LABETALOL (Intravenous – severe hypertension pre and post alteplase administration in ischaemic stroke)

SCOPE (Area): FOR USE IN: ED, Critical Care Unit
EXCLUSIONS: Paediatrics (seek Paediatrician advice) and General Wards
SCOPE (Staff): Medical, Nursing and Pharmacy

This drug guideline must be used in conjunction with Thrombolysis for Acute Ischaemic Stroke (CPP0012)

BRAND NAMES
Labetalol - brands are often changing, and may be SAS (paperwork for approval with product)
Labetalol is also known as labetalol hydrochloride.

PHARMACOLOGY AND PHARMACOKINETICS
Labetalol is a selective alpha and non-selective beta1 and beta2 blocking agent, with minimal intrinsic sympathomimetic activity. The alpha and beta blocking activity both contribute to lowering blood pressure via vasodilatation and a slowing of heart rate (often offsetting the reflex tachycardia that occurs with vasodilatation). The peak hypotensive activity of IV labetalol injection can be seen within 5 minutes, with a gradual and progressive loss of effect over 16 to 18 hours after the last dose was administered. Labetalol is extensively metabolised by the liver, with a half-life of about 5 and a half hours when used intravenously.

INDICATIONS
- To lower severely elevated blood pressure before or after the administration of alteplase for thrombolysis in acute ischaemic stroke, defined as:
  - Systolic BP greater than 185 mmHg
  - Diastolic BP greater than 110 mmHg
  obtained on two readings 5 minutes apart.
- (To lower severely elevated blood pressure in haemorrhagic stroke – labetalol can also be used in this setting, but patient specific blood pressure parameters will be determined by the Neurology or Medical Registrar at the time and are not covered by this guideline).

CONTRAINDICATIONS
- Asthma or COAD.
- Second or third degree AV block.
- Sinus bradycardia (less than 45-50 beats per minute) or sick sinus syndrome.
- Heart failure (including right ventricular failure secondary to pulmonary hypertension).
- Shock (including cardiogenic and hypovolaemic shock).
- Severe hypotension.
- Significant right ventricular hypertrophy (except in specific cases of congenital heart disease)
eg. tetralogy of Fallot) – seek cardiologist advice if uncertain.

- Allergic disorders which may suggest a predisposition to bronchospasm.
- Hypersensitivity to labetalol.

**PRECAUTIONS**

- **Postural hypotension** – may be severe due to the alpha effect of labetalol, ensure patient is in the supine position during administration.
- **Diabetes** - labetalol can mask important signs of hypoglycaemia (e.g. tachycardia, tremor) and may increase the incidence and severity of hypoglycaemia.
- **History of anaphylactic or allergic reactions** - labetalol may prevent response to usual doses of adrenaline for anaphylaxis, and the allergic response may be exaggerated.
- **Hepatic impairment** - a lower dose of labetalol may be required.
- **Hyperthyroidism** - labetalol can mask clinical signs (e.g. tachycardia).
- **Raynaud’s phenomenon or peripheral vascular disease** - labetalol can impair peripheral circulation and can exacerbate symptoms.
- **Elderly** – may be more susceptible to the hypotensive effects of labetalol and may require lower doses.
- **Vasospastic angina** – labetalol may worsen coronary artery spasm.
- **Myasthenia gravis** - labetalol may worsen the symptoms.
- **Pheochromocytoma** - may cause a paradoxical hypertensive response (if no alpha blockade).
- **Surgery** – if the patient requires surgery whilst they still have labetalol in their system, the Anaesthetist should be made aware due to the potential hypotensive and bradycardic effects.

**PREGNANCY AND BREASTFEEDING**

Seek specialist advice before prescribing, information may update regularly.

**DRUG INTERACTIONS**

- **Verapamil (and to a lesser degree diltiazem)** – can lead to significant decrease in heart rate and cardiac conductivity, use labetalol with extreme caution only under specialist advice.
- **Drugs that reduce cardiac conductivity or contractility** – use with labetalol increases the risk of heart block, bradyarrhythmia or heart failure. Monitor carefully.
- **Drugs that cause hypotension** - may exacerbate the hypotensive effect of labetalol, especially other vasodilators that can worsen postural hypotension.
- **Insulin or sulfonylureas** – labetalol increases the hypoglycaemic effect of these drugs, see Precautions – Diabetes.
- **Adrenaline** – see Precautions – History of anaphylactic or allergic reactions.
- **Clonidine, dexametomidine, methyldopa** – labetalol increases the incidence of bradycardia and hypotension. Sudden withdrawal of clonidine or dexametomidine in a patient with beta blockade can lead to rebound hypertension.
- **Beta2 agonists, theophylline, aminophylline** – labetalol will diminish the bronchodilatory effects of these drugs.
- **Bromocriptine, cabergoline, ergometrine** - use with labetalol may lead to additive vasoconstriction, monitor for peripheral ischaemia.
- **Isoprenaline** - labetalol may antagonise the therapeutic effects of isoprenaline.
- **Phenobarbitone, rifampicin, thiopentone** – may increase the metabolism of labetalol leading to lower levels of labetalol.
- **Chloroquine, hydroxychloroquine, primaquine** – may decrease the metabolism of labetalol leading to higher levels of labetalol.
- Labetalol (Intravenous – severe hypertension pre and post alteplase administration in ischaemic stroke) (2014)

**DOSAGE AND ADMINISTRATION**

Requires continuous ECG monitoring during administration and for 8 hours following administration of the last dose.

For administration only

▪ in Critical Care Unit, ED

To be administered by Neurology or Medical Registrar.

Measure supine blood pressure prior to administration by IV injection or infusion. Patients should be kept in the supine position during administration of labetalol, and for 3 hours after labetalol was last administered to prevent postural hypotension.

Administer via CVC, midline or peripheral line.

**IV injection (via CVC, midline or peripheral vein):**

Vials contain labetalol 100 mg/20 mL vials (5 mg/mL). IV injections only use PART of this vial.

**Dose:** Labetalol 5-10 mg (1-2 mL from PART vial) undiluted over 1-2 minutes.

Dose can be repeated every 5-10 minutes for unresponsive blood pressure to a maximum TOTAL dose of 100 mg.

**General Administration Information**

▪ **Routes of administration:**
  
  - IV injection: Yes (slow)
  - IV intermittent infusion: No
  - IV continuous infusion: Yes (not covered in this guideline)
  - IM injection: No
  - Subcut injection: No

▪ **Compatible/incompatible IV drugs/fluids:**

Consult the Australian Injectable Drugs Handbook (‘Yellow book’) in your ward area. **Assume all unlisted drugs and IV fluids are incompatible – contact Pharmacy for further advice.**

**MONITORING (INCLUDING BLOOD TESTS)**

▪ The Medical Officer must set clear blood pressure and heart rate parameters for Nursing Staff to follow.

▪ No blood tests are required specific to labetalol administration.
NURSING PRACTICE POINTS

- Requires continuous ECG monitoring during administration and for 8 hours following administration of the last dose.
- A Registered Nurse Division 1 is required to remain with the patient until the Neurology or Medical Registrar has deemed that heart rate and blood pressure are stable and constant monitoring is not required.
- Patients should be kept in the supine position during administration of labetalol, and for 3 hours after labetalol has stopped to prevent postural hypotension.
- Blood pressure, heart rate, heart rhythm and SpO2 requires close monitoring as outlined in the box below, with results outside parameters set by the Neurology or Medical Registrar to be reported. Record results on Thrombolysis in Acute Ischaemic Stroke Pathway (MR/265.05).

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<th>Time from most recent IV injection</th>
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| 0-10 mins                         | - Supine blood pressure, heart rate, heart rhythm and SpO2 to be recorded immediately before and after administration of each dose.  
- Repeat at 5 mins and 10 mins post IV injection. |
| 10 mins-2 hrs                     | - If vital signs are stable, monitor blood pressure, heart rate, heart rhythm and SpO2 15 minutely.  
- If unstable, the Neurology or Medical Registrar will determine the level of monitoring required. |
| 2-8 hrs                           | - 30 minute blood pressure and heart rate measurements. |
| 8-24 hrs                          | - Hourly blood pressure and heart rate. |

Blood glucose should be checked six hourly (or more frequently if indicated clinically) by glucometer, and the patient should be monitored for symptoms suggestive of hypoglycaemia.

ADVERSE EFFECTS

In general labetalol is well tolerated.

- **Cardiovascular:** Postural hypotension may occur if the initial dosage is too high or if the dose is increased too rapidly. Occasionally bradycardia and heart block have been reported. May uncover latent heart failure.
- **Nervous system:** Transient dizziness, headache, tiredness, hallucinations and lethargy may occur. There have been reports of a tingling sensation of the skin (especially of the scalp), usually occurring early in treatment and which is transient in nature.
- **Collagen disorders:** There have been occasional reports of positive antinuclear antibodies un-associated with disease as well as the occasional case of systemic lupus erythematosus and very occasionally drug fever.
- **Ocular:** Blurred vision, eye irritation and dry eyes have been reported.
- **Hepatic:** Raised liver function tests; jaundice (both hepatocellular and cholestatic) and hepatitis (the signs and symptoms are usually reversible on withdrawal of the drug). Hepatic necrosis.
- **Musculoskeletal:** There has been one report of toxic myopathy. Muscle cramps.
- **Respiratory:** Bronchospasm (may occur in susceptible individuals), dyspnoea.
- **Dermatological:** Rashes of various types such as generalised maculopapular, lichenoid, urticarial, bullous, lichen planus, psoriasiform, facial erythema, Peyronie's disease, reversible alopecia and thrombocytopenic purpura.
- **Genitourinary**: Acute retention of urine and difficulty in micturition.
- **Gastrointestinal**: Epigastric pain, diarrhoea, nausea and vomiting.
- **Hypersensitivity**: Rash, pruritis, angioedema and dyspnoea.
- **Other**: Ankle swelling, nasal congestion, cold extremities, sweating, exacerbation of Raynauds

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**DRUG PRESENTATIONS, LOCATION AND STORAGE**

Labetalol hydrochloride vial 100 mg/20 mL.

Imprest locations (at the time of guideline development): ED, Theatre and 5N.

Store below 25 degrees