LABETALOL
(Intravenous – severe hypertension in pregnancy)

<table>
<thead>
<tr>
<th>SCOPE (Area):</th>
<th>FOR USE IN: Labour Ward, HDU, ED and Theatre</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXCLUSIONS:</td>
<td>Paediatrics and other General Wards</td>
</tr>
<tr>
<td>SCOPE (Staff):</td>
<td>Medical, Nursing and Pharmacy</td>
</tr>
</tbody>
</table>

This Drug Guideline must be used in conjunction with “Hypertension in Pregnancy” Clinical Practice Guidelines – see Related Documents. Injectable labetalol is only available via the Special Access Scheme and the form kept with the injection must be filled out by Medical Staff for all patients.

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 alpha₁ and non-selective beta₁ and beta₂ blocking agent, with no 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). Labetalol injection has an onset of action of 5 minutes, with peak hypotensive effect occurring at 10-15 minutes, and a duration of action of 45 minutes to 6 hours.

Intravenous Labetalol is considered to be the primary medicine of choice for the urgent control of severe hypertension in pregnancy.

INDICATIONS
- First line drug therapy to lower severely elevated blood pressure of pregnancy, defined as:
  - Systolic BP greater than 160 mmHg and/or
  - Diastolic BP greater than 110 mmHg
  Obtained on two readings 10 minutes apart (BP taken manually with appropriate size cuff)

CONTRAINDICATIONS
- Asthma or COAD.
- Bradycardia.
- Severe hypotension or shock.
- Hypersensitivity to labetalol.
- Second or third degree AV block.
- Heart failure (including right ventricular failure secondary to pulmonary hypertension).
- 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.
PRECAUTIONS

- **Postural hypotension** – may be severe due to the alpha effect of labetalol, ensure patient is in the supine position (with lateral tilt) 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 reactions** - labetalol may prevent response to usual doses of adrenaline for anaphylaxis.
- **Hyperthyroidism** - labetalol can mask clinical signs (e.g. tachycardia).
- **Raynaud’s syndrome or peripheral vascular disease** - labetalol can impair peripheral circulation and can exacerbate symptoms.
- **Vasospastic angina** – labetalol may worsen coronary artery spasm.
- **Myasthenia gravis** – labetalol may worsen.
- **Pheochromocytoma** - may cause a paradoxical hypertensive response. Use with caution.
- **Hepatic impairment.**

PREGNANCY AND BREASTFEEDING

**Pregnancy** – listed as ADEC (Australian Drug Evaluation Committee) Category C, may be used with caution. Monitor foetus for bradycardia.

**Breastfeeding** – excreted in small amounts into breastmilk, but unlikely to have an adverse effect on the infant.

**Neonate** - the neonate is at risk of hypoglycaemia and close monitoring of blood glucose levels (BGLs) after delivery is indicated (Refer **CPG0110 Neonatal Hypoglycaemia – Prevention and Management**). Monitor also for bradycardia and hypotension. Seek specialist advice for further information.

DRUG INTERACTIONS

- **Verapamil (and to a lesser degree diltiazem)** – can lead to a 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, bradycardia 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. Also the vasoconstrictor (alpha receptor-mediated) effects of adrenaline predominate, marked hypertension followed by bradycardia may occur.
- **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.
- **Rifampicin, phenobarbitone, 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.
- **NSAIDs, methylphenidate** - can decrease the antihypertensive effect of labetalol.
- **Tricyclic antidepressants** - patients may exhibit a tremor when treated with labetalol.
- **Isoprenaline** - labetalol may antagonise the therapeutic effects of isoprenaline.
- **Lignocaine, bupivacaine, mepivacaine** – labetalol may decrease the metabolism of these drugs leading to increased levels.
▪ Complementary medicines that may reduce antihypertensive effect of labetalol – bayberry, blue cohosh, cayenne, ephedra, ginger, ginseng, kola, licorice.
▪ Complementary medicines that may increase antihypertensive effect of labetalol – black cohosh, california poppy, coleus, goldenseal, hawthorn, mistletoe, periwinkle, shepherd’s purse.

### DOSAGE AND ADMINISTRATION

One to one nursing or midwifery care is required during administration of IV labetalol (injection or infusion), and for 24 hours (or longer if indicated by the Lead Obstetrician) following the end of the last dose of IV labetalol (injection or infusion). This nursing care may be provided in Labour Ward, HDU, ED or Theatre as determined by the Lead Obstetrician depending on the clinical condition of the patient.

If the woman is already on oral Labetalol at a reasonable dose and needs treatment for severe hypertension, intravenous hydralazine should be considered.

Patients who have received labetalol IV injection may require admission to HDU (discussion between the Lead Obstetrician and Anaesthetist is required to assess clinical condition). Patients receiving labetalol IV infusion may be transferred to HDU as soon as practical i.e. the patient is stable and where appropriate the baby has been delivered. Where transfer to HDU is planned post or during IV labetalol administration, the Lead Obstetrician or senior Obstetric Registrar and a Midwife must remain with the patient until transfer occurs.

For administration only in
▪ HDU, Labour Ward, ED or Theatre (injection or infusion)

**Bolus Injection only to be administered by**

▪ Lead Obstetrician or Senior Obstetric Registrar
▪ ICU Consultant, Registrar or nursing staff under their direct supervision
▪ Anaesthetic Consultants or Registrar (after consultation with Consultant)
▪ Nursing and midwifery staff under the direct supervision of the Medical staff listed above

Medical staff must remain present in the room for the duration of IV injection administration and stabilisation of a woman having an IV infusion

Fluid loading is important when managing severe hypertension. 300-500 mL of sodium chloride 0.9% may be administered under the supervision of the senior clinician prior to commencing labetalol.

The goal for reduction of severely elevated blood pressure is to achieve and maintain a blood pressure of 140/90 mmHg. Blood pressure should be monitored and reduced gradually to avoid adverse fetal side effects from rapid decrease in uteroplacental perfusion.

Administer via CVC, midline or peripheral line. Use a dedicated line for infusion.

Note: Co-administration with magnesium is commonly required and may increase the risk of hypotension. Co-administration with hydralazine or nifedipine may result in an enhanced hypotensive effect, monitor carefully. Hydralazine may be required in addition to labetalol if labetalol fails to control BP.
IV injection (via CVC, midline or peripheral vein):
**Only to be administered in HDU/Labour Ward/ED/THEATRE by staff listed in box above**
Ampoules contain labetalol 100 mg/20 mL (5 mg/mL), IV injections only use part of this ampoule.
**Dose:** Labetalol 20 mg (4 mL from ampoule) undiluted over 2 minutes.
Dose can be repeated every 10 minutes for unresponsive blood pressure.
If more than 3 doses are required over 30 minutes an IV infusion should be considered.
**Maximum total dose:** 300 mg (Injection plus infusion).
**Target blood pressure:** 140/90 mmHg, see box above.

IV infusion (via CVC, midline or peripheral vein):
**Only to be administered in HDU/Labour Ward/ED/THEATRE by staff listed in box above**
Use labetalol 100 mg/20 mL ampoules to make up infusion.
Withdraw 40 mL from a 100 mL sodium chloride 0.9% minibag.
Labetalol 200 mg (40 mL from TWO ampoules) added to remaining 60 mL sodium chloride 0.9% in the minibag.
**Total Volume:** 100 mL.
**Final concentration:** 2 mg/mL.
**Starting rate:** 20mg/hr (10 mL/hr).
**Rate increase:** For unresponsive blood pressure, infusion may be increased by 20 mg/hr (10 mL/hr) every 20 minutes. Titrate to blood pressure response.
**Maximum rate:** 160 mg/hr (80 mL/hr).
**Maximum total dose:** 300 mg (Injection plus infusion).
**Weaning rate:** Decrease by 20 mg/hr (10 mL/hr) every 20 minutes. Weaning of the infusion will be done under direction of the lead clinician and will usually occur post delivery.
**Target blood pressure:** 140/90 mmHg, see box above.

**General Administration Information**

- **Infusion preparation:** Mix infusion thoroughly after adding labetalol to avoid inadvertently giving a more concentrated dose. Discard any remaining solution after 24 hours.
- **Infusion pump:** Alaris® PC unit with pump module utilising Guardrails®.
- **Routes of administration:**
  - IV injection: Yes (slow)
  - IV intermittent infusion: No
  - IV continuous infusion: Yes
  - IM injection: No
  - Subcut injection: No
- **Compatible/incompatible IV drugs/fluids:**
  Labetalol is compatible with sodium chloride 0.9 %, Hartmann’s solution and glucose 5%.
  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 prescribing 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

- **One to one nursing care required.**
- **Measure supine blood pressure** prior to administration by IV injection or infusion. Patients should be kept in the supine position (with lateral tilt) during administration of labetalol, and for 3 hours after labetalol was last administered to prevent postural hypotension.
- **Strict fluid balance monitoring** should occur with accurate documentation under the supervision of the senior clinician. Monitor urine output hourly.
- **Cardiotocographic (CTG) monitoring** – ensure monitoring commences before the administration of labetalol, and remains insitu until delivery, or as directed by the senior clinician. The record must be signed by the senior clinician and attached to the medical history.
- **Hypoglycaemia** – labetalol increases the incidence and severity of hypoglycaemia, and may blunt some of the usual signs of hypoglycaemia (tachycardia and tremor).
  - The neonate is at risk of hypoglycaemia and close monitoring of blood glucose levels (BGL’s) after delivery is indicated (Refer CPG0110 Neonatal Hypoglycaemia – Prevention and Management).
  - Women with pre-existing diabetes or gestational diabetes must be closely monitored for hypoglycaemia and blood glucose levels checked 2 hourly (or more frequently if clinically indicated).
  - Women without diabetes of any type also require monitoring for hypoglycaemia and blood glucose levels checked 6 hourly (or more frequently if clinically indicated).
- **Observe** for other clinical features of Pre-eclampsia (CPP0119 Hypertension in Pregnancy – Pre-eclampsia) and Eclampsia (CPP0037 Hypertension in Pregnancy – Eclampsia).
- Blood pressure, heart rate, and SpO2 require close monitoring as outlined in the table below, with results outside parameters set by the prescribing Medical Officer to be reported. Record results on the Midwifery Frequent Observations Chart MR/571.0.
- If rapid drop in blood pressure occurs the woman must be placed in the left lateral position, oxygen given via mask and a fluid bolus administered.

### Labetalol IV Observations Summary Table

<table>
<thead>
<tr>
<th><strong>IV injection</strong> (Time from most recent dose)</th>
<th><strong>Observations</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10 mins</td>
<td>Supine wedged blood pressure, heart rate, and SpO2 to be recorded immediately before and after administration of each dose. Repeat at 5 mins and 10 mins post IV injection. Heart rate and SpO2 monitoring must be continuous during administration and recorded with other vital signs.</td>
</tr>
<tr>
<td>10 mins-2 hrs</td>
<td>If vital signs are stable, monitor blood pressure, heart rate, and SpO2 15 minutely. If unstable, the prescribing Medical Officer will determine the level of monitoring required.</td>
</tr>
<tr>
<td>2-8 hrs</td>
<td>30 minutely blood pressure and heart rate, unless otherwise determined by Medical Officer.</td>
</tr>
<tr>
<td>8-24 hrs</td>
<td>Hourly blood pressure and heart rate, unless otherwise determined by Medical Officer.</td>
</tr>
</tbody>
</table>

**IV infusion**

<table>
<thead>
<tr>
<th>At start of infusion and during rate change</th>
<th><strong>Observations</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>10 minutely blood pressure and heart rate, unless otherwise determined by Medical Officer. Heart rate and SpO2 monitoring must be continuous during administration and recorded with other vital signs.</td>
<td></td>
</tr>
</tbody>
</table>
| During infusion once blood pressure stable | - 30 minute blood pressure and heart rate, unless otherwise determined by Medical Officer.  
- Heart rate and SpO2 monitoring must be continuous during administration and recorded with other vital signs. |
| 24 hours after infusion ceased | - Hourly blood pressure and heart rate, unless otherwise determined by Medical Officer. |

**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.

- **Nervous system:** Transient dizziness, headache, tiredness, depressed mood, 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 have been reported. The signs and symptoms are usually reversible on withdrawal of the drug. Hepatic necrosis has been reported.

- **Musculoskeletal:** There has been one report of toxic myopathy. Muscle cramps have been reported.

- **Respiratory:** Bronchospasm may occur in susceptible individuals.

- **Dermatological:** Rashes of various types such as generalized maculopapular, lichenoid, urticarial, bullous, lichen planus, psoriasiform, facial erythema, Peyronie's disease and reversible alopecia.

- **Genitourinary:** Acute retention of urine and difficulty in micturition have occurred during labetalol treatment.

- **Gastrointestinal:** Epigastric pain, nausea and vomiting.

- **Hypersensitivity:** Rash, pruritus, angioedema and dyspnoea.

- **Other:** Ankle swelling, nasal congestion, cold extremities and sweating.

**DRUG PRESENTATIONS, LOCATION AND STORAGE**

- Labetalol hydrochloride ampoule 100 mg/20 mL.

- Imprest locations (at the time of guideline development): ED, 5N, Obstetric Emergency Trolley, Theatre and Pharmacy.

- Store below 30 degrees. Protect from light.