Ballarat Health Services

DRUG GUIDELINE

VASOPRESSIN (ARGIPRESSIN) - Intravenous infusion

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

DEFINITIONS
MAP – Mean Arterial Pressure

BRAND NAMES
Pitressin®. Note: other brands may be available via the Special Access Scheme.
Vasopressin is currently in the process of being renamed argipressin in Australia.
Also known as arginine vasopressin (AVP) and antidiuretic hormone (ADH).

PHARMACOLOGY AND PHARMACOKINETICS
Vasopressin ampoules contain a solution of synthetic vasopressin (a peptide hormone released endogenously from the posterior pituitary with vasoactive and antidiuretic properties). Vasopressin acts on three receptors. V_{1a} (initiates vasoconstriction, hepatic gluconeogenesis, platelet aggregation and Factor VIII release), V_{1b} (mediates adrenocorticotropic hormone (ACTH) secretion from the pituitary) and V_2 (located in renal collecting duct and increases free water reabsorption at renal tubules). Low doses of vasopressin potentiate alpha adrenergic vasoconstriction, and by stimulating endothelial nitric oxide release also vasodilatation (coronary, renal, cerebral, pulmonary, mesenteric). High doses of vasopressin lead to nonselective vasoconstriction. In normal health vasopressin plays a minimal role in the maintenance of blood pressure and is only released when its action as an antidiuretic hormone is required to increase reabsorption of fluid from the renal tubules. Vasopressin levels rise initially in sepsis (as part of the stress response), but in prolonged sepsis the levels drop inappropriately low for the degree of hypotension (mechanism unclear). Uniquely the pressor response to vasopressin may be enhanced in vasodilatory septic shock, whilst the pressor response with other catecholamines may be reduced. As such, vasopressin in septic shock reduces the catecholamine dose required to restore vascular tone and blood pressure. Vasopressin is rapidly metabolised in the liver and kidney with minimal renal excretion, with a half-life of 10-20 minutes.

INDICATIONS
- **Refractory vasodilatory shock where low systemic vascular resistance persists despite adequate fluid resuscitation and noradrenaline at a dose of 20 micrograms/min or greater**.
- **Haemodynamic instability for potential organ donors with or without diabetes insipidus, particularly when other inotropes (i.e. noradrenaline) are in use.**
- **Extremely acidotic patients on noradrenaline –** vasopressin is not inactivated by low pH (noradrenaline is).

CONTRAINDICATIONS

- Hypersensitivity to vasopressin.

PRECAUTIONS

- **Hypovolaemia with hypotension** - correct before using vasopressin.
- **Patients with vascular disease, especially of the coronary arteries** – even small doses of vasopressin may precipitate angina pain, and larger doses may precipitate myocardial infarction.
- **Extravasation** – can cause tissue necrosis.
- **Conditions that may be aggravated by water retention** (e.g. cardiac failure, asthma, epilepsy, migraine, preeclampsia, nephritis, coronary thrombosis).

PREGNANCY AND BREASTFEEDING

Seek specialist advice before prescribing, information may update regularly.

DRUG INTERACTIONS

- **Lithium, noradrenaline, demeclocycline, heparin and alcohol** - may block the antidiuretic activity of vasopressin.
- **Carbamazepine, tricyclic antidepressants and fludrocortisone** - may potentiate antidiuretic response of vasopressin.
- **H_2 antagonists** - isolated cases of severe bradycardia and heart block with vasopressin.

DOSAGE AND ADMINISTRATION

Risk of anaphylaxis with administration.
Requires continuous ECG monitoring.
For administration only:

- **in Intensive Care Unit, ED, CVS and Theatre**

Administer via CVC, PICC or midline only – see Precautions re extravasation. Do not administer on lines where other infusions may be bolused or flushed.

Vasopressin must be diluted prior to administration by IV infusion.

Note: Vasopressin is only used in vasodilatory shock as an adjunct to noradrenaline (see Indications), and only after adequate fluid resuscitation.

Adjunct to noradrenaline in vasodilatory shock IV infusion (via CVC, PICC or midline):

For doses and rates LESS than 1.8 units/hr (1.8 mL/hr) prepare:
Vasopressin 20 units (1 mL from ONE ampoule) diluted to 20 mL with glucose 5% in a luer lock syringe.
Total Volume: 20 mL. **Final concentration**: 1 unit/mL. Note: 1 unit/hr = 1 mL/hr.

For doses and rates GREATER than 1.8 units/hr (1.8 mL/hr) prepare:
Vasopressin 40 units (2 mL from TWO ampoules) diluted to 40 mL with glucose 5% in a luer lock syringe.
Total Volume: 40 mL. **Final concentration**: 1 unit/mL. Note: 1 unit/hr = 1 mL/hr.

In Guardrails select 'Vasopressin', then '_Vasodilatory Shock'

Starting rate: 0.6 units/hr (0.6 mL/hr). See table below.
Rate increase: increase by 0.3 units/hr (0.3 mL/hr) every 10 minutes to achieve target MAP.
Usual rate range: 0.6-2.4 units/hr (0.6-2.4 mL/hr).
Standard maximum rate: 2.4 units/hr (2.4 mL/hr).
ICU Consultant maximum rate: 3.6 units/hr (3.6 mL/hr). Rates above 2.4 units/hr MUST be authorised by an ICU Consultant. Higher rates are only to be used when other options to maintain MAP are exhausted, as severe vasoconstriction may result in regional ischaemia (including coronary or mesenteric ischaemia).
Ceasing infusion: Wean by decreasing rate by 0.3 units/hr (0.3 mL/hr) every 30-60 minutes whilst maintaining MAP. Weaning may need to be quicker if the patient is hypertensive.

Adjunct to noradrenaline in Vasodilatory shock rate table for vasopressin 1 unit/mL IV infusion		
	Units/hr	**mL/hr**
	0.3	0.3
Starting Rate	**0.6**	**0.6**
	0.9	0.9
	1.2	1.2
	1.5	1.5
	1.8	1.8
	2.1	2.1
Usual Maximum Rate	2.4	2.4
Doses above 2.4 units/hr (2.4 mL/hr) require ICU Consultant approval		
ICU Consultant Approval Required	2.7	2.7
	3	3
	3.3	3.3
	3.6	3.6

Potential organ donors with or without diabetes insipidus IV infusion (via CVC, PICC or midline):

Vasopressin 40 units (2 mL from TWO ampoules) diluted to 40 mL with glucose 5% in a luer lock syringe.

Total Volume: 40 mL.

Final concentration: 1 unit/mL. Note: 1 unit/hr = 1 mL/hr.

In Guardrails select 'Vasopressin', then 'DL +/- DI' (Donate Life +/- Diabetes Insipidus)

Starting rate: 2 units/hr (2 mL/hr). See table below.

Usual rate range: 0.5-2.4 units/hr (0.5-2.4 mL/hr) to maintain MAP 70 or greater.

Standard maximum rate: 2.4 units/hr (2.4 mL/hr).

ICU Consultant maximum rate: 4 units/hr (4 mL/hr). Rates above 2.4 units/hr MUST be authorised by the ICU Consultant. These higher doses may cause severe vasoconstriction resulting in regional ischaemia (including coronary or mesenteric ischaemia).

Potential organ donors with or without diabetes insipidus rate table for vasopressin 1 unit/mL IV infusion		
	Units/hr	**mL/hr**
	0.5	0.5
	0.8	0.8
	1.2	1.2
	1.6	1.6
Starting Rate	**2**	**2**
Usual Maximum Rate	2.4	2.4
Doses above 2.4 units/hr require ICU Consultant approval		
ICU Consultant Approval Required	2.7	2.7
	3	3
	3.3	3.3
	3.6	3.6
	4	4

General Administration Information

- **Infusion preparation:**
  Mix infusion thoroughly after adding vasopressin to avoid inadvertently giving a more concentrated dose.
  Glucose 5% can be substituted with sodium chloride 0.9% as requested by the Medical Officer.
  Infusion stable for 24 hours (brands may vary, check carefully).
- **Infusion pump:** Alaris Syringe Unit with Guardrails®.
- **Routes of administration:**
  IV injection: No
  IV intermittent infusion: No
  IV continuous infusion: Yes
  IM injection: Yes (not covered in this guideline)
  Subcut injection: Yes (not covered in this guideline)
- **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)

- Observe the colour and temperature of the skin (especially of patients with occlusive vascular disease) for compromised peripheral circulation.
- Assess for organ ischaemia due to vasoconstriction including kidneys, gastrointestinal tract and peripheral extremities.
- Monitor electrolytes (especially sodium as hyponatraemia can occur) at baseline and at least daily.
- Monitor LFTs and platelets at baseline and daily.
- Dose range and clinical goals should be documented by the Medical Officer.

NURSING PRACTICE POINTS

- Continuous ECG monitoring.
- **Cardiac ischaemia –** monitor for any signs or symptoms of angina or myocardial infarction.
- **Allergy** – monitor for any signs and symptoms of an allergic reaction (including anaphylaxis).
- Monitor blood pressure continuously via arterial line.
- Baseline 12 lead ECG, and then daily.
- Monitor urine output and fluid balance and watch for signs of water intoxication (drowsiness, listlessness and headaches).
- The Pitressin® brand states for IM/subcut use only, but may be administered by IV infusion as per Australian Injectables Drug Handbook.
- All injections and infusions are to be labelled as per CPP0022 Labelling of Injectable Medicines and Lines.

ADVERSE EFFECTS

- **Myocardial, mesenteric or peripheral (digital) ischaemia** – can manifest as acute myocardial infarction, gastrointestinal infarction, decreased urine output/creatinine clearance or gangrene.
- **Cardiac arrhythmia and cardiac arrest.**
- **Tissue necrosis with IV infiltration.**
- **Allergic reactions -** including urticaria, bronchospasm and anaphylactic shock.
- **Water intoxication –** the early signs of drowsiness, listlessness and headaches should be recognised to prevent terminal coma and convulsions.
- **Hyponatraemia due to water retention.**
- **Decreased cardiac output due to increased afterload** (caution in heart failure).
- **Other** - hypertension, bradycardia, pallor, abdominal cramps, nausea, vomiting, diarrhoea, headache, vertigo, circumoral pallor, sweating, tremor, pounding in the head, thrombosis, rhabdomyolysis, rise in liver enzymes and reduction in platelet count.

DRUG PRESENTATIONS AND STORAGE

Vasopressin 20 units/1mL ampoules.
Storage conditions vary with brand – check carefully. Do not freeze.
