Package leaflet: Information for the patient

Dopamine Hydrochloride 40mg/ml Concentrate for Solution for Infusion

Read all of this leaflet carefully before you start being given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

The name of your medicine is Dopamine Hydrochloride 40mg/ml Concentrate for Solution for Infusion. It will be referred to as "Dopamine Concentrate" for ease of use hereafter.

What is in this leaflet

1. What Dopamine Concentrate is and what it is used for

Dopamine Hydrochloride 40mg/ml Concentrate for Solution for Infusion contains 200mg of dopamine hydrochloride which helps to increase the strength of muscle contraction in the heart.
It is used to correct poor circulation to the tissues
- when there is a low output of blood from the heart and shock associated with damage to the heart muscle due to obstruction of its blood supply.
- also after an injury, blood infection, heart failure and open heart surgery.

2. What you need to know before you are given Dopamine Concentrate

You should not be given Dopamine Concentrate
- if you are allergic to dopamine hydrochloride or any of the other ingredients of this medicine (listed in section 6)
- if you have been told by your doctor that you have a tumour of the adrenal gland (phaeochromocytoma).
- if you have abnormal heartbeats and uncoordinated contraction of the heart muscles.
- if you have an overactive thyroid gland
- if you are being given certain anaesthetics, such as halothane and cyclopropane.

Warnings and precautions
Talk to your doctor or nurse before you are given Dopamine Concentrate
- if you have any heart related problems
- if you have recently used monoamine oxidase inhibitors (known as MAOIs which are used for the treatment of depression; see section "Taking other medicines" for further information)
- if you are sensitive to sulphite
- if you have a weaker pulse in your wrists than normal on examination

- if you have a blood disorder in which the volume of circulating blood is decreased (hypovolaemia)
- if you know that you are suffering or have suffered from problems related to circulation of blood in your hands and feet (peripheral vascular disease)
- if you have any kidney or liver diseases
- if you are pregnant or breast feeding
- if you have diabetes.

Speak to your doctor before you are given this injection if this applies to you.

Your doctor will monitor you for any side-effects affecting the heart or kidneys while you are receiving dopamine.
Dopamine infusion should be withdrawn gradually, to avoid low blood pressure.

Other medicines and Dopamine Concentrate
Tell your doctor if you are taking, have recently taken or might take any other medicines.

Some medicines can interact with Dopamine Concentrate, which can significantly alter their effects. If you are already taking one of the following medicines, speak to your doctor before you receive this medicine:
- Monoamine oxidase inhibitors (used for the treatment of depression) or if you have taken them in the last 14 days, e.g. phenelzine, moclobemide, rasagiline, selegiline, entacapone.
- Water tablets (diuretics), e.g. furosemide, amiloride or triamterene.
- Medicines which are often used for treating blood pressure and heart disorders (alpha and beta blockers e.g. propranolol, tolazoline).
- Medicines used to treat epilepsy (phenytoin).
- Medicines used to treat migraine (e.g. ergotamine derived from ergot alkaloids, methysergide).
- Medicines used to treat depression such as Tricyclic antidepressants (e.g. amitriptyline).
- Medicines used to reduce high blood pressure like guanethidine.
- Medicine used to help your breathing (doxapram).
- Medicines used to treat psychological problems like schizophrenia (e.g. haloperidol, clozapine).

Tell your doctor before you are given Dopamine Concentrate if you have recently received any anaesthetic agent such as halothane, isoflurane or cyclopropane.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

As with all drugs, this medicine should only be given in pregnancy and when breast feeding if absolutely necessary. Your doctor will be able to advise you.

Driving and using machines
Not applicable

Dopamine Concentrate contains sodium metabisulfite
Sodium metabisulfite may rarely cause severe hypersensitivity (allergic) reactions and bronchospasm (breathing difficulties).

Information on Sodium content
This medicine contains less than 1 mmol sodium (23 mg) per ml, that is to say essentially ‘sodium-free’.

3. How Dopamine Concentrate is given to you

This injection will be administered under the supervision of a doctor. The solution is diluted before administration and will then be given by infusion (as a drip through a needle or tube) into a vein.
Your doctor will decide on the most suitable dose for you. This product is not recommended for use in children.

If you think you have been given more Dopamine Concentrate than you should have
As the injection will be administered under the supervision of a doctor, it is unlikely that you will be given more than is necessary. However, if you have any concerns about the dose of your medicine discuss them with your doctor.
If you develop symptoms like narrowing of the blood vessels, tissue death around blood vessels, restriction in blood supply due to tissue damage due to over use of this product your doctor will stop giving you this medicine and give you other medications for treatment.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If any of the following happen, tell your doctor immediately:
- serious allergic reactions- any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face, lips, rash or itching (especially affecting your whole body)
- pain in your fingers or toes (at higher doses, especially in people who have had problems with their circulation, gangrene can occur)
- severe irregular heartbeat.

Other side effects:

Common: may affect up to 1 in 10 people
- headache
- a rapid or slow heart beat, chest pain, irregular heart beat and awareness of a rapid or irregular pulse
- difficulty in breathing
- low blood pressure (which may cause symptoms such as faintness or dizziness)
- narrowing of blood vessels (which may cause the skin to become cold and to turn pale or to have a bluish colour)
- nausea and vomiting.

Uncommon: may affect up to 1 in 100 people
- dilation of the pupil of the eye which may cause difficulty with bright lights
- goose pimples or hair 'standing at ends'
- irregular transfer (aberrant conduction), slow heartbeat (bradycardia)
- abnormalities in the ECG (a tracing of electrical currents in the heart)
- high blood pressure
- an excess of urea or other waste products in the blood (which may make you feel generally unwell and is identified by blood tests).

If dopamine hydrochloride escapes from the vein into the surrounding tissues during administration, it may cause damage of the surrounding tissues; tell your doctor if you notice any pain or swelling at the injection site so that the appropriate treatment may be given.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Dopamine Concentrate

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the ampoule label and carton after EXP. The expiry date refers to the last day of that month.

Do not store above 25°C.
Keep the ampoule in the outer carton in order to protect from light.

If only part used, discard the remaining solution.
If the solution appears darker than slightly yellow or discoloured in any other way, it should be returned unused to the pharmacist.

6. Contents of the pack and other information

What Dopamine Concentrate contains
- The active substance is dopamine hydrochloride.
- The other ingredients are sodium metabisulfite (E 223) in water for injections.

What Dopamine Concentrate looks like and contents of the pack
Dopamine Concentrate is a clear, colourless or pale yellow solution presented in 5ml clear glass ampoules (small glass bottles).
Each 5ml ampoule contains 200mg dopamine hydrochloride.
There are ten 5ml ampoules packed in to one cardboard box.

Marketing Authorisation Holder
Mercury Pharmaceuticals Limited, Dashwood House, 69 Old Broad Street, London, EC2M 1QS, United Kingdom

Manufacturer
Delpharm Tours, Rue Paul Langevin, Chambray Lès Tours, 37170 France.

This leaflet was last revised in August 2023.

Healthcare Professional's Information Leaflet

1 NAME OF THE MEDICINAL PRODUCT
Dopamine Hydrochloride 40mg/ml Concentrate for Solution for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 40 mg dopamine hydrochloride.
Each 5 ml ampoule contains 200mg dopamine hydrochloride

Excipient(s) with known effect
Each 5mL ampoule contains 50 mg sodium metabisulfite.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for infusion
Clear, colourless or pale yellow solution

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

Posology

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.

Paediatric population
The safety and efficacy of dopamine hydrochloride therapy in children have not been established.

Method of administration

For intravenous use
The solution must be diluted before administration.

For instructions on dilution of the medicinal product before administration, see section 6.6.

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.

4.3 Contraindications

Dopamine should not be used in patients with –

• Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

• 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

Warnings:

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% Glucose 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.

Glucose 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.

Excipients
Dopamine Hydrochloride 40mg/ml Concentrate for Solution for Infusion contains an antioxidant, sodium metabisulfite, a sulphite that may rarely 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.

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 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 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.

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.

Doxapram may cause hypertension in patients receiving 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 following adverse reactions are classified by system organ class and ranked under heading of frequency: Common (>1/100 to <1/10);
Uncommon (≥1/1,000 to <1/100).

System Organ Class	Frequency	Adverse reactions
Nervous system disorders	Common	Headache
Eye disorders	Uncommon	Mydriasis
Cardiac disorders	Common	Ectopic heart beats, tachycardia, anginal pain, palpitation
	Uncommon	Aberrant conduction, bradycardia, widened QRS complex, fatal ventricular arrhythmias have been reported on rare occasions.
Vascular Disorders	Common	Hypotension, vasoconstriction
	Uncommon	Hypertension, gangrene
Respiratory, thoracic and mediastinal disorders	Common	Dyspnoea
Gastrointestinal disorders	Common	Nausea, vomiting
Skin and subcutaneous tissue disorders	Uncommon	Piloerection
Renal and urinary disorders	Uncommon	Azotaemia

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.

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 Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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

Pharmacotherapeutic group: adrenergic and dopaminergic agents, ATC code: C01CA04

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.

Mechanism of action

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.

Pharmacodynamic effects

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 7.1µg/kg/min) to seven normal subjects increased estimated average renal plasma flow from 507 to 798ml/min, inulin clearance from 109 to 136ml/min and average sodium excretion from 171 to 571µEq./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

Biotransformation and Elimination

Dopamine is a metabolic precursor of noradrenaline and, whereas a proportion is excreted as the metabolic products of noradrenaline.

The plasma half-life of dopamine is approximately two minutes. Dopamine is metabolised in the liver, kidneys, and plasma by monoamine oxidase (MAO) and catechol-0-methyltransferase to the inactive compounds homovanillic acid (HVA) and 3,4-dihydroxyphenylacetic acid which are rapidly excreted in the urine. In patients receiving MAO inhibitors, the duration of action of dopamine may be as long as 1 hour. About 25% of a dose of dopamine is metabolised to norepinephrine within the adrenergic nerve terminals.

Dopamine is excreted in urine principally as HVA and its sulfate and glucuronide conjugates and as 3, 4-dihydroxyphenylacetic acid. A very small fraction of a dose is excreted unchanged.
Following administration of radio
labelled dopamine, approximately 80% of the radioactivity reportedly is excreted in urine within 24 hours.

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 metabisulfite (E 223)
Water for injections

6.2 Incompatibilities

Iron salts, alkalis or oxidising agents.

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

3 years

For single use only If only part of an ampoule is used, discard the remaining solution.

Diluted solutions should be used immediately. Discard any remaining solution.

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.

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.

Inspect the solution before use. Do not use the injection if it is darker than slightly yellow or discoloured in any other way or if it contains particulate matter.

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 (20 ml of the Dopamine Hydrochloride 40mg/ml Concentrate for Solution for Infusion) to 480 ml one of the following sterile I.V. solutions to achieve 1,600 microgram per ml concentration:

Sodium Chloride Injection
5% Glucose Injection
5% Glucose and 0.9% Sodium Chloride Injection
5% Glucose and 0.45% Sodium Chloride Solution
5% Glucose in Ringer Lactate Solution
Sodium Lactate 1/6 Molar Injection
Lactated Ringer's Injection

7 MARKETING AUTHORISATION HOLDER

Mercury Pharmaceuticals Limited
Dashwood House,
69 Old Broad Street,
London, EC2M 1QS,
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 12762/0571

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14 September 1989

Date of latest renewal: 19 March 2008

10 DATE OF REVISION OF THE TEXT

08/2023