Labetalol Injection

50mg/10ml **NOW available**[1]

Indicated for:[1]

- Severe hypertension, including severe hypertension of pregnancy, when rapid control of blood pressure is essential
- Anaesthesia when a hypotensive technique is indicated

This 10ml ampoule has been developed to offer:[1]

- An additional source of this critical hospital product thus reducing the risk of possible shortages of labetalol for patients
- Improved flexibility in administration by providing a dose closer to licensed indication
- Less potential wastage and hence efficiency savings from using a 20ml ampoule of labetalol

- Available from Alloga
- EAN code: 5060231320198
- PIP code: USP0571

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Synchrony Pharma

Prescribing Information

Abbreviated Prescribing Information. Labetalol Synchrony 5mg/ml solution for injection

Presentation: Clear and colourless liquid, pH 4 (3.5-4.5). Osmolarity 0.03 (0.02400.036) Osmol/kg **Indications:** Severe hypertension, including severe hypertension of pregnancy, when rapid control of blood pressure is essential. Anaesthesia when a hypotensive technique is indicated. **Dosage and Administration:** Labetalol injection is intended for intravenous use in hospitalized patients. Adults *Severe hypertension*, 50mg if labetalol hydrochloride bolus injection (over a period of at least one minute). It may be repeated at five minute intervals until a satisfactory response occurs. Total dosage should not exceed 200mg. Intravenous infusion (instructions for dilution refer to later). Use 1mg/ml labetalol infusion solution. This is made by diluting 4x 10ml ampoules (200mg) to 200ml with Sodium Chloride and Dextrose Injection, 5% dextrose Intravenous Infusion, Potassium Chloride and Glucose solution or Ringer Lactate. Rate of infusion should be about 160mg/hour. The effective dose is usually in the range of 50-200mg but the infusion may be adjusted according to response at the discretion of the physician. A larger dose may be required especially in patients with phaeochromoctyoma. In severe cases of hypertension of pregnancy a lower increasing infusion rate needs to be administered (starting at 20mg/hour and this may be doubled every 30 minutes until a satisfactory result has been obtained or a dosage of 160mg/hour is reached. *Hypotensive Anaesthesia* To control hypertension during anaesthesia, a starting does of 10-20 mg i.v. depending on age and condition of patient. If a satisfactory result is not achieved after five minutes increments of 5-10mg should be given until the desired blood pressure is attained. The mean duration of hypotension following 20- 25mg of labetalol is 50 minutes. *Hypertension due to other causes* The infusion rate should be 120-160mg/hour until a satisfactory result is achieved. Then stop the infusion. Effective dose is in the range of 50 to 200mg but a larger dose may be required, especially in patients with phaeochromocytoma. Paediatrics The safety and efficacy of labetalol in children from 0-18 years if age has not been established. Method of administration Patient should always receive the drug whilst in supine or left lateral position. They should not be raised into an upright position until 3 hours post administration to avoid the possibility of postural hypotension. **Contraindications:** Non-selective beta blockers must not be used on patients with a history of asthma or of obstructive pulmonary disease. Labetalol injections are contraindicated for second- or third-degree heart block (unless a pacemaker is in-situ), cardiogenic shock and other disorders which are associated with serious and long-lasting hypotension and/or bradycardia. Decompensated heart failure. Uncontrolled/ unstable heart failure. Sick sinus syndrome (including sino-atrial block), unless a pacemaker is in-situ. Prinzmetal's angina. Sinus node dysfunction Hypersensitivity to the active substance, or any of the excipients. **Precautions:** *Liver disease* rare reports of hepatocellular injury, which is usually reversible and has occurred on short- and long-term therapy. There have been reports of fatal hepatic necrosis. Appropriate laboratory testing should be carried out at first sign of liver dysfunction, if there is any evidence of liver injury or jaundice, labetalol should be discontinued. Extra caution should be taken in patients with pre-existing liver dysfunction as labetalol will be metabolised more slowly than in patients without liver dysfunction. *Renal impairment* Caution needs to be taken in patients with severe renal impairment (GFR=15-29ml/min/1,73m^2) *Peripheral circulatory disorders* Should be used with great caution as aggravation of these disorders may occur. Likewise great caution should be advised in patients with peripheral arterial diseases (Raynaud's disease or syndrome, intermittent claudication), as aggravation of these disorders may occur. Alpha blockers may counteract the adverse events of beta blockers. *Symptomatic Bradycardia* If a patient experiences symptoms relating to bradycardia, the labetalol dosage should be reduced. *First degree atrioventricular block* Due to the negative effect of atrioventricular conduction time, labetalol needs to be administered with caution to patients with first degree atrioventricular block. *Diabetes Mellitus* Great caution needs to be taken with untreated or uncontrolled diabetes mellitus. As with other beta-adrenergic blocking agents, labetalol can mask the symptoms of hypoglycemia (tachycardia and tremor) in diabetic patients. The hypoglycemic effect of insulin and oral hypoglycemic agents can be higher when beta-adrenergic blocking agents are used. *Thyrotoxicosis* Beta-blockers can mask the symptoms of thyrotoxicosis but will not change the thyroid function. *Hypersensitivity to beta-blockers* While taking beta-blockers, patients with a history of severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge. Such patients may be unresponsive to usual doses of epinephrine used to treat allergic reactions. *Adrenaline* If patients taking labetalol need adrenaline, a lower dose of adrenaline needs to be used since the use of both adrenaline and labetalol at the same time may cause bradycardia and hypertension. When adrenaline has a serious influence, as is the case with phaeochromocytoma, labetalol can lead to a paradoxical blood pressure increase. *Skin rashes and/or dry eyes* There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenoceptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when the treatment was withdrawn. Gradual discontinuation of the drug should be considered if any such reaction is not otherwise explicable. *Intraoperative floppy iris syndrome* The occurrence of intraoperative floppy iris syndrome (IFIS, a variation of Horner's syndrome) has been observed during cataract surgeries in some patients who were being treated with tamsulosine, or have been treated with tamsulosine in the past. IFIS has also been reported when other alpha-1-blockers were being used, and the possibility of a class effect cannot be excluded. Since IFIS can lead to a higher chance of complications during cataract surgeries, the ophthalmologist needs to be informed if alpha-1-blockers are currently being used, or have been used in the past. *Heart failure or decreased left ventricular function* Extra caution needs to be taken in patients who suffer from heart failure or decreased left ventricular function. Labetalol is contraindicated for uncontrolled heart failure, but may be used with caution in patients whose heart failure is under control and who are free of symptoms. Heart failure needs to be controlled with an appropriate treatment before labetalol should be used. The use of beta-blockers may induce or aggravate heart failure or obstructive pulmonary disease. In the case of heart failure, the myocardial contractility needs to be maintained and the failure needs to be compensated. Patients with reduced contractility, especially elderly patients, need to be checked regularly on the development of heart failure. It is strongly recommended not to interrupt or discontinue labetalol therapy abruptly, especially patients with heart failure and patients with angina pectoris (to prevent exacerbation of angina pectoris, myocardial infarction and ventricular fibrillation). *Inhalation Anaesthetics* Caution needs to be taken when inhalation anaesthetics are used concurrently. It is not necessary to discontinue labetalol therapy in patients requiring anaesthesia, but the anaesthetist must be informed and the patient should be given intravenous atropine prior to induction. Labetalol can increase the hypotensive effect of inhalational anaesthetics. *Metabolic Acidosis and Phaeochromocytoma* Caution needs to be taken with cases of metabolic acidosis and phaeochromocytoma. In patients with phaeochromocytoma, labetalol may only be used after adequate alpha-blockage has been reached. *Calcium Antagonists* Caution needs to be taken when labetalol is used at the same time as calcium antagonists, and especially calcium entry-blockers, which negatively influence the contractility and the atrioventricular conductions. Caution needs to be taken when adrenaline, verapamil or class I antiarrhythmic agents are administered at the same time as labetalol. Beta-blockers have a negative inotropic effect but will not influence the positive inotropic effect of digoxin. *Sudden haemorrhage* During anaesthesia labetalol may mask the compensatory physiological responses to sudden haemorrhage (tachycardia and vasoconstriction). Close attention must therefore be paid to blood loss, and the blood volume maintained. *Administration* It is desirable to check the blood pressure and the heart rate after injection and during infusion. In most patients, the heart rate will decrease slightly. Severe bradycardia is not usual but can be controlled by injecting 1 to 2mg of atropine intravenously. Breathing should be carefully checked in patients with a known airway disease. As soon as blood pressure is reduced by bolus injection or infusion, the treatment should be maintained with labetalol tablets, with a starting dose of 100mg two times a day. Labetalol-injection is administered to patients who suffer from an uncontrolled hypotension and who have been given other hypotensive substances, including beta-blockers, without suffering from side effects. **Interactions:** The hypotensive effect of labetalol may be reduced when used in combination with prostaglandin synthetase inhibiting drugs (NSAID's, nonsteroidal anti-inflammatory drugs). Dose adjustments may be necessary. The combination with other antihypertensives may lead to additive synergism. Labetalol is fluorescent in alkaline solution with an excitation wavelength of 334 nanometer and a fluorescent wavelength of 412 nanometer and may therefore interfere with the tests of some fluorescent substances, including catecholamines. The presence of labetalol metabolites in the urine can lead to false high levels of catecholamines, metanephrines, normetanephrines, and vanillylmandelic acid (VMA) in the urine when measured with fluorimetric or photometric methods. When patients who are suspected to suffer from phaeochromocytoma are screened, and are treated with labetalol hydrochloride, a specific method such as HPLC-assay with solid phase extraction will need to be used to determine the level of catecholamines. Labetalol has been shown to reduce the uptake of radioisotopes of metaiodobenzylguanidine (MIBG). Care should therefore be taken in interpreting results from MIBG scintigraphy. The use of both adrenaline and labetalol at the same time may cause bradycardia and hypertension. Extra care should be taken if labetalol is used at the same time as either class I antiarrhythmic agents or calcium antagonists of the Verapamil class. Class I antiarrhythmic agents (e.g. disopyramide, quinidine) and amiodarone (antiarrhythmic Class II) may have potentiating effects on atrial conduction and induce negative inotropic effect. If labetalol is used simultaneously with calcium antagonists with a negative inotropic effect (e.g. verapamil, diltiazem), the risk of bradycardia and hypotension may increase, especially in patients with atrioventricular conduction disease or contractility disease. If the patient is switched from calcium antagonists to beta-blockers, or the other way around, a new intravenous treatment should not be started until at least 48 hours after the previous treatment has ended. Simultaneous use of labetalol with calcium antagonists belonging to the dihydropyridine derivates (e.g. nifedipine), may increase the risk of hypotension and may lead to cardiac failure in patients with latent cardiac insufficiency. Digitalis glycosides used in association with beta-blockers may increase atrioventricular conduction time. Labetalol can heighten the effect of digoxin on reduction of ventricular flow. Beta-blockers, especially non-selective beta-blockers, can increase the risk of hypoglycemia in diabetic patients and may prevent the appearance of signs of hypoglycemia, such as tachycardia and tremors, and may delay the normalization of glucose levels after insulin induced hypoglycemia. Changes of the dose of oral anti diabetics may be necessary. Extra caution needs to be taken when general anesthesia is used on patients who are treated with beta-blockers. Beta-blockers reduce the risk of arrhythmia during anesthesia but can lead to a reduction of the reflex tachycardia and a higher risk of hypotension during anesthesia. An anesthetic with the lowest possible negative inotropic effect should be used. Heart function needs to be monitored closely and bradycardia due to vagal dominance needs to be corrected by administrating 1-2 mg atropine intravenously (stopping before surgery). When treatment is discontinued in patients who use both beta-blockers and clonidine, the beta-blocker should be phased out a couple of days before the treatment with clonidine is discontinued. This needs to be done to avoid a recurrence of hypertensive crisis as a result of the discontinuance of the clonidine treatment. For the same reasons it is also important to phase out the clonidine when a switch to beta-blockers is being made, and to start the treatment with the beta-blocker some time before the clonidine is discontinued. Concomitant use of labetalol and cholinesterase inhibitors can increase the risk of bradycardia. Concomitant use with alpha adrenergic agonists (e.g. phenylpropanolamine and adrenalin) can increase the risk of high blood pressure, while concomitant use with beta adrenergic agonists may counteract the beta adrenergic agonists (antidotumeffect). Concomitant use of ergot derivatives may increase the risk of peripheral vasoconstriction in some patients. It has been demonstrated that labetalol increased the biological availability of imipramine by more than 50% through the inhibition of 2-hydroxylation. Labetalol in combination with imipramine can increase the effect of imipramine and the concurrent use of tricyclic antidepressants. Concomitant use of tricyclic antidepressants may increase tremors. Labetalol may increase the hypotensive effect of volatile anaesthetics. An increase in blood pressure reduction may occur during concomitant use of, e.g. nitrates, anti-psychotics (phenothiazine derivatives like chloropromazine) and other anti-psychotics and anti-depressants. **Fertility, pregnancy and lactation:** Fertility There is no information available on the effect labetalol has on fertility. Pregnancy: On the basis of experience during human pregnancy, it is unexpected that labetalol increases the risk of birth defects. Animal studies have not demonstrated reproductive toxicity. However, toxicity has been demonstrated in embryo-foetal development (see section 5.3). Labetalol crosses the placenta and because of the pharmacological activity of alpha- and beta-adrenoceptor blockade, side effects in the foetus and neonate should be borne in mind (bradycardia, hypotension, respiratory depression, hypoglycemia, hypothermia). Close observation up to 24 to 48 hours after birth is required. Beta-blockers may reduce placental perfusion. Labetalol should only be used during the pregnancy if the potential benefit for the mother outweighs the potential risk for the foetus. Breast-feeding Labetalol is excreted in breast milk in small amounts (approximately 0.004-0.07% of the dose administered to the mother). No side-effects have been reported. Monitoring is needed if Labetalol is used in lactating mothers. **Undesirable effects** See SPC for full listing and details. The most frequently reported undesirable effects during the use of labetalol injection and those reported in post-marketing studies include: congestive heart failure, postural hypotension, hypersensitivity, drug fever, increased liver functions, nasal congestion and erectile dysfunctions. **Shelf-life**: 18 months **Legal category**: POM **Marketing Authorisation Numbers**: PL39280/0009. ***See approved Summary of Product Characteristics for further information.*** **For Further information contact:** Synchrony Pharma Ltd, Business & Technology Centre, Bessemer Drive, Stevenage, SG1 2DX. Date of Preparation: March 2019 Item Code: LABE/001/03/2019

Adverse events should be reported.
For reporting within the UK, forms and information can be found at www.mhra.gov. uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Pharmacovigilance at Synchrony Pharma on Phone: +44(0) 1438791091
Email: pv@synchronypharma.com

References

1. Labetalol Synchrony 5mg/ml solution for injection SmPC May 2018

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