



MONOGRAPH

BOSENTAN

Scope (Staff):	Medical, Pharmacy, Nursing, Anaesthetic Technicians
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this [DISCLAIMER](#)

QUICKLINKS

Dosage/Dosage Adjustments	Administration	Monitoring	Adverse Effects
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DRUG CLASS

Endothelin antagonist^{1,2}

INDICATIONS AND RESTRICTIONS

- Bosentan is used at PCH for pulmonary arterial hypertension (PAH).¹⁻⁴ The prescribing of bosentan must be in accordance with the PBS Section 100 Highly Specialised Drug Program prescribing guidelines.
- All other uses of bosentan require prior application to and approval from the hospital's Drug and Therapeutics Committee via an "Individual Patient Application (IPA)".

CONTRAINDICATIONS

- Hypersensitivity to bosentan or any component of the formulation.²
- Pregnancy - exclude pregnancy prior to initiation of therapy.
Ensure effective contraception is used during, and for at least 3 months after stopping treatment. Double-barrier contraception is recommended as bosentan may reduce the efficacy of hormonal contraceptives.^{1,2}
- Bosentan is contraindicated in moderate to severe hepatic impairment and/or when the baseline aminotransferase concentrations are greater than 3 times the upper limit of normal (ULN).^{1,2,5}

- Co-administration of bosentan and ciclosporin is contraindicated due to markedly increased plasma concentrations of bosentan.^{1, 2}
- Co-administration of bosentan and glibenclamide is contraindicated due to an increased risk of liver enzyme elevations.^{1, 2}

PRECAUTIONS

- Pulmonary veno-occlusive disease.^{2,5}
- Fluid overload may worsen due to bosentan. Close monitoring is required in patients at risk of fluid overload.^{1,2}
- Anaemia may worsen due to bosentan, close monitoring is required (see [Monitoring](#)).^{1,2}
- Bosentan is probably porphyrinogenic.⁵ Avoid use in acute porphyrias.³
- Pre-existing hypotension prior to starting bosentan (see [Monitoring](#)).^{2,3,5}

FORMULATIONS

Listed below are products available at Perth Children's Hospital (PCH), other formulations may be available, check with pharmacy if required:

- Bosentan 62.5 mg tablets
- Bosentan 125 mg tablets

Imprest location: [Formulary One](#)

DOSAGE & DOSAGE ADJUSTMENTS

Neonates: [Refer to Neonatal Medication Protocols](#)

The doses below are within the standard reference range; however, the dose of bosentan may need to be titrated depending on the patient's clinical needs and response.

Oral (6 months – 18 years):¹⁻⁴

5–10 kg: initially 15.625 mg ONCE daily for 4 weeks, then increase to 15.625 mg TWICE daily.

10–20 kg: initially 31.25 mg ONCE daily for 4 weeks, then increase to 31.25 mg TWICE daily.

20–40 kg: initially 31.25 mg TWICE daily for 4 weeks, then increase to 62.5 mg TWICE daily.

>40 kg: initially 62.5 mg TWICE daily for 4 weeks, then increase to 125 mg TWICE daily.

The increased risk of liver toxicity is generally considered to outweigh any clinical benefit of using higher doses.^{2,4,6}

Renal impairment:

- No dosage adjustment is required in renal impairment.^{2,6}

Hepatic impairment:

- Bosentan is contraindicated in moderate and severe hepatic impairment or when baseline aminotransferase (AST/ALT) concentrations are greater than 3 times ULN.¹⁻³
- Reduce dose or discontinue treatment when AST/ALT concentrations increase to greater than 3 times ULN.^{1,2,5}

ADMINISTRATION

- Bosentan is teratogenic.² Women of childbearing potential must avoid splitting or handling broken bosentan tablets or exposure to generated dust.²
- To avoid exposure to dust from bosentan **do not crush the tablets.**
- Tablets may be cut using a commercial tablet cutter designated solely for use with bosentan.
- If cutting bosentan tablets, staff should double-glove and wear a disposable protective gown, face mask and protective glasses.
- For children unable to swallow a tablet, the tablet may be dispersed in 5-25mL of water.²
- The containers used to suspend the tablet should be discarded or thoroughly cleaned after the preparation of each dose.

MONITORING

- Check haemoglobin at baseline, 1 and 3 months after initiating therapy and then every 3 months.^{1,2}
- Measure aminotransferase (ALT/AST) concentrations at baseline, each month during treatment, 2 weeks after an increase in dosage and within 3 days of restarting after interruption due to raised aminotransferases.^{1,2}
- Treatment and monitoring recommendations based on aminotransferases:
 - 3-5 times ULN: Confirm by another aminotransferase test; if confirmed reduce the dose or interrupt treatment and monitor aminotransferase levels at least every 2 weeks^{1, 2}. Consider reintroduction (if withheld) of bosentan if levels return to pre-treatment values.¹
 - 5-8 times ULN: Confirm by another aminotransferase test; if confirmed stop bosentan and monitor aminotransferase levels at least every 2 weeks. Once the aminotransferase levels return to pre-treatment values, consider reintroduction of bosentan.^{1,2}
 - >8 times ULN: Bosentan should be ceased and should not be reintroduced.²
 - If bosentan is reintroduced it should be at the starting dose and aminotransferase levels should be tested within 3 days of restarting.^{1,2}
 - Cease bosentan if aminotransferase elevations are accompanied by signs or symptoms of liver dysfunction or injury (e.g. abdominal pain, fatigue, fever, jaundice, nausea and vomiting). There is no experience with the re-introduction of bosentan in these circumstances.²

- Cease bosentan if bilirubin levels are greater than twice the ULN.¹

- Particular caution should be exercised when initiating bosentan in patients with pre-existing hypotension; blood pressure in such patients should be monitored closely.²

ADVERSE EFFECTS

Common: Increased liver aminotransferases, fatigue, itch, hypotension, muscle cramps, palpitations, diarrhoea, gastro-oesophageal reflux, flushing, headache, anaemia.^{1,3}

Infrequent: Hepatitis, jaundice, thrombocytopenia, neutropenia, leucopenia.^{1,3}

Rare: Liver cirrhosis, liver failure, anaphylaxis, multi-organ hypersensitivity syndrome, angioedema.^{1,3}

STORAGE

Store tablets below 25°C.²

Protect from moisture.²

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. [Clinical Pharmacology](#)), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Please note: The information contained in this guideline is to assist with the preparation and administration of **bosentan**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines

[Bosentan – Health Facts \(PCH\)](#)

[Contraception in women with heart disease – Health Facts \(PCH\)](#)

Related external legislation, policies and guidelines



[Pharmaceutical Benefits Scheme](#)

References

1. Australian Medicines Handbook Pty Ltd. Australian Medicines Handbook [online] Adelaide (SA): Australian Medicines Handbook Pty Ltd [accessed 23/07/2024].
2. MIMS Australia Pty Ltd. MIMS [online]. St Leonards (NSW): CMP Medica Australia Pty Ltd; [accessed 23/07/2024].

3. Paediatric Formulary Committee. Bosentan. BNF for Children [online] London: BMJ Group, Pharmaceutical Press, and RCPCH Publications. [accessed 26/07/2024].
4. AMH Children's Dosing Companion [online]. Adelaide: Australian Medicines Handbook Pty Ltd [accessed 26/07/2024].
5. Bosentan monograph. In Martindale: The complete drug reference. [online] London: Pharmaceutical Press; 2024 [accessed 26/07/2024].
6. UpToDate. Bosentan: Pediatric Drug Information. [online] Lexi-Comp Inc: 2024 [accessed 26/07/2024].

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