

1. NAME OF THE MEDICINAL PRODUCT

Sterile Dopamine Concentrate BP 200mg/5ml.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Dopamine Hydrochloride USP, 200mg in 5ml.

3. PHARMACEUTICAL FORM

Clear, colourless or pale yellow sterile solution intended for parenteral administration to human beings.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the correction of haemodynamic imbalances in low-perfusion circulatory insufficiency associated with myocardial infarction, trauma, septicaemia, cardiac failure and open heart surgery.

4.2 Posology and method of administration

The solution must be diluted before administration. Alkaline solutions such as 5% sodium bicarbonate should NOT be added to dopamine hydrochloride because the drug will be inactivated. The usual dilution is 1,600 micrograms per ml and this may be achieved by transfer, aseptically of 800mg of dopamine hydrochloride to one of the following sterile I.V. 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

A suitable metering device is required in the infusion system to control the rate of flow, and this should be adjusted to the optimum patient response and monitored constantly in the light of the individual patient's response.

Adults: Use as large a vein as possible for infusion. The initial rate of infusion is 2 to 5 micrograms per kilogram bodyweight 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.

Children: The safety and efficacy of dopamine hydrochloride therapy in children have not been established.

4.3. Contraindications

Dopamine should not be used in patients with –

- Hypersensitivity to dopamine or any of the excipients.
- Pheochromocytoma 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

The solution contains an antioxidant, sodium metabisulphite, a sulphite that may cause allergic-type reactions including bronchospasm, anaphylaxis and life-threatening episodes in certain susceptible individuals. The prevalence of sulphite-sensitivity in the general population is unknown and is probably low. Sulphite-sensitivity is seen more frequently in persons with a history of asthma or atopic allergy.

Each ampoule of this injection contains 2.42 mg Sodium per ml.

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.

Precautions:

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 mesylate 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 of dopamine hydrochloride during infusion may cause ischaemic necrosis and sloughing of surrounding tissue. Ischaemia can be reversed by infiltration of the affected area with 10-15 ml of saline containing 5 to 10 mg phentolamine mesylate. A syringe with a fine hypodermic needle should be used to liberally infiltrate the ischaemic area as soon as extravasation is noted.

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.

Dextrose solutions should be used with caution in patients with known subclinical or overt diabetes mellitus.

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.

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.

4.5 Interaction with other medicinal products and other forms of interaction

i) 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.

ii) Alpha and Beta Blockers:

The cardiac effects of dopamine are antagonised by β -adrenergic blocking agents such as propranolol 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.

iii) 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 1/10th of the usual dose).

iv) 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 Pregnancy and lactation

Use in 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.

Use in Lactation:

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

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.

More common reactions include-

Cardiovascular: Ectopic heart beats, tachycardia, anginal pain, palpitation, hypotension, vasoconstriction.

Gastrointestinal: Nausea, vomiting

Nervous System: Headache

Respiratory: Dyspnoea

Less common reactions include-

Biochemical Abnormalities- Azotaemia

Cardiovascular: Aberrant conduction, bradycardia, widened QRS complex, hypertension, gangrene, fatal ventricular arrhythmias have been reported on rare occasions.

Eye Disorders: Mydriasis

Nervous system- Piloerection

Serious or Life-threatening Reactions:

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.

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 mesylate, should be considered.

Dopamine at the infusion site can cause local vasoconstriction hence the desirability of infusing into a large vein. The resulting ischaemia can be reversed by infiltration of the affected area with 10-15 ml of saline containing 5 mg to 10 mg phentolamine mesylate. A syringe with a fine hypodermic needle should be used to liberally infiltrate the ischaemic area as soon as extravasation is noted.

Accidental Overdosage:

Accidental overdosage 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 mesylate should be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Dopamine (3,4-dihydroxyphenylethylamine) is the third naturally occurring catecholamine and is a metabolic precursor of noradrenaline and adrenaline. Dopamine is used therapeutically as the hydrochloride and its main effects are seen in the cardiovascular system and the kidneys.

Heart

Dopamine exerts positive inotropic and chronotropic effects on the myocardium, acting as an agonist at beta-adrenergic receptors. In addition to its direct action on beta-adrenergic receptors, dopamine acts indirectly by releasing noradrenaline from sympathetic storage sites.

Blood Vessels

Depending on the vascular bed being studied and the dose administered, Dopamine can cause relaxation or contraction of vascular smooth muscle.

Dopamine Receptors

Unlike other endogenous catecholamines or sympathomimetic amines, Dopamine caused vasodilation in renal, coronary, mesenteric and intracerebral arterial vascular beds in anaesthetised dogs. This vasodilator effect is not antagonised by beta-adrenergic blockers, atropine or antihistamines. However, butyrophenones, phenothiazines, apomorphine and bulbocapnine selectively attenuate dopamine-induced vasodilatation, thus suggesting the existence of specific dopamine vascular receptors similar to those in the basal ganglia and other areas in the central nervous system.

Alpha-adrenergic Receptors

Dose response studies indicate that with a sufficiently large dose, the vasoconstrictor effect of dopamine predominates over its vasodilator effect. This dopamine-induced vasoconstrictor effect is antagonised by alpha-adrenoreceptor blocking agents such as phentolamine and phenoxybenzamine, indicating that vasoconstriction results from the action of dopamine on alpha-adrenergic receptors.

Kidney

Intravenous infusions of dopamine (2.6 to 7.1 µg/kg/min) to seven normal subjects increased estimated average renal plasma flow from 507 to 798 ml/min, inulin clearance from 109 to 136 ml/min and average sodium excretion from 171 to 571 µEq./min. Although the diuretic and natriuretic effects of dopamine may result from vasodilatation in renal vascular bed (vide supra), disassociation between natriuresis and increments in renal blood flow has been observed, suggesting that other mechanisms such as redistribution of intrarenal blood flow may be involved.

5.2 Pharmacokinetic properties

Dopamine is inactive when taken orally and its vasoconstrictor properties preclude its administration by subcutaneous or intramuscular injection. Dopamine hydrochloride is administered by intravenous infusion

Dopamine is a metabolic precursor of noradrenaline and, whereas a proportion is excreted as the metabolic products of noradrenaline, the majority is mainly metabolised into 3,4 -Dihydroxyphenylacetic Acid (DOPAC) and 3-methoxy-4-hydroxyphenylacetic (HVA) which are rapidly excreted in the urine.

The plasma half-life of dopamine is approximately two 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 BP
Water for Injections BP

6.2 Incompatibilities

Iron salts, alkalis or oxidising agents.

6.3 Shelf Life

36 months

* If only part of an ampoule is used, discard the remaining solution.

6.4 Special precautions for Storage

Do not store above 25°C.

Keep the container in the outer carton in order to protect from light.

6.5 Nature and Contents of Container

5 ml clear glass one point-cut (OPC) ampoules, glass Type I Ph Eur. borosilicate glass ampoules packed in cardboard cartons to contain 10 x 5ml ampoules.

6.6 Special precautions for disposal

This solution must be diluted before use.

Do not dilute with alkaline solution.

Do not use the injection if it is darker than slightly yellow or discoloured in any other way.

For the preparation of Dopamine Hydrochloride Intravenous Infusion.

Use as directed by the physician.

Keep out of reach of children.

7. MARKETING AUTHORISATION HOLDER

Antigen International Limited
Roscrea
Co. Tipperary
Ireland.

8. MARKETING AUTHORISATION NUMBER(S)

PL 02848/0130

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

14 September 1989 / 25 July 2000

10 DATE OF REVISION OF THE TEXT

18/03/2010.