PACKAGE LEAFLET

Package leaflet: Information for the patient

Rapibloc 300 mg powder for solution for infusion

landiolol hydrochloride

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 nurse.
- 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.

The full name of your medicine is Rapibloc 300 mg powder for solution for infusion. In this leaflet the shorter name Rapibloc is used.

What is in this leaflet

1. What Rapibloc is and what it is used for

Rapibloc contains the active substance landiolol hydrochloride. It belongs to a group of medicines called "beta-blockers". It works by changing your irregular or fast heartbeat to a normal heartbeat.

This medicine is used in adults to treat heartbeat problems, when your heart beats too fast.
It is used during or straight after surgery or in other situations where control of your heartbeat is needed.

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

Your doctor will NOT give you Rapibloc if:

- You are allergic to landiolol or any of the other ingredients of this medicine (listed in section 6).
- You have a very slow heartbeat (less than 50 beats per minute).
- You have a fast or alternating fast and slow heartbeat (a problem called the "sick sinus" syndrome).
- You have a problem called "severe heart block". Heart block is a problem with the electrical messages that control your heartbeat.
- You have a problem with the blood supply to your heart (a problem called "cardiogenic shock").
- You have very low blood pressure.
- You have serious heart failure symptoms.
- You have increased pressure in the lungs (pulmonary hypertension).
- You have a gland disease called phaeochromocytoma which has not been treated. Phaeochromocytoma arises from the adrenal gland and may cause a sudden increase of blood pressure, severe headache, sweating and increased heartbeat.
- You have asthma symptoms that are worsening rapidly.
- You have very high levels of acids in your body (severe metabolic acidosis) which can not be corrected.

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

Warnings and precautions

- Talk to your doctor or nurse before being given this medicine.
- Rapibloc is a powder and must be dissolved by your doctor or nurse before it is given to you.
- Usually, your heartbeat, blood pressure and the electrical activity of your heart will be continuously monitored while you are treated with this medicine.

If any of the below apply to you (or you are not sure), talk to your doctor or nurse before being given this medicine.

Your doctor will take special care with this medicine if:

- You have diabetes or low blood sugar. Landiolol can mask the symptoms of a low blood sugar.
- You have low blood pressure.
- You have a problem called "pre-excitation syndrome" in combination with an irregular and rapid heartbeat (atrial fibrillation).
- You have problems with the electrical messages that control your heartbeat (heart block).
- You have problems with the progression of electrical impulses through the heart and receiving verapamil or diltiazem.
- You have a particular type of angina (chest pain) called "Prinzmetal´s angina".
- You have or had heart problems (such as congestive heart failure). Your doctor will monitor you very closely for any heart symptoms. If necessary, the treatment will be stopped, the dosage lowered or special treatment initiated.
- You have certain heart rhythm disorders called supraventricular arrhythmias and you:
    - have other heart problems or
    - are taking other heart medicines
- You have kidney problems.
- You have a gland disease called phaeochromocytoma which has been treated with medicines called alpha-receptor blockers.
- You have narrowing of your airways or wheezing, such as with asthma.
- 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 any allergies or you are at risk of anaphylactic reactions (severe allergic reactions). Rapibloc can make allergies more severe and more difficult to treat.

Other medicines and Rapibloc

Tell your doctor or nurse 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 Rapibloc works.

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

- Medicines used to treat heart rhythm problems (such as diltiazem, verapamil, propafenone, disopyramide, amiodarone, digoxin, digitalis) and high blood pressure (such as nifedipine).
- Medicines used to treat diabetes, including insulin and medicines taken by mouth.
- Medicines usually used during an operation to relax your muscles (such as suxamethonium) or medicines used to reverse the effect of muscle relaxants called cholinesterase inhibitors (such as neostigmine, distigmine, edrophonium). Your doctor will also take special care when using Rapibloc during operations, when you will be having anaesthetics and other treatments.
- 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).
- Barbiturates (such as phenobarbital, used to treat epilepsy).
- Phenothiazines (such as chlorpromazine, used to treat mental disorders).
- Medicines used to treat asthma.
- Medicines used to treat colds or a blocked nose, called "nasal decongestants".
- Medicines that can lower the blood pressure (such as reserpine and clonidine).
- Epinephrine, which is used to treat allergic reactions.
- Heparin, which is used to thin the blood.

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

Pregnancy and breast-feeding

If you are pregnant or you think you may be pregnant talk to your doctor before having this medicine. There are no data available about the use of Rapibloc during pregnancy. Because of the lack of experience, the use of this medicine during pregnancy is not recommended.

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

3. How you will be given Rapibloc

- Rapibloc is a powder and must be dissolved by your doctor or nurse. It is given to you as an infusion through a needle into your vein.
- The dosage must be individually adapted. A starting dose can be given before the maintenance dose. Your doctor will determine the dosage scheme and adapt the dosage as needed.
- The duration of use depends on the effect and possible occurring side effects. Your doctor will determine the duration of treatment. Rapibloc will not normally be given longer than 24 hours.
- While you are being given Rapibloc, your heartbeat, blood pressure and the electrical activity of your heart will be checked.
- After reaching a stable condition, you may be given another heart drug, while your dose of Rapibloc is reduced.

Changing the dose of this medicine is not usually necessary if you are elderly.

If you have kidney problems, your doctor will take appropriate caution.

Liver impairment

If you have liver problems, your doctor will start your treatment with a lower dose.

Children and adolescents

There is limited experience on the use of Rapibloc in children and adolescents. Your doctor will decide about the treatment with Rapibloc.

If you are given more Rapibloc than you should

If you have the feeling that you have received too much Rapibloc, tell your doctor or nurse straight away.

Your doctor will take appropriate measures (your treatment may be stopped immediately and you may receive supportive therapy).

You may experience the following symptoms, if you have been given too much of this medicine:

- Severe drop in blood pressure (you may feel dizzy or light headed)
- Very slow heart beat
- Reduced heart function
- Shock occurring because of decreased heart function
- Breathing problems
- Loss of consciousness ranging to coma
- Convulsions (cramps)
- Nausea
- Vomiting
- Low blood sugar
- High blood potassium level (hyperkalaemia)

When the use of Rapibloc is stopped

Suddenly stopping Rapibloc does usually not cause symptoms of a rapid heartbeat (tachycardia) to return. Your doctor will monitor you closely if your treatment with this medicine will be stopped.

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

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 Rapibloc. Tell your doctor or nurse straight away if you notice any of the following side effects, which can be serious.

The infusion may need to be stopped if your doctor observes any serious changes of:
- Your heart beat
- Your blood pressure
- The electrical activity of your heart

Common (may affect up to 1 in 10 people):

- Slow heartbeat
- Low blood pressure

Uncommon (may affect up to 1 in 100 people):

- Lung infection (pneumonia)
- Low sodium levels in the blood (hyponatraemia)
- Reduced blood supply to the brain, headache
- Failure of the normal circulation of the blood (cardiac arrest), fast heartbeat
- High blood pressure
- Accumulation of fluid in the lungs
- Vomiting, feel sick
- Liver disease
- Abnormal reading (ECG, medical ultrasound) of the heart
- Changes in blood tests
- Abnormal urine test (protein in the urine)

Rare (may affect up to 1 in 1,000 people):

- Inflammation of the chest tissue
- Abnormal number of blood clotting cells (platelets)
- High blood sugar
- Stroke, seizure
- Heart attack, heart rhythm disorders, decreased heart function, certain kinds of heartbeat problems (such as a short pause in the normal activity of the heart or a missed heart beat; awareness of your heart beating (palpitations))
- Shock, hot flush
- Breathing problems (including shortness of breath), lung disease, abnormally low levels of oxygen in the blood
- Abdominal discomfort, oral discharge, bad breath
- Abnormally high level of bilirubin (a pigment produced from the breakdown of red blood cells) in the blood
- Skin redness, cold sweat
- Muscle cramps
- Kidney failure, kidney injury, reduced urine volume
- Fever, chills, chest discomfort, pain at the injection site
- Increased pressure in the vessels of the lungs
- Sugar (glucose) in urine

Not known (frequency cannot be estimated from the available data):

- Skin changes at the injection site, sensation of pressure at the injection site

Reporting of side effects

If you get any side effects, talk to your doctor 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.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Rapibloc

- Keep this medicine out of the sight and reach of children.
- Do not use Rapibloc after the expiry date which is stated on the carton and vial after EXP. The expiry date refers to the last day of that month.
- This medicine does not require any special storage conditions.
- Rapibloc must be dissolved before it is used. The diluted medicine is stable for 24 hours at 25°C. However, it should be used immediately after dilution.
- This medicine must not be administered if you notice particles or discoloration of the solution.

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 Rapibloc contains

The active substance is landiolol hydrochloride. A vial contains 300 mg landiolol hydrochloride (as a powder) which is equivalent to 280 mg landiolol. After dilution, one ml contains 6 mg of landiolol hydrochloride.

The other ingredients are mannitol and sodium hydroxide (to ensure the correct pH).

What Rapibloc looks like and contents of the pack

Rapibloc is a powder for solution for infusion which is white to almost white.

The pack size is one 50 ml vial.

Marketing Authorisation Holder and Manufacturer:

AOP Orphan Pharmaceuticals GmbH
Leopold-Ungar-Platz 2
1190 Vienna
Austria

This medicine is authorised in the Member States of the European Economic Area under the following names:

Austria	Rapibloc 300 mg Pulver zur Herstellung einer Infusionslösung
Bulgaria	Rapibloc 300 mg прах за инфузионен разтвор
Croatia	Rapibloc 300 mg prašak za otopinu za infuziju
Cyprus	Rapibloc 300 mg κόνις για διάλυμα προς έγχυση
Czech Republic	Rapibloc 300 mg prášek pro infuzní roztok
Denmark	Rapibloc 300 mg pulver til infusionsvæske, opløsning
Estonia	Raploc 300 mg infusioonilahuse pulber
Germany	Rapibloc 300 mg Pulver zur Herstellung einer Infusionslösung
Greece	Rapibloc 300 mg κόνις για διάλυμα προς έγχυση
Finland	Rapibloc 300 mg infuusiokuiva-aine, liuosta varten
France	Rapibloc 300 mg poudre pour solution pour perfusion
Hungary	Rapibloc 300 mg por infúziós oldathoz
Iceland	Rapibloc 300 mg innrennslisstofn, lausn
Italy	Landiobloc
Lithuania	Raploc 300 mg milteliai infuziniam tirpalui
Latvia	Raploc 300 mg pulveris infūziju šķīduma pagatavošanai
Malta	Rapibloc 300 mg powder for solution for infusion
The Netherlands	Rapibloc 300 mg poeder voor oplossing voor infusie
Norway	Raploc
Poland	Runrapiq
Romania	Rapibloc 300 mg pulbere pentru soluţie perfuzabilă
Slovak Republic	Rapibloc 300 mg prášok na infúzny roztok
Slovenia	Rapibloc 300 mg prašek za raztopino za infundiranje
Sweden	Rapibloc

This leaflet was last revised in 06/2022

The following information is intended for 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.

Landiolol is intended for intravenous use in a monitored setting. Only a well-qualified health care professional should administer landiolol. The dosage of landiolol should be titrated individually.

Rapibloc must not be administered without reconstitution.
Reconstitute 1 vial with 50 ml of one of the following solutions:

- NaCl 9 mg/ml (0.9%) solution
- Glucose 50 mg/ml (5%) solution

- Ringer's solution
- Ringer-lactate solution

The white to almost white powder dissolves completely after reconstitution. Mix gently until a clear solution is obtained. Reconstituted solutions should be visually examined for visible particles and discoloration. Only clear and colourless solutions should be used.

The infusion is usually started with an infusion rate of 10 - 40 micrograms/kg/min, which will establish the heartrate lowering effect within 10 - 20 min.

If rapid onset of the heartrate lowering effect is desired (within 2 to 4 min), an optional loading dose of 100 micrograms/kg/min for 1 min can be considered, followed by continuous intravenous infusion of 10 - 40 micrograms/kg/min.

Lower doses should be used for patients with cardiac dysfunction. Dosing instructions are provided under "special populations" and in the integrated dosing scheme.

Maximum dose: The maintenance dose may be increased up to 80 micrograms/kg/min for a limited time period (see section 5.2 of the SmPC), if the cardiovascular status of the patient requires and allows such an increase of the dose and the maximum daily dose is not exceeded.

The maximum recommended daily dose of landiolol hydrochloride is 57.6 mg/kg/day (based on 40 micrograms/kg/min and a maximum infusion duration of 24 hours).
There is limited experience with landiolol infusion durations beyond 24 hours.

Conversion formula for continuous intravenous infusion: micrograms /kg/min to ml/h
(Rapibloc 300 mg/50 ml = 6 mg/ml):

Target dose (micrograms /kg/min) x body weight (kg)/100 = infusion rate (ml/h)

Conversion table (example):

	range for cardiac dysfunction patients							
kg body weight	1 µg/kg/min	2 µg/kg/min	5 µg/kg/min	10 µg/kg/min	20 µg/kg/min	30 µg/kg/min	40 µg/kg/min	
40	0.4	0.8	2	4	8	12	16	ml/h
50	0.5	1	2.5	5	10	15	20	ml/h
60	0.6	1.2	3	6	12	18	24	ml/h
70	0.7	1.4	3.5	7	14	21	28	ml/h
80	0.8	1.6	4	8	16	24	32	ml/h
90	0.9	1.8	4.5	9	18	27	36	ml/h
100	1	2	5	10	20	30	40	ml/h

Optional bolus administration for hemodynamically stable patients:
Conversion formula from 100 micrograms/kg/min to ml/h (Rapibloc 300 mg/50 ml = 6 mg/ml):

Loading dose infusion rate (ml/h) for 1 minute = body weight (kg)
(Example: 70 ml/h loading dose infusion rate for 1 minute for a 70 kg patient)

In case of an adverse reaction, the dose of landiolol should be reduced or the infusion be discontinued, and patients should receive appropriate medical management if needed. In the event of hypotension or bradycardia, administration of landiolol can be restarted at a lower dose after the blood pressure or heart rate have returned to an acceptable level. In patients with a low systolic blood pressure extra caution is needed when adjusting the dosage and during the maintenance infusion.

In case of overdose the following symptoms can occur: Severe hypotension, severe bradycardia, AV block, heart insufficiency, cardiogenic shock, cardiac arrest, bronchospasm, respiratory insufficiency, loss of consciousness to coma, convulsions, nausea, vomiting, hypoglycaemia, hyperkalemia.

In case of overdose, no further landiolol doses should be administered.

Transition to an alternative drug: After achieving adequate control of the heart rate and a stable clinical status, transition to alternative medicinal products (such as oral antiarrhythmics) may be accomplished.
When landiolol is replaced by alternative medicinal products, the physician should carefully consider the labelling and dosage of the alternative drug, and the dosage of landiolol can be reduced as follows:

- Within the first hour after the first dose of the alternative medicinal product has been administered, the infusion rate of landiolol should be reduced by one-half (50%).
- After administration of the second dose of the alternative medicinal product, the patient's response should be supervised and if satisfactory control is maintained for a least one hour, the landiolol infusion can be discontinued.

Special populations

Elderly population (≥ 65 years)

No dose adjustment is necessary.

Renal impairment

No dose adjustment is necessary.

Hepatic impairment

Data regarding the treatment in patients with hepatic impairment is limited. Careful dosing starting with the lowest dose is recommended in patients with all degrees of hepatic impairment.

Cardiac dysfunction

In patients with impaired left ventricular function (LVEF <40%, CI <2.5 L/min/m^2, NYHA 3-4) e.g. after cardiac surgery, during ischemia or in septic states, lower doses starting from 1 microgram/kg BW/min and increased in a stepwise fashion under close blood pressure monitoring up to 10 micrograms/kg BW/min have been used to achieve heart rate control.

Paediatric population

The safety and efficacy of landiolol in children aged 0 to 18 years have not yet been established.

Method of administration

Rapibloc must be reconstituted before administration and used immediately after opening.

Rapibloc must not be mixed with other medicinal products except those listed in section 6.6 of the SmPC.

Landiolol should be administered intravenously via a central line or a peripheral line and should not be administered through the same intravenous line as other medicinal products.

Contrary to other beta-blockers, landiolol did not show withdrawal tachycardia in response to abrupt termination after 24 h continuous infusion. Nevertheless, patients should be closely monitored when administration of landiolol is to be discontinued.

Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the SmPC.
- Severe bradycardia (less than 50 beats per minute)
- Sick sinus syndrome
- Severe atrioventricular (AV) nodal conductance disorders (without pacemaker): 2nd or 3rd degree AV block
- Cardiogenic shock
- Severe hypotension
- Decompensated heart failure when considered not related to the arrhythmia
- Pulmonary hypertension
- Non-treated phaeochromocytoma
- Acute asthmatic attack
- Severe, uncorrectable metabolic acidosis