PACKAGE LEAFLET: INFORMATION FOR THE PATIENT

Dobutamine 12.5 mg/ml

Concentrate for solution for infusion

dobutamine hydrochloride

Read all of this leaflet carefully before you start using 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.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- 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.

WHAT IS IN THIS LEAFLET

1. WHAT DOBUTAMINE IS AND WHAT IT IS USED FOR

Dobutamine contains the active ingredient dobutamine, which belongs to a group of medicines called beta receptor agonists (heart stimulants).

In **adults** it is used:
- in open heart surgery,
- to treat heart disease,
- to treat heart failure,
- as an alternative to exercise for stress testing the heart.

Paediatric population
Dobutamine is indicated in all paediatric age groups (from neonates to 18 years of age) as inotropic support in low cardiac output hypoperfusion states resulting from decompensated heart failure, following cardiac surgery, cardiomyopathies and in cardiogenic or septic shock.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE DOBUTAMINE

Do not use Dobutamine:
- if you are allergic to dobutamine, sodium metabisulphite or any of the other ingredients of this medicine (listed in section 6). Dobutamine (see list of ingredients in section 6). An allergic reaction may include rash, itching, difficulty breathing or swelling of the face, lips, throat or tongue.
- if you suffer from high blood pressure due to a tumour near the kidney (Phaeocromocytoma).
- if you have a low blood volume that has not been corrected (your doctor will know this).
- if you have an obstruction that interferes with blood flow out of your heart (your doctor will know this).
- if you have an uncontrolled arrhythmia (heart rhythm)

Do not use Dobutamine to test your heart if:
- You have unstable (uncontrolled) angina.
- You have an electrolyte (salt) imbalance.
- You have suffered a heart attack within the last 30 days.
- You have suffered an aortic aneurysm (a weakened and bulging area in the aorta, the major blood vessel that feeds blood to the body).
- You have uncontrolled high blood pressure.
- You have severe anaemia (low red blood cells).
- You have suffered an aortic dissection (bleeding caused by a tear in the wall of the aorta, the major blood vessel that feeds blood to the body)

Warnings and precautions
Talk to your doctor or nurse before using Dobutamine.

Talk to your doctor or nurse if you have any of the following conditions:
- Any heart disorder.
- Hyperthyroidism (over-active thyroid).
- A tumour of the adrenal gland.
- A condition in which the concentration of potassium in the blood is low (Reduction in serum potassium concentration and hypokalaemia).
- A liver or kidney disorder.
- Severe hypotension (low blood pressure).
- Asthma.
- Diabetes mellitus.
- Hypovolaemia (dehydration).

Children
Increments in heart rate and blood pressure appear to be more frequent and intense in children than in adults. The new-born baby cardiovascular system has been reported to be less sensitive to dobutamine and hypotensive effect (low blood pressure) seems to be more often observed in adult patients than in small children. Accordingly, the use of dobutamine in children should be monitored closely.

Other medicines and Dobutamine
Tell your doctor if you are using, have recently used or might use any other medicines.
This is especially important with the following medicines as they may interact with your Dobutamine:
- Monoamine oxidase inhibitors (treatments for depression)
- Beta-adrenergic blockers such as propranolol or metoprolol
- Alpha-adrenergic blockers (for high blood pressure or enlarged prostate gland)
- ACE-inhibitors, e.g. captopril (for high blood pressure or heart failure)
- Antipsychotics (treatments for mental illness)
- Oxytocin (used in labour)
- Peripheral vasoconstrictor agents such as noradrenaline
- Peripheral vasodilators (e.g. nitrates, sodium nitroprusside)
- Ergotamine or methysergine (treatments for migraine)
- Dipyridamole (a blood thinner)
- General anaesthetics
- Theophylline (a treatment for asthma)
- Entacapone (a medicine to treat Parkinson's disease)
- Doxapram (for breathing problems)
- Atropine sulphate (for inflammation of the iris of the eye or for eye examinations)

Pregnancy and breast-feeding
You will not be given Dobutamine if you are pregnant or breast-feeding unless your doctor thinks it is necessary.

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

Dobutamine contains sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per dose (12.5 mg/ml), i.e. essentially 'sodium- free'.

Dobutamine contains sodium metabisulphite (E223)
May rarely cause severe hypersensitivity reactions and bronchospasm.

The following information is intended for healthcare professionals only:

Dobutamine 12.5 mg/ml

Concentrate for solution for infusion
dobutamine hydrochloride

Posology and method of administration
For intravenous use only.

Posology
Adult

Inotropic support of the myocardium:
The usual dose is 2.5 to 10 µg/kg/minute, which should be adjusted according to the patient's heart rate, blood pressure, cardiac output and urine output. The infusion must be started at a rate of 2.5 µg/kg/min and the dose may be increased in intervals of 10-30 minutes until desired hemodynamic response is achieved or until side effects, such as excessive tachycardia, arrhythmia, headache or tremor limit a further increase in dosage. The dose should be adjusted individually according to heart rate and rhythm, blood pressure and urinary flow. Occasionally, a dose as low as 0.5 µg/kg/minute will produce a response. Up to 40 µg/kg/minute may be required.

During prolonged continuous infusion (48-72 hours), a decrease in haemodynamic response may occur, which makes an increase in dose necessary.

Dosage for cardiac stress testing:
The use of dobutamine in cardiac stress testing 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 including the availability of a defibrillator and personnel specially trained in resuscitation are present.

The recommended dosage is an incremental increase in infusion rates from 5 µg/kg/minute to 10, 20, 30 and a maximum of 40 µg/kg/minute, each dose being infused for 3 minutes. In addition atropine can be added during further infusion of the peak dose. Continuous electrocardiogram (ECG) monitoring is required and the infusion may be terminated in the event of ST-segment depression of > 0.2 mV (2 mm) measured 80 ms after the J point, a ST-segment elevate of > 0.1 mV (1 mm) in patients without history of myocardial infarction, or any significant cardiac arrhythmias.
The infusion of dobutamine should be terminated if the heart rate reaches 85% of the age-predicted maximum, systolic blood pressure rises above 220 mmHg or a symptomatic decrease in systolic blood pressure > 40 mmHg from baseline, new cardiac wall motion abnormalities, severe chest pain or any non-tolerable adverse effect occurs.

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

Cardiac stress testing: when used as an alternative to exercise for cardiac stress testing the recommended dose should start at 5 µg/kg/minute, and the dose should be increased incrementally by 5 µg/kg/minute every 8 minutes to a maximum rate of 20 µg/kg/minute. Continuous ECG monitoring is essential and the infusion terminated in the event of > 3 mm ST segment depression or any ventricular arrhythmia. The infusion should also be terminated if heart rate reaches the age/sex maximum, systolic blood pressure rises above 220 mm Hg or any side effects occur.

Paediatric population
For all paediatric age groups (neonates to 18 years) an initial dose of 5 µg/kg/minute, adjusted according to clinical response to 2 – 20 µg/kg/minute is recommended. Occasionally, a dose as low as 0.5-1.0 µg/kg/minute will produce a response.

There is reason to believe that the minimum effective dosage for children is higher than for adults. Caution should be taken in applying high doses, because there is also reason to believe that the maximum tolerated dosage for children is lower than the one for adults. Most adverse reactions (tachycardia in particular) are observed when dosage was higher than/equal to 7.5 µg/kg/minute, but reducing or termination of the rate of dobutamine infusion is all that is required for rapid reversal of undesirable effects.

A great variability has been noted between paediatric patients in regard to both the plasma concentration necessary to initiate a hemodynamic response (threshold) and the rate of hemodynamic response to increasing plasma concentrations, which demonstrates that the required dose for children cannot be determined a priori and should be titrated in order to allow for the supposedly smaller "therapeutic width" in children.

Method of administration
Dobutamine should be diluted before use and administered by IV infusion only.

The concentration of the dobutamine administered depends upon the dosage and fluid requirements of the individual patient. The final concentrations generally used for perfusion are 250 µg/ml, 500 µg/ml or 1000 µg/ml. For special precautions for storage of the prepared diluted infusion see section 6.4. High concentrations of dobutamine should only be given with an infusion pump or other suitable apparatus to ensure accurate dosage. Due to its short half-life dobutamine should be administered as a continuous intravenous infusion. Dobutamine should be administered intravenously through an intravenous needle or catheter. The following sterile solutions for IV infusion may be used for the dilution of dobutamine before use: 5% Dextrose Injection, 5% Dextrose and 0.45% Sodium Chloride Injection, 5% Dextrose and 0.9% Sodium Chloride Injection, 10% Dextrose Injection, multi-electrolyte with 5% Dextrose Injection, Lactated Ringer's Injection, 5% Dextrose in Lactated Ringer's Injection, 20% Mannitol in Water for Injection, 0.9% Sodium Chloride Injection and Sodium Lactate Injection.

Dosage for Infusion delivery systems:
One vial Dobutamine 12.5 mg/ml (250 mg/20 ml) diluted to a solution volume of 500 ml (final concentration 0.5 mg/ml) with any of the approved diluents (see section 6.6).

Dosage range		**Specifications in ml/h* (drops/min)**		
		Patient's weight		
		50 kg	**70 kg**	**90 kg**
Low 2.5 µg/kg/min	ml/h (drops/min)	15 (5)	21 (7)	27 (9)
Medium 5 µg/kg/min	ml/h (drops/min)	30 (10)	42 (14)	54 (18)
High 10 µg/kg/min	ml/h (drops/min)	60 (20)	84 (28)	108 (36)

* For double concentration, i.e. 500 mg Dobutamine added to 500 ml, or 250 mg added to 250 ml solution, infusion rates must be halved.

3. HOW TO USE DOBUTAMINE

You will be given Dobutamine in hospital by a doctor or nurse. Dobutamine is diluted and infused into a vein.

Your doctor will decide the correct dosage for you and how and when the injection will be given.

Dosage for stimulation of the heart

Adults and the elderly:
The usual dose is 2.5 to 10 µg/kg (body weight)/min, which is adjusted according to the heart rate, blood pressure, heart output and urine output. Doses up to 40 µg/kg/min may occasionally be required.

Dosage for stress testing of the heart

Adults:
The recommended dosage is an incremental increase from 5 to maximum 40 µg/kg/minute.

Elderly:
The recommended dosage is an incremental increase from 5 to maximum 20 µg/kg/minute.

Use in Children:
For all paediatric age groups (neonates to 18 years) an initial dose of 5 µg/kg/minute, adjusted according to clinical response to 2 – 20 µg/kg/minute is recommended. Occasionally, a dose as low as 0.5-1.0 µg/kg/minute will produce a response. The required dose for children should be titrated in order to allow for the supposedly smaller "therapeutic width" in children.

If you use more Dobutamine than you should
Since the injection will be given to you by a doctor or nurse, it is unlikely that you will be given too much.

4. POSSIBLE SIDE EFFECTS

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

The following side-effects have been reported:

Very common (may affect up to 1 in 10 people)
- increased heart rate
- severe chest pain
- arrhythmia (too fast or too slow heartbeat)
- electrocardiogram ST segment elevation
- coronary artery spasm (temporary, sudden contraction in one location of heart muscles)
- palpitations
- irregular heartbeats
- ventricular tachycardia (fast heart rhythm that originates in one of the ventricles of the heart)

Common (may affect up to 1 in 100 people)
- hypersensitivity reactions including rash
- eosinophilia (high concentration of eosinophils granulocytes in blood)
- hypertension
- marked increase in systolic blood pressure indicates overdose
- shortness of breath
- nausea
- fever
- bronchospasm (sudden constriction of the muscles in the walls of the bronchioles)
- non-specific chest pain
- asthma
- headache

Uncommon (may affect up to 1 in 1,000 people)
- atrial fibrillation (abnormal heart rhythm involves the two upper chambers-atria)
- ventricular fibrillation (uncontrolled contractions of the cardiac muscle of the ventricles)
- left ventricular outflow tract obstruction
- hypotension
- slight vasoconstriction, especially in patients with pre-treated with β-blockers

Rare (may affect up to 1 in 10,000 people)
- phlebitis (formation of blood clots)
- local inflammatory changes
- anaphylactic reactions (severe hypersensitivity allergic reaction)
- severe life-threatening asthmatic episodes may be due to sulphite sensitivity

Very rare (affects less than 1 patient in 10,000)
- as with other catecholamines, decreases in serum potassium concentrations have occurred
- myoclonus (involuntary twitching of muscle) has been reported in patients with severe renal failure receiving dobutamine
- cutaneous necrosis
- myocardial ischemia (reduced blood supply to the heart muscle)
- myocardial infarction (heart attack)
- eosinophilic myocarditis (inflammation of the heart muscle)
- fatal cardiac rupture during dobutamine stress testing

Not known (cannot be estimated from the available data)
- Urinary urgency

Reporting of side effects
If you get any side effects, talk to your doctor 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 at 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 DOBUTAMINE

Your doctor and pharmacist are responsible for the correct storage, use and disposal of this medicine.

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 label and carton after EXP.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Dobutamine contains
- The active substance is dobutamine hydrochloride.
- The other ingredients are sodium metabisulphite, sodium hydroxide, hydrochloric acid and water for injections.

What Dobutamine looks like and contents of the pack
Dobutamine is packed in clear glass vials packed in carton boxes with 10 vials.

Marketing Authorisation Holder and Manufacturer
Hikma Farmacêutica (Portugal), S.A.
Estrada do Rio da Mó, nº8, 8A, 8B
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The dose to be administered can be calculated taking into account the table below.
Infusion rates in millilitres/min can be obtained by multiplying infusion rates for each concentration (ml/kg/min) by patient's weight (kg).

	One (1) vial 250 mg dobutamine in 1000 ml of solution for infusion	Two (2) vials 500 mg dobutamine in 1000 ml of solution for infusion	Four (4) vials 1000 mg dobutamine in 1000 ml of solution for infusion
	250 µg/ml	500 µg/ml	1000 µg/ml
Dose µg/kg/min	**Infusion rate ml/kg/min**	**Infusion rate ml/kg/min**	**Infusion rate ml/kg/min**
2.5	0.01	0.005	0.0025
5	0.02	0.01	0.005
7.5	0.03	0.015	0.0075
10	0.04	0.02	0.01
12.5	0.05	0.025	0.0125
15	0.06	0.03	0.015

Dosage for syringe pumps:
One vial Dobutamine 12.5 mg/ml (250 mg/20 ml) diluted to a solution volume of 50 ml (final concentration 5 mg/ml) with any of the approved diluents (see section 6.6).

Dosage range		**Specifications in ml/h* (drops/min)**		
		Patient's weight		
		50 kg	**70 kg**	**90 kg**
Low 2.5 µg/kg/min	ml/h (ml/min)	1.5 (0.025)	2.1 (0.035)	2.7 (0.045)
Medium 5 µg/kg/min	ml/h (ml/min)	3.0 (0.05)	4.2 (0.07)	5.4 (0.09)
High 10 µg/kg/min	ml/h (ml/min)	6.0 (0.10)	8.4 (0.14)	10.8 (0.18)

Paediatric population
For continuous intravenous infusion using an infusion pump, dilute to a concentration of 0.5 to 1 mg/mL (max 5 mg/mL if fluid restricted) with Glucose 5% or Sodium Chloride 0.9%. Infuse higher concentration solutions through central venous catheter only. Dobutamine intravenous infusion is incompatible with bicarbonate and other strong alkaline solutions.

Neonatal intensive care
Dilute 30 mg/kg body weight to a final volume of 50 mL of infusion fluid. An intravenous infusion rate of 0.5 mL/hour provides a dose of 5 µg/kg/minute.

Incompatibilities
Do not add Dobutamine to 5% Sodium Bicarbonate intravenous infusion or to any other strongly alkaline solutions. Because of potential physical incompatibilities, it is recommended that dobutamine hydrochloride not be mixed with other drugs in the same solution.

Dobutamine injections should not be used with other agents or diluents containing both sodium metabisulphite and ethanol.

Special precautions for disposal and other handling
Dobutamine must be diluted to at least 50 ml, prior to administration in an IV container with one of the intravenous solutions listed below:
- 5% Dextrose Injection,
- 5% Dextrose and 0.45% Sodium Chloride Injection,
- 5% Dextrose and 0.9% Sodium Chloride Injection,
- 10% Dextrose Injection,
- multi-electrolyte with 5% Dextrose Injection;
- Lactated Ringer's Injection;
- 5% Dextrose in Lactated Ringer's Injection;
- 20% Mannitol in Water for Injection;
- 0.9% Sodium Chloride Injection,
- Sodium Lactate Injection.

For example, diluting to 250 ml or 500 ml will provide the following concentrations for administration:
250 ml contains 1,000 µg/ml of dobutamine
500 ml contains 500 µg/ml of dobutamine

The prepared solution should be used within 24 hours.

Chemical and physical in-use stability has been demonstrated for 24 hours at 25ºC (room temperature).

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8ºC, unless dilution has taken place in controlled and validated aseptic conditions.

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