Ballarat Health Services

DRUG GUIDELINE

LABETALOL
(Intravenous – severe hypertension in pregnancy)

SCOPE (Area): **FOR USE IN:** Labour Ward, ICU, ED and Theatre
EXCLUSIONS: Paediatrics, Coronary Care Unit and other General Wards
SCOPE (Staff): Medical, Nursing and Pharmacy

This Drug Guideline must be used in conjunction with 'Hypertension Disorders in Pre-eclampsia/Eclampsia' Clinical Practice Protocol – see Related Documents.

BRAND NAMES
Labetalol - brands are often changing.
Labetalol is also known as labetalol hydrochloride.

PHARMACOLOGY AND PHARMACOKINETICS
Labetalol is a selective alpha$_1$ and non-selective beta$_1$ and beta$_2$ 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). 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 4-8 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)**
- For non-obstetric use of intravenous labetalol see Labetalol – Intravenous, Non-Obstetric Medication Guideline.

CONTRAINDICATIONS
- **Asthma or COAD.**
- **Second or third degree AV block.**
- **Bradycardia (less than 45-50 beats per minute) or sick sinus syndrome (without pacemaker).**
- **Decompensated heart failure.**
- **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 (with lateral tilt) during administration.
- **First Degree AV block** – labetalol may worsen.
- **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 or allergic reactions -** labetalol may prevent response to usual doses of adrenaline for anaphylaxis, and the allergic response may be exaggerated.
- **Compensated heart failure** – labetalol may worsen.
- **Hepatic impairment** - a lower dose of labetalol may be required.
- **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 the symptoms.
- **Pheochromocytoma -** may cause a paradoxical hypertensive response (requires complete alpha blockade prior to administering labetalol).
- **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

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. If labetalol is the medicine of choice, observe the breastfed infant for signs of hypotension or bradycardia.

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. A cohort study has concluded that the effects of prenatal labetalol exposure did not appear to adversely affect the long term neurodevelopment of young children.

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.
- **Mefloquine** – labetalol may potentiate cardiac adverse effects of mefloquine.
- **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.

- **Alpha2 agonists - clonidine, dexmedetomidine, methyldopa, brimonidine (topical)** – labetalol increases the incidence of bradycardia and hypotension. Sudden withdrawal of long term clonidine or dexmedetomidine 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.
- **Dobutamine, isoprenaline, noradrenaline** - labetalol may antagonise the therapeutic effects of these drugs.
- **Rifampicin, phenobarbitone, primidone, 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.
- **Lignocaine, bupivacaine, mepivacaine –** labetalol may decrease the metabolism of these drugs leading to increased levels.
- **NSAIDs -** may impair the antihypertensive effect of labetalol, and should not be used in hypertensive patients.
- **Amphetamines or methylphenidate** - may decrease the antihypertensive effect of labetalol.
- **Tricyclic antidepressants** - patients may exhibit a tremor when treated with labetalol.
- **Complementary medicines that may reduce antihypertensive effect of labetalol** – bayberry, blue cohosh, cayenne, ephedra, ginger, ginseng (American), kola nut, 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, ICU, 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 ICU (discussion between the Lead Obstetrician and Anaesthetist is required to assess clinical condition). Patients receiving labetalol IV infusion may be transferred to ICU as soon as practical i.e. the patient is stable and where appropriate the baby has been delivered. Where transfer to ICU 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

- **ICU, 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 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.

Most patients will require a maintenance infusion of 80 mL/hr compound sodium lactate (Hartmann's). Fluid boluses are no longer given routinely prior to the administration of blood pressure lowering agents due to the risk of complications such as pulmonary oedema. A 250 mL bolus may be given to treat sudden hypotension. The Obstetrician will determine all decisions regarding fluid management.

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 foetal side effects from rapid decrease in uteroplacental perfusion.

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

Note: Coadministration with magnesium is commonly required and may increase the risk of hypotension. Coadministration 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 ICU/Labour Ward/ED/THEATRE by staff listed in box above
Vials/ampoules contain labetalol 50 mg/10 mL (5 mg/mL), IV injections only use part of this ampoule.
Dose: Labetalol 20 mg (4 mL from vial/ampoule) undiluted over 2 minutes.
Dose can be repeated every 10 minutes for unresponsive blood pressure.
If more than 3 doses are required (total 60 mg) 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 ICU/Labour Ward/ED/THEATRE by staff listed in box above
Use labetalol 50 mg/10 mL vials/ampoules to make up infusion.
Withdraw 40 mL from a 100 mL sodium chloride 0.9% minibag.
Labetalol 200 mg (40 mL from FOUR vials/ampoules) added to remaining 60 mL sodium chloride 0.9% in the minibag.
Total Volume: 100 mL.
Final concentration: 2 mg/mL.
Starting rate: 20 mg/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:**
  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 and Eclampsia *(CPP0119 Hypertension Disorders in Pre-eclampsia/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 Variable Maternal Observations Summary Table	
IV injection (Time from most recent dose)	**Observations**
0-10 mins	▪ 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.
10 mins-2 hrs	▪ 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.
2-8 hrs	▪ 30 minutely blood pressure, heart rate and SpO2 unless otherwise determined by Medical Officer.
8-24 hrs	▪ Hourly blood pressure, heart rate and SpO2 unless otherwise determined by Medical Officer.
IV infusion	**Observations**
At start of infusion and during rate change	▪ 10 minutely blood pressure, respiratory rate 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. ▪ Continuous ECG monitoring should be commenced as soon as practicable.
During infusion once blood pressure stable	▪ 30 minutely blood pressure, respiratory rate 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. ▪ Continuous ECG monitoring.
24 hours after infusion ceased	▪ Hourly blood pressure, respiratory rate, heart rate and SpO2 unless otherwise determined by Medical Officer.

ADVERSE EFFECTS

In general labetalol is well tolerated.

- **Common (greater than 1%) -** bradycardia, hypotension, orthostatic hypotension, transient worsening of heart failure (when treatment starts), nausea, diarrhoea, bronchospasm, dyspnoea, cold extremities, exacerbation of Raynaud's phenomenon, fatigue, dizziness, abnormal vision, alteration of glucose metabolism.
- **Infrequent or rare – -** hallucinations, insomnia, nightmares, depression, heart block, rash, exacerbation of psoriasis, sweating, muscle cramp, nasal congestion, hypersensitivity reaction, thrombocytopenia, urinary retention, increased aminotransferase concentrations, hepatotoxicity.

DRUG PRESENTATIONS AND STORAGE

- Labetalol hydrochloride vial/ampoule 50 mg/10 mL.
- Store below 25 degrees. Protect from light.