MONOGRAPH

INFLIXIMAB

Scope (Staff):	Medical, Pharmacy, Nursing
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

Tumour Necrosis Factor alpha antagonist.[1]

Note: The reference biological medicine infliximab and its biosimilar formulations are considered substitutable with each other[2] and are all covered by this document.

INDICATIONS AND RESTRICTIONS

Infliximab is used most frequently in the management of Crohn's disease (including fistulising disease), ulcerative colitis and a number of rheumatological conditions where there has been an inadequate response to conventional therapies.[3]

PCH RESTRICTIONS

All Non-PBS indications require Individual Patient Approval (IPA) from the hospital's Drug and Therapeutics Committee (the IPA form is accessible at PCH from the Formulary One page) except as listed below;

1. As per the PBS indication, the hospital is required to fund the initial dose of infliximab when used in patients to treat acute severe ulcerative colitis.
2. Patients that are approved under the compassionate ixtend program. Patients approved under the ixtend program are to be dispensed patient named infliximab (CA) Inflectra®.

Infliximab is a PBS Complex Authority Item and requires written approval from Medicare PRIOR to the initiation of therapy.

CONTRAINDICATIONS

- Hypersensitivity to infliximab or any component of the formulation.
- Patients with severe infections such as sepsis, abscesses, tuberculosis and opportunistic infections.[3]
- Concurrent administration with anakinra.[3]
- Central Nervous System demyelinating disorders.[3]
- Patients with congestive heart failure.[3]
- Infliximab is possibly porphyrinogenic.[4]

PRECAUTIONS

The following screening assessments must be performed prior to commencing infliximab for the first time:[3,5]

- Tuberculosis – Assess for tuberculosis exposure and screen for latent infection using the QuantiFERON test. Contact the Infectious Diseases team for further information,
- Hepatitis-B and hepatitis-C (with complete serology including both antibodies and antigen),
- Pregnancy test and counselling.
    - In pregnancy infliximab is categorised by the TGA as a category C drug. These are "drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Accompanying texts should be consulted for further details".[6]
    - Although there is evidence that infliximab may be safely used in pregnancy[5,7,8,9], 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 infliximab.

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 contra-indications (including demyelination. cardiac failure, malignancy and history of allergy to infliximab or other murine proteins).

- Assessment of vaccination status and vaccination where required (annual flu vaccines are safe and recommended).

Update all vaccinations before treatment initiation where possible. Inactivated vaccines should be given at least 2 weeks prior to commencing infliximab.[5]

Live vaccines must be given at least 4 weeks prior to initiating therapy. Whilst on infliximab live vaccines should not be given.[5]

An Immunologist or Infectious Diseases Physician must be consulted regarding when to administer any immunisation in patients no longer receiving infliximab.

Re-administration is not recommended after an infliximab free interval of more than 16 weeks due to the potential risk of hypersensitivity reactions.[3]

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:

Infliximab 100mg powder vial [3,10]

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Infliximab dosing is expected to begin with a three-dose induction followed by maintenance doses thereafter.[3,10]

Child 6 to 18 years: Crohn's disease and Ulcerative Colitis[1]

(Child < 6 years with fistulising Crohn's disease under the direction of the Gastroenterologist)

Induction

IV infusion: 5 mg/kg/dose (not dose capped) at weeks 0, 2 and 6.[1]

Maintenance

IV infusion: 5 mg/kg/dose (not dose capped) thereafter at 8 weekly intervals.[1]

*For patients in **maintenance** where there is loss of effect and infliximab is to continue* – The treating doctor may choose to temporarily give infliximab at 6 weekly intervals, or to attempt re-induction (as above).

An IPA is required for higher doses.

Renal impairment:

No information.

Hepatic impairment:

No information.

RECONSTITUTION & ADMINISTRATION

- All doses of infliximab are prepared by Pharmacy Compounding Service (PCS).
- All orders for infliximab doses of up to 1000 mg are prepared to a final volume of 250 mL. Higher doses should be prepared to a concentration of 4 mg/mL or weaker.

- Personal Protective Equipment at ward unit level during administration[11,12]:
  - An N95 mask must be worn.
  - Gloves must be worn.
  - Protective eye wear – must be worn during preparation and when dis/connecting administration.
  - Gowns are not warranted.

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 [13,14] unless the patient has previously reacted to infliximab. If necessary, single doses of

a) oral loratadine (see AMH-CDC for dosing guidelines) [15],

b) oral paracetamol and

c) IV hydrocortisone (4 mg/kg, maximum 100 mg/dose[16])

should be given 30 minutes prior to the infusion. These medications should be written by the doctor on the front of the patient's WA Paediatric Hospital Medication Chart MR860.00.

Adrenaline (epinephrine) must be readily available for all patients.

NOTE: It is mandatory to administer infliximab through an in-line, low protein binding filter (1.2 micrometres or smaller)[3] such as the B.Braun "Infusomat Spaceline Safe Set with Sterifix 0.2 micrometre filter set" (B.Braun reference 8700098SP). These are imprest on Ward 1A, Clinic H and Day Treatment Unit.
The 'Smart Infusion Pump Pharmacist' is available during business hours via Vocera to provide advice on suitable giving sets.

IMPORTANT – DO NOT SHAKE. Shaking leads to frothing and breakdown of the drug.

Standard Infusion Protocol

All infliximab orders to be given by the 'Standard Infusion Protocol' MUST be prescribed on an "Infliximab Infusion Chart: STANDARD Infusion Protocol" form (MR 353.06/ 860.15). This form is available here.

NOTE: All three Induction doses (0, 2 and 6 weeks) must be given according to this regimen. The first Maintenance dose is usually given according to this regimen also.

10 mL/hr for 15 minutes, then if tolerated

20 mL/hr for 15 minutes, then if tolerated

40 mL/hr for 15 minutes, then if tolerated

80 mL/hr for 15 minutes, then if tolerated

150 mL/hr for 30 minutes, then if tolerated

250 mL/hr for the remainder of the infusion.

Rapid Infusion Protocol [17,18,19]

All infliximab orders to be given by the 'Rapid Infusion Protocol' MUST be prescribed on an "Infliximab Infusion Chart: RAPID Infusion Protocol" form (MR 353.07/ 860.1). This form is available here.

NOTE:

a) *The Rapid Infusion Protocol is **not** suitable for children of less than 25 kg.*

b) *Only patients who have not reacted to the Standard Infusion Protocol can be considered for infliximab administration by the Rapid Infusion Protocol.*

c) *This regimen may be used for administering from the second Maintenance dose and onwards. The Consultant may, however, decide to give the first Maintenance dose according to this rapid regimen. This must be specifically documented by the Consultant in the patient's notes.*

60 mL/hr for 10 minutes, then if tolerated

120 mL/hr for 10 minutes, then if tolerated

250 mL/hr for the remainder of the infusion.

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

Sodium chloride 0.9%[20]

Compatible at Y-site:

No information.

Only commonly used drugs are listed below. This is not a complete list of incompatible drugs. Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

INCOMPATIBLE drugs:

No information.

MONITORING

Prior to and during administration –

- Blood for Full Blood Picture (FBP), C Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), Liver Function Tests (LFTs) and iron studies must be taken before all doses of infliximab.
- Blood for anti-TNF and anti-infliximab antibodies may also be requested in patients where there is concern of a loss of effect.
- 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 infliximab. Thereafter it will be done at the discretion of the treating doctor.
- Before commencing the patient must be afebrile, without respiratory symptoms and have no signs of an active abscess.

After infusion completed –

- Monitor temperature, pulse, respiratory rate and blood pressure 30 minutes and 1 hour after completion of the infusion.
- In addition, monitoring should be repeated 2 hours after completion of the infusion in those patients who have received infliximab by the Standard Infusion Protocol.

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 starting at the slowest rate of the protocol being followed.

ADVERSE EFFECTS

Common: Nausea, abdominal pain, vomiting, fever, cough, fatigue, vertigo, dizziness, flushing, serum sickness-like reaction.[1,3]

Infusion-related reactions - Headache, fever, chills, flushing, vertigo, pruritis, urticaria, chest pain, dyspnoea, hypertension or hypotension and palpitations. [1,3]

Infrequent: Anaphylaxis, depression, agitation, back pain, myalgia, arthralgia, increased ALT and AST. [1,3]

Rare: Aseptic meningitis, pleural effusion, jaundice, hepatitis, liver failure, delayed hypersensitivity. [1,3]

STORAGE

Store at 2 to 8ºC

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.

Concurrent use with other biological therapeutics, including anakinra and abatacept, are not recommended because of the possibility of increased immunosuppression and increased risk of infections and malignancies.[3]

Infliximab and immunosuppressants may contribute to increased infection and malignancy risk.

If Infliximab is initiated or discontinued in a patient taking warfarin, ciclosporin or theophylline, check levels as dose adjustment may be needed.

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

Related CAHS internal policies, procedures and guidelines

Adrenaline (epinephrine) - PCH Medication Monograph

Paracetamol – PCH Medication Monograph

Resuscitation and Responding to Clinical Deterioration.

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Useful resources (including related forms)

Australian consensus guidelines for the safe handling of monoclonal antibodies for cancer treatment by healthcare personnel

Pharmaceutical Benefits Scheme - Infliximab listing

This document can be made available in alternative formats on request for a person with a disability.

File Path:	W:\Safety & Quality\CAHS\CLOVERS MEDICAL Pharmacy\Procedures Protocols and Guidelines\Medication Monographs_Word\PCH.MED.Infliximab.docx		
Document Owner:	Chief Pharmacist		
Reviewer / Team:	Clinical Pharmacist, Consultant Gastroenterologist, Consultant Gastroenterologist, Consultant Rheumatologist, Acting Clinical Nurse Specialist, Gastroenterology, Clinical Nurse Manager, ACDF, Gastroenterology Liaison Nurse, Gastroenterology Liaison Nurse		
Date First Issued:	January/2016	**Last Reviewed:**	August/2023
Amendment Dates:		**Next Review Date:**	August/2026
Approved by:	CAHS Medication Safety Committee	**Date:**	Aug 2023
Endorsed by:	CAHS Drug & Therapeutics Committee	**Date:**	Sep 2023
Standards Applicable:	NSQHS Standards: NSMHS: N/A Child Safe Standards: N/A		

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