

PATIENT INFORMATION LEAFLET

Multiflex ERMOLOC Premix 10 mg/mL IV Solution for Infusion

Administered intravenously without diluting.

Sterile

Active substance: Each 250 mL bag contains 2500 mg esmolol hydrochloride.

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

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.*
- *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.*
- *Tell your doctor that you are taking this medicine when you go to the doctor or hospital during the use of this medicine.*
- *Follow exactly what is written in this instruction. Do not use **high or low** doses other than the recommended dosage.*

What is in this Leaflet:

- 1. What ERMOLOC is and what it is used for?***
- 2. What you need to know before you use ERMOLOC***
- 3. How to use ERMOLOC?***
- 4. What are the possible side effects?***
- 5. How to store ERMOLOC***

Headings are covered.

1. What ERMOLOC is and what it is used for?

ERMOLOC contains a drug substance called as esmolol. This drug substance belongs to a group of medicines called beta blockers. It shows its effect by controlling the heart beat pattern and pulse rate. It can also help lower the blood pressure.

It is used in the treatment of the following diseases:

- Heart problems when your heart beats too fast
- Heartbeat problems and an increase in blood pressure during or immediately after an operation

2. What you need to know before you use ERMOLOC

DO NOT USE ERMOLOC

If;

- You have hypersensitivity (allergy) to esmolol active substance, other beta-blocker drugs or other ingredients (symptoms of an allergic reaction include breathlessness, wheezing, rash,

itching or swelling of your face and lips).

- Your heart is beating too slowly (your heart rate is less than 50 per minute).
- There is acceleration or a slowdown and acceleration in your heartbeat.
- You have a severe heart block (heart block is a problem with the electrical current that regulates the work of the heart).
- You have low blood pressure.
- You have a problem getting blood to your heart.
- You have symptoms of severe heart failure.
- You are using the drug called verapamil (used in the treatment of diseases such as high blood pressure, heart spasm, heart rhythm disorder, heartbeat too fast) or if you have recently used it (ERMOLOC should not be administered before 48 hours after the drug called verapamil is discontinued).
- You have untreated pheochromocytoma (pheochromocytoma is caused by the adrenal glands and can cause spikes in blood pressure, severe headaches, sweating, and rapid heartbeat)
- You have high blood pressure in the vein leading to the lungs (if you have pulmonary hypertension).
- You have asthma symptoms that get worse quickly.
- You are unable to remove excess acids from your body due to the disruption of the production-destruction works in your body (if you have metabolic acidosis).
- You are pregnant or breastfeeding. Do not use ERMOLOC.

USE ERMOLOC CAREFULLY in the following cases

Before using ERMOLOC, consult your doctor, nurse or pharmacist. If you have the following situations, your doctor will take special precautions while administering ERMOLOC to you:

- If you have a specific arrhythmia called supraventricular arrhythmia and you also have any of the following
 - If you have other heart problems or
 - If you are taking any other heart medication

In such cases, administration of ERMOLOC can cause to the following situations, which can be fatal:

- Loss of consciousness
- Shock (when your heart is not able to pump enough blood)
- Heart attack (cardiac arrest)

- If you have low blood pressure (hypotension). You may feel dizzy or lightheaded, especially when standing. Low blood pressure usually improves within 30 minutes after cessation of ERMOLOC therapy.
- If you have a low heart rate before treatment.
- A decrease in your heart rate to 50-55 beats per minute. In this case, your doctor may reduce your ERMOLOC dose or stop your treatment.
- If you have heart failure.
- If you have problems in conducting the electrical current that regulates your heart (heart block).
- If you have a glandular disease called pheochromocytoma for which you are being treated with alpha-receptor blockers.
- If you are being treated for high blood pressure (hypertension) due to too low body temperature (hypothermia).
- If you suffer from narrowing of your airways or wheezing or whistling, as in asthma.
- If you have diabetes or low blood sugar (ERMOLOC can increase the effect of your diabetes medications).
- If you have skin problems. Such problems may be caused by your medicine getting out of the vein from the place where it was administered. When such an event occurs, your doctor will administer the drug from another vein.
- If you have a specific angina (chest pain) called Prinzmetal's angina
- You have low blood volume (with low blood pressure). In this case, your circulatory system can collapse much more easily.
- If you have problems with your blood circulation, such as pallor in your fingers (Raynaud's disease) or pain, fatigue and sometimes burning pain in your legs.
- If you have kidney problems. If you have kidney disease or are on dialysis for your kidneys, you may have increased potassium levels in your blood (hyperkalaemia). This condition can cause serious heart problems.
- If you are allergic to anything or you are at risk of an anaphylactic reaction (severe allergic reaction). Due to the administration of ERMOLOC, existing allergies may become more severe and more difficult to treat.
- If you or your families have psoriasis (this skin disease, also called psoriasis, has patches on the skin).
- If you have a disease called hyperthyroidism (overactive thyroid gland).

It is generally not necessary to change the dose if:

- If you have liver problems. When using ERMOLOC, you need to be monitored:

- Long-term use of medicines such as ERMOLOC may cause a decrease in your heart rate.
- Since ERMOLOC is administered only for a limited time, this will not happen to you. You will be carefully monitored while receiving ERMOLOC treatment and if a decrease in your heart rate is observed ERMOLOC treatment doses will be reduced or stopped. During your treatment with ERMOLOC, your doctor will check your blood pressure.

Please consult your physician if these warnings applicable to you, even at any time in the past.

Use of ERMOLOC with food and drink

It is not possible to use food and drinks while administration of ERMOLOC.

Pregnancy

Consult to your doctor or your pharmacist before using this drug.

Do not use this drug if you are pregnant or if you think that you are pregnant.

If you notice that you are pregnant during your treatment, consult your doctor or pharmacist immediately.

Breast-feeding

Consult your doctor or your pharmacist before using the drug.

If you are a breastfeeding mother, tell that to your doctor before using ERMOLOC. ERMOLOC can pass into breast milk and therefore ERMOLOC may not be used if you are a breastfeeding mother.

Driving and using machines

It is not possible to drive and use machines while administration of ERMOLOC.

Important information about some of the excipients contained in ERMOLOC

This medicinal product contains approximately 700 mg of sodium in each bag. This should be considered for patients on a controlled sodium diet.

Use with other medicines

If you are using the following medicines or have used them recently, please tell your doctor or pharmacist. This includes other medicines purchased without a prescription, herbal remedies, and natural products.

- Medicines that lower your blood pressure or slow your heart rate
- Medicines such as verapamil and diltiazem used for heart rhythm problems or chest pain (angina). You should not take ERMOLOC for 48 hours after the drug called Verapamil is discontinued.
- Nifedipine used for chest pain (angina), high blood pressure and Raynaud's disease
- Medicines used for heart rhythm problems (such as quinidine, disopramide, amiodarone) and

heart failure (such as digoxin, digitoxin, digitalis)

- Medicines used to treat diabetes, including insulin and oral medications
- Medicines called ganglion blockers (medicines used to treat high blood pressure such as trimethaphan)
- Drugs used as pain relievers and called non-steroidal anti-inflammatory drugs (NSAIDs) (such as aspirin, ibuprofen, nabumetone)
- Floctafen, a pain reliever
- Amisulpride, a drug used in the treatment of mental health problems
- Tricyclic antidepressant drugs (such as imipramine and amitriptyline) or any medication used to treat mental health problems
- Barbiturates (such as phenobarbital used in the treatment of epilepsy) or phenothiazines (such as chlorpromazine used in the treatment of mental health disorders)
- Clozapine (used in the treatment of mental health disorders)
- Epinephrine used to treat allergic reactions
- Medicines used in asthma treatment
- Medicines called nasal decongestants and used for colds or nasal congestion
- A drug called reserpine used in some cases with high blood pressure
- A drug called clonidine used in some cases with high blood pressure and migraine
- A drug called moxonidine, used in some cases with high blood pressure
- Medicines called ergot derivatives, mainly used in Parkinson's disease
- Warfarin, a medicine used to thin your blood.
- Morphine, a powerful pain reliever
- Succamethonium chloride (also known as succinylcholine or scoline), which is often used as a muscle relaxant during surgery. In addition, if you are going to have surgery and you will be given narcosis drugs or other treatments during your surgery, your doctor will take special precautions while using ERMOLOC during your surgery.

If you are currently using or taking any prescription or over-the-counter medication, please inform your doctor or pharmacist.

3. How to use ERMOLOC?

Your doctor will decide how much medicine you need and how long you will use it.

ERMOLOC is not normally used for longer than 24 hours.

- **Administration route and method**

ERMOLOC is a ready-to-use medicine. ERMOLOC will be administered slowly (infusion) through a needle inserted into a vein in your arm.

ERMOLOC should not be mixed with other drugs or sodium bicarbonate solution. The medicine will be given to you in two stages:

- **First stage:** A high loading dose is administered within one minute. In the blood like this drug level rises rapidly. In some cases, your doctor may start your medication directly with the maintenance dose without administering this loading dose to you.

- **Second stage:** A lower dose (maintenance dose) than the first loading dose is administered within four minutes.

Depending on the response of your heart, the first and second stage doses can be repeated and the dose can be adjusted. As soon as a positive response is obtained, the first stage (high dose administered stage) administration is terminated and the second stage (maintenance stage with low dose) is continued with the dose and this dose is reduced if necessary.

If your condition stabilizes, your dose of ERMOLOC can be gradually reduced and switched to another heart drug.

If your heart rate increases or your blood pressure rises during a surgery or during the recovery period, you will be given higher doses of ERMOLOC for a shorter period of time.

- **Various age groups**

Use in children:

It should not be administered in children under 18 years of age.

Use in the elderly:

If you are older, your doctor will start you on a lower dose of this drug.

- **Special conditions of use:**

Renal failure:

Caution should be exercised when administration of ERMOLOC in patients with renal failure.

Liver failure:

Special precautions are not required in case of liver failure.

Please talk to your physician or pharmacist if you feel that the effect of ERMOLOC is too strong or too weak.

If you have used more ERMOLOC than you should:

If you have used more than you should use from ERMOLOC, talk to a doctor and pharmacist.

Since ERMOLOC will be administered to you by a trained and qualified healthcare professional, it is unlikely that you have used more medication than you should. However, if you use more

medication than you should, your doctor will stop using ERMOLOC and, if necessary, administer additional treatment to you.

If you forget to use ERMOLOC

Do not take a double dose to make up for forgotten doses.

Since ERMOLOC will be administered to you by a trained and qualified healthcare professional, it is not possible to forget to take the medicine. However, if you think that a dose has been missed, talk to a doctor, pharmacist or nurse as soon as possible.

Effects which may occur when treatment with ERMOLOC is discontinued

If the treatment with ERMOLOC is discontinued suddenly, symptoms of rapid heartbeat (tachycardia) and high blood pressure (hypertension) may return. To avoid this, your doctor will gradually reduce your treatment. If you have coronary heart disease (this disease may include angina (severe pain in the heart area and chest caused by insufficient blood supply to the heart) or a history of heart attacks) your doctor will take special care when terminating your treatment with ERMOLOC.

4. What are the possible side effects?

Like all medicines, there may be side effects in people who are sensitive to the substances contained in ERMOLOC. Most of the side effects disappear within 30 minutes after termination of treatment with ERMOLOC.

The following side effects have been reported with the use of ERMOLOC:

Very common (affects more than one in 10 people)

- A decrease in blood pressure. This can be quickly corrected by reducing the dose or discontinuing the drug. Your blood pressure will be measured frequently during treatment.

- Excessive sweating,

Common (affects less than 1 in 10 people)

- Poor appetite
- Anxiety or feeling depressed
- Dizziness / lightheadedness
- Sleeping state
- Headache
- Tingling or 'pins and needles' sensation
- Difficulty concentrating
- Confusion or agitation (excessively inconsistent behavior manifested as behavioral and mental excitement depending on personal mood disorders)
- Feeling sick (nausea and vomiting)
- Feeling weak
- Feeling exhausted (tired)
- Irritation and hardening on your skin where ERMOLOC is administered

Uncommon (affects less than one in 100 people)

- Abnormal thoughts
- Sudden loss of consciousness

- Feeling like you will faint
- Seizures
- Speech disorders
- Vision problems
- Slow heartbeat
- Problems with electrical impulses controlling your heartbeat
- Increases in pressure in the pulmonary arteries
- Inability of the heart to pump enough blood (heart failure)
- Occasional disturbance of the heart rhythm known as palpitations (ventricular extrasystole)
- A type of heart beat disorder (nodal rhythm)
- Discomfort in the chest caused by insufficient blood circulation in the blood vessels feeding the heart muscle (angina pectoris)
- Insufficient blood circulation in the arms and legs
- Looking pale or red on the face and neck
- Fluid accumulation in the lungs
- Feeling short of breath or tightness in the chest that makes it difficult to breathe
- Wheezing
- Congestion in the nose
- Hearing crackling sounds in lung sounds while breathing in and out
- Disturbances in the sense of taste
- Indigestion
- Constipation
- Drying in the mouth
- Pain in the stomach area
- Loss of skin color
- Redness of the skin
- Pain in muscles and tendons, including shoulders and back
- Difficulty urinating (not fully emptying the bladder)
- Chills or high fever
- Pain and swelling (edema) where ERMOLOC is administered
- Burning sensation or bruising at the injection site

Very rare (affecting less than one in 10,000 people)

- Severe reduction in heart rate (sinus arrest)
- Absence of electrical activity in the heart (asystole)
- Sensitization of blood vessels (thrombophlebitis) with a hot and red area on the skin
- The formation of dead parts on the skin due to the leakage of the solution around the injection site.

Unknown (number of people affected is unknown)

- Increase in blood potassium levels (hyperkalemia)
- Increase in blood acid levels (metabolic acidosis)
- Increase in the rate of contraction of the heart (accelerated idioventricular rhythm).
- Spasm in the artery that supplies the heart
- Failure of the normal circulation of the blood (cardiac arrest)
- Psoriasis (this skin disease, also called psoriasis, is seen in the form of patches on the skin)
- Swelling of the face, lips, tongue or throat (angioedema)
- Hives (urticaria)
- Inflammation of a vein or fluid collection where the infusion is being administered

Reporting of the side effects:

If you get any side effects not listed in this leaflet, talk to your doctor or pharmacist. You can also report side effects directly to your doctor or pharmacist. You can also report side effects directly to your country's related health authority. By reporting side effects, you can help provide more information on the safety of this medicine.

If you experience any side effect not mentioned in this patient information leaflet, inform your doctor or your pharmacist.

5. How to store ERMOLOC

Keep ERMOLOC out of the sight and reach of children, and in its packaging.

- Do not use ERMOLOC after the expiry date indicated on the package. The expiry date refers to the last day of the specified month.
- Do not open the protective cover outside the bag until just before use.
- Store ERMOLOC at room temperature below 25 °C.
- The medicine should not be stored in the refrigerator or frozen.
- If ERMOLOC is stored between 2 and 8 °C after opening, it will not deteriorate for 24 hours. However, it should be used immediately after opening.
- If you see particles or discoloration in the solution, do not use ERMOLOC.

Medicines should not be disposed of in household waste and sewers. Ask your pharmacist how to throw away medicines you no longer need. So you can help protect the environment.

Use in accordance with expiration dates

Do not use ERMOLOC after the expiration date stated on the packaging.

Do not throw away drugs that have expired or are not used! Give them to the collection system determined by the Ministry of Environment and Urbanization.

Marketing Authorization Holder:

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This patient information leaflet was approved on ../../.....

THE FOLLOWING INFORMATION IS FOR THE HEALTH PERSONNEL WHO WILL ADMINISTER THIS MEDICINE

This section contains practical information about the application. Regarding posology and method of administration, contraindications, warnings etc. Summary of Product Characteristics should be fully read.

Posology/administration frequency and duration

Dosing in the Treatment of Supraventricular Tachycardia or Uncompensated Sinus Tachycardia

ERMOLOC is administered by continuous intravenous infusion with or without a loading dose. Additional loading doses and / or titration of the maintenance infusion (stepwise dosing) may be required, depending on the desired ventricular response.

Table 1-Stepwise Dosing

Step	Operation
1	Optional loading dose (500 mcg / kg within 1 min), then 50 mcg / kg / min for 4 min
2	Optional loading dose if required, 100 mcg/kg/min for 4 min.
3	Optional loading dose if required, 150 mcg/kg/min for 4 min.
4	If required, increase the dose to 200 mcg/kg/min.

In cases where the loading dose is not administered, pharmacokinetically and pharmacodynamically fixed concentrations of esmolol administered at a fixed concentration are reached in about 30 minutes.

The effective maintenance dose is 50 to 200 micrograms/kg/min, although doses as low as 25 micrograms/kg/min are sufficient for continuous and stepwise dosing. Doses higher than 200 micrograms/kg/min decrease the effect and cause a small increase in heart rate and increase the rate of adverse reactions.

The maintenance infusion can be continued for up to 48 hours.

Intraoperative and postoperative tachycardia and / or hypertension

It is not always recommended to titrate slowly for therapeutic effect in this use. Therefore, two dosing options are offered: Immediate control and step control.

1. Dose recommendation for immediate control

- It is administered as bolus dose 1 mg/kg within 30 seconds, followed by 150 microgram/kg/min infusion if necessary.
- The infusion rate as needed to maintain the desired heart rate and blood pressure is adjusted. See Maximum Recommended Doses below.

2. Dose recommendation for step titration

- It is administered as a bolus dose of 500 microgram/kg within 1 minute, followed by a maintenance infusion of 50 microgram/kg/minute within 4 minutes.
- Depending on the response achieved, the dosing determined for supraventricular tachycardia is continued. See Maximum Recommended Doses below.

Maximum recommended doses

- Maintenance doses higher than 200 micrograms/kg/min are not recommended for the treatment of tachycardia. Doses higher than 200 micrograms/kg/min decrease the effect, causing a small increase in heart rate and increasing the rate of adverse reactions.
- Higher maintenance infusion doses (250-300 micrograms/kg/min) may be required for the treatment of hypertension. The reliability of doses above 300 micrograms/kg/min has not been studied.

Transition from ERMOLOC treatment to alternative drugs

Patients can be switched to alternative antiarrhythmic drugs after providing adequate control of heart rate and a stable clinical picture.

When switching from ERMOLOC treatment to alternative drugs, the physician should carefully examine the instructions for use of the selected alternative drug and reduce the dose of ERMOLOC as follows:

- Within 30 minutes after the first dose of the alternative medicine, ERMOLOC infusion rate is reduced in half (50%).
- After the administration of the second dose of the alternative medicine, the patient's response is monitored and if adequate control is achieved in the first hour, ERMOLOC infusion is discontinued.

Method of Administration:

Since Multiflex ERMOLOC Premix 10 mg/mL is a ready-to-use solution, it is used intravenously without dilution.