PACKAGE LEAFLET: INFORMATION FOR THE USER

hameln

Dobutamine 12.5 mg/ml concentrate for solution for infusion
dobutamine

Read all of this leaflet carefully before you are 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 pharmacist.
- 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
2. What you need to know before you use Dobutamine
3. How to use Dobutamine
4. Possible side effects
5. How to store Dobutamine
6. Contents of the pack and other information

1. WHAT DOBUTAMINE IS AND WHAT IT IS USED FOR

Dobutamine belongs to a group of medicines called catecholamines. It helps your heart to work more effectively. It works by strengthening the pumping action of the heart, increasing the amount of blood flow in the body and by expanding your veins and arteries.

Dobutamine is used:
- to treat heart failure (cardiac decompensation) if the heart is not beating strongly enough (depressed contractility),
- in heart failure where there is severe low blood pressure (hypotension),
- to detect poor blood supply to the heart (cardiac stress testing).

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** (hypersensitive) to **dobutamine** or **any of the other ingredients** of this medicine (listed in section 6). An allergic reaction may include rash, itching, difficulty in breathing or swelling of the face, lips, throat or tongue. You may know this from earlier experience.
- there is **a narrowing in your heart or blood vessels that prevents the heart from filling or ejecting blood properly** (your doctor will know this).
- there is a **lack of adequate circulatory filling** (hypovolaemia).

If you have certain heart or blood vessel disorders, Dobutamine should not be used to detect poor blood supply to your heart.

Warnings and precautions

Talk to your doctor before using Dobutamine. Tell your doctor if you have any of the following conditions:
- asthma and you have been told that you are allergic to sulfites,
- severe coronary heart disease,
- acute (sudden) heart failure.

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.

Caution is advised in giving high doses of dobutamine to children. Your doctor will adjust the required dose for your child carefully.

Other medicines and Dobutamine

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is especially important with the following medicines as they may interact with your Dobutamine:
- beta blockers (treatment of high blood pressure and irregular heart rhythms),
- alpha blockers (treatment of high blood pressure and prostate enlargement),
- vasodilators (expanding blood vessels, used to treat an angina attack or severe heart failure),
- antidiabetics (treatment of diabetes),
- ACE inhibitors (treatment of high blood pressure and heart failure),
- dopamine (used to increase heart rate and blood pressure),
- inhaled anaesthetics.

It may still be all right for you to receive Dobutamine and your doctor will be able to decide what is suitable for you.

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 or pharmacist for advice before you are given this medicine.

Dobutamine should not be given to pregnant women unless medically justified. It is recommended that you stop breast-feeding during your treatment with dobutamine.

Driving and using machines

If you have any concerns ask your doctor or pharmacist.

Dobutamine contains sodium metabisulfite (E223), which may rarely cause allergic reactions (hypersensitivity) and asthma-like symptoms (bronchospasm).

Dobutamine contains sodium

This medicine contains less than 1 mmol **sodium** (23 mg) per 20 ml, that is to say essentially `sodium-free´.

3. HOW TO USE DOBUTAMINE

Dobutamine will be given to you by specifically trained health care professionals and emergency equipment will be available.

Dosage

The required rate of infusion depends on your response to therapy and any side effects. Your doctor will decide the dose of Dobutamine you will be given and will adjust the flow rate and duration of your infusion.

Dosage in adults:

Most patients respond to doses of 2.5-10 micrograms of dobutamine per kg body weight per minute. Doses up to 40 micrograms of dobutamine per kg body weight per minute have been given.

Dosage in children:

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

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 more than 1 in 10 people)
- increased heart rate
- chest pain
- heartbeat disturbances

Common (may affect up to 1 in 10 people)
- blood pressure increase or decrease
- narrowing of the blood vessels (vasoconstriction)
- irregular heartbeat (palpitations)
- fast heart rate (ventricular tachycardia)
- headache
- asthma-like symptoms (bronchospasm)
- shortness of breath
- increase in white blood cells (eosinophilia)
- inhibition of blood clot formation
- increased desire to urinate (at high doses)
- feeling sick (nausea)
- rash (exanthema)
- fever
- inflammation of the vein at the injection site (phlebitis)

Uncommon (may affect up to 1 in 100 people)
- uncontrolled contractions of the ventricles of the heart (ventricular fibrillation)
- heart attack (myocardial infarction)

Very rare (may affect up to 1 in 10,000 people)
- slow heartbeat (bradycardia)
- not enough blood supplied to the heart (myocardial ischaemia)
- low potassium (hypokalaemia)
- spots on the skin (petechial bleeding)
- heart block
- narrowing of the blood vessels supplying the heart (coronary vasospasm)
- black areas of dying skin (cutaneous necrosis)

Not known (frequency cannot be estimated from the available data)
- chest pain caused by stress (stress cardiomyopathy)
- impaired cardiac function (decrease in pulmonary capillary pressure)
- problems with your heart muscle (stress cardiomyopathy also known as Takotsubo syndrome) that present with chest pain, shortness of breath, dizziness, fainting, irregular heartbeat when dobutamine is used for stress echocardiography test

Further undesirable effects which have been observed:
- restlessness
- pins and needles (paraesthesia)
- involuntary muscle twitches (tremor)
- feeling of heat and anxiety
- muscle spasm

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 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
- 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 pack after EXP. The expiry date refers to the last day of that month.

The following information is intended for healthcare professionals only:

PREPARATION GUIDE FOR:

Dobutamine 12.5 mg/ml concentrate for solution for infusion

Please refer to the Summary of Product Characteristics for full prescribing and other information.

1. NATURE AND CONTENT OF CONTAINER

1 ml solution contains 12.5 mg dobutamine.

Dobutamine is supplied in 20 ml clear glass ampoules. It is available in original packages containing 1, 5, 10 or 50 ampoule(s).

2. POSOLOGY AND METHOD OF ADMINISTRATION

When used for detection of myocardial ischaemia and of viable myocardium, dobutamine may only be administered by a physician with sufficient experience in conducting cardiology stress tests. Continuous monitoring of all wall areas via echocardiography, and ECG as well as control of blood pressure is necessary.

Monitoring devices as well as emergency medicines must be available (e.g. defibrillator, I.V. beta-blockers, nitrates, etc.) and staff trained in the resuscitation procedure must be present.

The required rate of infusion depends on the patient’s response to therapy and the adverse reactions experienced.

The dose of dobutamine should be gradually reduced when discontinuing therapy.

Any unused solution should be discarded.

Dosage

Dosage in adults:

According to experience, the majority of patients respond to doses of 2.5-10 µg dobutamine/kg/min. In individual cases, doses up to 40 µg dobutamine/kg/min have been administered.

Dosage in paediatric patients:

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

The infusion solution concentrate must be diluted before administration. It must be diluted to a volume of 50 ml or more.

Intravenous infusion of Dobutamine is also possible after dilution with compatible infusion solutions such as: 5% glucose solution (50 mg/ml), 0.9% sodium chloride (9 mg/ml) or 0.45% sodium chloride (4.5 mg/ml) in 5% glucose solution (50 mg/ml). Infusion solutions should be prepared immediately before use.

Due to its short half-life, dobutamine must be administered as a continuous intravenous infusion.

Paediatric patients: 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% (50 mg/ml) or Sodium Chloride 0.9% (9 mg/ml). 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 micrograms/kg/minute.

Tables, showing infusion rates with different initial concentrations for various dosages:

One ampoule Dobutamine 12.5 mg/ml (250 mg/20 ml) diluted to a solution volume of 500 ml (final concentration 0.5 mg/ml)

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 volume, infusion rates must be halved.

- Do not use this medicine if you notice the solution is not clear and free of particles or if the container is damaged.
- This medicine does not require any special temperature storage conditions.
- Keep the ampoules in the outer carton in order to protect from light.
- Do not freeze.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Dobutamine contains

The active substance is dobutamine.

1 ml solution contains 12.5 mg dobutamine.

Each 20 ml ampoule Dobutamine contains dobutamine hydrochloride equivalent to 250 mg dobutamine.

The other ingredients are sodium metabisulfite (E223), hydrochloric acid and water for injections.

What Dobutamine looks like and contents of the pack

Dobutamine is a clear, colourless or slightly yellow concentrate for solution for infusion.

Dobutamine is supplied in 20 ml clear glass ampoules. It is available in original packages containing 1, 5, 10 or 50 ampoule(s).

Not all pack sizes may be marketed.

Marketing Authorisation Holder

hameln pharma ltd
Nexus, Gloucester Business Park
Gloucester, GL3 4AG
United Kingdom

Manufacturer

Siegfried Hameln GmbH
Langes Feld 13
31789 Hameln
Germany

For any information about this medicine, please contact the Distributor.

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

DE	Dobutamin-hameln 12,5 mg/ml Konzentrat zur Herstellung einer Infusionslösung
FI	Dobutamin Hameln 12.5 mg/ml infuusiokonsentraatti, liuosta varten
NL	Dobutamine-hameln 12,5 mg/ml steriel concentraat, concentraat voor oplossing voor infusie
NO	Dobutamin Hameln 12,5 mg/ml konsentrat til infusjonsvaeske
SE	Dobutamin Hameln 12,5 mg/ml koncentrat till infusionsvätska, lösning
UK (NI)	Dobutamine 12.5 mg/ml concentrate for solution for infusion

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Dosage for syringe pumps

One ampoule Dobutamine 12.5 mg/ml (250 mg/20 ml) diluted to a solution volume of 50 ml (final concentration 5 mg/ml)

Dosage range		Specifications in ml/h (ml/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)

The chosen syringe pump must be suitable for the volume and rate of administration.

3. CONTRAINDICATIONS

Dobutamine must not be used in case of:

- known hypersensitivity to dobutamine or to any of the excipients,
- mechanical obstruction of ventricular filling and/or of outflow, such as pericardial tamponade, constrictive pericarditis, hypertrophic obstructive cardiomyopathy, severe aortic stenosis,
- hypovolaemic conditions.

Dobutamine stress echocardiography

Dobutamine must not be used for detection of myocardial ischaemia 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,
- severe heart failure (NYHA III or IV),
- predisposition for or documented medical history of clinically significant or chronic arrhythmia, particularly recurrent persistent ventricular tachycardia,
- significant disturbance in conduction,
- acute pericarditis, myocarditis or endocarditis,
- aortic dissection,
- aortic aneurysm,
- poor sonographic imaging conditions,
- inadequately treated / controlled arterial hypertension,
- obstruction of ventricular filling (constrictive pericarditis, pericardial tamponade),
- hypovolaemia,
- previous experience of hypersensitivity to dobutamine.

4. INTERACTION WITH OTHER MEDICINAL PRODUCTS

Interactions of dobutamine with the following medicinal products are observed:

- beta blockers,
- alpha blockers,
- primarily venous acting vasodilators (e.g. nitrates, sodium nitroprusside),
- ACE inhibitors (e.g. captopril),
- dopamine,
- thiamine (vitamin B1),
- inhaled anaesthetics,
- atropine.

Administering dobutamine to diabetic patients may cause increased insulin demand. Thus, in diabetic patients levels should be checked when starting dobutamine therapy, changing the rate of infusion and discontinuing the infusion. If necessary the insulin dose must be adjusted as required.

5. INCOMPATIBILITIES

For known incompatibilities of dobutamine solutions with several substances and of sodium metabisulfite see section 6.2 of the Summary of Product Characteristics.

This medicinal product must not be mixed with other medicinal products except with those for which compatibility is proven.

6. STORAGE

This medicine does not require any special temperature storage conditions.

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

Do not freeze.

After dilution:

Chemical and physical in-use stability has been demonstrated for 24 hours at 25°C.

From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.