SESLHDMG/150

Medicine Guideline

Infliximab

Areas where Protocol/Guideline applicable	SESLHD
Authorised Prescribers:	SESLHD Medical Officers
Indication for use	Infliximab may be indicated in the management of the following conditions: • Crohn's disease* • Ulcerative Colitis* ○ Acute Ulcerative Colitis Salvage Therapy on the advice of a gastroenterology service • Acute Severe Steroid Refractory Immune Colitis on the advice of a gastroenterology service • Chronic Plaque Psoriasis* • Severe Psoriatic Arthritis* • Rheumatoid arthritis* • Severe rheumatoid vasculitis for use by rheumatology services • Ankylosing spondylitis* * PBS S100 indication When infliximab is to be prescribed for an indication that is not listed on the hospital formulary, Individual Patient Use (IPU) approval is required as outlined in the SESLHDPD/183 *Medicine Formulary*.
Adjunctive Therapy	**Premedication** The treating medical officer may order the patient pre-medications such as antihistamines, paracetamol or intravenous steroids. Pre-medications MUST be administered 30 minutes prior to infusion when patient is on **Rapid Infusion Schedule**. Administered 30 minutes prior to infusion Paracetamol 1 g PO stat and Hydrocortisone 100 mg IV stat.
Contra-indications	• Severe active infections such as sepsis, abscesses, tuberculosis, and opportunistic infections • Congestive Heart Failure (CHF) • History of hypersensitivity to infliximab or to other murine proteins or to any excipient of the products • Concurrent Anakinra therapy (disease-modifying antirheumatic drug (DMARD) • Pregnancy – multiple sources show absence of adverse outcomes with administration of infliximab during pregnancy. However, high serum levels are detected in neonates and infants exposed to infliximab in the last trimester of pregnancy and under these circumstances it is recommended that live vaccines are avoided in exposed infants in the first 6-12 months • Lactation – infliximab is minimally excreted in breast milk and very little is absorbed systemically after ingestion by the infant ***NB:** The use of Infliximab during pregnancy and lactation should only be considered following consultation by treating specialist with a patient fully informed of risks and benefits.

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Precautions	• May affect immune response • Chronic or recurrent infection (especially HIV, hepatitis B and C) • Fistula (perianal or enterocutaneous) where local sepsis not excluded • Re-treatment, after a period of discontinuation • Demyelination • Surgery (infection risk) • Children • Elderly • Live vaccines should be avoided in immunosuppressed patients, unless medical officer considers it necessary • Previous Tuberculosis
Important Drug Interactions	There is limited data on possible drug interactions with infliximab. • It is recommended that live vaccines not be given concurrently with infliximab. • Avoid combination with other biological therapies (e.g., anakinra, abatacept); may increase risk of infection.
Dosage	Dependent on indication, refer to appropriate reference text (e.g., MIMs, eTG).
Duration of therapy	Dependent on indication, refer to appropriate reference text (e.g., MIMs, eTG). Refer to Rate Schedule below
Patient education	Staff must inform and educate patient on possible side effects prior to infusion commencement and provide patient with Infliximab patient information leaflet if not previously provided.
Prescribing Instructions	• Obtain patient consent. • Infliximab and associated premedications must be prescribed on the eMR (eFluids), eRIC, or in Mosaiq/ARIA, with administration rates clearly specified. In the absence of eMM systems, the appropriate paper medication chart may be used. • For outpatients a current referral form is to be provided by patient's treating specialist and for eligible patients a current approved PBS authority script and a s100 form (valid for 12 months) needs to be completed and signed by a consultant.

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Preparation Instructions	All medications must be prepared and administered in accordance with the five rights as per NSW Health PD2022_032 *Medication Handling*. Reconstitution is to take place in the designated reconstitution clean utility room with the door closed using aseptic technique. Staff administering infliximab must wear PPE as per SESLHDPR/368 *Safe Handling and Management of Monoclonal Antibodies*. Reconstitution Procedure • Perform hand hygiene. • Don PPE. • Use closed transfer systems for reconstitution, if available. • Remove flip-top from vial and swab the rubber stopper with an alcohol-wipe. • Reconstitute each vial with 10 mL of sterile water for injection. Following reconstitution, the concentration is equivalent to 10 mg/mL. • Insert syringe with a 21 g or smaller needle through the centre of the rubber stopper and **direct the stream of sterile water to the glass wall of the vial (foaming on reconstitution is not unusual).** • Swirl vial gently until the powder is completely dissolved. Avoid prolonged or vigorous agitation**. DO NOT** shake the vial. • Allow the reconstituted solution to stand for five minutes. The solution should be colourless to light yellow and opalescent. Repeat reconstitution until required number of vials are made up. • Using aseptic technique, withdraw and discard a volume of normal saline solution, equal to the volume of the reconstituted infliximab dose from a sterile 250 mL 0.9% sodium chloride infusion bag. • Slowly add the reconstituted dose of infliximab to the sterile 0.9% sodium chloride solution, using aseptic technique. This will dilute the infliximab dose to a **final volume of 250 mL and a final concentration of 0.4 mg-4 mg/mL (maximum dose in 250 mL is 1000 mg).** • Gently mix. **DO NOT shake.** • Labelling to occur as per NSW Health PD2022_032 *Medication Handling* and Australian Commission on safety and Quality in Healthcare *National Standard for User-applied Labelling of Injectable Medicines, Fluids and Lines* • The Infliximab infusion should begin within three hours of preparation.

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Administration Instructions	• Infliximab must be administered in accordance with NSW Health PD2022_032 *Medication Handling* • Infliximab MUST only be administered as an intravenous infusion. Do not administer as an intravenous (IV) bolus injection. • Connect infliximab infusion to an infusion line with filter (sterile, nonpyrogenic, low-protein binding filter; pore size 1.2 micron or less). • Infuse infliximab via Agilia pump. • Patients who have not received infliximab for a period of six months or more or received infliximab at another care facility where medical records are not readily accessible are required to re-commence at the slowest infusion rate schedule. • Administer infliximab solution as per appropriate infusion rate schedule or as per patient's infusion plan. • **Prior to each rate change a complete set of observations must be documented** • The trade name and the batch number of the administered product should be clearly recorded in the patient file.
Infusion Rate Schedule	• Commence infusion at 10 mL/hour x 15 minutes • Increase to 20 mL/hour x 15 minutes • Increase to 40 mL/hour x 15 minutes • Increase to 80 mL/hour x 15 minutes • Increase to 150 mL/hour x 30 minutes • Increase to 250 mL/hour for remainder of infusion *Approximate infusion time 2 hours & 40 minutes* ***Patient to be observed for 2 hours post infusion***
Fast-Track Infusion Rate Schedule	**Appropriate for patients who have safely received the first three infusions (i.e., received infusions at week 0, week 2 and week 6 with no evidence of adverse events and their dose is less than 6 mg/kg.** • Commence infusion at 80 mL/hour x 15 minutes • Increase to 250 mL/hour for remainder of infusion *Approximate infusion time 1 hours & 15 minutes* ***Patient to be observed for 1 hours post infusion***
Rapid Infusion Rate Schedule	**Appropriate for patients who have safely received a total of nine infusions (three via induction rate schedule followed by six at fast-track rate schedule) with no adverse events. Pre-medication must be administered 30 mins prior to commencing infusion.** • Commence infusion at 500 mL/hour x 30 minutes *Approximate infusion time 30 minutes* ***Patient to be observed for 30 minutes post infusion***

Adverse Effects	Hypersensitivity and anaphylactic reactions may occur. Epinephrine (adrenaline), antihistamines, corticosteroids and cardiovascular resuscitation equipment should be readily available prior to commencing infliximab infusion. Cardiovascular resuscitation equipment MUST be readily available. – Acute infusion reaction including cardiopulmonary effects – Delayed hypersensitivity – Autoimmune disease – Opportunistic infection including TB, PCP, flu, herpes – Fatigue – Dyspnoea – Dizziness – Headache – Flushing – Gastrointestinal upset – Abnormal hepatic function – Cholecystitis – Skin, haematological, neurological reactions – Worsening heart failure – Anti-infliximab antibodies – Possible lymphoproliferative disorders – Post-procedural complication – Paradoxical drug-induced immune disorders ***NB:** Acute infusion reactions may develop immediately, or within a few hours post infusion. They are most likely to occur during the first and second infusion. These effects may be related to the rate of the Infliximab infusion. An acute infusion reaction is an anaphylaxis type reaction.
Monitoring requirements	• Baseline observations are to be recorded prior to commencing infusion. • Observations are to be recorded prior to each rate change. • Observations are recorded at the completion of the infusion, then hourly for duration of the post infusion period as determined by the infusion rate schedule. • Observations are recorded on the eMR prior to patient discharge. • Patient must remain under observation for the specified period in due to risk of acute infusion reactions e.g. dyspnoea, urticaria, hypotension, flushing and headache. • Outpatients to have intravenous cannula remain insitu until patient discharged.

Management of Complications	**Treatment of Anaphylaxis** 1. **STOP the infusion** 2. Call for help as per local clinical emergency response 3. Lie patient flat and raise their feet, if breathing is compromised sit in high fowlers position 4. Administer 100 % oxygen via mask via non rebreather mask 5. Obtain intravenous access in adults in the event of hypotension and give IV normal saline (20 mL/kg) rapidly and consider large bore IV access 6. Medical Officer to give adrenaline (1:1000) immediately (0.01 mg/kg to a maximum dose of 0.5 mg) IM (repeat at 5 minute intervals if necessary) followed by hydrocortisone (4 mg/kg to a maximum of 100 mg if < 12 years or 300 mg if > 12 years) IV and promethazine (0.5 mg/kg to a maximum 50 mg) IV if required. 7. Commence CPR in the event of a respiratory or cardiac arrest. **For mild reactions:** 1. **STOP the infusion** 2. Medical Officer review to consider prescribing promethazine, hydrocortisone and/or paracetamol. If deemed safe to restart the infusion following medical review, recommence infusion at a slower rate as instructed by the treating Medical Officer **If extravasation is suspected:** 1. **STOP the infusion** 2. Assess the site 3. Disconnect the giving set 4. Consider aspirating any fluid back from PIVC 5. Remove the cannula 6. Apply a cold compress and elevate the affected limb 7. Seek medical review 8. Document the volume of fluid infused The type of infusion related complication and action taken needs to be clearly documented in the patient's health care record and notified through ims+ for investigation.

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Basis of Protocol/Guideline: (including sources of evidence, references)	1. MIMS Online 2020, Accessed 22nd October 2020 2. Australian Injectable Drugs Handbook (8th Edition) 2020, The Society of Hospital Pharmacists of Australia, Accessed 22nd October 2020 3. Product Information – Remicade ® (Infliximab) 4. Product Information - Inflectra® (Infliximab) 5. Babouri A., Roblin X., Filippi J., Hebuterne, H., Bigard, M-A. & PeyrinBiroulet, L. (2014) Tolerability of one hour 10mg/kg infliximab infusions in inflammatory bowel diseases: A prospective multicenter cohort study. Journal of Crohns and Colitis. 8(2):161-165 Michielan A., Martinato M., Favarin A., Zanotto, V., Caccaro, R., Carouso, A., Sturniolo, GC. & D'Inca, R. (2015) A nurse-led accelerated procedure for infliximab infusion is well tolerated and effective in patients with inflammatory bowel disease. Digestive and Liver Disease. 47(5):372-377 6. Donnellan, C, Ford, A, Sprakes, M, Greer, D, Fairclough, A, Warren, L and Hamlin, P 2009, *Accelerated infliximab infusions are safe and well tolerated in patients with inflammatory bowel disease*, European Journal of Gastroenterology and Hepatology, vol 21, issue 1, pp 71-75. 7. Drugs and Lactation Database (LactMed) 2021, Accessed 11th June 2021 8. MotherToBaby Fact Sheet (Infliximab) 2021, Accessed 11th June 2021 9. National standards for user-applied labelling of injectable medicines, fluids and lines, 2015
Groups consulted in development of this guideline	SGH Gastroenterology, Inflammatory Bowel Disease, Neurology, Day Medical & Infusion Centre and Pharmacy. Adapted from BR376 SGH-TSH Infliximab Business Rule.

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GOVERNANCE	
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