Specialised Medication - Intravenous Tocilizumab for Cytokine Release Syndrome from bi-specific T-cell engaging therapies guideline

1. Purpose

This document provides guidance for the prescribing, preparation, and administration of tocilizumab to **adult non-pregnant** patients for the treatment of cytokine release syndrome (CRS) resulting from treatment with bi-specific T-cell engaging therapies.

Tocilizumab is one component of treating CRS. Refer to the causative bi-specific antibody eviQ treatment protocol, product information and treating consultant in the first instance when CRS is suspected.

For management of CRS in paediatric patients refer to Perth Children's Hospital (PCH) Tocilizumab monograph.

For cancer treatment protocols refer to Cancer Treatments Online | eviQ.

Refer to the product-specific medication monographs for full prescribing information, available from AusDI.

2. Guideline [1, 2]

Tocilizumab is a recombinant humanised monoclonal antibody of the immunoglobulin IgG1. Tocilizumab binds to IL-6 receptors and inhibits the IL-6 signalling pathway. Inhibition of IL-6 results in down-regulation of T-Cell activation and thereby it's inflammatory pathogenesis.

CRS usually occurs within the first few weeks of initiation of a bispecific T-cell engager and within 48 hours of the preceding dose (generally in cycle 1-2 during ramp up dosing or with the first full dose).

The goal of CRS management is to prevent life threatening sequelae. Tocilizumab is one of many medications that may be used in the management of CRS. Immediate recognition and management are essential. Differential bi-specific antibody class wide adverse effects such as infection, sepsis and haemophagocytic lymphohistiocytosis (HLH) share many overlapping clinical and laboratory features with CRS. Broad spectrum antibiotics should be initiated without delay along with CRS-directed therapy.

See Medical management of Neutropenic Sepsis / Febrile Neutropenia in adult Oncology / Haematology patients Procedure and Nursing Management of the Neutropenic Adult Haematology and Oncology Patient Procedure.

Management of all patients, presenting with signs and symptoms of CRS is to be discussed with the treating haematologist or medical oncologist or as per the regional medication specific flashcard and/or service level agreement to the relevant tertiary hospital on call service.

2.1 Product [2, 3, 4]

Tocilizumab (Actemra ®) concentration solution (20 mg/mL) for intravenous (IV) infusion is available in 80 mg/4 mL, 200 mg/10 mL and 400 mg/20 mL vials.

Tocilizumab for CRS is non-PBS but is listed on the WA Adult Medicines - WA Statewide Medicines Formulary.

Regional availability specifics – contact your pharmacy department or refer to Formulary One imprest location list.

2.2 Contraindications [2, 3]

Tocilizumab is contraindicated in patients with:

- a previous hypersensitivity reaction to tocilizumab, Chinese hamster ovary cell products or other recombinant human or humanised antibodies.

2.3 Precautions [2, 3]

Precautions to be considered:

- Patients with an active infection.
- Patients with a history of serious or untreated infection e.g. sepsis, abscess, hepatitis B (prior to initiation of antivirals) or active tuberculosis (TB) (prior to completing TB treatment).
- Vaccination status - live and live attenuated vaccines must not be given concurrently. Delay any live vaccinations and consider if any have been recently administered. See The Australian Immunisation Handbook for advice.
- Viral reactivation has been reported following administration. Tocilizumab is not recommended in patients with HIV, hepatitis B, prior hepatitis C or symptomatic Epstein-Barr Virus. Appropriate pre-screening for these infections should occur. In cases of life-threatening CRS, blood requests for hepatitis B, C or HIV should not delay the administration of tocilizumab. Appropriate prophylaxis can be given for patients deemed to be at high risk of reactivation of disease.
- Tocilizumab can cause neutropenia and thrombocytopenia. Monitor when neutrophils are below 2 x 10^9/L and platelets below 50 x 10^9/L, however for CRS treatment, can still be given at the discretion of the treating haematologist or medical oncologist.

2.4 Dosage [2, 3, 5]

Dosing provided is based on the product information, clinical advice should be sought from the treating haematologist, medical oncologist or associated tertiary contact, as dosing may vary and be specific to a bi-specific antibody or an eviQ cancer treatment protocol.

- Dosing for patients >30 kg: 8 mg/kg (maximum of 800 mg) as a single dose.
- Dosing may be repeated every 8 hours (maximum of 3 infusions in 24 hours) if there is no response to initial therapy, up to 4 doses in total may be given.
- The treating team must be involved, and the patient will need transfer to a tertiary center if there is no response to the initial dose.
- Pre-medications are not routinely administered but may be considered if a patient has had a previous infusion related reaction.

2.5 Preparation & administration [2, 3, 4, 5, 6]

Preparation

Tocilizumab is a monoclonal antibody and is not a hazardous medication as defined by the National Institute for Occupational Safety and Health (NIOSH). Although the risk of exposure is low, minimum personal protective equipment (PPE) for preparation and administration of monoclonal antibodies (goggles, gloves & N95 mask) is required as per the WACHS Safe Handling, Preparation and Administration of Monoclonal Antibodies Policy.

Tocilizumab may be prepared at the ward level in a treatment room as per Monoclonal Antibodies Occupational Exposure Handling & Preparation Risk Assessments .

- Using aseptic technique and the appropriate PPE above, withdraw the required dose from the vial(s) and add to a 100 mL sodium chloride 0.9% infusion bag. Closed system transfer devices (CSTD's) are not required.
- Do not shake the vial(s) or infusion bag. Gently invert to dilute the added solution.
- Label and administer immediately. If there is a delay in administration store at 2-8°C for up to 24 hours. Ensure preparation details including the time and dose prepared are on the label in accordance with WACHS Medication Prescribing and Administration Policy and the National Standard for User-Applied Labelling of Injectable Medicines, Fluids and Lines.

Administration

Prescribe on WA Health MR860 pre-filled Tocilizumab for CRS chart. Available from FSH Pharmacy - Actemra® (TOCILIZUMAB) for Cytokine Release Syndrome (CRS).pdf - All Documents. Alternatively MR176 Intravenous Fluid Treatment may be used.

Administer as intravenous infusion over 60 minutes. Tocilizumab is only compatible with sodium chloride 0.9%.

For patients with previous hypersensitivity reactions, prescribers may consider the use of premedication administered 30 minutes to 1 hour prior to the infusion including paracetamol and antihistamine.

ATTENTION

In the event of anaphylaxis.

Stop the infusion, contact the prescriber and permanently discontinue tocilizumab.

In the event of an infusion reaction, stop the infusion and contact the prescriber or an onsite medical practitioner for assessment and advice on further action (for example abandon, pre-medicate or rechallenge). If the patient meets medical emergency response (MER) criteria, treat as a per regional procedure for deteriorating patients.

2.6 Storage [2, 4]

Vials:
- Store at 2 °C to 8 °C.
- Protect from light.

Infusion Solution:
- The prepared infusion solution of tocilizumab is physically and chemically stable in 0.9% sodium chloride solution at 30°C for 24 hours.
- To reduce microbiological hazard, the prepared infusion should be used immediately. If storage is necessary, hold at 2°C to 8°C for not more than 24 hours.

2.7 Adverse effects [2, 3]

Relevant to this medicine guideline, refer to product information for a full list of adverse effects.

- Infections, due to immunosuppression. Including cellulitis, herpes simplex, herpes zoster, upper respiratory infections and opportunistic infections including TB, invasive fungal infections and pneumocystis jirovecii.
- Neutropenia
- Increased liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST)
- Infusion related reactions
- Gastritis, mouth ulcers
- Hypersensitivity reactions, including anaphylaxis

2.8 Monitoring [2, 3]

Monitoring is required before, during and for 30 minutes after completion of infusion, as follows:
- Temperature, blood pressure, oxygen saturation and pulse rate.
- Monitor for hypersensitivity reactions during the infusion and for 30 minutes following the completion of the infusion.
- Signs of an infusion hypersensitivity reaction include bronchospasm, urticaria and angioedema.
- Anaphylaxis has been reported (0.2 %). Medications for managing severe hypersensitivity reactions, including anaphylaxis, should be available for immediate use in the event of an adverse event.
- Laboratory inflammatory markers C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) may be suppressed by tocilizumab.
- Full blood count, ALT and AST as clinically required by the haematologist or medical oncologist.

Guidelines are designed to provide staff with evidence-based recommendations to support appropriate actions in specific settings and circumstances. As such, WACHS guidelines should be followed in the first instance. In the clinical context, where a patient's management should vary from an endorsed WACHS guideline, this variation and the clinical opinion as to reasons for variation must be documented in accordance with the

Documentation Clinical Practice Standard. WACHS staff are reminded that compliance with all policies and procedures is mandatory.

3. Roles and Responsibilities

The **Medical Officer** is responsible for:
- appropriate prescribing, monitoring and review of patients per this guideline
- ensuring that all orders are documented on a WACHS endorsed medication chart
- ensuring that all orders are complete and unambiguous.

Nurses are responsible for:
- appropriate preparation and administration of tocilizumab per this guideline
- monitoring of patients, including recording observations and escalation of care as per the MR140A WACHS Adult Observation and Response chart (A-ORC).

Pharmacists are responsible for:
- reviewing a charted order and endorsing as suitable to administer
- escalating any issues with regards to prescription or administration
- ensuring appropriate supply arrangements.

All staff are required to comply with the directions in WACHS policies and procedures as per their roles and responsibilities. Guidelines are the recommended course of action for WACHS, and staff are expected to use this information to guide practice. If staff are unsure which policies procedures and guidelines apply to their role or scope of practice, and/or are unsure of the application of directions they should consult their manager in the first instance.

4. Monitoring and Evaluation

Adverse events and clinical incidents relating to medications are to be reported via the approved clinical incident management system (CIMS) e.g. DATIX, and managed as per the WACHS Medication Prescribing and Administration Policy and the MP0122/19 Clinical Incident Management Policy. The WACHS Medication Safety Committee and regional Medicines and Therapeutics Committees reviews clinical incident data relevant to medications. CIMS involving tocilizumab will be used to monitor and evaluate the effectiveness of this guideline.

This guideline will be reviewed as required to determine effectiveness, relevance and currency. At a minimum it will be reviewed every five years by WACHS Pharmacy Cancer Services.

5. References

1. Lee, D.W., B.D. Santomasso, F.L. Locke, et al. 2019. "ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells" Biol Blood Marrow Transplant 25(4):625638 https://doi.org/10.1016/j.bbmt.2018.12.758
2. Aus DI [Internet] Actemra Product Information. Modified 2 Sept 2022 [cited 10 Sep 2025] Available from: Actemra - AusDI

3. Australian Medicines Handbook [Internet]. Tocilizumab. Modified 2025 July [10 Sep 2025] Available from: Tocilizumab - Australian Medicines Handbook
4. SHPA. Australian Injectable Drugs Handbook 9th Edition. Modified 2025 Jun 16. Available from: AIDH - TOCILIZUMAB
5. Sir Charles Gairdner Osborne Park Health Care Group. Tocilizumab For Cytokine Release Syndrome. Nedlands; 2023. Available from: https://healthpoint.hdwa.health.wa.gov.au/policies/Policies/NMAHS/SCGH/SCGH.MMG.Tocilizumab_for_cytokine_release_syndrome.pdf
6. NIOSH [2024]. NIOSH list of hazardous drugs in healthcare settings, 2024. By Ovesen JL, Sammons D, Connor TH, MacKenzie BA, DeBord DG, Trout DB, O'Callaghan JP, Whittaker C. Cincinnati, OH: U.S. Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2025-103 (Supersedes 2016-161), NIOSH List of Hazardous Drugs in Healthcare Settings, 2024.

6. Definitions

Term	Definition
Bi-specific antibody	Bispecific antibodies are proteins that are designed to bind to two different targets at the same time. This differs from traditional monoclonal antibodies which can only bind to one target. Bispecific antibodies are designed to bind to a variety of targets and can be T-cell or non-T-cell engaging.
Closed system transfer devices (CSTD)	Devices used for personnel protection when preparing and/or administering hazardous medicines.
Cytokine release syndrome (CRS)	CRS is an acute systemic inflammatory response characterised by fever. T-cell engaging therapies, such as T-cell engaging bispecific antibodies, can set off a cascade of events which leads to an excessive and rapid release of cytokines into the blood stream, resulting in (CRS).
eviQ	An Australian developed online resource that provides evidence-based cancer treatment protocols and information for health professionals.

7. Document Summary

Coverage	WACHS wide
Audience	Clinical Staff in Cancer Services and Emergency departments
Records Management	Clinical: Health Record Management Policy
Related Legislation	• Medicines and Poisons Act 2014 (WA) • Medicines and Poisons Regulations 2016 (WA)
Related Mandatory Policies / Frameworks	• MP0122/19 Clinical Incident Management Policy • Clinical Governance, Safety and Quality Framework
Related WACHS Policy Documents	• Documentation Clinical Practice Standard • High Risk Medications Procedure • Medical management of Neutropenic Sepsis / Febrile Neutropenia in adult Oncology / Haematology patients Procedure • Medication Prescribing and Administration Policy • Nursing Management of the Neutropenic Adult Haematology and Oncology Patient Procedure • Safe Handling, Preparation and Administration of Monoclonal Antibodies Policy
Other Related Documents	• 3500-Cytokine release syndrome (CRS) | eviQ
Related Forms	• MR140A WACHS Adult Observation and Response Chart (A-ORC) • MR176 Intravenous Fluid Treatment • MR860 FSH Pharmacy - Actemra® (TOCILIZUMAB) for Cytokine Release Syndrome (CRS).pdf - All Documents
Related Training	Nil
Aboriginal Health Impact Statement Declaration (ISD)	ISD Record ID: 5057
National Safety and Quality Health Service (NSQHS) Standards	1.27, 4.13, 4.14, 4.15

8. Document Control

Version	Published date	Current from	Summary of changes
1.00	16 June 2026	16 June 2026	New guideline

9. Approval

Policy Owner	WACHS Executive Director Nursing & Midwifery
Co-approver	Executive Director Clinical Excellence
Contact	WACHS Cancer Services Coordinator of Nursing
Business Unit	WACHS Cancer Services
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This document can be made available in alternative formats on request.