

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

DOBUN (Dobutamine for Injection USP 250 mg)

2. Qualitative and Quantitative composition

Each vial contains:

Dobutamine Hydrochloride USP

Eq. to Dobutamine.....250mg

Excipients.....q.s

For full list of excipient section 6.1

3. Pharmaceutical form

Lyophilized cake

4. Clinical particulars

4.1 Therapeutic indications

Sterile Dobutamine hydrochloride solution is indicated in adults who require inotropic support in the treatment of low-output cardiac failure associated with cardiomyopathies, cardiogenic or septic shock, myocardial infarction and cardiac surgery. Dobutamine can increase or maintain cardiac output during positive end-expiratory pressure (PEEP) ventilation.

Dobutamine hydrochloride may also be used for cardiac stress testing as an alternative to exercise in patients for whom routine exercise cannot be satisfactorily performed. This use of dobutamine should only be undertaken in units, which already perform exercise stress testing and all normal care and precautions required for such testing are also required when using dobutamine for this purpose.

4.2 Posology and method of administration

This is a potent drug. The solution must be diluted to at least 50ml before administration and may then be administered by intravenous infusion.

Alkaline solutions such as 5% sodium bicarbonate should not be added to dobutamine hydrochloride because the drug will be inactivated.

Sterile Dobutamine hydrochloride solution must be diluted to at least 50ml with Sterile Water for Injection BP intravenous solutions:

Recommended dosage for adults and the elderly:

The usual dose is 2.5 to 10 micrograms/kg/minute. Occasionally, however, a dose as low as

0.5 micrograms/kg/minute will elicit a response. Up to 40 micrograms/kg/minute may occasionally be required.

The rate of administration and 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.

It is advisable to reduce the dosage of Dobutamine hydrochloride gradually rather than abruptly stopping therapy.

Side effects which are dose-related, are infrequent when Dobutamine hydrochloride 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.

Rates of Infusion for Concentrations of 250, 500, and 1000 microgram/mL Infusion Delivery

Rate

Drug Delivery Rate	250 µg/mL*	500 µg/mL**	1000 µg/mL***
2.5	0.0	0.00	0.0025
5	0.0	0.0	0.00
7.5	0.0	0.01	0.0075
10	0.0	0.0	0.0
12.	0.0	0.02	0.0125
15	0.0	0.0	0.01

* 250 mg per liter of admixture

** 500 mg per liter or 250 mg per 500 mL of admixture

***1000 mg per liter or 250 mg per 250 mL of admixture

The final volume administered should be determined by the fluid requirements of the patient. The rate of administration and duration of therapy should be adjusted according to the patient's response as determined by heart rate, presence of ectopic activity, blood pressure, urine flow and, whenever possible, measurement of central venous or pulmonary wedge pressure and cardiac output.

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 with restricted fluid intake.

Cardiac stress testing: when used as an alternative to exercise for cardiac stress testing the recommended dose is an incremental increase of 5 micrograms/kg/minute from 5 up to 20 micrograms/kg/minute, each dose being infused for 8 minutes. Continuous ECG monitoring is essential, and the infusion is terminated in the event of >3mm ST segment depression or any ventricular arrhythmia. The infusion should also be terminated if the heart rate reaches the age/sex maximum, systolic blood pressure rises above 220mm HG or any side effects occur.

Childre

n:

The safety and efficacy of Dobutamine hydrochloride therapy in children have not been established.

Method of administration

Intravenous use only.

4.3 Contraindications

- ☐ Hypersensitivity
- ☐ Phaeochromocytoma.
- ☐ Dobutamine stress echocardiography.
- ☐ Dobutamine must not be used for the detection of myocardial ischemia and of viable myocardium in case of:
 - recent myocardial infarction (within the last 30 days)
 - unstable angina pectoris
 - stenosis of the main left coronary artery
 - haemodynamically significant outflow obstruction of the left ventricle including hypertrophic obstructive cardiomyopathy
 - haemodynamically significant cardiac valvular defect
 - predisposition for or documented medical history of clinically significant or chronic arrhythmia, particularly recurrent persistent ventricular tachycardia
 - significant disturbance in the conduction
 - acute pericarditis, myocarditis or endocarditis
 - poor sonographic imaging conditions
 - inadequately treated/controlled arterial hypertension

4.4 Special warnings and precautions for use

The dose of dobutamine should be reduced or the drug should be discontinued temporarily if

an undue increase in heart rate or systolic blood pressure occurs or if an arrhythmia is precipitated. Dobutamine may precipitate or exacerbate ventricular ectopic activity: rarely has it caused ventricular tachycardia or fibrillation. Because dobutamine facilitates A-V conduction, patients with atrial flutter or fibrillation may develop rapid ventricular responses.

Dobutamine should only be used with great care in patients with acute myocardial infarction because any significant increase in heart rate or excessive increase in arterial pressure that occurs may intensify ischaemia and cause anginal pain.

Dobutamine Injection USP should not be used in the presence of uncorrected tachycardia or ventricular fibrillation.

Inotropic agents, including dobutamine, do not improve haemodynamics in most patients with mechanical obstruction that hinders either ventricular filling 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.

Minimal vasoconstriction has occasionally been observed, most notably in patients recently treated with a β -blocking drug. The inotropic effect of dobutamine stems from stimulation of cardiac β_1 receptors and this effect is prevented by β -blocking drugs. However, dobutamine has been shown to counteract the cardio-depressive effects of β -blocking drugs. Conversely, adrenergic blockade may make the β_1 and β_2 effects apparent, resulting in tachycardia and vasodilatation.

Dobutamine stress echocardiography

Because of possible life-threatening complications, the administration of dobutamine for stress echocardiography should only be undertaken by a physician with sufficient personal experience of the use of dobutamine for this indication.

The use of dobutamine as an alternative to exercise for cardiac stress testing is not recommended for patients with unstable angina, bundle branch block, valvular heart disease, aortic outflow obstruction or any cardiac condition that could make them unsuitable for exercise stress testing.

Cardiac rupture is a potential complication of myocardial infarction. The risk of cardiac rupture (septal and free wall) may be influenced by a variety of factors including the site, and time since, the infarct. There have been very rare, fatal reports of acute cardiac rupture during dobutamine stress testing. These events have occurred during pre-discharge examination in patients hospitalised with recent (within 4-12 days) myocardial infarction. In the reported cases of free wall rupture, the resting echocardiogram showed a dyskinetic and thinned inferior wall. Patients considered at risk of cardiac rupture during dobutamine testing should therefore be carefully evaluated prior to testing.

Dobutamine stress echocardiography must be discontinued if one of the following diagnostic endpoints occurs:

- systolic blood pressure decrease greater than 20 mmHg
- blood pressure increase above 220/120 mmHg
- progressive symptoms (angina pectoris, dyspnoea, dizziness, ataxia)

- progressive arrhythmia (e.g., coupling, ventricular salvos)
- progressive conduction disturbances
- recently developed wall motility disorders in more than 1 wall segment (16-segment model)
- increase of end-systolic volume
- reaching peak dose

4.5 Interaction with other medicinal products and other forms of interaction

Halogenated anaesthetics:

Although it is less likely than adrenaline to cause ventricular arrhythmias, Dobutamine solution should be used with great caution during anaesthesia with cyclopropane, halothane and other halogenated anaesthetics.

Entacapone:

The effects of dobutamine may be enhanced by entacapone.

No evidence of drug interactions were noted in clinical studies when dobutamine was administered concurrently with other drugs including digitalis preparations and/or furosemide, spironolactone, lidocaine, nitroglycerin, isosorbide dinitrate, morphine, atropine, anticoagulants and potassium chloride supplements.

4.6 Pregnancy and lactation

Animal studies have not revealed any evidence of teratogenic effects from dobutamine hydrochloride. As animal reproduction studies are not always predictive of human response the drug should not be used in pregnancy unless, in the opinion of the physician, the expected therapeutic benefits outweigh the potential risk to the foetus.

4.7 Effects on the ability to drive and use machines

Dobutamine hydrochloride has no/negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

Infusions for up to 72 hours have revealed no adverse effects other than those seen with shorter infusions.

Evaluation of undesirable effects is based on the following frequency scale:

Very common: $\geq 1/10$

Common: $\geq 1/100$ to $< 1/10$

Uncommon: $\geq 1/1,000$ to $< 1/100$

Rare: $\geq 1/10,000$ to $< 1/1,000$

Very rare: $< 1/10,000$

Not known: cannot be estimated from the available data

Immune system disorders:

Not Known: Hypersensitivity reactions including rash, fever, eosinophilia and bronchospasm, have been reported. Anaphylactic reactions and severe life-threatening asthmatic episodes may be due to sulphite sensitivity (see section 4.4 Special warnings and other precautions for use).

Blood and lymphatic system disorders

Common: Eosinophilia, inhibition of thrombocyte aggregation (only when continuing infusion over several days)

Metabolism and nutrition disorders:

Very rare: Hypokalaemia
Consideration should be given to monitoring serum potassium.

Cardiac disorders:

Very common: Increase of the heart rate by ≥ 30 beats/min

Common: Blood pressure increase of ≥ 50 mmHg. Patients suffering from arterial hypertension are more likely to have a higher blood pressure increase.
Blood pressure decrease, ventricular dysrhythmia, dose-dependent ventricular extrasystoles.
Increased ventricular frequency in patients with atrial fibrillation. These patients should be digitalised before dobutamine infusion.
Vasoconstriction in patients who have previously been treated with beta receptor blockers.
Anginal pain, palpitations.

Uncommon: Ventricular tachycardia, ventricular fibrillation

Very rare: Bradycardia, myocardial ischaemia, myocardial infarction
Cardiac arrest

Not known: Electrocardiogram ST-segment elevation Decrease in pulmonary capillary pressure.

Eosinophilic myocarditis has been noted in explanted hearts of patients who had undergone treatment with multiple medications including dobutamine or other inotropic agents before transplantation.

Stress cardiomyopathy (Takotsubo syndrome) (see section 4.4)

Vascular disorders:

Hypertension. A marked increase in systolic blood pressure indicates overdose
Hypotension

Nervous system disorders:

Common: Headache

Not known: Paraesthesia, tremor, myoclonic spasm. Myoclonus has been reported in patients with severe renal failure receiving dobutamine.

Gastrointestinal disorders

Not known: Nausea

Respiratory system, thoracic and mediastinal disorders

Common: Bronchospasm, shortness of breath

Skin and subcutaneous tissue disorders

Common: Exanthema

Very rare: Petechial bleeding

Musculoskeletal and connective tissue disorders

Common: Chest pain

Renal and urinary disorders

Common: Increased urgency at high dosages of infusion

General disorders and administration site conditions

Common: Fever, phlebitis at the injection site

In case of accidental paravenous infiltration, local inflammation may develop. Very rare: Cutaneous necrosis

"Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) <https://pv.pharmacyboardkenya.org>"

4.9 Overdose

Overdoses of dobutamine have been reported rarely. The symptoms of toxicity may include

anorexia, nausea, vomiting, tremors, 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.

If the product is ingested, unpredictable absorption may occur from the mouth and gastrointestinal tract.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Dobutamine directly stimulates β_1 adrenergic receptors and is generally considered a selective β_1 -adrenergic agonist, but the mechanisms of action of the drug are complex. It is

believed that the β -adrenergic effects result from stimulation of adenyl cyclase activity. In therapeutic doses, dobutamine also has mild β_2 and β -adrenergic receptor agonist effects, which are relatively balanced and result in a minimal net direct effect on system vasculature. Unlike dopamine, dobutamine does not cause the release of endogenous norepinephrine. The main effect of therapeutic doses of dobutamine is cardiac stimulation. The positive inotropic effect of the drug on the myocardium appears to be mediated principally via β_1 -adrenergic stimulation.

The β_1 -adrenergic effects of dobutamine exert a positive inotropic effect on the myocardium and result in an increase in cardiac output due to increased myocardial contractility and stroke volume in healthy individuals and in patients with congestive heart failure. Increased left ventricular filling pressure decreases in patients with congestive heart failure. In therapeutic doses, dobutamine causes a decrease in peripheral resistance; however systolic blood pressure and pulse pressure may remain unchanged or be increased because of augmented cardiac output. With usual doses, heart rate is usually not substantially changed. Coronary blood flow and myocardial oxygen consumption are usually increased because of increased myocardial contractility.

Electrophysiologic studies have shown that dobutamine facilitates atrioventricular conduction and shortens or causes no important change in intraventricular conduction. The tendency of dobutamine to induce cardiac arrhythmias may be slightly less than that of dopamine and is considerably less than that of isoproterenol or other catecholamines. Pulmonary vascular resistance may decrease if it is elevated initially and mean pulmonary artery pressure may decrease or remain unchanged. Unlike dopamine, dobutamine does not seem to affect dopaminergic receptors and causes no renal or mesenteric vasodilation, however, urine flow may increase because of increased cardiac output.

5.2 Pharmacokinetic properties

Absorption

Orally administered dobutamine is rapidly metabolised in the gastrointestinal tract. Following IV administration, the onset of action of dobutamine occurs within 2 minutes. Peak plasma concentrations of the drug and peak effects occur within 10 minutes after initiation of an IV infusion. The effects of the drug cease shortly after discontinuing an infusion.

Distribution

It is not known if dobutamine crosses the placenta or is distributed into milk.

Elimination

The plasma half-life of dobutamine is about 2 minutes. Dobutamine is metabolised in the liver and other tissues by catechol-o-methyltransferase to an inactive

compound, 3-O- methyl Dobutamine and by conjugation with glucuronic acid. Conjugates of Dobutamine and 3- O-methyl Dobutamine are excreted mainly in urine and to a minor extent in faeces

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety

pharmacology and repeated dose toxicity. There are no studies concerning the mutagenic and carcinogenic potential of Dobutamine. In view of the vital indications and the short duration of treatment, these studies appear of minor relevance. Studies in rats and rabbits revealed no evidence of a teratogenic effect. An impairment of implantation and pre-and postnatal growth retardations were observed in rats at doses toxic to mothers. No influence on fertility was seen in rats.

6. Pharmaceutical particulars

6.1 List of excipients

Mannitol BP
Sodium hydroxide
BP Disodium
EDTA BP Ascorbic
acid BP

6.2 Incompatibilities

Dobutamine solutions have proven to be incompatible with:

- alkaline solutions (e.g., sodium hydrogen carbonate),
- solutions containing both sodium metabisulfite and ethanol,
- aciclovir,
- alteplase,
- aminophylline,
- bretylium,
- calcium chloride,
- calcium gluconate,
- diazepam,
- digoxin,
- etacrynic acid (sodium salt),
- heparin sodium,
- hydrogen cortisone sodium succinate,
- insulin,
- potassium chloride,
- magnesium sulfate,
- penicillin,
- phenytoin,
- streptokinase,

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

6.3 Shelf life

24 months

6.4 Special precautions for storage

Do not store above 30°C. Protect from light. Keep out of reach and sight of children
In combination with intravenous formulations it may be stored for 24 hours at 25°C.

6.5 Nature and contents of the container

A white to off - white coloured cake filled in 20 ml clear USP Type-I Tubular glass vial plugged with grey bromo butyl rubber stopper with flip off Aluminium seal and packed in printed monocarton along with pack insert.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder

Indasi Lifescience Pvt. Ltd

Manufacturer address:

Name of manufacturer	Indasi Lifescience Pvt. Ltd
Address	Plot No. 73-77, Silver Industrial Estate, Bhimpore, Daman 396210.
Phone	+918000590111, +918000492233
Fax	-
E-mail ID	info@indasilifescience.com
Quality Manufacturing Site	qa1@indasilifescience.com

8. Marketing authorization number(s)

NA

9. Date of first authorization/renewal of the authorization

NA

10. Date of revision of the text

July 2026 (last updated)