Specialised Medication – Tocilizumab Guideline

1. Guiding Principles

This guideline provides guidance for the prescription and administration of Tocilizumab for **adult** patients by infusion or subcutaneous injection.

This guideline must be used in conjunction with the associated mandatory MR173F WACHS Specialised Medication - Tocilizumab Pre-Infusion Checklist.

Information in this guideline is specific to Actemra®.

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

- familiar with specified guidelines
- 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 – Medication Management Manual - Tocilizumab (accessible via HealthPoint).

2. Guideline

Tocilizumab inhibits the activity of interleukin-6 (IL-6) by binding to its receptors. IL-6 is a cytokine that is involved in the pathogenesis of Rheumatoid Arthritis (RA).[1]

2.1 Presentation[2]

Vials contain 20mg/mL of concentrated Tocilizumab solution (available in 4mL, 10mL and 20mL) for dilution prior to intravenous infusion.
Alternatively, some WACHS Pharmacy Departments may purchase infusions prepared by sterile manufacturing facilities.

Subcutaneous injection is presented in a prefilled syringe containing 162mg /0.9 ml Tocilizumab.

2.2 Indication[3]

Availability of Tocilizumab is currently restricted to indications listed on the PBS on presentation of an approved PBS authority prescription.

- Rheumatoid arthritis (RA) – prescribed by a rheumatologist

2.3 Contraindications[1,2]

- Hypersensitivity reactions to Tocilizumab, any component contained in the product, Chinese hamster ovary cell products or other recombinant human or humanised antibodies

- Serious or untreated infection
- Not recommended for use with other biological agents including TNF antagonists, anakinra, rituximab and abatacept.

2.4 Precautions[1,2]

Precautions for the use of Tocilizumab are extensive. Please refer to the Product Information for the complete list and full details. Below is a summary of important points:

- Serious and sometimes fatal infections have been reported in patients receiving Tocilizumab. If a patient develops a serious infection, treatment is to be interrupted until resolution.
- Patients are to be screened for latent tuberculosis (TB), and appropriately treated if necessary, prior to initiation. Patients are to be instructed to seek medical advice if they develop any symptoms suggestive of TB.
- Viral reactivation (hepatitis B) has been reported with biological therapies.
- Pregnancy. Avoid use unless 'clearly necessary' (no data); Australian category C. Use of appropriate contraception during and for several months after treatment is recommended.
- Breastfeeding. It is unknown whether Tocilizumab is excreted into human breast milk. Efficacy and safety in lactating women has not been established. The decision whether to continue/ discontinue treatment with Tocilizumab or to continue/ discontinue breastfeeding is on an individual case basis.
- Decreases in neutrophil and platelet count have occurred in patients that are treated in combination with methotrexate. Neutrophil and platelet count is to be monitored 4-8 weeks after starting therapy then as per standard practice. Dose reductions may be necessary.
- Transient elevations of hepatic transaminases have been reported. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels are to be monitored every 4-8 weeks for the first 6 months then every 12 weeks. Dose reductions may be necessary.
- Diverticular perforation as a complication of diverticulitis has been reported in RA patients. Tocilizumab is to be used with caution in patients with a previous history of intestinal ulceration or diverticulitis. Patients presenting with symptoms of such are to be promptly identified and managed appropriately.

2.5 Dosage[1,2]

Intravenous Infusion:

Condition	***Usual Dose Recommendation	Frequency
Rheumatoid arthritis (adults)	8mg/kg (up to maximum of 800mg)	Every 4 weeks

*** It is possible, due to the results of pathology (neutrophil count, platelet count, liver enzyme abnormalities) that a reduced dose may be prescribed. This is only to be under the direction of the treating rheumatologist. Any query relating to the dose for the patient is to be referred to the treating rheumatologist.

Subcutaneous injection:

Condition	***Usual Dose Recommendation	Frequency
Rheumatoid arthritis (adults)	162mg weekly If transitioning from the infusion 4mg/kg – 162mg every 2 weeks 8mg/kg – 162mg weekly.	Weekly

The first dose of the subcutaneous injection must be given under medical observation. May be suitable for self-administration in selected patients however the potential for anaphylaxis must be considered.

2.6 Administration[2,4,5]

Intravenous Infusion
Specific considerations for handling of monoclonal antibodies:

- Prepare using aseptic technique.
- Personal Protective Equipment (PPE) - A respirator mask (N95) and protective eyewear is to be worn during preparation.
- These PPE is also to 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 Calculate the volume required of the Tocilizumab concentrate to provide the prescribed dose.
2.6.2 Withdraw and discard the volume calculated in step 1 from a **100mL sodium chloride 0.9% bag.**
2.6.3 Under aseptic conditions, add the prescribed dose of Tocilizumab to the sodium chloride 0.9% bag.
2.6.4 To mix the infusion, gently invert to avoid foaming
2.6.5 Only solutions that are clear to opalescent, colourless to pale yellow and free of visible particles can be infused.
2.6.6 DO NOT administer concurrently with any other IV medication.
2.6.7 Infuse over ONE hour (protect from light).

Subcutaneous Infusion:

- Allow the syringe to reach room temperature for 20-30minutes

- Inject into the thigh, abdomen or upper arms.
- Do not shake before administration

2.7 Storage[2,4]

Store vials between 2 and 8 deg C, protected from light.

Following dilution, infuse immediately, or commence infusion within 24 hours of preparation, if stored between 2 and 8 deg C.

Syringe for subcutaneous injection are stored between 2 and 8 deg C within the supplied carton to protect from light.

Once removed from the fridge the subcutaneous syringe must be stored below 30 deg C and administered within 8 hours.

2.8 Infusion reactions[2]

Infusion related adverse effects were reported in 6.9% of patients during clinical trials. The adverse event reported during the infusion was primarily hypertension whereas headaches and skin reactions were reported within 24 hours of completing the infusion. These events did not prevent further treatment.

2.8.1 'Mild' infusion reactions

These reactions involve symptoms such as (but not limited to): Headache, nausea, dizziness, fever, flushing, pruritis, urticaria, muscle pain, flu-like 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.

In most circumstances, when the symptoms have completely resolved, the infusion can be recommenced at a 50% reduction in rate.[2]

2.8.2 'Severe' hypersensitivity/ anaphylactic reactions

These reactions involve symptoms such as (but not limited to): Anaphylaxis, hypo/hypertension, chest pain, dyspnoea, swelling, severe pruritis

Patient management should be:

- escalated according to the Observation and response chart criteria
- in accordance with Adverse Drug Reaction section of the WACHS Medication Prescribing and Administration Policy.

For guidance on the management of anaphylaxis, refer to the ASCIA Guidelines – Acute management of anaphylaxis.

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

Hypersensitivity reactions:

Serious hypersensitivity reactions including anaphylaxis, hypotension, dyspnoea, swelling, flushing and pruritus have occurred with Tocilizumab treatment.

In the event of a 'severe' reaction, **STOP** the infusion immediately. Consult the prescriber and treat the patient according to symptoms. This may include, but is

not limited to adrenaline, antihistamines, glucocorticoids, intravenous fluids, vasopressors, oxygen, bronchodilators and paracetamol.

In all cases consult the prescribing doctor.

2.9 Monitoring requirements

- The minimum physiological observations to be documented as recommended by the approved product information or as a minimum pre infusion, mid infusion, post infusion and as clinically indicated during the infusion based on patient response (e.g. light-headedness, flushing).
- Record temperature, pulse, respiration rate and blood pressure prior to commencement of the infusion and at completion.
- Check the IV regularly to ensure correct flow rate and cannula position.
- Monitoring should continue for at least 30 minutes post infusion.

3. Roles and Responsibilities

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

- receiving 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 all treatment and duties within scope of practice.

The **Registered Nurse** is responsible for completing all nursing duties for the patient within scope of practice.

Where supplied by the pharmacy department, the **Chief Pharmacist** is responsible to ensure the prescription is processed for payment via PBS.

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 Tocilizumab infusions are to be zero (0).

6. Standards

National Safety and Quality Health Service Standards
Clinical Governance Standard: 1.7, 1.10
Precenting and Controlling Healthcare Associated Infection Standard: 3.9
Medication Safety Standard: 4.3, 4.4, 4.7, 4.8, 4.11, 4.15
Comprehensive Care Standard: 5.10, 5.11
Communicating for safety Standard: 6.5
Recognising and Responding to Acute Deterioration Standard: 8.4, 8.5, 8.6.

7. Legislation

Medicines and Poisons Act 2014 (WA)
Medicines and Poisons Regulations 2016 (WA)

8. References

1. Australian Medicines Handbook Pty Ltd [Accessed: 18 March 2021]
2. MIMS Online [Accessed: 18 March 2021]
3. Pharmaceutical Benefits Scheme (PBS) [Accessed: 18 March 2021]
4. Australian Injectable Drugs Handbook [Accessed: 18 March 2021]
5. Alexander M, King J, Bajel A, Doecke C, Fox P, Lingaratnam S, et al. Australian consensus guidelines for the safe handling of monoclonal antibodies for cancer treatment by healthcare personnel [Internet].

9. Related Forms

MR173F WACHS Specialised Medication - Tocilizumab Pre-Infusion Checklist

10. Related Policy Documents

WACHS Aseptic Technique Policy
WACHS High Risk Medications Procedure
WACHS Medication Handling and Accountability Policy
WACHS Medication Prescribing and Administration Policy
WACHS Safe Handling and Administration of Monoclonal Antibodies Guideline

11. Related WA Health Policies

MP 0053/17 WA Clinical Alert (Med Alert) Policy
MP 0131/20 WA High Risk Medication Policy

12. WA Health Policy Framework

Clinical Governance, Safety and Quality Policy Framework

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

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