Specialised Medication - Infliximab Guideline

1. Guiding Principles

Provides guidance for the prescription and administration of Infliximab for **adult** patients.

This guideline must be used in conjunction with the associated mandatory MR173A WACHS Specialised Medication - Infliximab Pre-Infusion Checklist

Information in this guideline is applicable to Remicade® and the biosimilar product Inflectra®.

The brand(s) of infliximab stocked may vary across different regions.

> When prescribing a biologic/biosimilar, the **generic and tradename** of the intended biologic must be clearly written on the prescription. The brand administered and Batch must be recorded on the Pre-infusion checklist.
>
> This must take into account which biologic product is listed on the formulary for initiation of treatment, along with other responsibilities listed in Section 3 of the Western Australia Drug Evaluation Panel's Approach to Biosimilars Guideline.(1)
>
> Where a prescription is presented to pharmacy for the initiation of a biologic that is not listed on the formulary and an IPA has not been granted by the DTC, the pharmacist is to notify the prescriber of the product change.(1)

This infusion may only be administered when there is a doctor who is:

- familiar with this guideline
- aware of the patient receiving the infusion
- credentialed and appointed to the hospital site where the infusion is being administered
- willing and able to respond in the event of an emergency in the absence of a dedicated Medical Emergency Response (MER) team.

> For paediatric patients, refer to the Perth Children's Hospital – Pharmacy Manual (Infliximab) accessible via HealthPoint.

2. Guideline

Infliximab is a chimeric human-murine monoclonal antibody that binds to Tissue Necrosis Factor alpha (TNFα) and inhibits its activity. TNFα is a cytokine involved in inflammatory and immune responses and in the pathogenesis of rheumatoid arthritis, psoriasis and inflammatory bowel disease.(2)

2.1 Presentation

Vial containing 100mg Infliximab powder for intravenous infusion[3].

Alternatively, some WACHS Pharmacy Departments may purchase infusions prepared by sterile manufacturing facilities.

2.2 Indication

Availability of Infliximab is currently restricted to indications listed on the PBS on presentation of an approved PBS authority prescription or treatment of conditions approved under the WATAG WA Hospitals High-cost Medicine Formulary[4, 5].

- **Ulcerative colitis (UC)**:
  - Acute, severe UC – prescribed by a gastroenterologist or consultant specialising in gastroenterology.
  - Moderate to severe UC – prescribed by a gastroenterologist, physician specialising in gastroenterology, paediatrician, or specialised paediatric gastroenterologist.
- **Ankylosing spondylitis (AS)**:
  - Active AS – prescribed by a rheumatologist
- **Crohn's Disease**:
  - Complex, refractory fistulating Crohn's disease – gastroenterologist or consultant specialising in gastroenterology.
  - Severe Crohn's disease – prescribed by a gastroenterologist or consultant specialising in gastroenterology
  - Moderate to severe Crohn's disease – prescribed by a gastroenterologist, consultant specialising in gastroenterology, paediatrician or a paediatric gastroenterologist.
- **Psoriasis / Psoriatic arthritis**:
  - Severe psoriatic arthritis – prescribed by a rheumatologist or clinical immunologist.
  - Severe, chronic plaque Psoriasis – prescribed by a dermatologist.
- **Rheumatoid arthritis (RA)**:
  - Severe, active RA in combination with methotrexate – prescribed by a rheumatologist or clinical immunologist.

2.3 Contraindications[2, 3]

- Severe or untreated infections (sepsis, abscess, active tuberculosis, opportunistic infections, hepatitis B).
- Hypersensitivity reactions to Infliximab, any excipient contained or other murine proteins.
- Demyelinating disorders. e.g. multiple sclerosis – Infliximab may increase disease activity.
- Congestive heart failure (NYHA Class III-IV); Product Information states "do not initiate therapy in patients with congestive heart failure".
- TNF-alpha antagonists (e.g. infliximab) are contraindicated with anakinra.

Printed or saved electronic copies of this policy document are considered uncontrolled.
Always source the current version from WACHS HealthPoint Policies.

- History of lymphoproliferative disease within the last five years.
- Pregnancy. Limited data; avoid use, Australian category C
- Breastfeeding – limited data - is not recommended during or for six months after therapy cessation.

2.4 Precautions[2, 3, 6]

- Previous adverse event associated with Infliximab infusion.
- Break/interruption in treatment – increased risk of infusion-related effects.
- Any signs of active/ recent infections
- Heart failure – use cautiously in mild disease; see contraindications above.
- Respiratory disease – increased risk of interstitial lung disease.
- Psoriasis – exacerbation and change in type of psoriasis.
- Initiating treatment in patients with a history of malignancy or continuing therapy in patients who have developed malignancy.
- Concurrent administration with another cytokine modulator (TNF-alpha antagonist, abatacept, rituximab, tocilizumab).
- Surgery – increased risk of perioperative infections.
- The development of lupus-like syndrome, neurological disorders, haematological disorders and altered liver function (see Product Information for further information).
- Administration of live vaccines – risk of clinical infection, including disseminated infections.
- Therapeutic infectious agents (e.g. BCG bladder instillation in oncology) – not recommended.
- An annual skin check to detect early skin cancer is recommended.

2.5 Dosage[3]

Dosage is based on weight and differs depending on indication:

For ADULT patients:

Condition	Usual Dose Recommendation	Frequency
Rheumatoid arthritis	Initially, 3mg/kg as an intravenous infusion (may be increased by 1.5mg/kg increments after the first three infusions to a maximum 7.5mg/kg)	0, 2, 6 then 8 weekly
Ankylosing spondylitis	5mg/kg as an intravenous infusion	**0, 2, 6 then **6** weekly**
Psoriatic arthritis	5mg/kg as an intravenous infusion	0, 2, 6 then 8 weekly

Printed or saved electronic copies of this policy document are considered uncontrolled.
Always source the current version from WACHS HealthPoint Policies.

Condition	Usual Dose Recommendation	Frequency
Psoriasis	5mg/kg as an intravenous infusion	0, 2, 6 then 8 weekly
Crohn's disease – moderate to severe	5mg/kg as an intravenous infusion (may be increased after the first three infusions to a maximum 10mg/kg)	0, 2, 6 then 8 weekly
Crohn's disease – refractory fistulating	5mg/kg as an intravenous infusion (may be increased after the first three infusions to a maximum 10mg/kg)	0, 2, 6 then 8 weekly
Ulcerative colitis	5mg/kg	0, 2, 6 then 8 weekly

2.6 Administration[3, 7, 8]

Specific Considerations for Handling of Monoclonal Antibodies[9]

- Prepare using aseptic technique.
- Personal Protective Equipment (PPE) - A respirator mask (N95) and protective eye wear should be worn during preparation. These PPE should also be worn during administration processes for IV formulations where the dis/connecting of administration lines may present a risk of aerosolisation, particularly with new or inexperienced staff.
- Closed system drug transfer devices are not required for the preparation of doses for administration but can be utilised by individual sites based on availability.
- All waste is to be handled as per standard procedures for parenterally administered agents.
- Avoid preparation and handling if pregnant, breastfeeding or immunosuppressed.

2.6.1 Reconstitute each vial with 10mL Water for Injection, by injecting the water down the side of the vial and swirl gently to dissolve - **DO NOT SHAKE**. The solution produced contains Infliximab 10mg/mL. Allow to stand for five minutes to disperse any foam that forms. Prepared solution is to be colourless to light yellow.

2.6.2 Calculate the volume required of the reconstituted Infliximab to provide the prescribed dose.

2.6.3 Withdraw and discard the volume of sodium chloride 0.9% calculated in step 2 from a 250mL **sodium chloride 0.9% bag**.

2.6.4 Add the required dose of Infliximab to the sodium chloride 0.9% bag.

2.6.5 **Do NOT** use if the vials contain visible particulates or are discoloured.

2.6.6 **Do NOT** administer concurrently with any other IV medication.

Printed or saved electronic copies of this policy document are considered uncontrolled.
Always source the current version from WACHS HealthPoint Policies.

2.6.7 Infuse using an infusion set with an in-line 1.2 micron (or less) low protein-binding filter.

2.6.8 Administer as an intravenous infusion **over TWO hours (or more).**

2.6.9 All patients administered infliximab infusions are to be observed for two hours post-infusion for side effects (medications, an artificial airway and other appropriate materials must be available for the treatment of these effects). See Section 2.8 below.

In carefully selected patients who have tolerated at least three initial two-hour infusions, consideration may be given to administering subsequent infusions over a period of not less than one hour.

2.7 Storage[3]

Store vials between 2 and 8 deg C.

The product information states that the infusion should begin within 3 hours after preparation and the solution should not be stored for reuse (due to potential for microbiological hazard, and the absence of any preservative).

2.8 Infusion reactions

Infusion reactions vary in severity and management is case dependent. They are typically defined as any adverse event occurring during an infusion or up to one hour after the infusion.[3]

Infusion-related effects in patients were more likely to occur during the first infusion and less likely on subsequent infusions.[3]

Re-administration of infliximab after a period of no treatment has resulted in a higher incidence of infusion reactions relative to regular maintenance treatment[3].

Development of antibodies to infliximab may result in delayed hypersensitivity reactions (including fever and arthralgia) and reduced response with subsequent doses.[6] These may occur 3-12 days after the infusion.[2]

In all cases, the infusion must be interrupted immediately[3], and consult the prescribing doctor.

2.8.1 'Mild' reactions

Symptoms include: Fever/chills, pruritus/urticaria, headache, flu-like symptoms, and gastrointestinal disturbances.

Slowing the infusion rate may control mild symptoms. Patients should be managed on an individual case basis but reduction in infusion rates and symptom management with medications such as paracetamol, antihistamines or glucocorticoids (e.g. dexamethasone) may allow the completion of the infusion[6].

Patients who have experienced mild infusion reactions may be pre-treated with an anti-histamine, paracetamol and/or corticosteroids prior to subsequent infusions.[3]

2.8.2 'Severe' hypersensitivity/ anaphylactic reactions

Symptoms include: Cardiopulmonary symptoms such as chest pain, hypotension or hypertension, dyspnoea +/- the symptoms experienced in 'mild' reactions.

Printed or saved electronic copies of this policy document are considered uncontrolled.
Always source the current version from WACHS HealthPoint Policies.

The infusion should be **stopped** immediately and the prescriber informed. Patients should be managed on an individual case basis with therapy including (but not limited to) adrenaline, antihistamines, glucocorticoids (e.g. dexamethasone), intravenous fluids, vasopressors, oxygen, bronchodilators and paracetamol.

Patient management should be escalated according to the deteriorating patient protocol as per the observation chart. For guidance on the management of anaphylaxis, refer to the WACHS Medication Administration Policy: Anaphylaxis Flowchart (Appendix 7).

Patients who experience a severe hypersensitivity/ anaphylactic reaction should have the details recorded as a Medication Alert for entry into webPAS (using a regional Medical Alert Notification form), clearly documented in the patient integrated notes and recorded on the medication chart and a red ID (allergy) band applied. Refer to the WA Clinical Alert (Med Alert) Policy).

Where applicable, the WACHS doctor should discuss this event with the referring specialist.

2.8.3 Monitoring requirements

- Record temperature, pulse, respiration and blood pressure prior to commencement and every 30 minutes for the duration of the infusion.
- Monitor closely during and for **two** hours post infusion for the development of an infusion reaction (**see above**)
- Check the IV regularly to ensure correct flow rate and cannula position.

3. Roles and Responsibilities

The **Nurse Unit Manager / Senior Nursing Staff** is responsible for:

- receiving a valid referral and documentation including a valid PBS prescription as required from the prescribing consultant or other treating doctor
- informing the prescriber, if external to the hospital, that the infusion has been administered and any related outcomes (e.g. adverse events).

The **Medical Officer** is responsible for:

- completing orders for the medication on the appropriate chart. When prescribing a biologic/biosimilar, the prescriber has the following responsibilities[1]:
  - ensuring the **generic** and **trade name** of the intended biologic is written clearly on the prescription
  - being aware of which biologic product is listed on the formulary for initiation of treatment
  - knowing which product the patient is being treated with and have record of an IPA for an alternative, non-formulary biologic if applicable
  - playing an active role in the pharmacovigilance of biologics/biosimilars by identifying, monitoring and reporting adverse events
- ensuring the appropriate venous access is inserted if required
- reviewing recorded observations regularly and alter treatment where required
- completing all treatment and duties within scope of practice.

Printed or saved electronic copies of this policy document are considered uncontrolled.
Always source the current version from WACHS HealthPoint Policies.

The **Registered Nurse** is responsible for:

- recording observations as directed and notify the medical officer of any abnormal reading
- preparing the medication in readiness for treatment checking with another registered nurse, medication endorsed enrolled nurse or medical officer
- completing all nursing duties for the patient within scope of practice
- completing all required documentation.

4. Compliance

Failure to comply with this policy document may constitute a breach of the WA Health Code of Conduct (Code). The Code is part of the Integrity Policy Framework issued pursuant to section 26 of the *Health Services Act 2016* (WA) and is binding on all WACHS staff which for this purpose includes trainees, students, volunteers, researchers, contractors for service (including all visiting health professionals and agency staff) and persons delivering training or education within WACHS.

WACHS staff are reminded that compliance with all policies is mandatory.

5. Evaluation

Adverse events and clinical incidents relating to the administration of Infliximab infusions are to be zero (0).

6. Standards

National Safety and Quality Health Service Standards (Second edition 2017) - 1.7, 1.10, 3.9, 4.3, 4.4, 4.7, 4.8, 4.11, 4.15, 5.10, 5.11, 6.5, 8.4, 8.5, 8.6.

7. Legislation

Medicines and Poisons Act 2014

8. References

1. Western Australia Drug Evaluation Panel. Statewide Medicines Formulary: Approach to Biosimilars. 2016 (Jan) Accessed: 12/10/2016.
2. Australian Medicines Handbook. Adelaide, South Australia: Australian Medicines Handbook Pty. Ltd.; 2016.
3. Remicade (Approved Product Information) [database on the Internet]. MIMS Australia Pty. Ltd. 2016 [cited 7/9/2016].
4. (WATAG) Western Australian Therapeutic Advisory Group. WA Hospitals High-Cost Medicine Formulary. Infliximab monograph [serial on the Internet].
5. Pharmaceutical Benefits Scheme and Repatriation Pharmaceutical Benefits Scheme Section 85 Supply Data [database on the Internet] 2016.

Printed or saved electronic copies of this policy document are considered uncontrolled.
Always source the current version from WACHS HealthPoint Policies.

6. Getting to know your rheumatological drugs (Amended February 2015). Therapeutic Guidelines: Rheumatology. West Melbourne, Australia: Therapeutic Guidelines Ltd.; July 2016 edition.
7. Pharmacy Department. Day infusion information - patient monitoring, handling Mabs, management of infusion reactions. Bunbury, Western Australia: WACHS-SW; Page last updated 24/8/2016 [Accessed: 14/9/2016].
8. Australian Injectable Drugs Handbook. Collingwood, Australia: Society of Hospital Pharmacists (SHPA); 2016.
9. Alexander M., J. King, Bajel A., C. Doecke, P. Fox. Australian consensus guidelines for the safe handling of monoclonal antibodies for cancer treatment by healthcare personnel. 2014.

9. Related Forms

MR173A WACHS Specialised Medication - Infliximab Pre-Infusion Checklist

10. Related Policy Documents

WACHS High Risk Medications Procedure

WACHS Medication Administration Policy

11. Related WA Health Policies

WA Clinical Alert (Med Alert) Policy

WA High Risk Medication Policy

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

Contact:	WACHS Chief Pharmacist		
Directorate:	Medical Services	**TRIM Record #**	ED-CO-13-12129
Version:	5.00	**Date Published:**	04 February 2021

Copyright to this material is vested in the State of Western Australia unless otherwise indicated. Apart from any fair dealing for the purposes of private study, research, criticism or review, as permitted under the provisions of the *Copyright Act 1968*, no part may be reproduced or re-used for any purposes whatsoever without written permission of the State of Western Australia.

Printed or saved electronic copies of this policy document are considered uncontrolled.
Always source the current version from WACHS HealthPoint Policies.