B. PACKAGE LEAFLET

Package leaflet: information for the user

Dobutamine 5 mg/ml solution for infusion in pre-filled syringe

dobutamine

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 pharmacist.
- If you get any side effects, talk to your doctor or pharmacist. 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 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 in adults
- to treat heart failure (cardiac decompensation) if the heart is not beating strongly enough (depressed contractility) caused by an organic heart disease or by heart surgery
- 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 are given Dobutamine

You should NOT be given Dobutamine if any of the following apply to you. Tell your doctor if
- you are allergic to dobutamine hydrochloride 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)
- you are using monoamine oxidase inhibitors (treatments for depression).

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

Do not use Dobutamine also to test your heart if you have
- suffered a heart attack within the last 30 days
- unstable (uncontrolled) angina
- 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)
- suffered an aortic aneurysm (a weakened and bulging area in the aorta, the major blood vessel that feeds blood to the body)
- uncontrolled high blood pressure
- a low blood volume that has not been corrected (your doctor will know this)
- an obstruction that interferes with blood flow out of your heart (your doctor will know this).

Warnings and precautions
Tell your doctor, pharmacist or nurse before using Dobutamine 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.
- phaeocromocytoma (high blood pressure due to a tumour near the kidney)
- hyperthyroidism (over-active thyroid).

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, including medicines obtained without a prescription.

Dobutamine can interact with a number of medicines and supplements, which may either raise or lower the level of the medicine in your blood.

Tell your doctor if you are taking any of the following medicines
- beta blockers (treatment of high blood pressure and irregular heart rhythms)
- alpha blockers such as captopril (treatment of high blood pressure and prostate enlargement)
- vasodilators such as nitrates, sodium nitroprusside (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 increasing heart rate and blood pressure)
- peripheral vasoconstrictor agents such as noradrenaline
- inhaled anaesthetics
- monoamine oxidase inhibitors (treatments for depression)
- entacapone (a medicine to treat Parkinson’s disease)
- antipsychotics (treatments for mental illness)
- doxapram (for breathing problems)
- ergotamine or methysergine (treatments for migraine)
- oxytocin (used in labour)
- dipyridamole (a blood thinner)
- atropine sulphate (for inflammation of the iris of the eye or for eye examinations).

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, breast-feeding and fertility

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

Dobutamine should not be given to pregnant women unless medicinally justified.

Breast-feeding
If you are breast-feeding ask your doctor or pharmacist for advice before taking this medicine.

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
This medicinal product contains 162 mg sodium (main component of cooking/table salt) in each pre-filled syringe. This is equivalent to 8.1% of the maximum daily dietary intake of sodium for an adult.

3. How Dobutamine will be given

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

Method of administration
Dobutamine will be given as an infusion (drip) into your veins. 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 for stimulation of the heart

Adults and the elderly
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 for stress testing of the heart

Adults and the elderly
The recommended dosage is an incremental increase from 5 to maximum 40 µg/kg/minute.
In the elderly, another dosage scheme may also be considered.

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. Your doctor will discuss these side effects with you and explain the risks and benefits of your treatment.

Very common side effects (may affect more than 1 in 10 people)
- increased heart rate
- chest pain
- heartbeat disturbances

Common side effects (may affect up to 1 in 10 people)
- blood pressure increase or decrease
- narrowing of the blood vessels (vasoconstriction)
- irregular heartbeat (palpitations)
- headache
- electrocardiogram ST segment elevation
- 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 side effects (may affect up to 1 in 100 people)
- fast contractions of the ventricles of the heart (ventricular tachycardia)
- uncontrolled contractions of the ventricles of the heart (ventricular tachycardia)
- atrial fibrillation (abnormal heart rhythm involves the two upper chambers-atria)
- heart attack (myocardial infarction)

Very rare (may affect up to 1 in 10,000 people, including isolated cases)
- 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)
- restlessness
- pins and needles (paraesthesia)
- tremor
- feelings of heat and anxiety
- muscle cramp (myoclonic spasm)
- fatal cardiac rupture during dobutamine stress testing

Not known (frequency cannot be estimated from the available data)
- coronary artery disease by stress (stress cardiomyopathy)
- 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.

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 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 label, pouch and carton after EXP. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

After opening the syringe, the product should be used immediately in order to avoid microbial contamination. 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°C to 8°C unless preparation has taken place in controlled and validated aseptic conditions.

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 (as hydrochloride). One ml of the solution for infusion contains dobutamine (as hydrochloride) corresponding to 5 mg dobutamine. Each pre-filled syringe of 50 ml contains dobutamine (as hydrochloride) corresponding to 250 mg dobutamine.
- The other ingredients are: disodium edetate (E386), cysteine hydrochloride monohydrate, sodium chloride, sodium hydroxide (for pH adjustment), hydrochloric acid (for pH adjustment) and water for injection.

What Dobutamine looks like and contents of the pack
Dobutamine is a clear, colourless to slightly yellow solution for infusion.

Dobutamine is available in packs containing 1 or 5 pouches with one pre-filled syringe containing 50 ml solution for infusion, one plunger rod and one scavenger.

Marketing Authorisation Holder
Sun Pharmaceutical Industries Europe B.V.
Polarisavenue 87
2132JH Hoofddorp
The Netherlands

Manufacturer
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The Netherlands

Terapia S.A.
124 Fabricii Street
400632, Cluj-Napoca
Cluj County

Romania

This medicinal product is authorised in the Member States of the EEA under the following names

Germany:	Dobutamin SUN
France:	Dobutamine SUN
Italy:	Dobutamina SUN
The Netherlands:	Dobutamine SUN
United Kingdom:	Dobutamine

This leaflet was last revised in February 2022

The following information is intended for healthcare professionals only

INFORMATION FOR THE HEALTHCARE PROFESSIONALS

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

Posology and method of administration
When used for detection of myocardial ischaemia and of viable myocardium within the scope of an echocardiographic examination (dobutamine stress echocardiography), 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

Myocardial inotropic support

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.

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

Tables, showing infusion rates with different initial concentrations for various dosages:
Dobutamine administration should be done in continuous intravenous infusion with a constant delivery pump/system.

Dosage for infusion delivery systems

Dobutamine 5 mg/ml solution for infusion in pre-filled syringe diluted to a solution volume of 500 ml (final concentration 0.5 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)	15 (0.25)	21 (0.35)	27 (0.45)
Medium 5 µg/kg/min	ml/h (ml/min)	30 (0.5)	42 (0.7)	54 (0.9)
High 10 µg/kg/min	ml/h (ml/min)	60 (1.0)	84 (1.4)	108 (1.8)

* 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.

Dosage for syringe pumps

Dobutamine 5 mg/ml solution for infusion in pre-filled syringe undiluted (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.

Dobutamine stress echocardiography
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.

Administration in stress echocardiography is undertaken by gradually increasing dobutamine infusion.

The most frequently applied dosage scheme starts with 5 micrograms /kg/minute dobutamine increased every 3 minutes to 10, 20, 30, 40 micrograms /kg/minute until a diagnostic endpoint (see section 4.4
is reached. If no endpoint is reached, when appropriate, atropine sulfate may be administered at 0.25 to 1 mg in divided doses of 0.25 mg at 1 minute intervals to increase the heart rate.

Paediatric population
The experience in children and adolescents is limited to the treatment of patients requiring positive inotropic support.

Method of administration
Intravenous infusion of Dobutamine is also possible after dilution with compatible infusion solutions such as: 5% glucose solution, 0.9% sodium chloride or 0.45% sodium chloride in 5% glucose solution. Infusion solutions should be prepared immediately before use.

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

Dobutamine intravenous infusion is incompatible with bicarbonate and other strong alkaline solutions.

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% or sodium chloride 0.9%. Infuse higher concentration solutions through central venous catheter only.

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.

Precautions
Dobutamine must not be used in case of:
- known hypersensitivity to dobutamine or to any of the excipients
- mechanical obstruction of ventricular filing 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 condition

- acute pericarditis, myocarditis or endocarditis
- aortic dissection
- aortic aneurysm
- in case of poor sonographic imaging conditions
- inadequately treated/controlled arterial hypertension
- obstruction of ventricular filling (constrictive pericarditis pericardial tamponade)
- hypovolaemia
- previous experience of hypersensitivity to dobutamine.

Incompatibilities

Dobutamine has proven to be incompatible with:

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

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.

Storage

This medicinal product does not require any special storage conditions.

After opening the syringe, the product should be used immediately in order to avoid microbial contamination. 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°C to 8°C unless preparation has taken place in controlled and validated aseptic conditions.

Syringe pump programming

When programming the pump for the infusion, it is recommended to select “BD Plastipak” as the syringe setting. Do not use in bolus.