MONOGRAPH

Dinutuximab BETA

Dinutuximab (Unituxin®) should not be confused with Dinutuximab BETA (Qarziba®) - these two medications are not interchangeable.

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	Oncology Department

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

⚠ HIGH RISK MEDICINE ⚠

QUICKLINKS

DRUG CLASS[1]

Dinutuximab beta is a chimeric monoclonal IgG1 antibody. It reacts specifically with disialoganglioside 2 (GD2) which is highly expressed by neuroblastoma, melanomas, brain tumours and some sarcomas but in normal tissues is restricted to neurons, skin melanocytes and peripheral pain fibres.

Dinutuximab beta binds to cell surface GD2 and induces cell lysis of GD2 expressing cells through antibody-dependent cell-mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC).

Dinutuximab beta (Qarziba®) is not interchangeable with Dinutuximab (Unituxin®)

Dinutuximab beta is a High Risk Medicine.

Extravasation: Dinutuximab beta is non-irritant (neutral).

Emetogenic Rating: Low.

INDICATIONS AND RESTRICTIONS[1-7]

- Dinutuximab beta can only be prescribed by oncologists as per a PCH approved treatment protocol for the first line treatment of high risk neuroblastoma

CONTRAINDICATIONS[1-7]

- Hypersensitivity to dinutuximab beta or any component of the formulation.
- Due to their immunosuppressive activity, concomitant treatment with corticosteroids is contraindicated within 2 weeks prior to the first treatment course until 1 week after the last treatment course with dinutuximab beta, except for life-threatening conditions.
- Antihypertensive medication should be withheld 12 hours prior to the infusion.
- Any other protocol specific contraindications.

PRECAUTIONS[1, 2, 7]

- Dinutuximab beta (Qarziba®) is not interchangeable with Dinutuximab (Unituxin®).
- Patients should be pre-treated with paracetamol and an antihistamine prior to infusion. The patient must be under supervision for the initiation and during the infusion (see 'Monitoring').
- Hypersensitivity reactions including anaphylaxis, may develop immediately or at any time during the infusion.
- Adrenaline (epinephrine) must be available for immediate use. It is recommended that emergency medication doses are calculated and prescribed on the paediatric Hospital Medication Chart (pHMC) for use if required for anaphylactic reactions.
- Severe infusion-related reactions, including cytokine release syndrome (CRS) may occur despite the use of premedication. Occurrence of a severe infusion related reaction (including CRS) requires immediate discontinuation of dinutuximab beta therapy and may necessitate emergency treatment.
- Severe hypotension may occur. Institute supportive management as appropriate or as per protocol. **Antihypertensive medication should be withheld 12 hours prior to the infusion.**
- Capillary leak syndrome (CLS) may occur. Careful monitoring of circulatory and respiratory function is required. Institute supportive management as appropriate or as per protocol.
- Neuropathic pain is a common adverse effect of dinutuximab beta. It is recommended that pre-medication is administered with analgesics, including an opioid and gabapentin (see

'Reconstitution and Administration') to continue throughout the duration of dinutuximab beta therapy. Gabapentin should begin 3 days prior to administration.

- Impaired vision (due to reversible pupillary palsy) is an infrequent adverse effect of dinutuximab beta and does not usually warrant a change in therapy if visual impairment is assessed as tolerable by the physician. Treatment should be interrupted in patients who experience Grade 3 vision toxicity (i.e. subtotal vision loss) and the patient should be referred to an ophthalmologist.
- Vaccinations should be avoided during administration of dinutuximab beta until 10 weeks after the last treatment course, due to immune stimulation through dinutuximab beta and possible risk for rare neurological toxicities.
- Concomitant use of intravenous immunoglobulins is not recommended as they may interfere with dinutuximab beta dependent cellular cytotoxicity. IV Immunoglobulin should not be administered within 2 weeks before or 1 week after each course of dinutuximab beta.

FORMULATIONS[1, 8]

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

- Dinutuximab beta (Qarziba®) 20 mg/4.5 mL vial

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS[1-5, 7]

Dosage Regimen of Dinutuximab beta

- As per protocol

Renal impairment:

- No data

Hepatic impairment:

- No data

Treatment related toxicity:

- Dose adjustment as per treatment protocol

RECONSTITUTION & ADMINISTRATION [1-3, 8]

Dinutuximab beta (Qarziba®) is a high-cost drug with a 7-day expiry once compounded into a CADD bag. Each CADD bag is infused over 5 days – CADD bags should be prepared ensuring the expiry date and time of the CADD bag is after the planned infusion end date and time.

- Handle as cytotoxic.

- Dinutuximb beta must be compounded in a cytotoxic drug safety cabinet by pharmacy personnel who have appropriate training and validation in aseptic and cytotoxic drug reconstitution and handling techniques.
- Dinutuximab beta should be administered at a continuous rate of 2 mL/hour. The solution for infusion must be infused through a 0.22 – 5 micron filter through a dedicated line.
- Each 240 mL bag of dinutuximab beta contains an excess of 10 mL (total volume 250 mL) to allow line priming and to ensure the full dose is administered.

Pre administration

1. Ensure oral gabapentin has been commenced and titrated prior to admission.
2. Prior to administering dinutuximab beta, ensure an emergency tray is at the patient's bedside and all doses of the following medications are pre-calculated (refer to the Adrenaline (epinephrine) Monograph, Salbutamol Monograph and Diphenhydramine Monograph):
   a) Intramuscular adrenaline (epinephrine) 1:1000 (1 mg/1 mL) ampoule as per protocol
   b) Nebulised salbutamol:
      < 6 years = 2.5 mg
      ≥ 6 years = 5 mg
   c) Intravenous diphenhydramine as per protocol
   d) Intravenous hydrocortisone as per protocol
3. Contact the Acute Pain Service (APS) for a pain management plan and opioid infusion prescribing.
4. Prior to commencing dinutuximab beta infusion administer:
   a) Intravenous paracetamol (20 minutes prior) or oral paracetamol (60 minutes prior)
   b) Intravenous diphenhydramine (20 minutes prior)
   c) Administer opioid bolus and commence continuous opioid infusion as prescribed by APS

Analgesia requirements

- Gabapentin is to be commenced at least 3 days prior to beginning dinutuximab beta. Gabapentin may be stopped after the completion of each dinutuximab beta infusion and recommenced prior to the next cycle or may be continued between cycles.
- An opioid infusion should be commenced 2 hours prior to the start of dinutuximab beta as prescribed by the APS. Weaning of intravenous opioids should be as prescribed by the APS.
- Patients should be converted to oral analgesics as soon as practicable under the guidance of the APS and this should be continued on discharge.

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*[1, 8]

Compatible fluids: Sodium Chloride 0.9%

Dinutuximab beta should be infused through a dedicated lumen. It **must not** be co-infused with any other drug or fluid.

MONITORING[1, 2, 7, 9, 10]

Pre administration:

- Ensure necessary tests are completed as per protocol including a baseline urinalysis, full blood picture (FBP), urea and electrolytes (U&Es), and liver function tests (LFTs)
- Complete baseline observations including weight, temperature, pulse, respiratory rate, blood pressure and oxygen saturation

During and post administration:

- Vital signs
  - Record vital signs (e.g. temperature, pulse, respiratory rate, blood pressure & oxygen saturation) every 15 minutes during the first hour.
  - Record vital signs hourly after the first hour to 4 hours after commencing the infusion.
  - After the first 4 hours record vital signs every 2 hours for 24 hours.
  - Vital signs should then be recorded at least every 4 hours until completion of the infusion or until the patient is discharged.
- Check U&Es, calcium, magnesium and phosphate daily while an inpatient.
- Conduct urinalysis twice daily to check for haematuria and Specific Gravity (SG)
- Strict fluid balance every 4 hours
- Twice daily weight measurement whilst an inpatient
- Pain scores

Special Considerations

Do not flush the dinutuximab beta lumen, especially when changing CADD bags as this can result in an increased rate of administration and associated complications.

- All patients will have a double lumen central venous access device inserted prior to commencing on dinutuximab beta.
- If the patient develops a fever ≥ 38°C, perform blood cultures at least once per day from the available lumen of the double lumen central venous access device only, ensuring the dinutuximab beta line is clamped whilst this occurs. **Do not disconnect the dinutuximab beta infusion to perform blood cultures – only culture the dinutuximab beta lumen at CADD change or disconnect.**
- A patient may not need to be readmitted to the ward if a disconnection and interruption to therapy occurs. This decision should be referred to the treating consultant who will assess this on a case-by-case basis based on the clinical picture and pain management plan.

ADVERSE EFFECTS[1, 2, 7, 8]

Common: Hypotension, fever, pain, infusion reactions, hypersensitivity reactions, cytokine release syndrome, capillary leak syndrome, hypoxia, hypokalaemia, hyponatraemia, hypoalbuminemia, hypocalcaemia, vomiting, diarrhoea, urticaria, neutropenia, thrombocytopenia, anaemia, lymphopenia, alanine aminotransferase (ALT) increased, aspartate aminotransferase (AST) increased.

Infrequent: Hypertension, nausea, hypophosphataemia, hypomagnesaemia, tachycardia, increased serum creatinine, hyperglycaemia, haemorrhage, sepsis, infection, oedema, proteinuria, urinary retention, peripheral neuropathy, decreased appetite, weight gain, febrile neutropenia, mydriasis, periorbital oedema, and eyelid oedema.

Rare: Anaphylaxis, seizures, cardiac arrest, sudden death, renal and urinary disorders (atonic bladder), atypical haemolytic uremic syndrome, neurological disorders of the eye, posterior reversible encephalopathy syndrome (PRES), myelitis, blurred vision, photophobia, ophthalmoplegia, optic atrophy.

STORAGE[1, 8]

IV infusion: Refrigerate at 2 – 8°C prior to use, stable for 7 days. Do not shake

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. AusDI), 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 **Dinutuximab beta**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines

Adrenaline Monograph

Anaphylaxis Emergency Department Guideline

Cytotoxic Biotherapy Agents Administration

Cytotoxic Biotherapy Agents Extravasation

Cytotoxic Biotherapy Agents Safety

Anti-cancer Induced Nausea and Vomiting Management

Diphenhydramine Monograph

Salbutamol Monograph

Related external legislation, policies and guidelines

ASCIA Guidelines Acute management of anaphylaxis - Australasian Society of Clinical Immunology and Allergy (ASCIA)

References

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3. Ladenstein R, Potschger U, Valteau-Couanet D, Luksch R, Castel V, Ash S, et al. Investigation of the Role of Dinutuximab Beta-Based Immunotherapy in the SIOPEN High-Risk Neuroblastoma 1 Trial (HR-NBL1). Cancers (Basel). 2020;12(2).
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File Path:	W:\Safety & Quality\CAHS\CLOVERS MEDICAL Pharmacy\Procedures Protocols and Guidelines\Medication Monographs_Word\PCH.MED.DinutuximaBETA.docx		
Document Owner:	Chief Pharmacist		
Reviewer / Team:	Clinical Nurse Specialist, Consultant Oncologist, Supervisor Pharmacist (Oncology)		
Date First Issued:	Nov 2026	**Last Reviewed:**	First Issue
Amendment Dates:	First Issue	**Next Review Date:**	Nov 2026
Approved by:	CAHS Medication Safety Committee	**Date:**	Oct 2023
Endorsed by:	CAHS Drug & Therapeutics Committee	**Date:**	Nov 2023
Standards Applicable:	NSQHS Standards: NSMHS: N/A Child Safe Standards: N/A		

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