PACKAGE LEAFLET: INFORMATION FOR THE USER

Labetalol Synchrony, 5mg/ml solution for injection

Labetalol Hydrochloride

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, pharmacist 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.

What is in this leaflet:

1. What Labetalol Synchrony is and what it is used for

Labetalol Synchrony contains the active substance Labetalol. It is used in the treatment of severe hypertension (high blood pressure), including severe hypertension during pregnancy (gestational hypertension), when the blood pressure needs to be lowered rapidly. This medicine may also be used to control the blood pressure during anesthesia.

This medicine belongs to a group of medicines called alpha and beta blockers.
These medicines work by causing the heart to beat more slowly and with less force. It also widens the arteries in the body. This helps to lower the pressure of the blood as it travels around the body.

2. What you need to know before you are given Labetalol Synchrony

You should NOT be given this medicine if:
- you have a heart condition (e,g. second or third degree heart block, unless you have a pacemaker, or uncontrolled heart failure)
- you have low blood pressure, or a very slow heartbeat (severe bradycardia).
- you suffer from Prinzmetal angina pectoris
- you suffer from asthma or a similar lung disease (obstructive airways).
- you are allergic to labetalol or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor or nurse before you are treated with Labetalol Synchrony if:
- you suffer from liver failure, or if you have liver damage
- you suffer from impaired kidney function
- you suffer from peripheral artery disease, e.g. Raynaud's syndrome or intermittent claudication
- you suffer from diabetes mellitus (type 1 or 2).
- you suffer from an overactive thyroid (thyrotoxicosis, hyperthyroidism)
- you have suffered from any serious allergic reactions in the past
- you suffer from heart failure, or any other heart conditions (e.g. left ventricular systolic dysfunction, first degree atrioventricular block)
- you know that you will have to undergo surgery
- you suffer from metabolic acidosis (increased acid levels in the blood).
- you suffer from phaeochromocytoma (a tumour near your kidneys)
- you suffer from a coronary artery disease
- you suffer from lung conditions or respiratory depression.

If treatment with this medicine leads to a slow heartbeat (bradycardia) your doctor may lower your dosage.

If you suffer from skin rash, dry eyes, or an allergic reaction during your treatment with this medicine, please contact your doctor for the dosage to be lowered or the treatment to be discontinued.

If treatment with this medicine leads to a slow heartbeat (bradycardia) your doctor may lower your dosage.

Surgery

If you need to undergo surgery and you are about to receive an anaesthetic, please tell the surgeon about your treatment with this medicine before the surgery.

Labetalol may affect your pupils during cataract surgery. Please tell your eye surgeon before your surgery about your treatment with this medicine. You do not need to stop treatment with this medicine unless your surgeon advises otherwise.

Other medicines and Labetalol Synchrony

Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines.
In particular tell your doctor if you are taking any of the following:
- NSAIDs (non-steroidal anti-inflammatory drugs) e.g. sulindac or indometacin, used to treat pain or inflammatory conditions
- Digoxin (heart medication)
- Adrenaline, which can be used in the treatment of severe anaphylactic (allergic) reactions.
- Medicines used to treat your heart (Class I antiarrhythmics e.g. disopyramide and quinidine and class II antiarrhythmics e.g. amiodarone)
- Other medicines that lower the blood pressure (calcium antagonists such as verapamil)
- General anaesthetics (used during surgery)
- Tricyclic antidepressants e.g. imipramine (used to treat depression)
- Oral anti-diabetic drugs such as biguanides (e.g. metformin), sulfonylurea (e.g. glimepiride), mitiglinides (e.g. repaglinide) and alpha-glucosidase inhibitors (e.g. acarbose), used to lower the glucose levels in the blood.
- Ergot derivatives e.g. ergotamine or dihydroergotamine, used in the treatment of migraines.
- Cholinesterase inhibitors e.g. donepezil, galantamine or rivastigmine, used to treat light cognitive disorders, Alzheimer's disease and Parkinson's disease
- Nitrates, antipsychotics (e.g. phenothiazine, chlorpromazine) and other antipsychotic drugs, antidepressants.
- Clonidine, used in the treatment of high blood pressure.

Tests

This medicine may have a disruptive effect on certain medical or laboratory tests. This may lead to incorrect test results. Tell your doctor and the laboratory staff that you have been given this medicine.

Pregnancy, breast-feeding and fertility.

If you are pregnant or think you may be pregnant or are planning to have ask your doctor for advice before being treated with this medicine.
Contact your doctor before you are given this medicine as the foetus may be affected. However this medicine may be used if the blood pressure needs to be lowered rapidly.

Nipple pain and Raynaud's phenomenon of the nipple have been reported (see section 4).

Labetalol is excreted in breast milk in small amounts. You should be monitored by your doctor if you need to be given this medicine whilst breast-feeding.

Driving and using machines

Not applicable

3. How to use Labetalol Synchrony

This medicine always needs to be used as prescribed by your doctor. It is intended for intravenous treatment in hospitalized patients and needs to be given by a healthcare professional.

This drug should only be given if you are lying down.
You should avoid sitting upright for three hours after being given this medicine, as you may feel very dizzy and lightheaded (due to low blood pressure).
This medicine may be given as a bolus injection (which means that it will be given directly into a vein), or by intravenous infusion (which means that it will be given as a slow drip into a vein).
Your doctor will decide how this medicine will be given to you and the correct dose for you.

If you are given more of this medicine than you should

Symptoms of an overdose of Labetalol Synchrony are, among others, extreme dizziness when you sit up and sometimes a slowing heartbeat, which can be measured by a low pulse (bradycardia).
If you think you have been given too much of this medicine, tell your doctor immediately.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Tell your doctor or nurse immediately if you have an allergic reaction.
This includes any of the following symptoms:
- difficulty in breathing
- swelling of your eyelids, face or lips
- rash or itching
- very rarely fever and swelling of the skin.

Other side effects

Common (may affect up to 1 in 10 people)
- Congestive heart failure
- Dizziness due to low blood pressure when sitting upright or standing up too quickly (postural hypotension). This can happen within the first three hours after this medicine has been given, and is short-lasting in nature. This will occur in the first weeks of treatment.
- Nasal congestion, this is usually short-lived and will occur in the first weeks of treatment
- Increased liver function. This will usually be short-lived after treatment has stopped.
- Erectile dysfunction (impotency).

Uncommon (may affect up to 1 in 100 people)
- Constriction of the muscles in the walls of the bronchioles causing breathlessness (bronchospasm).

Rare (may affect up to 1 in 1,000 people)
- Slow heart beat which can be measured by a low pulse (bradycardia).

Very rare (may affect up to 1 in 10,000 people)
- Blocking of the electrical signals controlling the heart rhythm (heart block)
- Worsening of blood circulation leading to nipple pain, cold or blue extremities with numbness or tingling in your fingers and toes
- Inflammation of the liver (hepatitis), usually short-lived when the treatment is discontinued.

- Hepatocellular jaundice (skin and whites of the eyes become yellow), cholestatic jaundice (symptoms include tiredness and nausea followed by itchiness, dark urine, and jaundice, and also skin rash and fever) and liver necrosis (damaged liver tissue). These symptoms will disappear after the treatment with this medicine has stopped.

Not known (cannot be estimated from the available data)
- Nipple pain
- Intermittent decrease in blood flow to your nipples, which may cause your nipples to go numb, pale, and painful (Raynaud's phenomenon)

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, at www.mhra.gov.uk/yellowcard. By reporting side effects you can help provide more information the safety of this medicine.

5. How to store Labetalol Synchrony

Keep the ampoules in the original packaging (to protect from light).
Keep this medicine out of the sight and reach of children.

Do not use Labetalol Synchrony after the expiry date which is stated on the carton and the ampoule label. The expiry date refers to the last day of that month.

Any unused dilution should be disposed of after 24 hours.

Discard any unused material.
Medicines should not be disposed of via wastewater or household waste.
Ask your pharmacist what to do with any leftover medicine. These measurements will protect the environment.

6. Contents of the pack and other information

What Labetalol contains
- The active ingredient is labetalol hydrochloride.
- The other ingredients are dilute hydrochloric acid (E507), sodium hydroxide (E524) for pH adjustment, and water for injections.

What Labetalol looks like and contents of the pack
Labetalol is a clear colourless solution.
Labetalol comes in 10ml amber glass ampoules with a white break ring, with ten ampoules in each pack.

Marketing Authorization Holder
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Manufacturer
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THE FOLLOWING INFORMATION IS INTENDED FOR HEALTHCARE PROFESSIONALS ONLY:

Administration
Labetalol Synchrony is meant for intravenous use in hospitalized patients and should always be given by healthcare professionals. Patients should always receive the drug whilst in the supine or left lateral position. Raising the patient into the upright position within 3 hours of intravenous labetalol administration should be avoided since severe postural hypotension may occur.
It is desirable to check the blood pressure and heart rate after the injection and during the infusion. The heart rate will decrease slightly. Severe bradycardia is not usual, but can be controlled by an intravenous injection of 1 to 2mg of atropine. The breathing should be carefully checked in patients with known airway disease. Labetalol Synchrony can be given as a bolus injection or intravenously. Labetalol Synchrony injection is administered to patients who suffer from uncontrolled hypotension and who have been given other hypotensive substances, including beta- blockers, without suffering from side effects.

Oral maintenance
When the blood pressure has been lowered sufficiently through either the bolus injection or intravenously, the treatment should be maintained by labetalol tablets with a starting dose of 100mg, twice a day.

Dosage: Labetalol injection

Indication	Dosage
Severe hypertension	*Bolus injection:* If it is essential to reduce blood pressure quickly, a dose of 50mg of labetalol hydrochloride should be given by intravenous injection (over a period of at least one minute) and, if necessary, may be repeated at five minute intervals until a satisfactory response occurs. The total dosage should not exceed 200mg. The maximum effect usually occurs within five minutes and the effective duration of action is usually about 6 hours but may be as long as 18 hours.
	Intravenous infusion: A labetalol infusion solution containing 1mg/ml needs to be used. This solution can be made by diluting the contents of four 10ml ampoules (200mg) to 200ml with Sodium Chloride and Dextrose Injection or 5% Dextrose Intravenous Infusion or Potassium Chloride and Glucose solution or Ringer Lactate. The rate of infusion of Labetalol hydrochloride should be about 160mg/hour, but may be adjusted according to the response at the discretion of the physician. The effective dose is usually in the range of 50-200mg but infusion needs to be administered until a satisfactory result has been achieved. A larger dose may be required, especially in patients with phaeochromocytoma. In severe cases of hypertension of pregnancy a lower, increasing infusion rate needs to be administered. The infusion needs to be started at the rate of 20mg/ hour, and this dose may be doubled every 30 minutes until a satisfactory result has been obtained, or a dosage of 160mg/hour is reached.
In Hypotensive Anaesthesia	To control hypotension during anesthesia, the recommended starting dose of Labetalol injection is 10-20mg intravenously, depending on the age and condition of the patient. If satisfactory hypotension is not achieved after five minutes, increments of 5-10mg should be given until the desired level of blood pressure is attained. The mean duration of hypotension following 20 to 25mg of labetalol is 50 minutes.
Hypertension due to other causes	The rate of infusion of Labetalol hydrochloride should be 120 - 160mg/ hour, until a satisfactory result has been achieved. Then stop the infusion. The effective dose is usually in the range of 50 to 200mg, but a larger dose may be required, especially in patients with phaeochromocytoma.

Pediatric patients
The safety and efficacy of labetalol administered to children between 0 to 18 years of age have not been established. No data is available.

Compatibility
Labetalol injection is compatible with the following solutions for infusion
- Dextrose 5% (w/v)
- Sodium Chloride 0.18% (w/v) and dextrose 4% (w/v)
- Potassium Chloride 0.2% (w/v) and glucose 5% (w/v)
- Ringer Lactate

Incompatibilities
Labetalol injection has been shown to be incompatible with sodium bicarbonate injection 4.2% w/v

Overdose
Signs and symptoms:
Acute cardiac insufficiency is to be expected, e.g. excessive hypotension and sometimes bradycardia. Oliguric renal failure has been reported after massive overdosage of labetalol orally. In one case, the use of dopamine to increase the blood pressure may have aggravated the renal failure.

Treatment:
The patient should be placed on their back, with the legs up.
Parental adrenal/ anticholinergic treatment should be provided if necessary to improve the flow of blood.

Haemodialysis removes less than 1% labetalol hydrochloride from the circulation.

Shelf Life
Chemical and physical in-use stability diluted in dextrose 5% (w/v); sodium chloride 0.18% (w/v) and dextrose 4% (w/v); potassium chloride 0.3% (w/v) and dextrose 5% (w/v) and Ringer Lactate has been demonstrated for 24 hours at 25 ºC.

From a microbiological point of view, the product should be used immediately after dilution. If not used immediately in-use storage time and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Any unused dilution should be disposed after 24 hours.

Synchrony Pharma

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