propylene glycol
Water for injections

6.2 Incompatibilities

Perfan 5mg/ml concentrate for solution for infusion may only be diluted with sodium chloride solution or water for injections (see section 6.6).

Other drugs or fluids must not be mixed in the same container or administered concomitantly in the same infusion line as Perfán 5 mg/ml concentrate for solution for injection.

Crystal formation has occurred when enoximone injection was mixed in glass containers or syringes.

Glucose solutions should not be used as crystal formation may occur.

6.3 Shelf Life

Unopened: 3 years

Use immediately once diluted.

6.4 Special precautions for storage

Do not store above 30°C.

In-use: see section 6.3 and section 6.6

6.5 Nature and contents of container

Glass ampoules (Type I Ph. Eur.) of 20 ml in cartons containing 10 ampoules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Prior to administration, Perfán 5 mg/ml concentrate for solution for injection or infusion must be diluted 1:1 with isotonic sodium chloride solution or water for injections. Dilution should take place immediately prior to intravenous administration.

Perfan 5 mg/ml concentrate for solution for injection or infusion may only be diluted with sodium chloride solution or water for injections. Other solutions, in particular glucose solution must not be used for dilution because of potential incompatibilities.

The diluted solution is clear and has a yellow colour. The product must not be used if the solution is not clear or contains a precipitate.

For dilution and administration of Perfán 5 mg/ml concentrate for solution for injection or infusion, only equipment and syringes consisting of plastic material as generally used in hospitals may be used since crystallisation is possible when dilution is carried out in glass vessels.

Following dilution 1:1, 40 ml of ready-to-use solution contain 100 mg enoximone, 1 ml of this solution contains 2.5 mg enoximone.

Perfan 5 mg/ml concentrate for solution for injection or infusion ampoules are for single use only. After dilution, use immediately and discard any unused portion. Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

PA1682/1/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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