Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dobutrex 250mg/20ml, concentrate for solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Dobutamine Hydrochloride equivalent to Dobutamine 250mg/20ml (12.5mg/ml).

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for infusion
A clear, colourless to faint straw-coloured solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Actions: The primary action of dobutamine is to augment cardiac contractility by stimulating the beta-1 receptors of the heart. It is a direct-acting agent.

Indications: Dobutrex is indicated for adults who require inotropic support in the treatment of cardiac failure associated with myocardial infarction, open heart surgery or cardiomyopathies. Dobutrex is also indicated for adults with cardiogenic or septic shock who are not severely hypotensive. Dobutrex can increase or maintain cardiac output during positive end expiratory pressure (PEEP) ventilation.

4.2 Posology and method of administration

For intravenous administration only.

Dobutrex should only be used in specialist units in which adequate facilities are available for patient surveillance and the monitoring of responses.

Dobutrex Solution must be further diluted to at least 50ml prior to administration in an i.v. container with one of the intravenous solutions listed below:

Sodium Chloride Intravenous Infusion BP
5% Dextrose Intravenous Infusion BP
5% Dextrose + 0.9% Sodium Chloride Intravenous Infusion BP
5% Dextrose + 0.45% Sodium Chloride Intravenous Infusion BP
Sodium Lactate Intravenous Infusion BP

If diluting to 250ml or 500ml, dilution will give a concentration for administration as follows:

250ml contains 1,000 micrograms/ml of dobutamine
500ml contains 500 micrograms/ml of dobutamine

The prepared solution should be used immediately or within 24 hours if stored at 2°C - 8°C.

Administration: Due to its short half-life, Dobutrex must be administered as a continuous intravenous infusion. After dilution, Dobutrex should be administered intravenously through an intravenous needle or catheter. An i.v. drip chamber or other suitable metering device is essential for controlling the rate of flow in drops per minute.

Recommended dosage for adults and the elderly: Dosage is inversely dependent upon the extent of healthy myocardium. Most patients will respond satisfactorily to doses ranging from 2.5 to 10 micrograms/ kg/minute. Occasionally a dose as low as 0.5 micrograms/kg/minute will elicit a response. Rarely, a dose as high as 40 micrograms/kg/minute is required.

The rate of administration and the duration of therapy should be adjusted according to the patient's response as determined by heart rate, blood pressure, urine flow, and, if possible, measurement of cardiac output.

Rather than abruptly discontinuing therapy with Dobutrex, it is often advisable to decrease the dosage gradually.

Side-effects, which are dose-related, are infrequent when Dobutrex is administered at rates below 10 micrograms/kg/minute. Rates as high as 40 micrograms/kg/minute have been used occasionally without significant adverse effects.

The final volume administered should be determined by the fluid requirements of the patient. Concentrations as high as 5,000 micrograms/ml have been used in patients on a restricted fluid intake.

High concentrations of dobutamine should only be given with an infusion pump, to ensure accurate dosage.

Paediatric use: The safety and efficacy of dobutamine for use in children have not been established.

4.3 Contraindications

Previous hypersensitivity to dobutamine. Hypovolaemia (see Section 4.4).

4.4 Special warnings and precautions for use

If tachycardia or an undue increase in systolic blood pressure occurs or if an arrhythmia is precipitated, the dose of dobutamine should be reduced or the drug should be discontinued temporarily.

Dobutamine may precipitate or exacerbate ventricular ectopic activity; rarely has it caused ventricular tachycardia or fibrillation. Because dobutamine facilitates atrioventricular conduction, patients with atrial flutter or fibrillation may develop rapid ventricular responses.

Extreme caution should be exercised when dobutamine is used in patients with acute myocardial infarction because any significant increase in heart rate or excessive increases in arterial pressure that occur may intensify ischaemia and cause anginal pain and ST segment elevation. Extreme caution should also be exercised in patients with atrial fibrillation or idiopathic hypertrophic subaortic stenosis.

Inotropic agents, including dobutamine, do not improve haemodynamics in most patients with mechanical obstruction that hinders either ventricular filling or outflow, or both. Inotropic response may be inadequate in patients with markedly reduced ventricular compliance. Such conditions are present in cardiac tamponade, valvular aortic stenosis, and idiopathic hypertrophic subaortic stenosis.

During the administration of dobutamine, as with any parenteral catecholamine, heart rate and rhythm, arterial blood pressure, and infusion rate should be monitored closely. When initiating therapy, electrocardiographic monitoring is advisable until a stable response is achieved. The development of increase in heart rate or blood pressure, or arrhythmias may require the temporary reduction or discontinuation of dosage.

Precipitous decreases in blood pressure (hypotension) have occasionally been described in association with dobutamine therapy. Decreasing the dose or discontinuing the infusion typically results in rapid return of blood pressure to base-line values, but rarely intervention may be required and reversibility may not be immediate.

Dobutamine should be used with caution in the presence of severe hypotension complicating cardiogenic shock (mean arterial pressure less than 70mm Hg).

Hypovolaemia should be corrected when necessary with whole blood or plasma before dobutamine is administered.

If arterial blood pressure remains low or decreases progressively during administration of dobutamine despite adequate ventricular filling pressure and cardiac output, consideration may be given to the concomitant use of a peripheral vasoconstrictor agent, such as dopamine or noradrenaline.

Dobutrex contains sodium metabisulphite. Sulphites may cause allergic - type reaction, including anaphylactic symptoms and life – threatening or less severe asthmatic episodes in certain susceptible people. Sulphite sensitivity is seen more frequently in asthmatic than non – asthmatic people.

4.5 Interaction with other medicinal products and other forms of interaction

The potency of dobutamine may be decreased if the patient is given beta-adrenergic receptor antagonists. In such a case, the unopposed alpha-agonist effects of dobutamine may become apparent, including peripheral vasoconstriction and hypertension. Conversely, alpha-adrenergic blockade may make the beta-1 and beta-2 effects apparent, resulting in tachycardia and vasodilatation.

4.6 Pregnancy and lactation

Reproduction studies performed in rats and rabbits have revealed no evidence of harm to the foetus or teratogenic effects due to dobutamine. Animal studies to evaluate effects on fertility have not been performed. As there are no adequate and well-controlled studies in pregnant women and as animal reproduction studies are not always predictive of human response, dobutamine should not be used during pregnancy unless the potential benefits outweigh the potential risks to the foetus.

It is not known whether this drug is excreted in human milk, so caution should be exercised. If a mother requires dobutamine treatment, breast feeding should be discontinued for the duration of treatment.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

For cardiovascular effects, see ‘Section 4.4’.

Reactions at site of intravenous infusion: Phlebitis has occasionally been reported. Local inflammatory changes have been described following inadvertent infiltration. Isolated cases of cutaneous necrosis have been reported.

The following side-effects have been reported rarely: nausea, headache, anginal pain, non-specific chest pain, palpitations, shortness of breath, and reactions suggestive of hypersensitivity, including rash, fever, eosinophilia and bronchospasm. Isolated cases of thrombocytopenia have been reported.

As with other catecholamines, decreases in serum potassium concentrations have occurred, rarely to hypokalaemic values. Consideration should be given to monitoring serum potassium.

Long-term safety: Infusions for up to 72 hours have revealed no adverse effects other than those seen with shorter infusions. There is evidence that partial tolerance develops with continuous infusions of dobutamine for 72 hours or more; therefore, higher doses may be required to maintain the same effects.

4.9 Overdose

Overdoses of dobutamine have been reported rarely. The symptoms of toxicity may include anorexia, nausea, vomiting, tremor, anxiety, palpitations, headache, shortness of breath and anginal and non-specific chest pain. The positive inotropic and chronotropic effects of dobutamine may cause hypertension, tachyarrhythmias, myocardial ischaemia and ventricular fibrillation. Hypotension may result from vasodilatation.

The duration of action of dobutamine hydrochloride is generally short (half-life, approximately 2 minutes).

Temporarily discontinue dobutamine until the patient's condition stabilises. The patient should be monitored and any appropriate resuscitative measures initiated promptly.

Forced diuresis, peritoneal dialysis, haemodialysis, or charcoal haemoperfusion have not been established as beneficial.

If the product is ingested, unpredictable absorption may occur from the mouth and gastro-intestinal tract.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The primary action of dobutamine is to augment cardiac contractility by stimulating the beta-1 receptors of the heart. It is a direct-acting agent.

5.2 Pharmacokinetic properties

The onset action of Dobutrex is within one to two minutes; the principal routes of metabolism are methylation of the catechol and conjugation. In human urine the major excretion products are the conjugates of dobutamine and 3-0-methyl dobutamine. The 3-0-methyl derivative of dobutamine is inactive.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium metabisulphite
Water for injections
Hydrochloric acid
Sodium hydroxide

6.2 Incompatibilities

Because of potential physical incompatibilities, it is recommended that Dobutrex not be mixed with other drugs in the same solution.

Do not add Dobutrex to 5% Sodium Bicarbonate Intravenous Infusion BP or to any other strongly alkaline solutions.

Dobutamine hydrochloride should not be used in conjunction with other agents or diluents containing both sodium bisulphite and ethanol.

6.3 Shelf Life

2 years.

6.4 Special precautions for storage

Do not store undiluted vials of Dobutrex Solution above 25°C.

From a microbiological point of view, the product should be used immediately. If 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 to 8°C unless dilution has taken place in controlled and validated aseptic conditions.

6.5 Nature and contents of container

A Type 1 Ph. Eur. clear glass vial with rubber stopper and aluminium seal.

Packs: single dose, 20 ml vial.

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

See section 4.2 and 6.2.

Solutions containing Dobutrex may turn pink; the colour may intensify with time. This colour change is due to slight oxidation of the drug, but there is no significant loss of potency during the recommended storage periods.

7 MARKETING AUTHORISATION HOLDER

Flynn Pharma Limited
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4 Herbert Street
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8 MARKETING AUTHORISATION NUMBER

PA 1226/3/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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