Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Sterile Dopamine Concentrate BP 160mg/ml, 5ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml sterile concentrate contains 160mg dopamine hydrochloride.
Each 5ml ampoule contains 800mg of dopamine hydrochloride.

Excipients with known effect
Each ml of sterile concentrate contains 2.42mg of sodium and 10.0mg sodium metabisulphite (E 223)
Each 5ml ampoule contains 12.1mg sodium and 50mg sodium metabisulphite (E 223)

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for infusion.
Clear, colourless or pale yellow sterile concentrate for solution for infusion.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the correction of haemodynamic imbalance such as is seen in circulatory decompensation accompanying myocardial infarction, trauma, endotoxic septicaemia, renal failure, congestive cardiac failure and open heart surgery.

4.2 Posology and method of administration

Posology

Adults including the elderly:
The initial rate of infusion is 2 to 5 micrograms per kilogram body weight per minute and this may be increased gradually by increments of 5 to 10 micrograms/kg/minute until the optimum dose for the individual is achieved.
Up to 50 micrograms/kg/minute may be required and even higher doses have been used.

The usual dilution is 1,600 micrograms per ml and this may be achieved by transfer, aseptically, of 800mg of dopamine hydrochloride to 500ml of one of the following sterile intravenous solutions :-
Sodium Chloride Injection
5% Dextrose Injection
5% Dextrose and 0.9% Sodium Chloride Injection
5% Dextrose and 0.45% Sodium Chloride Solution
5% Dextrose in Ringer Lactate Solution
Sodium Lactate 1/6 Molar Injection
Lactated Ringer's Injection
Alkaline solutions such as 5% sodium bicarbonate should NOT be added to dopamine hydrochloride because the drug will be inactivated.

Paediatric population
Safety and effectiveness in children have not been established.

Method of administration
For intravenous administration by infusion only, after dilution, into medium to large size veins.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Dopamine should not be used in patients with phaeochromocytoma or hyperthyroidism.
Dopamine should not be used in the presence of uncorrected atrial or ventricular tachyarrhythmias or ventricular fibrillation.
Cyclopropane and halogenated hydrocarbon anaesthetics should be avoided.

4.4 Special warnings and precautions for use

Patients who have been treated with MAO inhibitors prior to dopamine should be given reduced doses; the starting dose should be one tenth (1/10th) of the usual dose. Excess administration of potassium-free solutions may result in significant hypokalaemia.

The intravenous administration of these solutions can cause fluid and/or solute overloading resulting in dilution of serum electrolyte concentrations, overhydration, congested states or pulmonary oedema.

Hypovolaemia should be corrected where necessary prior to dopamine infusion. Low doses should be used in shock due to acute myocardial infarction.

If a disproportionate rise in diastolic pressure (i.e. a marked decrease in pulse pressure) is observed, the infusion rate should be decreased and the patients observed carefully for further evidence of predominant vasoconstriction activity, unless such an effect is desired.

Patients with a history of peripheral vascular disease should be closely monitored for any changes in colour or temperature of the skin of the extremities. If change of skin colour or temperature occurs and is thought to be the result of compromised circulation to the extremities, the benefits of continued dopamine infusion should be weighed against the risk of possible necrosis. These changes may be reversed by decreasing the rate or discontinuing the infusion. IV administration of phentolamine mesilate 5-10 mg may reverse the ischaemia.

Dopamine hydrochloride in 5% dextrose injection should be infused into a large vein whenever possible to prevent the possibility of infiltration of perivascular tissue adjacent to the infusion site. Extravasation may cause necrosis and sloughing of the surrounding tissue. Ischaemia can be reversed by infiltration of the affected area with 10-15 ml of saline containing 5 to 10 mg phentolamine mesilate. A syringe with a fine hypodermic needle should be used to liberally infiltrate the ischaemic area as soon as extravasation is noted. Dextrose solutions should be used with caution in patients with known subclinical or overt diabetes mellitus. As the effect of dopamine on impaired renal and hepatic function is not known, close monitoring is advised. Dopamine infusion should be withdrawn gradually, to avoid unnecessary hypotension. Administration of dopamine hydrochloride should always be under the direct supervision of a physician to whom facilities are available for monitoring cardiovascular and renal indices, including blood volume, cardiac output, blood pressure, electrocardiography and urine flow.

When dopamine is used in patients with a history of occlusive vascular disease, particular attention should be paid to the status of blood circulation in the extremities.

The occurrence of undesirable increases in blood pressure or vasoconstriction or decrease in urinary output requires a reduction in dosage of dopamine hydrochloride.

The routine use of low-dose dopamine hydrochloride in critically ill patients to prevent or treat acute renal failure is not recommended because this may cause adverse effects which could further compromise such patients.

Excipients
Sodium Metabisulphite in this injection may rarely cause hypersensitivity reactions and bronchospasms.
This medicine contains less than 1 mmol sodium (23 mg) per ml, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interactions

(1) Anaesthetics:
The myocardium is sensitised by the effect of dopamine, cyclopropane or halogenated hydrocarbon anaesthetics, and these should be avoided. This interaction applies both to pressor activity and cardiac beta adrenergic stimulation.

(2) Alpha and Beta Blockers:
The cardiac effects of dopamine are antagonised by β - adrenergic blocking agents such as propanolol and metoprolol, and the peripheral vasoconstriction caused by high doses of dopamine is antagonised by α adrenergic blocking agents. Dopamine-induced renal and mesenteric vasodilation is not antagonised by either α or β-adrenergic blocking agents, but, in animals, is antagonised by haloperidol or other butrophenones, phenothiazines, and opiates.

(3) Monoamine Oxidase (MAO) Inhibitors:
MAO inhibitors potentiate the effect of dopamine and its duration of action. Patients who have been treated with MAO inhibitors prior to administration of dopamine will therefore require a substantially reduced dosage. (The starting dose should be reduced to at least $^{1}/_{10}$th of the usual dose).

(4) Phenytoin:
Administration of IV phenytoin to patients receiving dopamine has resulted in hypotension and bradycardia; some clinicians recommend that phenytoin be used with extreme caution, if at all, in patients receiving dopamine.

- Dopamine may increase the effect of diuretic agents.
- The ergot alkaloids should be avoided because of the possibility of excessive vasoconstriction.
- Tricyclic antidepressants and guanethidine may potentiate the pressor response to dopamine.

4.6 Fertility, pregnancy and lactation

Pregnancy
Animal studies have shown no evidence of teratogenic effects with dopamine. However, the effect of dopamine on the human foetus is unknown. Therefore the drug should be used in pregnant women only when the expected benefits outweigh the potential risk to the foetus.

Breast-feeding
It is not known if dopamine is excreted in breast milk, nor is the effect on the infant known.

Fertility
No data available.

4.7 Effects on ability to drive and use machines

Not applicable in view of the indications for use and the short half-life of the drug.

4.8 Undesirable effects

Adverse reactions to dopamine are related to its pharmacological action. The frequency of the adverse reactions is not known (cannot be estimated from the available data).

Nervous System Disorders: Headache

Eye Disorders: Mydriasis

Cardiac Disorders: Ectopic heart beats, tachycardia, anginal pain, palpitation
Aberrant conduction, bradycardia, widened QRS complex, hypertension, gangrene, fatal ventricular arrhythmias have been reported on rare occasions.

Vascular Disorders: Hypotension, vasoconstriction.
Gangrene of the feet has occurred following doses of 10-14 microgram/kg/min and higher in a few patients with pre-existing vascular disease.

Respiratory, thoracic and mediastinal Disorders: Dyspnoea.

Gastrointestinal Disorders: Nausea, vomiting

Skin and subcutaneous tissue disorders: Piloerection.

Renal and urinary disorders: Azotaemia

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 HPRA Pharmacovigilance
Website: www.hpra.ie.

4.9 Overdose

Excessive elevation of blood pressure and vasoconstriction can occur due to the alpha adrenergic actions of dopamine, especially in patients with a history of occlusive vascular disease. If desired, this condition can be rapidly reversed by dose reduction or discontinuing the infusion, since dopamine has a half-life of less than 2 minutes in the body. Should these measures fail, an infusion of an alpha adrenergic blocking agent, e.g., phentolamine mesilate, should be considered.

Dopamine at the infusion site can cause local vasoconstriction see Section 4.4.

Accidental over dosage as evidenced by excessive blood pressure elevation can be controlled by dose reduction or discontinuing the dopamine infusion for a short period, since the duration of action of dopamine is short. Should these measures fail, an infusion of phentolamine mesilate should be considered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: adrenergic and dopaminergic agents, ATC code: C01CA 04

Mechanism of action
Dopamine is a sympathomimetic agent with actions at alpha, beta and dopamine receptors. The type of receptor stimulated is determined by the dose. In relatively low doses, dopamine dilates renal and mesenteric blood vessels causing increases in renal blood flow, urine output and sodium excretion. As the dosage is increased, dopamine exerts a direct inotropic effect on the heart causing increases in cardiac output with minimal effects on the heart rate. With larger doses, dopamine also exerts alpha-stimulant effects, notably vasoconstriction.

5.2 Pharmacokinetic properties

Dopamine is inactive when taken orally and its vasoconstrictive properties preclude its administration by subcutaneous or intramusuclar injection.

Biotransformation and Elimination
It is rapidly inactivated in the body and the majority is metabolised into dopamine-related metabolic products which are rapidly excreted in the urine. The plasma half-life of dopamine is approximately 2 minutes.

5.3 Preclinical safety data

No further relevant information other than that which is included in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium metabisulphite (E 223)
Water for injections

6.2 Incompatibilities

Dopamine should not be added to 5% Sodium bicarbonate or other alkaline solution because the drug will be inactivated.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

Product as packaged for sale: 3 years
This solution must be diluted before use and used immediately after opening.

6.4 Special precautions for storage

Do not store above 25°C.
Keep the ampoule in the outer carton in order to protect from light.
For storage conditions after dilution and first opening of the medicinal product see section 6.3.

6.5 Nature and contents of container

Clear glass one point-cut (OPC) ampoules, glass type I Ph.Eur. with white ring.
Pack size: 10 x 5ml ampoules.

6.6 Special precautions for disposal and other handling

For single use only.
Discard any unused contents.
Do not use the injection if it is darker than yellow or discoloured in any other way.
The solution must be diluted before use.
The usual dilution is 1,600 micrograms per ml.

Dopamine hydrochloride can be diluted with 500ml of one of the following sterile intravenous solutions:
Sodium Chloride Injection
5% dextrose injection
5% dextrose and 0.9% Sodium Chloride Injection
5% dextrose and 0.45% Sodium Chloride Solution
5% dextrose in Ringer Lactate Solution
Sodium Lactate 1/6 Molar Injection
Lactated Ringers Injection

Do not dilute with alkaline solutions such as 5% sodium bicarbonate because the drug will be inactivated.

7 MARKETING AUTHORISATION HOLDER

Mercury Pharmaceuticals (Ireland) Ltd
4045 Kingswood Road
Citywest Business Park
Co Dublin
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0073/108/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17th August 1989

Date of last renewal: 17th August 2009

10 DATE OF REVISION OF THE TEXT

August 2021