MONOGRAPH

Tocilizumab

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

Cytokine modulator – inhibits activity of interleukin-6.[4]

INDICATIONS AND RESTRICTIONS

Complex Authority Item (HSD S100) requires written approval from Medicare PRIOR to initiation of therapy. All Non-PBS indications require an Individual Patient Approval (IPA) from the CAHS Drugs and Therapeutics Committee (DTC) unless noted below:

HSD S100 / PBS Authority:

- Polyarticular Juvenile Idiopathic Arthritis (JIA) in patients of 2 years of age and over. [3, 4]
- Systemic JIA in patients of 2 years of age and over. [3, 4]

For S100 HSD / PBS Authority criteria see here.[3]

Approved non-PBS use (IPA not required):

- Treatment of severe or life-threatening cytokine release syndrome (CRS).

IPA required:

- Treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [COVID-19].
- IPA MUST be approved by DTC prior to commencement

CONTRAINDICATIONS

- Hypersensitivity to tocilizumab or any component of the formulation, including murine proteins.[1]

PRECAUTIONS

- Patients with an active infection (with the exception of SARS-CoV-2 [COVID-19]).[1, 4, 5]
- Patients with a history of serious or untreated infection, e.g. sepsis, abscess, hepatitis B, active tuberculosis (TB) (before completing TB treatment).
- Patients with any underlying conditions that predispose a patient to infection (e.g. diabetes, diverticulitis) should be closely monitored.
- Use with other cytokine modulators is not recommended as this can increase the risk of infection.
- Tocilizumab can cause neutropaenia, do not start when absolute neutrophil count (ANC) < 2 x 10^9/L and do not use when ANC is below 0.5 x 10^9/L unless patient has Macrophage Activation Syndrome (MAS) or CRS where the decision to treat with tocilizumab rests with the treating Consultant.
- Tocilizumab can cause thrombocytopenia, use with caution when platelets are < 100 x 10^9/L and do not use when platelets are below 50x10^9/L unless patient has MAS or CRS where the decision to treat with tocilizumab rests with the treating Consultant.
- May increase hepatic alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels during treatment, therefore careful monitoring is required. Commence tocilizumab therapy with caution if aminotransferases are greater than 1.5 times the upper limit of normal (ULN). If the patient has CRS the decision to treat rests with the treating Consultant.
- Live vaccines should not be given to patients receiving tocilizumab; vaccines may need to be delayed and consideration should be given if any live vaccines have been recently administered.[4]

FORMULATIONS

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

- 400 mg / 20 mL vial
- 200 mg / 10 mL vial
- 80 mg / 4 mL vial
- 162 mg / 0.9 mL prefilled subcutaneous pen
- 162 mg / 0.9 mL prefilled subcutaneous syringe

Imprest location: Formulary One

If no stock is available in an emergency after hours, contact the on-call pharmacist

DOSAGE & DOSAGE ADJUSTMENTS

Neonates: No data - IPA required for use.

INTRAVENOUS DOSING

Polyarticular JIA [1,4, 5]

≥ 2 years of age

- < 30 kg: 10 mg/kg/dose given once every four weeks as an IV infusion.
- ≥ 30 kg: 8 mg/kg/dose given once every four weeks as an IV infusion.

Systemic JIA [1, 4, 5]

≥ 2 years of age

- < 30 kg: 12 mg/kg/dose given once every two weeks as an IV infusion.
- ≥ 30 kg: 8 mg/kg/dose given once every two weeks as an IV infusion.

Treatment of CRS [5,15]

≥ 2 years of age

- < 30kg: 12 mg/kg/dose as an IV infusion
- ≥ 30kg: 8 mg/kg/dose (maximum 800mg) as an IV infusion[11]

Repeat Dosing for CRS

CRS associated with CAR T-Cell therapy: Repeat tocilizumab every 8 hours if not responsive to intravenous fluids and increasing oxygen supplementation. Limit to a maximum of 3 dose in 24 hours and maximum of 4 doses total[5,15]

CRS associated with blinatumomab: Refer to the relevant Oncology Protocol for additional information

Treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [COVID-19][10]

≥ 2 years of age

- < 30 kg: 12 mg/kg/dose as a single IV infusion
- ≥ 30 kg: 8 mg/kg/dose (to a maximum of 800mg) as a single IV infusion

A single additional dose may be administered at least 8 hours after the initial infusion if clinical signs or symptoms worsen, or do not improve after the initial dose.[1, 10]

SUBCUTANEOUS DOSING

Note: The prefilled pen (Actemra ACTPen®) should not be used in children < 12 years of age due to risk of inadvertent intramuscular administration with thinner subcutaneous tissue. Use the prefilled syringe in patients < 12 years of age.

Polyarticular JIA [1]

≥ 2 years of age

- < 30 kg: 162 mg given every three weeks by subcutaneous injection
- ≥ 30 kg: 162 mg given every two weeks by subcutaneous injection

Systemic JIA [1]

≥ 1 years of age

- < 10kg: Subcutaneous tocilizumab should not be used for systemic JIA in patients <10kg
- 10 kg – 29 kg: 162 mg given every two weeks by subcutaneous injection.
- ≥ 30 kg: 162 mg given once every week by subcutaneous injection

Renal impairment:

- No adjustment necessary. There are no studies conducted in patients with severe renal impairment.[1]

Hepatic impairment:

- Consider dosage adjustment or interruption to therapy if ALT/AST is elevated to greater than three times the upper limit of normal[5]

ADMINISTRATION

INTRAVENOUS INFUSION

The following personal protective equipment (PPE) must be worn during preparation and administration[2,5,6, 7,8,12,13,14]

- N95 mask
- Gloves
- Protective eye wear – must be worn during preparation and when dis/connecting administration.

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.[2, 5, 7]

Administer premedication, if ordered, 30 minutes to 1 hour prior to commencing infusion at the discretion of the treating consultant. (Not routinely used, however paracetamol and / or an antihistamine may be considered in patients who have experienced a previous infusion related reaction).

Must be further diluted in sodium chloride 0.9% before administration.

All tocilizumab orders are prepared in the **Day Treatment Unit (DTU) or the oncology ward (1A)**

The procedure is as follows:

1. Tocilizumab infusion should be charted on a Fluid Therapy Order Sheet (MR828).
2. Obtain the required number of tocilizumab vials. ***IMPORTANT - DO NOT SHAKE VIALS or FINAL PRODUCT***
   - For children < 30 kg: dose to be diluted in a 50 mL sodium chloride 0.9% IV bag.
   - For children and adolescents ≥ 3 0kg: dose to be diluted in a 100 mL sodium chloride 0.9% IV bag.
3. If the final volume is 50 mL:
   - Withdraw and discard 7 mL in addition to a volume equal to the volume of the tocilizumab dose, from a 50 mL sodium chloride 0.9% IV bag.

   OR If the final volume is 100 mL:
   - Withdraw and discard 8 mL in addition to a volume equal to the volume of the tocilizumab dose, from a 100 mL sodium chloride 0.9% IV bag.

   This will ensure that the final volume in the IV bag is either 50 mL or 100 mL respectively.
4. Draw up the volume equal to the dose of tocilizumab required into a syringe.
5. Slowly add the tocilizumab concentrate to the adjusted bag. Gently mix but **DO NOT SHAKE.**
6. Allow the diluted infusion solution to reach room temperature prior to administration and infuse as per rates below using a dedicated IV line.

Infusion rate

- Children < 30 kg commence at 10 mL/hr for first 15 minutes then increase to 65 mL/hr until infusion complete.
- Children and adolescents ≥ 30kg commence at 10 mL/hr for first 15 minutes then increase to 130 mL/hr until infusion complete.

Do not administer as an IV push or bolus.

- Do not use if opaque particles or discoloration are visible[5].

SUBCUTANEOUS INJECTION[1]

- The Actemra ACTPen® should not be used in children < 12 years of age
- Remove the subcutaneous syringe or pen from the refrigerator and allow to reach room temperature before administration (30 minutes for the syringe or 45 minutes for the pen)
- Give the injection within 3 minutes of removing the cap
- Inject dose subcutaneously into the abdomen, thigh or upper arm
- Rotate injection site each dose
- See the Subcutaneous Injections policy for further information

INTRAVENOUS COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids:

Sodium chloride 0.9%.

Do not mix with any other drug or diluent. [5, 6]

Compatible at Y-site:

- No information[6]

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[6]

MONITORING

Before treatment commences

- Full blood picture with differential, liver function tests, platelet count.
    - For JIA, measure alanine transaminase (ALT), aspartate transaminase (AST), platelets and absolute neutrophil count (ANC) at the time of the second infusion. Repeat every 4–8 weeks for polyarticular JIA; every 2–4 weeks for systemic JIA[4]

Before and during infusion

- Medications for treatment of severe hypersensitivity reactions, including anaphylaxis, should be available for immediate use in the event of an adverse event.[4]
- Monitor temperature, blood pressure and pulse rate every 30 minutes for the duration of the infusion and 30 minutes post infusion[6]

After infusion

- Patient to wait in the ward for 30 minutes after administration ***or earlier depending on Consultant approval for regular patients*** to facilitate monitoring of any allergic or adverse drug reactions.

Serum lipid profile is monitored if clinically indicated as there may be a transient increase in lipid levels while on therapy after infusion. Patient may be referred to their General Practitioner (GP) if necessary.

ADVERSE EFFECTS

Common: Infections (including opportunistic), rash, itch, headache, dizziness, hypertension, infusion related reactions, increased liver enzymes, neutropenia, gastritis, mouth ulcers, diarrhoea, hypofibrinogenaemia, increased lipids.[4]

Infrequent: Thrombocytopenia, gastrointestinal perforation (possibly dose-related), hypersensitivity reactions.[4]

Rare: Serious hepatotoxicity (including acute liver failure, hepatitis, jaundice).[4]

STORAGE

Vials must be stored refrigerated between 2-8°C and protected from light[1]

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.

Live and live attenuated vaccines should not be given concurrently with tocilizumab.

Hepatic CYP450 enzyme expression is supressed by cytokines that stimulate chronic inflammation e.g. IL-6. Suppression of CYP450 expression may be reversed when tocilizumab is introduced. Monitor patients taking medicines metabolised by CYP450 appropriately as doses may need to be adjusted.[1]

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

Related CAHS internal policies, procedures and guidelines

Subcutaneous Injections

Clinical Care of Paediatric Patients with COVID-19

References

1. Full product information Tocilizumab Monograph. Mims online. Accessed February 2023
2. Full product information Tocilizumab Monograph. Micromedex online. Accessed February 2023
3. PBS Information: Tocilizumab. Accessed online February 2023.
4. Australian Medicines Handbook Pty Ltd. Australian Medicines Handbook [online] Adelaide (SA): Australian Medicines Handbook Pty Ltd. Accessed online February 2023.
5. Tocilizumab Drug Information.UpToDate. Accessed February 2023,from Tocilizumab: Pediatric drug information - UpToDate (health.wa.gov.au)
6. Australian injectable drugs handbook[online]. Collingwood: The Society of Hospital Pharmacists of Australia; Accessed online February 2023
7. Australian Consensus guidelines for the safe handling of monoclonal antibodies for cancer treatment by healthcare personnel. Western & Central Melbourne Integrated Cancer Service. Accessed online on 14th May 2014
8. North Metropolitan Health Service Governance Policies. Accessed online on 14th May 2014.
9. Position Statement: Safe handling of monoclonal antibodies in healthcare settings, CPG AND COSA, September 2013. Accessed online on February 2023.

10. Tocilizumab Monograph Clinical Pharmacology. Accessed online February 2023.
11. Australian Medicines Handbook Children's Dosing Companion Pty Ltd Companion [online] Adelaide (SA): Australian Medicines Handbook Pty Ltd accessed online February 2023.
12. Australian Commission on Safety and Quality in Healthcare. Australian Guidelines for the Prevention and Control of Infection in Healthcare. Canberra: Commonwealth of Australia; 2010 Accessed online on 9th June 2016.
13. Alexander et al. Position Paper, Australian consensus guidelines for the safe handling of monoclonal antibodies for cancer treatment by healthcare personnel. Internal Medicine Journal. 44 (2014). Accessed online on 9th June 2016.
14. Jorgensen JA and Rinehart J. Considerations for Handling Monoclonal Antibodies. Pharmacy, Purchasing and Products. May 2015:12: Supp 5, 6. Accessed online on 9th June 2016.
15. Mahmoudjafari Z, Hawks KG, Hsieh AA, Plesca D, Gatwood KS, Culos KA. American Society for Blood and Marrow Transplantation Pharmacy Special Interest Group Survey on Chimeric Antigen Receptor T Cell Therapy Administrative, Logistic, and Toxicity Management Practices in the United States. Biol Blood Marrow Transplant. 2019 Jan; 25(1):26-33. PubMed PMID: 30266675. Epub 2018/09/30.

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.Tocilizumab.docx		
Document Owner:	Chief Pharmacist		
Reviewer / Team:	Senior Pharmacist, Rheumatology Consultant, Rheumatology Consultant, Rheumatology Consultant, Rheumatology Liaison Nurse Manager, Clinical Nurse Manager - HITH, Supervisor Pharmacist, Oncology, Paediatric Oncologist, Antimicrobial Stewardship Pharmacist		
Date First Issued:	17 October 2008	**Last Reviewed:**	Jun 2023
Amendment Dates:	*Jan 2021, Jan 2022, Jun 2023*	**Next Review Date:**	Jun 2026
Approved by:	CAHS Medication Safety Committee	**Date:**	May 2023
Endorsed by:	CAHS Drug and Therapeutics Committee	**Date:**	Jun 2023
Standards Applicable:	NSQHS Standards: NSMHS: N/A Child Safe Standards: N/A		

Printed or personally saved electronic copies of this document are considered uncontrolled

Healthy kids, healthy communities

Compassion | Excellence | Collaboration | Accountability | Equity | Respect

Neonatology | Community Health | Mental Health | Perth Children's Hospital