MONOGRAPH

VEDOLIZUMAB

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	Compatibility	Monitoring

DRUG CLASS

Vedolizumab is an α4-β7 integrin inhibitor used for the management of inflammatory bowel disease.[1]

INDICATIONS AND RESTRICTIONS

- Vedolizumab is used in patients with Crohn's disease or ulcerative colitis who have failed, ceased to respond to, or are intolerant of infliximab or adalimumab.[2,3]
- All patients require approval from the hospital's Drug and Therapeutics Committee prior to commencing vedolizumab. An Individual Patient Approval Application should be completed and submitted to this committee.

CONTRAINDICATIONS

- Hypersensitivity to vedolizumab or any component of the formulation.[2]
- Patients with severe infections such as sepsis, abscesses, tuberculosis and opportunistic infections.[2]
- Progressive multifocal leucoencephalopathy.[2,4]

PRECAUTIONS

- Patients previously treated with natalizumab should normally wait a minimum of 12 weeks after the last dose of natalizumab prior to initiating therapy with vedolizumab.[2]

The following screening assessments must be performed prior to commencing vedolizumab for the first time:

- Tuberculosis – Assess for tuberculosis exposure and screen for latent infection using the QuantiFERON test. Contact the Infectious Diseases team for further information.[2,4]
- Hepatitis-B and hepatitis-C (with complete serology including both antibodies and antigen).[5]
- Pregnancy test and counselling.
    - In pregnancy, vedolizumab is categorised by the TGA as a category B2 drug.
    - These are "Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage."[6]
    - There is only limited published evidence of the safety of vedolizumab in pregnancy.[7,8] Therefore the treating doctor must discuss reproductive health implications (including pregnancy and contraception) with the patient (and parent / carer, as appropriate) during the initial general counselling received by all patients commencing on vedolizumab.

In addition, there should be assessment for:

- Patient demographics, past exposure to and risk factors for chronic viral infections such as Hepatitis B, Hepatitis C, Human Immunodeficiency Virus, Varicella Zoster Virus and Human Papillomavirus.
- Clinical history and examination to exclude current sepsis.
- Exclusion of contraindications.
- Assessment of vaccination status and vaccination where required (annual influenza vaccines are safe and recommended).
    - Update all vaccinations before treatment initiation where possible.[2]
    - Live vaccines must be given at least 4 weeks prior to initiating therapy.[5] Whilst on vedolizumab live vaccines should not be given unless the benefits outweigh the risks.[2]
    - An Immunologist or Infectious Diseases Physician must be consulted regarding when to administer any immunisation in patients no longer receiving vedolizumab.

Vedolizumab may contribute to increased infection and malignancy risk.[2,3,4] These issues must be discussed with the patient and parent/carer before commencing therapy.

NOTE: Monitoring required prior to the initial and subsequent doses are described below under "Monitoring".

FORMULATIONS

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

- Vedolizumab 300 mg vial

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Intravenous infusion 8 years – 18 years

6 mg/kg/dose (maximum 300 mg) at 0, 2, and 6 weeks ("induction") and then every 8 weeks ("maintenance") thereafter.[9,10]

Renal impairment:

- No data for patients with renal impairment.[2]

Hepatic impairment:

- No data for patients with hepatic impairment.[2]

RECONSTITUTION & ADMINISTRATION

- Regardless of dose, all vedolizumab orders are prepared to a final volume of 250mL.
- All doses of vedolizumab are to be prepared by Pharmacy Compounding Service (PCS).

IV Infusion: Administer by intravenous infusion over 30 minutes.[2]

- An apron, mask and gloves must be worn during administration.[11,12] Disposal of waste is not subject to any special precautions and should be performed in accordance with the usual hospital practice for disposal of parenteral medications and patient waste.[11,12]
- Premedication is generally not required unless the patient has previously reacted to vedolizumab. If necessary, single doses of;
  (a) oral loratadine (see AMH-CDC for dosing guidelines)
  (b) oral paracetamol and
  (c) IV hydrocortisone (4 mg/kg, maximum 100 mg/dose)
- Premedication should be given 30 minutes prior to the infusion. These should be written by the doctor on the front of the patient's medication chart.
- Adrenaline (epinephrine) must be readily available for all patients.

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

Sodium chloride 0.9%, Compound Sodium Lactate (Hartmann's) solution.[13]

Compatible at Y-site:

No information[13]

Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

INCOMPATIBLE drugs:

No information[13]

MONITORING

Prior to and during treatment –

- The following blood tests are required prior to each dose of vedolizumab:
  - Full Blood Picture (FBP)
  - C Reactive Protein (CRP)
  - Erythrocyte Sedimentation Rate (ESR)
  - Liver Function Tests (LFTs)
  - Iron studies
- Perform a baseline measurement of temperature, pulse, respiratory rate and blood pressure and continue every 15 minutes until the infusion is completed.
- A pregnancy test is mandatory only before the first dose of vedolizumab. Thereafter it will be done at the discretion of the treating doctor.
- Vedolizumab levels are taken to monitor response and guide on-going treatment. The first such level is usually taken prior to the fourth dose (that is, after the completion of "induction") and thereafter at the discretion of the treating Gastroenterologist.
- Before commencing the patient must be afebrile, without respiratory symptoms and have no signs of an active abscess.
- Progressive multifocal leucoencephalopathy (PML) has been reported with other integrin antagonists. Therefore, patients receiving vedolizumab should be monitored for any new or worsening neurologic manifestations.
  Prior to receiving each dose of vedolizumab, the patient (or parent/carer, as appropriate) must be asked if any of the following neurological symptoms have occurred:
  - progressive weakness on one side of the body or clumsiness of limbs,
  - changes in speech or walking,
  - changes in vision,

- changes in thinking, memory and orientation leading to confusion and personality changes.[4]

This must be recorded in the patient's medical notes.

If any of the above signs of PML are reported, the patient must be immediately referred to a Neurologist and not receive any further vedolizumab.

After infusion completed –

- Monitor temperature, pulse, respiratory rate and blood pressure every 30 minutes after completion of the infusion.
- Patients receiving one of the three "induction" doses should be monitored for a minimum of two hours, whereas those receiving a "maintenance" dose should be monitored for a minimum of one hour.
- **In the event of an infusion reaction, the infusion must be stopped and the RMO or Registrar called.**

IMPORTANT - A "Code Blue" must be called immediately, and appropriate measures commenced, whenever anaphylaxis is suspected (Resuscitation and Responding to Clinical Deterioration).

Once the reaction has resolved and a decision made by the doctor to continue the dose, the infusion should be recommenced at half the previous rate of infusion. The patient must receive premedication (as described under "Administration") for all subsequent doses.

ADVERSE EFFECTS

Common: Arthralgia, headache, cough, infections (e.g. nasopharyngitis, upper respiratory tract infection), hypersensitivity and infusion-related reactions.[1,2]

Infrequent: Development of anti-vedolizumab antibodies.[1,2]

Rare: Hepatitis (raised aminotransferases and/or bilirubin).[1,2]

Infusion reactions:[1,2]

These commonly occur at the start of an infusion and up to 2 hours after. Delayed reactions (of up to 2 days) may occur. Symptoms can include fever, chills, nausea, headache, flushing, rash, urticaria, and pruritus.

Rarely increased BP, bronchospasm, and cardiac adverse effects and serious hypersensitivity reactions, including anaphylaxis, can occur.

STORAGE

Vials: Store at 2 – 8ºC. Protect from light.[13]

Vedolizumab diluted in sodium chloride 0.9% (as prepared by Pharmacy Compounding Services) is stable for 12 hours at room temperature and 24 hours if refrigerated.[13] Its administration, therefore, should be completed before this time has elapsed.

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 **vedolizumab**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines

Adrenaline (epinephrine) Monograph (Medication Management Manual)

WA Individual Patient Approval System (Formulary One)

Paracetamol Monograph(Medication Management Manual)

Resuscitation and Responding to Clinical Deterioration MET Review and Code Blue (Clinical Practice Manual)

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