

## PATIENT INFORMATION LEAFLET

### ESMOBLOC 10 mg/ml Solution for I.V. Infusion

Administered intravenously without diluting.

Sterile

**Active substances:** It contains 2.5 grams of esmolol hydrochloride per 250 milliliter bag.

**Excipients:** Sodium chloride, sodium acetate trihydrate, glacial acetic acid, sodium hydroxide and/or hydrochloric acid, water for injection.

**Please read this PATIENT INFORMATION LEAFLET carefully before starting to use the drug; because important information is included here.**

- *Please keep this patient information leaflet. You may need to refer to them in the future.*
- *If you have any further questions, please consult your physician or pharmacist.*
- *This drug has been prescribed specifically for you, please do not give it to others.*
- *If you go to a physician or a hospital while you are taking this drug, notify your doctor that you are taking this drug.*
- *Adhere to these instructions verbatim. Do not use **high or low** doses of the drug, use the exact dose recommended for you.*

### **The following topics are included in this Patient Information Leaflet:**

*1. What is ESMOBLOC and what is it used for?*

*2. Before you are given ESMOBLOC*

*3. How you will be given ESMOBLOC?*

*4. Possible side effects*

*5. How to store ESMOBLOC*

#### **1. What is ESMOBLOC and what is it used for?**

ESMOBLOC contains a drug called esmolol. This drug belongs to a family of drugs called “beta blockers”. It shows its effects by controlling the force and speed of the heart rate. It may also help reduce blood pressure.

It is used for the treatment of the following diseases:

- Heart rate issues when it is too high

- Heart rate issues and when blood pressure increases during or right after a surgical operation

## **2. Before you are given ESMOBLOC**

### **DO NOT USE ESMOBLOC under the following circumstances**

If:

- You are sensitive (allergic) to the active substance esmolol, other beta blockers or other substances contained in the product (symptoms of an allergic reaction include shortness of breath, noisy breathing, rashes, itching, and swelling around the face and the lips).
- Your heart rate is very low (if your heart rate is below 50 bpm)
- Your heart rate occasionally increases, or increases and decreases.
- You have a severe heart block (heart block is when there is an issue with the conduction of the electrical current that regulates the functions of your heart).
- You have low blood pressure.
- There are any problems with the blood flow to your heart.
- You have signs of severe heart failure.
- You are taking or recently took Verapamil (used for the treatment of diseases such as hypertension, heart spasm, arrhythmia, the heart beating too fast) (ESMOBLOC should not be administered for 48 hours after the last dose of verapamil).
- You have untreated pheochromocytoma (pheochromocytoma originates from the adrenal glands, and may cause sudden increases in blood pressure, severe headaches, sweating and increased heart rate).
- The blood pressure in the veins leading to your lungs is high (or, in other words, if you have pulmonary hypertension)
- You have signs of quickly accelerating asthma.
- You are unable to eliminate excess acids produced in your body as a result of your metabolism being disrupted, from your body (or, in other words, if you have metabolic acidosis).
- You are pregnant or breastfeeding,  
please do not use ESMOBLOC.

### **Use ESMOBLOC WITH CAUTION if**

Please consult your physician, nurse or pharmacist before taking ESMOBLOC. If any of the following applies to you, your physician will take special precautions when giving you ESMOBLOC:

- If you have a special case of arrhythmia called supraventricular arrhythmia and either of the following:
  - Other cardiac disorders, or
  - You are taking another cardiac drug

In such cases, the use of ESMOBLOC may lead to the following, potentially fatal circumstances:

- Loss of conscious
  - Shocks (when your heart cannot pump enough blood)
  - Heart attack (cardiac arrest)
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- If you have a low blood pressure (hypotension) This may present itself as light-headedness or dizziness especially when standing up. Low blood pressure usually reverts back to normal in 30 minutes after ESMOBLOC treatment is concluded.
  - Low heart rate before the treatment.
  - Heart rate decreasing to 50-55 beats per minute. In this case, your physician may either lower your dosage of ESMOBLOC or discontinue the treatment.
  - If you have a heart failure.
  - If there are issues with the conduction of the electrical current that regulates the functions of your heart (heart block).
  - If you have a gland disease called pheochromocytoma for the treatment of which you are receiving alpha-receptor blockers.
  - If you are being treated for increased blood pressure (hypertension) caused by decreased body temperature (hypothermia).
  - If you have complaints similar to those related with asthma, such as respiratory tract contraction or noisy breathing.
  - If you have diabetes or low blood sugar (ESMOBLOC may increase the effects of your diabetes drugs).
  - If you develop skin disorders. Such disorders may be caused by the drug seeping out of the veins where it is administered. In such cases, your physician will administer the drug through a different vein.
  - If you are experiencing a special kind of angina called “Prinzmetal angina”.
  - If you have low blood volume (together with low blood pressure).In this case, it is significantly easier for your circulation system to fail.
  - If you have blood circulation disorders such as your fingers looking pale (Raynaud disease) or pain, fatigue or pain in your legs resembling burning.
  - If you have renal disorders. If you have a renal disorder or are receiving dialysis treatment for your kidneys, the potassium levels in your blood may have increased (hyperkalemia). This may cause severe cardiac disorders.
  - If you are allergic to anything, or under the risk of anaphylactic reaction (severe allergic reaction). As a result of the use of ESMOBLOC, current allergies may become more severe and harder to treat.
  - If you or anyone in your family has psoriasis (this cutaneous diseases causes patch-like flaking on the skin).
  - If you have a disease called hyperthyroidism (over activity of the thyroid gland).

The following circumstance generally does not require the dosage to be re-adjusted:

- Hepatic disorders.

You need to be monitored while taking ESMOBLOC:

- Drugs such as ESMOBLOC may decrease the power of the beat of your heart, when used for long durations.
- When you take ESMOBLOC for a limited time only, this will not affect you. You will be monitored when you treated with ESMOBLOC, and if your heart beat becomes weaker, ESMOBLOC treatment dosage will be decreased or stopped. Your physician will check your blood pressure during the ESMOBLOC treatment.

If these warnings apply or applied to you in the past, please consult your physician.

### **Using ESMOBLOC with food and beverages**

It is not possible to consume food or beverages while taking ESMOBLOC.

### **Pregnancy**

*Please consult your physician or pharmacist before taking the drug.*

If you are or think that you are pregnant, do not use this drug.

*If you are aware of your pregnancy during treatment, immediately consult with your physician or pharmacist.*

### **Lactation**

*Please consult your physician or pharmacist before taking the drug.*

If you are a breastfeeding mother, inform your physician before taking ESMOBLOC. ESMOBLOC may pass into mother's milk, so if you are a breastfeeding mother, ESMOBLOC may not be used on you.

### **Ability on driving and using machines**

It is not possible to drive, or use machines while taking ESMOBLOC.

### **Vital information regarding some of the excipients contained in ESMOBLOC**

This medicinal product contains approximately 30.45 mmol mg sodium in each bag. This fact should be taken into consideration for the patients subjected to controlled sodium diet.

### **Use in combination with other drugs**

If you are taking, or recently took any of the following drugs, please inform your physician, nurse or pharmacist. This includes over-the-counter drugs, herbal drugs and natural products.

- Drugs that decrease your blood pressure and slow down your heart rate
- Drugs such as verapamil and diltiazem used for heart rhythm disorders or chest pain (angina). You should not take ESMOBLOC for 48 hours after the last dose of verapamil.
- Nifedipin which is used for chest pain (angina), high blood pressure and Raynaud disease.
- Drugs used for heart rhythm disorders (quinidine, disopramid, amiodaron, etc.) and heart

failure (digoxin, digitoxin, digitalis, etc.)

- Drugs used for the treatment of diabetes including insulin and orally taken drugs
- Drugs called ganglion blockers (drugs used for the treatment of hypertension, such as trimethaphan)
- Anti-inflammatory drugs that are used as painkillers and are not steroids (NSAIDs) (aspirin, ibuprofen, nabumeton, etc.)
- Floctafenine which is a painkiller
- Amisulpride which is used for the treatment of disorders related to mental health
- Tricyclic antidepressants (imipramine, amitriptyline, etc.) or drugs used for the treatment of disorders related to mental health
- Barbiturates (such as phenobarbital which is used for the treatment of epilepsy) or phenothiazines (such as chlorpromazine which is used for the treatment of mental health disorders)
- Clozapine (used for the treatment of mental health disorders)
- Epinephrine which is used for the treatment of allergic reactions
- Drugs used for the treatment of asthma
- Drugs called nasal decongestants and used for cold and nasal congestion
- A drug called reserpine which is used for when the blood pressure is high
- A drug called clonidine which is used for some cases where the blood pressure is high, and for migraine
- A drug called moxonidine which is used for some cases where the blood pressure is high
- Drugs called ergo derivatives which are principally used for Parkinson's disease
- A drug called warfarin used to dilute your blood
- Morphine which is a powerful painkiller
- Succinylcholine chloride (also known as succinylcholine or skolin) or mivacurium which are used as muscle relaxers during surgical operations. Moreover, if you will undergo a surgical operation, and sedatives or other treatments will be administered during the operation, your physician will take special measures during the operation.

*If you are currently taking or recently took any prescribed or over-the-counter drugs, please inform your physician or pharmacist.*

### **3. How you will be given ESMOBLOC?**

#### **Instructions regarding correct use and dosage/administration frequency:**

Your physician will determine the dosage and duration of administration.  
ESMOBLOC is typically not used for periods longer than 24 hours.

#### **Method of administration:**

ESMOBLOC is ready to use. ESMOBLOC will be slowly injected through a needle into a vein

in your arm (infusion).

ESMOBLOC should not be mixed with other drugs or sodium bicarbonate solution.

The drug will be administered in two stages:

- First stage: A high loading dosage is applied in one minute. This increases the level of drug in your blood. In such cases, your physician may start off with the sustainment dose without administering this loading dose.
- Second stage: In four minutes, a dose lower than the first loading dose (sustainment dose) is applied.

Depending on the response of your heart, first and second stage doses may be repeated and dose may be re-adjusted. As soon as positive response is observed, first stage (high dosage) is concluded and second stage dose (sustainment stage with a lower dose) is initiated and, if necessary, increased.

If you stabilize, your ESMOBLOC dosage may be gradually decreased and another heart drug may be used.

If your heart rate or blood pressure increases during a surgical operation or the discharge period afterwards, ESMOBLOC will be administered in shorter intervals and higher doses.

**Various age groups:**

**Use in children:**

It should not be used in children under 18.

**Use in the elderly:**

If you are old, your physician will administer the drug in a small dose.

**Special usage cases:**

**Renal failure:**

The use of ESMOBLOC requires caution in patients with renal failure.

**Hepatic failure:**

Hepatic failure does not require special measures.

*If you are under the impression that the effect of ESMOBLOC is too strong or weak, please consult your physician or pharmacist.*

**If you have taken more ESMOBLOC than you should have:**

*If you have used ESMOBLOC more than you should have, consult a physician or a pharmacist.*

As ESMOBLOC will be administered by a trained and qualified healthcare professional, the possibility of using more than you should is slim. Nevertheless, in cases where it was used more than it should have been, your physician will discontinue ESMOBLOC and, if necessary, administer additional treatments.

**If you forget to use ESMOBLOC:**

*Do not double-dose to make up for forgotten doses.*

As ESMOBLOC will be administered by a trained and qualified healthcare professional, the possibility of forgetting to use the drug is slim. However, if you believe that a dose has been forgotten, consult a physician, a pharmacist or a nurse as soon as possible.

**Possible effects once ESMOBLOC treatment is concluded:**

If treatment with ESMOBLOC is suddenly discontinued, symptoms that the heart is beating fast (tachycardia) and high blood pressure (hypertension) may return. If you have coronary heart disease (this disease may have a history of angina (severe pain in the heart area and chest due to insufficient blood flowing to the heart) or heart attacks), your physician will exercise extreme caution discontinuing your ESMOBLOC treatment.

**4. Possible side effects**

As is the case with all drugs, individuals sensitive to some of the substances contained in ESMOBLOC may develop side effects. Most of the side effects go away in 30 minutes after ESMOBLOC treatment is discontinued.

The side-effects listed below have been reported in connection with the use of ESMOBLOC:

**Very common** (affects more than 1 patient out of 10)

- Decreased blood pressure (tension). This could go away quickly by decreasing the dosage or discontinuing the treatment. Your blood pressure will be measured often during the treatment.
- Excessive sweating,

**Common** (affects less than 1 patient out of 10)

- Loss of appetite
- Anxiety or depression
- Light-headedness / confusion
- Sleepiness
- Headache
- Feeling of tingling or “pinprick”
- Difficulty to concentrate
- Foggy consciousness or agitation (inconsistent behaviors in the form of behavioral or spiritual excitement in connection with mental disorders)
- Feeling sick (nausea and vomiting)
- Feeling weak
- Feeling tired (fatigue)

- Rash or hardening in the skin around the administration site of ESMOBLOC

**Uncommon** (affects less than 1 patient out of 100)

- Abnormal thoughts
- Sudden loss of consciousness
- Feeling faint
- Spasm seizures
- Speech disorders
- Disorders related to sight
- Decreased heart rate
- Issues regarding electrical stimuli controlling the heart rates
- Increased pressure in lung arteries
- The failure of the heart to pump sufficient blood (heart failure)
- Arrhythmia which is also known as palpitation (ventricular extra systole)
- A type of arrhythmia (nodal rhythm)
- Discomfort in the chest area due to insufficient circulation of blood in the blood vessels feeding the heart muscle (angina pectoris)
- Insufficient blood circulation in the arms and the legs
- Looking pale or redness around the face and the neck
- Hydrothorax
- Shortness of breath or tightness in the chest area making it difficult to breathe
- Noisy breathing
- Nasal congestion
- Hearing clicking sounds in the lungs when breathing
- Disorders related to the sense of taste
- Indigestion
- Constipation
- Dry mouth
- Pain around the stomach area
- Skin discoloring
- Skin redness
- Muscle and tendon pain including shoulders and back
- Difficulty to urinate (not completely emptying the bladder)
- Feeling cold or high fevers
- Pain and swelling (edema) around the injection site of ESMOBLOC
- Inflammation or bruising around the injection site

**Very rare** (affects less than 1 patient out of 10,000)

- Severely decreased heart rate (sinus arrest)
- The electrical activity in the heart stopping (asystole)
- Blood vessels becoming more sensitive in addition to redness and hot area in the skin (thrombophlebitis)
- Necrosis in the skin as a result of leaking solution around the injection site

**Unknown** (the number of affected individuals is unknown)

- Increased levels of blood potassium (hyperkalemia)
- Increased levels of blood acid (metabolic acidosis)
- Increase in the contraction speed of the heart (expedited idioventricular rhythm).
- Spasms in the arteries feeding the heart
- The regular circulation of the blood being insufficient (cardiac arrest)
- Psoriasis (this cutaneous disease causes patch-like flaking on the skin).
- Swelling in face, tongue, lips or the throat (angio-edema)
- Urticaria
- Inflammation of a vein or build-up of water around the infusion site

*If you notice any side effect not mentioned in this leaflet, please inform your doctor or pharmacist.*

## **5. How to store ESMOBLOC**

*Store ESMOBLOC away from the reach and sight of children and in its original packaging.*

- Do not use ESMOBLOC after the expiration date printed on its packaging. The expiration date means the last day of the indicated month.
- Do not remove the protective cover around the bag until you will use it.
- Keep ESMOBLOC at room temperature below 25°C.
- This medicinal product should not be kept in a fridge, or be frozen.
- Once its packaging has been opened, ESMOBLOC does spoil for 24 hours if kept at temperatures between 2 and 8°C. However, it must be used immediately once opened.
- If you notice particles or discoloring in the solution, do not use ESMOBLOC.

Drugs should not be discarded with household waste, or to the sewage. Consult your pharmacist about how to dispose of the drugs that you do not need. You will help protect the environment by doing so.

**Use complying with expiration date.**

*Do not use ESMOBLOC after the expiration date printed on its packaging.*

***Marketing Authorization Holder and Manufacturing Site:***

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**FOLLOWING INFORMATION IS FOR THE HEALTHCARE PROFESSIONALS THAT WILL ADMINISTER THIS DRUG**

This section includes practical information regarding administration. Please refer to the entire Short Product Information for posology, administration method, contraindications, warnings, etc.

**Posology/administration frequency and duration**

**Dosage for the Treatment of Supraventricular Tachycardia or Non-Compensated Sinus Tachycardia**

ESMOBLOC is administered with or without a loading dosage through continued intravenous infusion. Depending on the desired ventricular response, additional loading dosage and/or sustainment infusion (gradual dosing) titration may be necessary.

Table 1-Gradual Dosing

Step	Procedure
1	Optional loading dosage (500 micrograms/kg in 1 min), then 50 micrograms/kg/min for 4 min
2	If necessary, the optional loading dosage, 100 micrograms/kg/min for 4 min
3	If necessary, the optional loading dosage, 150 micrograms/kg/min for 4 min
4	If necessary, dosage is increased to 200 micrograms/kg/min

In cases where loading dosage is not administered, the pharmacokinetically and pharmacodynamically stabilized concentrations of esmolol which is administered in a fixed concentration, is achieved in roughly 30 minutes.

While low dosages such as 25 micrograms/kg/min are sufficient for the effective sustainment dosage, continued and gradual dosing, they range from 50 to 200 micrograms/kg/min. High doses over 200 micrograms/kg/min have a lower effect, cause a small increase in the heart rate, and increase the rate of adverse reactions.

Sustainment infusion may be carried out for up to 48 hours.

### **Intraoperative or Postoperative Tachycardia and/or Hypertension**

Gradual titration is not always recommended for therapeutic effect in this usage. Therefore, there are two dosage options: instant control and gradual control.

#### 1. Dosage recommendation for instant control

- As bolus dosage, 1 mg/kg is administered in the first 30 seconds, and if necessary, 150 micrograms/kg/min is administered through infusion.
- Infusion rate is adjusted as necessary in order to sustain the desired heart rate and blood pressure. Please see the Maximum Recommended Doses section below

#### 2. Dosage recommendation for gradual titration

- As bolus dosage, 500 micrograms/kg is administered in the first 1 minute, and then 4 micrograms/kg/min is administered through sustainment infusion in 4 minutes.
- Depending on the resulting response, dosage indicated for supraventricular tachycardia is continued. Please see the Maximum Recommended Doses section below

#### Maximum Recommended Doses

- Sustainment doses over 200 micrograms/kg/min is recommended for the treatment of tachycardia. High doses over 200 micrograms/kg/min have a lower effect, cause a small increase in the heart rate, and increase the rate of adverse reactions.
- Higher sustainment infusion doses (250-300 micrograms/kg/min) may be required for the treatment of hypertension. The safety of doses over 300 micrograms/kg/min has not been studied.

### **Transitioning from ESMOBLOC Treatment to Alternative Drugs**

Once sufficient control and stabilized clinical picture have been achieved, alternative anti-arrhythmic drugs may be used.

When transitioning from ESMOBLOC treatment to alternative drugs, the physician should carefully read the user instructions and decrease the dose of ESMOBLOC as follows:

- In 30 minutes after the first dose of the alternative drugs, ESMOBLOC infusion rate is halved (50%).
- After the second dose of the alternative drug, the patient's response is monitored and if sufficient control is achieved in the first hour, ESMOBLOC infusion is discontinued.

**Method of administration:**

As ESMOBLOC is ready to use, it is administered intravenously without dilution.