MONOGRAPH

Dinutuximab (Unituxin®)

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

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

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[1,2]

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

Dinutuximab is a High Risk Medicine.

Extravasation: Dinutuximab is an irritant. Refer to Extravasation of Antineoplastic (Cytotoxic) Agents Policy.

Emetogenic Rating: Minimal. Refer to Anti-cancer Therapy Induced Nausea and Vomiting (AINV) Management Guideline.

INDICATIONS AND RESTRICTIONS

- Dinutuximab can only be prescribed as per the Paediatric – WA Statewide Medicines Formulary.

Special access scheme product. SAS application(s) must be completed in accordance to the TGA regulations.

CONTRAINDICATIONS[1-3]

- Hypersensitivity to dinutuximab or any component of the formulation.
- Concomitant use of immunosuppressive agents (e.g. glucocorticoids) except for life-threatening conditions.
- Any other protocol specific contraindications.

PRECAUTIONS[1-3]

- Acute adverse infusion effects, including anaphylaxis, may develop immediately or at any time during the infusion.
- 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.
- Adrenaline (epinephrine) must be available for immediate use. It is recommended that emergency medication doses are calculated and prescribed on the WA Paediatric Hospital Medication Chart (pHMC) for use if required for anaphylactic reactions.
- Capillary leak syndrome (CLS) may occur. Careful monitoring of circulatory and respiratory function is required. Institute supportive management as appropriate or as per protocol.
- Severe hypotension may occur. Institute supportive management as appropriate or as per protocol. Antihypertensive medication should be withheld 12 hours prior to the infusion.
- Neuropathic pain is a common adverse effect of dinutuximab. It is recommended that pre-medication is administered with analgesics, including intravenous opioid and gabapentin to continue throughout the duration of dinutuximab therapy. Gabapentin to begin 2-3 days before admission.
- Impaired vision (due to reversible pupillary palsy) is an infrequent adverse effect of dinutuximab 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.
- IV Immunoglobulin may interfere with the mechanism of action of dinutuximab and should not be administered within 2 weeks before or 1 week after each course of dinutuximab.

FORMULATIONS[3]

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

- Vial: 17.5 mg/5 mL solution

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Dosage as per treatment protocol in the OIMS (Oncology Information Management System).

Renal impairment:

- Dose adjustment as per treatment protocol. eGFR calculator

Hepatic impairment:

- Dose adjustment as per treatment protocol.

Treatment related toxicity:

- Dose adjustment as per treatment protocol.

RECONSTITUTION & ADMINISTRATION[1-3]

- Handle as cytotoxic. Refer to the Antineoplastic (Cytotoxic) Agents Safe Handling and Administration Policy.

Pre administration

1. Administer an IV sodium chloride 0.9% bolus: 10 mL/kg over 1 hour prior to the dinutuximab infusion.
2. Ensure oral gabapentin has been commenced and titrated prior to admission.
3. Prior to administering dinutuximab, 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
4. Contact the Acute Pain Service (APS) for a pain management plan and opioid infusion prescribing.
5. Prior to commencing dinutuximab 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. Gabapentin may be stopped after the completion of each dinutuximab infusion and recommenced prior to the next cycle or may be continued between cycles.
- An opioid bolus should be administered prior to the start of dinutuximab and infusion commenced at prescribed rate as per APS The opioid infusion runs throughout dinutuximab administration and should continue for at least 2 hours after completion.
- Where pain is not controlled with opioid analgesia or the opioid is not tolerated, a ketamine infusion may be prescribed by APS.
- Pain is the most common adverse event and manifests as abdominal cramps, or back and extremity pain.
- Despite the initial opioid bolus patients may have a surge of pain within the first hour of starting dinutuximab infusion.
    - If this occurs give further opioid bolus as prescribed by APS and reduce the dinutuximab infusion to the initial rate for the first hour then increase gradually by 2.5 mL/hr as tolerated to a maximum rate of 1.75 mg/m^2/hr (10 mL/hr).

Dinutuximab is infused over a **minimum of 10 hours** and maximum of 20 hours. Start rate at 0.88 mg/m^2/hr for 30 minutes, then increase to 1.75 mg/m^2/hr for the remainder of the dose. Discard balance if unable to deliver full dose in 20 hours, and record volume delivered.

- **Document** the tolerated infusion rate. Subsequent infusions should commence as per tolerated infusion rate of the previous cycle.

Action for Hypersensitivity or infusion related event:

- Grade 1 or 2 Hypersensitivity:
    - The infusion rate should be decreased to 50% (or interrupted) until recovery from symptoms. If tolerated, complete infusion at planned rate otherwise use the slower rate. Antihistamines may be prescribed by the medical team.
- Grade 3 or 4 Hypersensitivity:
    - Immediately discontinue dinutuximab infusion (and discontinue Granulocyte-macrophage colony-stimulating factor (GM-CSF) or aldesleukin infusion). Relevant anaphylaxis algorithm should be considered.
- Once stable refer to protocol for infusion continuation recommendations.

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*[3]

Compatible fluids: Sodium chloride 0.9%[4]

Compatible and INCOMPATIBLE drugs:

Antineoplastic therapies are not routinely administered with other medications. Consult two or more drugs references *(Compatibilities of IV drugs)* or pharmacy when there is a requirement for medications to be given concurrently.

MONITORING

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 until completion of antibody infusion.
- 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 and twice daily weights
- Twice daily weight measurement whilst an inpatient
- Pain scores
- For patients enrolled on Children's Oncology Group (COG) or other studies report any adverse events or toxicities as required by the Clinical Research Associate (CRA).

ADVERSE EFFECTS[1-3]

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[1,3]

IV infusion: Refrigerate 2-8°C, stable for 24 hours. Do not shake.

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.

- Concomitant use of immunosuppressive agents (e.g. glucocorticoids) except for life-threatening conditions.
- Antihypertensive medication should be withheld 12 hours prior to the infusion.
- IV Immunoglobulin may interfere with the mechanism of action of dinutuximab and should not be administered within 2 weeks before or 1 week after each course of dinutuximab.

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

Related CAHS internal policies, procedures and guidelines

Chemotherapy Induced Nausea and Vomiting Management

Extravasation of Antineoplastic (Cytotoxic) Agents

Anti-cancer Therapy Induced Nausea and Vomiting (AINV) Management

Adrenaline Monograph

Anaphylaxis Emergency Department Guideline

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

1. Drug information for commercial agents used by the Children's Oncology Group. [Online]. 2022; https://www.cogmembers.org/_files/disc/Pharmacy/CommercialAgentsMonographs.pdf.
2. Parenteral and oral chemotherapy administration guidelines used by the Children's Oncology Group. [Online]. 2023; https://www.cogmembers.org/_files/disc/Pharmacy/ChemoAdminGuidelines.pdf.
3. UpToDate. Lexicomp; 2024. https://www-uptodate-com.pklibresources.health.wa.gov.au/contents/search.

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