

AUSTRALIAN PRODUCT INFORMATION – DBL™ STERILE DOPAMINE CONCENTRATE (DOPAMINE HYDROCHLORIDE)

1. NAME OF THE MEDICINE

Dopamine hydrochloride

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Dopamine hydrochloride is a naturally occurring biochemical catecholamine precursor of noradrenaline and adrenaline. The chemical name of dopamine hydrochloride is 4-(2-aminoethyl) benzene-1,2-diol hydrochloride and has the chemical formula $C_8H_{11}NO_2.HCl$.

DBL Sterile Dopamine Concentrate is a sterile solution of Dopamine Hydrochloride BP in water for injection, containing 1% sodium metabisulfite. The strength supplied is 200 milligrams/5 mL in a clear glass ampoule.

Excipient with known effect

Sodium metabisulfite

For the full list of excipients, see **Section 6.1 List of Excipients**.

3. PHARMACEUTICAL FORM

Dopamine hydrochloride is a white, odourless powder, freely soluble in water and soluble in alcohol. It is sensitive to light, alkalis, iron salts and oxidising agents. The pH of the solution is approximately 4. **It must be diluted before use.**

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the correction of haemodynamic imbalance present in:

Acute hypotension or shock associated with myocardial infarction, endotoxic septicaemia, trauma and renal failure.

As an adjunct after open heart surgery, where there is persistent hypotension after correction of hypovolaemia.

In chronic cardiac decompensation as in congestive failure.

4.2 Dose and Method of Administration

WARNING: Dopamine is a potent drug. It must be diluted before administration. Do not add to alkaline solutions such as sodium bicarbonate, as these inactivate dopamine.

In appropriate cases, restoration of blood volume with plasma, whole blood, or a suitable plasma expander, should be instituted prior to administration: central venous pressure should be 10 to 15cm H₂O, or pulmonary wedge pressure 14 to 18mm Hg.

Dosage

Adult

When appropriate, increase blood volume with a suitable plasma expander, whole blood or plasma until central venous pressure is 10 to 15 cm H₂O or pulmonary wedge pressure is 14 to 18 mm Hg. Begin administration of diluted solution at doses of 2 to 5 micrograms/kg/min in patients who are likely to respond to modest increments of heart force and renal perfusion (see table under **Section 5 Pharmacological properties** for physiological effects at various doses).

In more seriously ill patients, begin administration of diluted solution at doses of 5 micrograms/kg/min and increase gradually using 5 to 10 micrograms/kg/min increments up to 20 to 50 micrograms/kg/min as needed. In patients who do not respond to these doses with adequate arterial pressures or urine flow, additional increments may be employed in an effort to produce an appropriate arterial pressure and central perfusion. If doses of dopamine in excess of 50 micrograms/kg/min are required, it is suggested that urine output be checked frequently. Should urine flow begin to decrease in the absence of hypotension, reduction of dosage should be considered. Once optimal haemodynamic effects have been achieved, the lowest dose that maintains these effects should be used. Multiclinic trials have shown that more than 50% of the patients were satisfactorily maintained on doses of dopamine less than 20 micrograms/kg/min.

Treatment of all patients requires constant evaluation of therapy in terms of the blood volume, augmentation of myocardial contractility, distribution of peripheral perfusion and urinary output. Dosage should be adjusted according to the patient's response with particular attention to diminution of established urine flow rate, increasing tachycardia or development of new dysrhythmias as indices for decreasing or temporarily suspending the dosage.

Care must be taken in patients with cardiac decompensation to avoid alpha-adrenoceptor induced vasoconstriction and increased afterload. These patients should be started on a dose of 1 to 2 micrograms/kg/minute and the rate of infusion increased with caution. Patients with occlusive vascular disease should also be commenced on a similar low dose.

For patients with severe, refractory, chronic congestive heart failure who are to be treated for a short period of time with dopamine, it is recommended that the infusion rate be commenced at a rate of 0.5 to 2 micrograms/kg/min, increasing the dose as the urine flow increases to a usual maintenance dose of 1 to 3 micrograms/kg/min. The infusion rate should be reduced if the diastolic blood pressure or heart rate increases.

Paediatric

It is not recommended for use in children as safety and efficacy in this age group has not been established.

Geriatric

No variation in dosage is suggested for geriatric patients.

Method of administration

The rate of administration should be controlled in order to prevent inadvertent bolus administration: constant evaluation of therapy should be undertaken (ie. blood volume, ECG, arterial blood pressure, urine output, augmentation of myocardial contractility and distribution of peripheral perfusion. Measurement of central venous pressure and pulmonary wedge pressure and cardiac output are also helpful). Dopamine should be administered into a large vein (preferably of the antecubital fossa) to reduce the risk of extravasation into surrounding tissue which may cause necrosis.

Antidote for peripheral ischaemia following extravasation

To prevent sloughing and necrosis in ischaemic areas, the area should be infiltrated as soon as possible with 10 to 15 mL of sodium chloride intravenous infusion 0.9% containing from 5 to 10 milligrams of phentolamine, an adrenergic blocking agent. A syringe with a fine hypodermic needle should be used, and the solution liberally infiltrated throughout the ischaemic area. Sympathetic blockade with phentolamine causes immediate and conspicuous local hyperaemic changes if the area is infiltrated within 12 hours. Therefore, phentolamine should be given as soon as possible after the extravasation is noted.

Suggested dilution

Aseptically transfer DBL Sterile Dopamine Concentrate into the intravenous solution as per the table below:

Strength milligrams/5 mL	Volume mL	Intravenous solution volume mL	Final concentration micrograms/mL
200	5	250	800
200	5	500	400

In patients in whom greater fluid load is undesirable, an alternative regimen is suggested:

Strength milligrams/5 mL	Volume mL	Intravenous solution volume mL	Final concentration micrograms/mL
200	10	250	1600
200	20	500	1600

Rate of administration

Dopamine, after dilution, is administered intravenously through a suitable intravenous catheter or needle. An intravenous drip chamber or other suitable metering device is essential for controlling the rate of flow in drops per minute. Each patient must be individually titrated to the desired haemodynamic and/or renal response with dopamine. In titrating to the desired increase in systolic blood pressure, the optimum dosage rate for renal response may be exceeded, thus, necessitating a reduction in rate after the haemodynamic condition is stabilised.

Administration at rates greater than 50 micrograms/kg/minute has safely been used in advanced circulatory decompensation states. If unnecessary fluid expansion is of concern, adjustment of drug concentration may be preferred over increasing the flow rate of a less concentrated dilution.

Compatibilities

Dopamine has been reported to be compatible with the following: sodium chloride 0.9%, glucose 5%, glucose 5% and sodium chloride 0.9%, glucose 5% in sodium chloride 0.45%, glucose 5% in lactated Ringer's solution, sodium lactate 1/6 M injection, lactated Ringer's injection.

It is recommended that, if dopamine is administered with other drugs, a "piggyback" administration set or administration into a second injection site is used to avoid mixing of potent drugs with dopamine.

IV fluids

Dopamine injection has been shown to be stable for 24 hours when 200 milligrams is diluted in 250 mL or 500 mL of the following intravenous fluids:

- sodium chloride infusion 0.9%
- glucose 5% injection
- glucose 5% and sodium chloride infusion 0.9%
- 5% glucose in lactated Ringer's solution
- 1/6 M sodium lactate injection
- lactated Ringer's injection

However, as with all intravenous admixtures, dilution should be made just prior to administration.

Antibiotics

Dopamine has been found to be chemically and physically stable for 24 hours (at 23° to 25°C and exposed to light) with the following antibiotics:

- kanamycin sulfate (500 milligrams/250 mL 5% glucose admixture)
- tetracycline hydrochloride (250 milligrams/250 mL 5% glucose admixture)
- carbenicillin disodium (1.0 g/250 mL 5% glucose admixture)
- chloramphenicol sodium succinate (1.0 g/250 mL 5% glucose admixture)
- cephalothin sodium neutral (1.0 gram/250 mL 5% glucose admixture) (see note below)
- oxacillin (500 milligrams/250 mL 5% glucose) (see note below)

Because of loss of potency of the antibiotic at 24 hours the following admixtures of antibiotics and dopamine in 5% glucose solution should be administered within six hours of mixing:

- gentamicin sulfate (80 milligrams/250 mL 5% glucose)
- cephalothin sodium (1.0 g/250 mL 5% glucose)
- penicillin G potassium (5,000,000 units/250 mL 5% glucose)

NOTE: It is recommended in the literature that cephalothin sodium, oxacillin sodium and gentamicin sulfate not be mixed with any other drug. It is considered that the recommendation should also include cephalothin sodium neutral. Although studies indicate that dopamine hydrochloride may be compatible with these drugs, their admixture produces a fixed

combination of potent drugs. It is suggested that admixtures containing gentamicin sulfate, cephalothin sodium, cephalothin sodium neutral or oxacillin sodium should be avoided unless all other viable alternatives have been exhausted.

Other medicines

Heparin sodium (50,000 units/250 mL 5% glucose) has been shown to be compatible with dopamine hydrochloride for 24 hours.

Lignocaine hydrochloride (1.0 g/250 mL 5% glucose) has been shown to be compatible with dopamine hydrochloride for 24 hours.

Mixing other drugs in dopamine infusion is not recommended, as sufficient evidence of compatibility is not available.

Incompatibilities - Refer to Section 6.2 **Incompatibilities**.

4.3 Contraindications

Administration of dopamine is contraindicated in the following cases:

- Phaeochromocytoma: dopamine may release catecholamines into the circulation, producing an additive effect to an already abnormally high catecholamine level, and causing acute hypertension.
- Atrial or ventricular tachyarrhythmias or ventricular fibrillation.
- Concurrent use with cyclopropane and halogenated hydrocarbon anaesthetics (see **Section 4.5 Interactions with other medicines and other forms of interactions**).
- Hyperthyroidism.
- Concurrent use with ergotamine (see **Section 4.5 Interactions with other medicines and other forms of interactions**).

4.4 Special Warnings and Precautions for Use

Patients who are taking Monoamine oxidase (MAO) inhibitors or who have taken them within the last two to three weeks require a substantially reduced starting dose, i.e. about 1/10th the usual dose (see **Section 4.5 Interactions with other medicines and other forms of interactions**).

Dopamine should not be added to alkaline diluents (see **Section 4.2 Dose and method of administration** and **Section 6.2 Incompatibilities**).

Hypovolaemia

Hypovolaemia should be fully corrected prior to treatment with dopamine with a suitable plasma expander or whole blood or plasma until the central venous pressure is 10 to 15 cm H₂O or the pulmonary wedge pressure is 14 to 18 mm Hg.

Decreased pulse pressure

Excessive dosage may be indicated by a disproportionate rise in diastolic pressure (ie a marked decrease in pulse pressure). The infusion rate should be decreased or ceased and the patients observed carefully for further evidence of predominant vasoconstriction activity, unless such an effect is desired.

Occlusive vascular disease

Those patients with pre-existing peripheral vascular disease, such as that due to atherosclerosis, arterial embolism, Buerger's disease, Raynaud's disease, diabetic endarteritis or cold injury (e.g. frostbite), may be more susceptible to peripheral ischaemia and subsequent gangrene and should be observed carefully for any changes in colour or temperature of the skin in the extremities. If ischaemia occurs and is thought to be due to vasoconstriction, the benefits of the dopamine infusion should be weighed against the risks of possible necrosis. Ischaemia may be reversed by either decreasing the rate or discontinuing the infusion. Intravenous administration of phentolamine 5 to 10 milligrams may also reverse the ischaemia.

As with any cardiac stimulant, care should be exercised when administering dopamine to patients with cardiac ischaemia.

Acidosis, hypercapnia or hypoxia may reduce the effectiveness and/or increase the incidence of adverse effects of dopamine. These conditions should be corrected prior to or concurrently with administration of dopamine.

Pulmonary hypertension may be exacerbated due to dopamine-induced pulmonary vasoconstriction. Where dopamine-induced pulmonary hypertension has occurred, isoprenaline may be considered as an alternative inotropic agent.

Routine monitoring of blood pressure, ECG, cardiac status and renal output, is necessary in all patients. Where possible, the cardiac output and pulmonary wedge pressure should also be measured.

Sulfite sensitivity

DBL Sterile Dopamine Concentrate contains sodium metabisulfite, which may cause allergic-type reactions, including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than non-asthmatic people.

Hypotension

Hypotension may occur when attempting to wean patients from dopamine and it may be necessary to substitute dopamine with another pressor agent or to expand blood volume whilst gradually reducing the infusion rate.

Extravasation

Dopamine should be infused into a large vein whenever possible to prevent the possibility of extravasation into tissue adjacent to the infusion site. The infusion site should be continuously monitored for free flow. Extravasation may cause necrosis and sloughing of the surrounding tissue. A syringe with a fine hypodermic needle should be used to liberally infiltrate the ischemic area as soon as extravasation is noted.

Diabetes

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

Use in hepatic impairment

Dopamine is metabolised in the tissues and blood by MAO inhibitors and COMT. Since the effect of impaired liver function is not known, close monitoring is advisable.

Use in renal impairment

Dopamine and its metabolites are almost completely excreted in the urine. Since the effect of impaired renal function is not known, close monitoring of such patients is advisable.

Use in the elderly

No variation in dosage is suggested for geriatric patients. Close monitoring is required for blood pressure, urine flow, and peripheral tissue perfusion.

Paediatric use

It is not recommended for use in children as safety and efficacy in this age group has not been established.

Effects on laboratory tests

Dopamine or its metabolites may interfere with urine tests for amino acids or catecholamines and also with tests for detecting uric acid or urobilinogen.

Infusion of dopamine suppresses pituitary secretion of thyroid stimulating hormone, and prolactin.

4.5 Interactions with Other Medicines and Other Forms of Interactions

Alcohol: No information available.

Food: Not applicable.

Cyclopropane and halogenated anaesthetics sensitise the myocardium to the effects of dopamine. Dopamine should therefore be used with extreme caution with these drugs due to the potential for developing ventricular arrhythmias or hypertension.

MAO inhibitors potentiate the effect of dopamine and prolong its duration of action. Patients being treated, or who have been treated within the previous two to three weeks, with MAO inhibitors will, therefore, require a substantially reduced dosage of dopamine (the starting dose should be reduced to 1/10th of the usual dose or less).

Alpha and beta adrenergic receptor blocking drugs will interfere with the alpha and beta adrenergic responses induced by dopamine. The use of other pressor amines may be associated with complex interactions. The cardiac effects of dopamine are antagonized by β -adrenergic blocking agents such as propranolol and metoprolol, and the peripheral vasoconstriction caused by high doses of dopamine is antagonized by α -adrenergic blocking agents.

Hypotension may be observed with concurrent use of vasodilators such as glyceryl trinitrate, nitroprusside and calcium channel blockers.

In animal studies, large doses of butyrophenones blocked the dopaminergic mediated renal vasodilation. Whether this occurs in man is not known.

Tricyclic antidepressants may potentiate the cardiovascular effects of dopamine, possibly resulting in arrhythmias, tachycardia or severe hypertension or hyperpyrexia (see **Section 4.4 Special warnings and precautions for use**).

Concurrent use of digitalis glycosides with dopamine may increase the risk of cardiac arrhythmias. Caution and close ECG monitoring are very important if concurrent use is necessary.

Concurrent use of methysergide or other ergot alkaloids with dopamine may result in excessive vasoconstriction and should be avoided. Ergot alkaloids or oxytocin may potentiate the pressor effect of dopamine and cause severe hypertension and rupture of cerebral blood vessels. Concurrent use of ergotamine with dopamine is not recommended as it may produce vascular ischaemia and gangrene.

Guanethidine may potentiate the pressor response to dopamine.

Concurrent use of intravenous phenytoin with dopamine may result in dose dependent, sudden hypotension and bradycardia and possibly cardiac arrest. If anticonvulsant therapy is necessary during administration of dopamine, an alternative to phenytoin should be considered. Caution is also advised with concurrent use of other hydantoins.

Also refer to **Section 6.2 Incompatibilities**.

4.6 Fertility, Pregnancy and Lactation

Effects on fertility

Studies in animals have not been performed to assess the effects of dopamine on fertility.

Use in pregnancy (Category B3)

Category B3: Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed. Studies in animals have shown evidence of increased foetal damage, the significance of which is considered uncertain in humans.

It is not known whether dopamine crosses the placental barrier. In one animal study, the administration of dopamine to pregnant rats resulted in a decreased survival rate of the newborn and cataract formation in the survivors. The benefits of using this product should be weighed against the possible risks 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. Dopamine is inactive when ingested orally, nonetheless it is not recommended for breast-feeding mothers unless the expected benefits outweigh any potential risks.

4.7 Effects on Ability to Drive and Use Machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration. Patients should refrain from driving or using machines until they know that the medicinal product does not negatively affect these abilities.

4.8 Adverse Effects (Undesirable Effects)

Common reactions

Adverse reactions have been observed in 19% of patients during clinical evaluation; however, only half of these were attributed to dopamine. Treatment was terminated in 5% of all patients due to adverse reactions.

Cardiovascular - Ectopic beats, tachycardia, anginal pain, palpitation, hypotension, vasoconstriction.

Gastrointestinal - Nausea, vomiting.

Nervous system - Headache.

Respiratory - Dyspnoea.

Less common reactions

Biochemical abnormalities – Azotaemia.

Cardiovascular – Atrial fibrillation, aberrant ventricular conduction, bradycardia, widened QRS complex, hypertension, ectopic heart beats. A few cases of peripheral cyanosis have been reported in patients receiving dopamine.

Nervous System – Piloerection, anxiety.

Serious or life threatening reactions

Gangrene of feet has occurred following doses of 10 to 14 micrograms/kg/min and higher and in a few patients with pre-existing vascular disease (see **Section 4.4 Special warnings and precautions for use**).

Fatal ventricular arrhythmias have been reported on rare occasions. Extravasation of dopamine may cause necrosis and sloughing of surrounding tissue (see **Section 4.2 Dose and method of administration**).

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 Overdose

Symptoms

Excessive elevation of blood pressure and vasoconstriction could be expected to occur due to the alpha-adrenergic actions of dopamine, especially in patients with a history of occlusive vascular disease. (see **Section 4.8 Adverse effects**).

Treatment

In case of accidental overdose the rate of administration should be reduced or the infusion discontinued temporarily until the patient's condition stabilises. Since the duration of action of dopamine is quite short, no additional measures are usually necessary. If these measures

fail to stabilise the patient's condition in a relatively short time, use of the short acting alpha adrenergic blocking agent, phentolamine, should be considered.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

Dopamine hydrochloride can stimulate alpha, beta and dopamine receptors. At infusion rates of 0.5 to 2 micrograms/kg/min, dopamine receptors are selectively activated and blood pressure either does not change or decreases slightly. The most important effects are renal and mesenteric vasodilatation. Renal plasma flow, glomerular filtration rate and sodium excretion usually increase. At infusion rates of 2 to 10 micrograms/kg/min, beta₁-receptors are activated and cardiac output and systolic blood pressure increase. The total peripheral resistance is relatively unchanged because of peripheral vasoconstriction (alpha effect) and muscle vasodilatation (beta effect). At infusion rates above 10 micrograms/kg/min, alpha-receptors are activated, causing vasoconstriction, and both systolic and diastolic pressures increase.

Dopamine does not cross the blood-brain barrier and so does not activate dopamine receptors in the brain.

Cardiovascular effects of dopamine at various infusion rates

	0.5 to 2 micrograms/ kg/min.	2 to 10 micrograms/ kg/min.	Over 10 micrograms/ kg/min.
Cardiac output	no change	increase	increase
Stroke volume	no change	increase	increase
Heart rate	no change	there is an initial increase followed by a decrease toward normal rate as infusion continues.	
Myocardial contractility	no change	increase	increase
Potential for excessive myocardial oxygen demands	low* coronary blood flow increased	low* coronary blood flow increased	data unavailable
Potential for tachyarrhythmias	low*	low*	moderate
Total systemic vascular resistance	slight decrease to no change	no change to slight increase	increase
Renal blood flow	increase	increase	decrease

Clinical implication of pharmacokinetic data

Dopamine should be given by continuous infusion because of the rapid metabolism and excretion of the drug.

5.3 Preclinical Safety Data

Genotoxicity

The genotoxic potential of dopamine has not been evaluated.

Carcinogenicity

Long term studies in animals have not been performed to evaluate the carcinogenic potential of dopamine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sodium metabisulfate

Water for injections

6.2 Incompatibilities

Dopamine should not be added to sodium bicarbonate and other alkaline solutions (see **Section 4.4 Special warnings and precautions for use**) as they will inactivate dopamine. If sodium bicarbonate is simultaneously indicated to treat acidosis, it should be given through a separate infusion line from a separate container.

Dopamine is incompatible with ampicillin or amphotericin B, so should not be mixed with either of these drugs. Dopamine decomposes when mixed with ampicillin in 5% glucose solution, because the solution is alkaline. A precipitate forms immediately on mixing dopamine with amphotericin B in 5% glucose solution. Also refer to **Section 4.5 Interactions with other medicines and other forms of interactions**.

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special Precautions for Storage

Store below 30°C. Protect from light.

6.5 Nature and Contents of Container

DBL

Sterile Dopamine Concentrate is available in clear glass ampoules in the following strength:
200 milligrams dopamine hydrochloride/5 mL (cartons contain 5 ampoules)

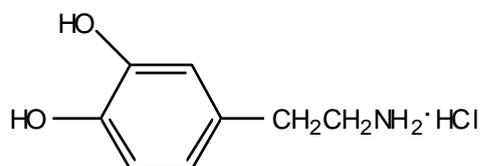
6.6 Special Precautions for Disposal

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 Physicochemical Properties

Chemical structure

The chemical structure is:



DOPAMINE HYDROCHLORIDE

MW 189.6

CAS number

CAS 51-61-6

7. MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4

8. SPONSOR

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9. DATE OF FIRST APPROVAL

20 June 2008

10. DATE OF REVISION

10 August 2021

Summary Table of Changes

Section changed	Summary of new information
4.2	Addition of monitoring urinary output; text relating to incompatibilities moved to section 6.2.
4.3	Addition of ventricular fibrillation

4.4	Addition of vasoconstriction activity monitoring, necrosis and sloughing caused by extravasation, warning relating to patients with diabetes, interference of thyroid hormone Editorial changes to add subtitles
4.5	Addition of β -adrenergic blocking agents propranolol and metoprolol
4.7	Addition of warning relating to driving or using machines
4.8	Addition of Atrial fibrillation and ectopic heart beats
4.9	Addition of overdose symptom vasoconstriction

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