Baxter

Package leaflet: Information for the patient

BREVIBLOC Premixed 10 mg/ml Solution for Injection
Esmolol hydrochloride

Read all of this leaflet carefully before you are given this medicine. 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, nurse or pharmacist
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet.

Throughout this leaflet, BREVIBLOC Premixed 10 mg/ml Solution for Injection will be called Brevibloc.

What is in this leaflet:

1. What Brevibloc is and what it is used for

Brevibloc contains a medicine called esmolol. It belongs to a group of medicines called 'beta-blockers'. It works by controlling the rate and force of your heartbeat. It can also help to reduce your blood pressure.

It is used to treat:

- Heartbeat problems, when your heart beats too fast
- Heartbeat problems and an increase in your blood pressure if this happens during or straight after an operation.

2. What you need to know before you are given Brevibloc

Your doctor will not give you Brevibloc if:

- You are allergic (hypersensitive) to esmolol, to other beta-blocker medicines, or any of the other ingredients of this medicine (listed in section 6).
  The signs of an allergic reaction include shortness of breath, wheezing, rash, itching or swelling of your face and lips
- You have a very slow heartbeat (less than 50 beats per minute)
- You have a fast or alternating fast and slow heartbeat
- You have something called "severe heart block". Heart block is a problem with the electrical messages that control your heartbeat
- You have low blood pressure
- You have a problem with the blood supply to your heart
- You have serious heart failure symptoms
- You are receiving or have recently received verapamil. You must not be given Brevibloc within 48 hours of when you stop receiving verapamil
- You have a gland disease called phaeochromocytoma which has not been treated. Phaeochromocytoma arises from the adrenal gland and may cause a sudden increase in blood pressure, severe headache, sweating and increased heartbeat
- You have increased blood pressure in the lungs (pulmonary hypertension)
- You have asthma symptoms that are worsening rapidly
- You have increased levels of acids in your body (metabolic acidosis).

You will not be given Brevibloc if any of the above applies to you. If you are not sure if you have any of these conditions, talk to your doctor, nurse or pharmacist before having Brevibloc.

Warnings and Precautions

Talk to your doctor, nurse or pharmacist before being given Brevibloc. Your doctor will take special care with this medicine if:

- You are being treated for certain heart rhythm disorders called supraventricular arrhythmias and you:
  – Have other heart problems or
  – Are taking other heart medicines
  Use of Brevibloc in this way can lead to severe reactions which may be fatal including:
  – Loss of consciousness
  – Shock (when your heart does not pump enough blood)
  – Heart attack (cardiac arrest)
- You develop low blood pressure (hypotension). The signs of this may be feeling dizzy or light headed, especially when standing up. Low blood pressure usually gets better within 30 minutes of the end of your Brevibloc treatment
- You have a low heart rate before treatment
- Your heart rate decreases to less than 50 to 55 beats per minute. If this happens your doctor may give you a lower dose or stop treatment with Brevibloc
- You have heart failure
- You have problems with the electrical messages that control your heartbeat (heart block)
- You have a gland disease called phaeochromocytoma which has been treated with medicines called alpha-receptor blockers
- You are being treated for high blood pressure (hypertension) which has been caused by low body temperature (hypothermia)
- You have narrowing of your airways or wheezing, such as with asthma
- You have diabetes or low blood sugar. Brevibloc can increase the effects of your diabetes medicines
- You develop skin problems. These can be caused by the solution leaking around the site of the injection. If this happens your doctor will use a different vein for your injection
- You have a particular type of angina (chest pain) called 'Prinzmetal's angina'
- You have low blood volume (with low blood pressure). You could develop circulatory collapse more easily
- You have circulation problems, such as paleness of your fingers (Raynaud's disease) or aching, tired and sometimes burning pains in your legs
- You have kidney problems. If you have kidney disease or you need kidney dialysis you could develop high blood potassium levels (hyperkalemia). This can cause serious heart problems
- You have any allergies or are at risk of anaphylactic reactions (severe allergic reactions). Brevibloc can make allergies more severe and more difficult to treat
- You or any of your family have a history of psoriasis (where your skin produces scaly patches)
- You have a disease called hyperthyroidism (an overactive thyroid gland).

Changing the dose is not usually necessary if you have liver problems.

If any of the above apply to you (or you are not sure), talk to your doctor, nurse or pharmacist before being given this medicine. You may need to be checked carefully and your treatment may be changed.

Other medicines and Brevibloc

Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines that you have obtained yourself, without a prescription, including herbal medicines and natural products. Your doctor will check that any other medicines you are taking will not alter the way that Brevibloc works.

In particular, tell your doctor, nurse or pharmacist if you are taking any of the following:

- Medicines that can lower the blood pressure or slow the heart rate
- Medicines used to treat heart rhythm problems or chest pain (angina) such as verapamil and diltiazem. You should not receive Brevibloc within 48 hours of stopping verapamil
- Nifedipine, which is used to treat chest pain (angina), high blood pressure and Raynaud's disease
- Medicines used to treat heart rhythm problems (such as quinidine, disopyramide, amiodarone) and heart failure (such as digoxin, digitoxin, digitalis)
- Medicines used to treat diabetes, including insulin and medicines taken by mouth
- Medicines known as ganglion blocking agents (such as trimetaphan)
- Medicines used as pain killers, such as non-steroidal anti-inflammatory drugs known as NSAIDs
- Floctafenine, which is a pain killer
- Amisulpride, a medicine that is used to treat mental problems
- 'Tricyclic' antidepressant medicines (such as imipramine and amitriptyline) or any other drugs for mental health problems
- Barbiturates (such as phenobarbital, used to treat epilepsy) or phenothiazines (such as chlorpromazine, used to treat mental disorders)
- Clozapine which is used to treat mental disorders
- Epinephrine, which is used to treat allergic reactions
- Medicines used to treat asthma
- Medicines used to treat colds or a blocked nose, called 'nasal decongestants'
- Reserpine, which is used to treat high blood pressure
- Clonidine, which is used to treat high blood pressure and migraine
- Moxonidine, which is used to treat high blood pressure
- Ergot derivates, medicines mainly used to treat Parkinson's disease
- Warfarin, which is used to thin your blood
- Morphine, which is a strong pain killer
- Suxamethonium chloride (also known as succinylcholine or scoline) or mivacurium, which are used to relax your muscles, usually during an operation. Your doctor will also take special care when using Brevibloc during operations, when you will be having anaesthetics and other treatments.

If you are not sure if any of the above applies to you talk to your doctor, nurse or pharmacist before having Brevibloc.

Tests you may have while Brevibloc is used

The use of medicines such as Brevibloc over a long period of time can cause a reduction in the force of your heartbeat.

Since Brevibloc is only used for a limited time, this is unlikely to happen to you. During treatment you will be carefully monitored and Brevibloc treatment will be reduced or stopped if the force of your heartbeat is reduced.

Your doctor will also check your blood pressure while you are being treated with Brevibloc.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.

You should not be given Brevibloc if you are pregnant, or if you think you may be pregnant.

Tell your doctor if you are breast-feeding. Brevibloc may pass into breast milk, so you should not be given Brevibloc if you are breast-feeding.

Brevibloc contains sodium

Brevibloc contains approximately 28 mg of sodium per vial. This may be important if you are controlling the sodium in your diet.

3. How you will be given Brevibloc

The recommended dose

Your doctor will decide how much of the medicine you will need and for how long it will be given to you. Brevibloc will not normally be given for longer than 24 hours.

How Brevibloc is given

Brevibloc is ready to use. You will be given Brevibloc by a slow injection (infusion) through a needle inserted into a vein in your arm.

Brevibloc must not be mixed with sodium bicarbonate or other medicinal products.

- The treatment is given in two stages:
  – Stage one: a large dose is given over one minute. This increases the levels in your blood quickly
  – Stage two: a smaller dose is then given over four minutes
  – Stage one and two may then be repeated and adjusted according to your heart's response. As soon as an improvement has happened, stage one (the large dose) will be stopped and stage two (the small dose) will be reduced as necessary
  – After reaching a stable condition, you may be given another heart drug, while your dose of Brevibloc is gradually reduced.
- If your heart rate or blood pressure increases during an operation or straight after recovering from it, you will be given larger doses of Brevibloc for a short time.

The following information is intended for medical or healthcare professionals only:

This section contains practical information regarding administration. Read the SPC for full information on posology and method of administration, contraindications, warnings etc.

Posology and method of administration

Brevibloc Premixed 10 mg/ml Solution for Injection is a ready-to-use 10 mg/ml solution recommended for intravenous administration. This dosage form is used to administer the appropriate Brevibloc loading dose or bolus dose by hand held syringe.

Posology is summarised in the following tables.

Table 1
Volume of BREVIBLOC 10 mg/ml required for an INITIAL LOADING DOSE of 500 mcg/kg/minute

	Patient weight (kg)								
	40	50	60	70	80	90	100	110	120
Volume (ml)	2	2.5	3	3.5	4	4.5	5	5.5	6

Table 2
Volume of BREVIBLOC 10 mg/ml required to provide MAINTENANCE DOSES at infusion rates between 12.5 and 300 mcg/kg/minute

Patient weight (kg)	Infusion Dose Rate (mcg/kg/min)						
	12.5	25	50	100	150	200	300
	Amount to administer per hour to achieve the dose rate (ml/hr)						
40	3	6	12	24	36	48	72
50	3.75	7.5	15	30	45	60	90
60	4.5	9	18	36	54	72	108
70	5.25	10.5	21	42	63	84	126
80	6	12	24	48	72	96	144
90	6.75	13.5	27	54	81	108	162
100	7.5	15	30	60	90	120	180
110	8.25	16.5	33	66	99	132	198
120	9	18	36	72	108	144	216

The Elderly
Your doctor will start your treatment with a lower dose.

Children
Children up to the age of 18 years should not receive Brevibloc.

If you have too much Brevibloc

As you are being given Brevibloc by a trained and qualified person, it is unlikely that you will have too much. However, if this happens the doctor will stop Brevibloc and give you additional treatment, if necessary.

If you think that a dose of Brevibloc has been forgotten

As you are being given Brevibloc by a trained and qualified person, it is unlikely that you will miss a dose. However, if you think that you have missed a dose, talk to your doctor, nurse or pharmacist as soon as possible.

If you stop having Brevibloc

Suddenly stopping Brevibloc may cause symptoms of rapid heartbeat (tachycardia) and high blood pressure (hypertension) to return. To avoid this your doctor should stop your treatment gradually. If you are known to have coronary artery disease (this may be associated with a history of angina or heart attack) your doctor will take special care when stopping treatment with Brevibloc.

If you have any further questions on the use of this product ask your doctor, nurse or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Most side effects disappear within 30 minutes of stopping treatment with Brevibloc. The following side effects have been reported with Brevibloc:

Tell your doctor, nurse or pharmacist straight away if you notice any of the following side effects, which can be serious. The infusion may also need to be stopped.

Very common (may affect more than 1 in 10 people)
- Fall in blood pressure. This can be rapidly corrected by reducing the dose of Brevibloc or stopping the treatment. Your blood pressure will be measured often during treatment
- Excessive sweating.

Common (may affect less than 1 in 10 people)
- Loss of appetite
- Feeling anxious or depressed
- Dizziness
- Feeling sleepy
- Headache
- Tingling or 'pins and needles'
- Difficulty concentrating
- Feeling confused or agitated
- Feeling or being sick (nausea and vomiting)
- Feeling weak
- Feeling tired (fatigue)
- Irritation and hardening of your skin where Brevibloc was injected.

Uncommon (may affect less than 1 in 100 people)
- Abnormal thoughts
- Sudden loss of consciousness
- Feeling faint or fainting
- Fits (seizures or convulsions)
- Problems with speech
- Problems with eyesight
- Slow heart rate
- Problems with the electrical messages that control your heartbeat
- Increased pressure in the arteries of the lungs
- Inability of the heart to pump enough blood (heart failure)
- A disruption in the rhythm of the heart sometimes known as palpitations (ventricular extrasystoles)
- A heartbeat disorder (nodal rhythm)
- Chest discomfort caused by poor blood flow through the blood vessels of the heart muscle (angina pectoris)
- Poor circulation in your arms or legs
- Looking pale or flushed
- Fluid on your lungs
- Shortness of breath or tightness of the chest making it difficult to breathe
- Wheezing
- Blocked nose
- Abnormal rattling/crackling sounds when breathing
- Changes in your sense of taste
- Indigestion
- Constipation
- Dry mouth
- Pain in your stomach area
- Discoloured skin
- Reddening of the skin
- Pain in your muscles or tendons, including around the shoulder blades and ribs
- Problems passing urine (urinary retention)
- Feeling cold or high temperature (fever)
- Pain and swelling (oedema) of your vein where Brevibloc was injected
- Burning feeling or bruising at the site of injection.

Very rare (may affect less than 1 in 10,000 people)
- Severe reduction in heart rate (sinus arrest)
- No electrical activity in the heart (asystole)
- Tender blood vessels with an area of hot red skin (thrombophlebitis)
- Dead skin caused by the solution leaking around the site of the injection.

Not known (the number of people affected is unknown)
- Increased levels of potassium in the blood (hyperkalemia)
- Increased levels of acids in your body (metabolic acidosis)
- Increased rate of contraction of the heart (accelerated idioventricular rhythm)
- Spasm of the artery in the heart
- Failure of the normal circulation of the blood (cardiac arrest)
- Psoriasis (where your skin produces scaly patches)
- Swelling of the skin of the face, limbs, tongue or throat (angioedema)
- Hives (urticaria)
- Inflammation of a vein or blistering at the site of infusion.

Reporting of side effects

If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet.

Ireland

You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace,
IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517.
Website: www.hpra.ie; Email: medsafety@hpra.ie.

United Kingdom

You can also report side effects Via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Brevibloc

- Keep this medicine out of the sight and reach of children
- Do not use Brevibloc after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month
- Do not store above 25°C
- The opened product is stable for 24 hours at 2 to 8°C. However, it should be used immediately after opening
- Do not use Brevibloc if you notice particles or discolouration of the solution.

Do not throw 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 Brevibloc contains

- The active substance is esmolol hydrochloride. One ml contains 10 mg of esmolol hydrochloride. Each vial contains 100 mg esmolol hydrochloride in 10 ml solution.
- The other ingredients are sodium acetate and glacial acetic acid, sodium chloride, sterile water (called 'water for injections'). Sodium hydroxide or hydrochloric acid may be added to ensure the correct pH.

What Brevibloc looks like and contents of the pack

Brevibloc is a clear, colourless to light yellow, sterile solution for intravenous injection. It is available in 10 ml amber glass vials.

Pack sizes of 3, 5, 10 and 20 vials containing 100 mg/10 ml. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

The Marketing Authorisation holder is:

United Kingdom
Baxter Healthcare Ltd
Caxton Way, Thetford,
Norfolk, IP24 3SE
United Kingdom

Ireland
Baxter Holding B.V.
Kobaltweg 49,
3542CE Utrecht,
Netherlands

Brevibloc is manufactured by:
Baxter S.A
Boulevard René Branquart, 80
7860 Lessines
Belgium

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

Member State	Name
Belgium	Brevibloc 10 mg/ml, solution injectable
Denmark	Brevibloc
Finland	Brevibloc 10 mg/ml injektioneste, liuos
Germany	Brevibloc 10 mg/ml Injektionslösung
Ireland	Brevibloc Premixed 10mg/ml, Solution for Injection
Luxembourg	Brevibloc 10 mg/ml, solution injectable
Netherlands	Brevibloc 10 mg/ml, oplossing voor injectie
Norway	Brevibloc 10 mg/ml, Injeksjonsvæske, oppløsning
Portugal	Brevibloc Premixed 10 mg/ml, Solução injectável
Spain	Brevibloc 10 mg/ml, solución para inyección
Sweden	Brevibloc 10 mg/ml, Injektionsvätska, lösning
UK	Brevibloc Premixed 10 mg/ml, Solution for Injection

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Other sources of information

For information about Brevibloc or to request this leaflet in formats such as audio or large print please contact the Marketing Authorisation Holder: Tel +44 (0)1635 206345

Perioperative tachycardia and hypertension

For perioperative tachycardia and hypertension the dosing regimen may vary as follows:

For intraoperative treatment **–** during anaesthesia when immediate control is required:
- A bolus injection of 80 mg is given over 15 to 30 seconds followed by a 150 micrograms/kg/minute infusion. Titrate the infusion rate as required up to 300 micrograms/kg/minute. The volume of infusion required for different patient weights is provided in Table 2.

Upon awakening from anaesthesia
- An infusion of 500 micrograms/kg/minute is given for 4 minutes followed by a 300 micrograms/kg/minute infusion. The volume of infusion required for different patient weights is provided in Table 2.

For post-operative situations when time for titration is available
- A loading dose of 500 micrograms/kg/minute is given over 1 minute before each titration step to produce a rapid onset of action. Use titration steps of 50, 100, 150, 200, 250 and 300 micrograms/kg/minute given over 4 minutes and stopping at the desired therapeutic effect. The volume of infusion required for different patient weights is provided in Table 2.

Incompatibilities

This medicinal product must not be mixed with other medicinal products or sodium bicarbonate solutions.

Special precautions for disposal and other handling
- Each vial is intended for **single use** only.
- Avoid contact with alkali.
- The solution should be visually inspected for particulate matter and discoloration prior to administration. Only a clear and colourless or slightly coloured solution should be used.
- Any unused solution and the containers should be disposed of in accordance with local requirements.

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