



DRUG GUIDELINE- SOTROVIMAB FOR TREATMENT OF COVID-19

Adapted from the NSW TAG Sotrovimab for COVID-19 in Adults Drug Guideline

Sotrovimab (Xevudy®) is [provisionally registered](#) by the Therapeutic Goods Administration for use in Australia for the treatment of COVID-19 in adults and adolescents (age >12 years and weighing at least 40 kg), who do not require oxygen and are at risk of disease progression to hospitalisation or death.¹

The decision was made on the basis of short-term efficacy and safety data. Sotrovimab appears to retain activity against Alpha; Beta; Gamma; Epsilon; Iota; and Delta variants of SARS-CoV-2¹ while some activity is expected to be retained against Omicron.

The [National COVID-19 Clinical Evidence Taskforce](#) (current as at 25/01/2022) provides a conditional recommendation for use of sotrovimab as a neutralising antibody therapy for adults and adolescents with COVID-19 who do not require initiation of oxygen and who have one or more risk factors for disease progression.^{3,4} (Certainty of evidence for outcomes: moderate for a composite endpoint of hospitalisation or death).³ This conditional recommendation is based on the results of the COMET-ICE trial, suggesting that there would be 46 fewer events (composite endpoint) per 1000 patients (CI 95% 52 fewer- 30 fewer).^{1,5}

Although pregnant women were not participants in the COMET-ICE trial, the NCCET has made a conditional recommendation for the use of sotrovimab in treatment of COVID-19 within 5 days of symptom onset in pregnant women in the second or third trimester who do not require oxygen and who have one or more risk factors for disease progression.⁴ In addition, the NCCET has made a consensus recommendation to address patients not included in the COMET-ICE trial, such as vaccinated and immunosuppressed patients.^{1,4} The NCCET also recommended rigorous data collection on indications and key outcomes of patients who receive sotrovimab therapy.⁴ Although children and adolescents were not participants in the COMET-ICE trial, the NCCET has made a consensus recommendation for the use of sotrovimab in the treatment of COVID-19 (within 5 days of symptom onset) for adolescents aged 12 years and over and weighing at least 40 kg in exceptional circumstances.⁴

This medication is regulated by the National Medical Stockpile. Access to stock requires completion of a WA Emergency COVID-19 Treatment Approval for Sotrivimab Form and confirmation by the prescriber that the patient fulfils required criteria.

Supply of COVID-19 therapeutics via the National Medical Stockpile (NMS) is uncertain and availability is expected to fluctuate with demand and constraints in the supply chain.

To ensure equity of access and conserve sotrovimab therapy for those patients at the highest risk of progression, a tiered access criterion is in place to allocate stock based upon current supply.

This guideline should be used in conjunction with the sotrovimab resources available:

- WA Emergency COVID-19 Treatment Approval for Sotrovimab Form
- Patient Consent Form and further information regarding consent, and
- Patient Information Leaflet.

Drug Class^{1,2}:

Recombinant human IgG1 monoclonal antibody targeting the spike protein of SARS-CoV-2, which is thought to prevent membrane fusion after the virus binds to the human ACE2 receptor.

Clinical Criteria:

As per the [National Taskforce Guidelines](#), adult patients (including pregnant women in the second and third trimester) and adolescents (aged 12 years and over and weighing at least 40 kg) are eligible for sotrovimab:

- within five (5) days of symptom onset (symptoms may be very mild); **AND**
- who do not require oxygen; **AND**
- who have not been fully vaccinated (note: fully vaccinated means 2nd dose > 2 weeks ago); **AND**
- who have **one or more of the following risk factors** for disease progression;

Adults:

- diabetes (requiring medication)
- obesity (BMI > 30 kg/m²)
- chronic kidney disease (*eGFR < 60 mL/minute)
- congestive heart failure (NYHA class II or greater)
- chronic obstructive pulmonary disease (history of chronic bronchitis, chronic obstructive lung disease, or emphysema with dyspnoea on physical exertion)
- moderate-to-severe asthma (requiring an inhaled steroid to control symptoms or prescribed a course of oral steroids in the previous 12 months)
- age ≥ 55 years.

Adolescents:

For consideration of use in adolescents aged 12 years and over and weighing at least 40 kg, recommend discussion with a Paediatric Infectious Diseases Specialist at Perth Children's Hospital to determine appropriateness of adolescent risk factors (including neurodisability, obesity (>95th centile for age and gender based on CDC growth charts), severe asthma, immune deficiency) and need for sotrovimab.

Clinical judgement should be used when assessing the severity of specific risk factors. The following risk factors should also be considered when prioritising patients for sotrovimab:

- Patients who are unvaccinated
- Consider using sotrovimab in immunocompromised patients** [presenting within five days of symptom onset and who do not require oxygen] regardless of vaccination status (see Appendix 1 for Australian Technical Advisory Group on Immunisation (ATAGI) advice for immunocompromised patients)
- Aboriginal and/or Torres Strait Islander patients > 35 years old.

Clinical judgement should be used when assessing the severity of specific risk factors.

*The COMET-ICE study used eGFR values derived from the Modification of Diet in Renal Disease (MDRD) formula, which is not routinely used in Australia. For the purposes of this guidance, eGFR calculations derived from CKD-Epi formula, which is routinely reported, are acceptable.

**For the purposes of this guidance, immunosuppressed patients are those that a) have a primary or acquired immunodeficiency such as haematological neoplasms, are post-transplant [solid organ (on immunosuppressive therapy) or haematopoietic stem cell transplant within 24 months], or have HIV/AIDS or other significant immunocompromising condition or b) are on/have been on recent immunosuppressive therapy such as chemotherapy, radiotherapy, high dose corticosteroids (equivalent to 20 mg or more of prednisone per day for 14 days or more) or are on biologic immunotherapies including most disease-modifying anti-rheumatic drugs (DMARDs).

Contraindications and Precautions^{1-3,6}:

- **Hypersensitivity:** Contraindicated in patients with known hypersensitivity to sotrovimab, or any of the excipients (histidine, histidine hydrochloride monohydrate, sucrose, methionine, polysorbate 90) in the product, Chinese Hamster Ovary cell products or other recombinant human or humanised antibodies. Exercise caution in patients with a history of anaphylaxis to other medicines.
- **Pregnancy and breastfeeding:** Sotrovimab is pregnancy category B2¹. There is potential for placental transfer of sotrovimab from the mother to the developing foetus. No information is available on the use of sotrovimab during breastfeeding. The amount present in breastmilk is likely to be very low as sotrovimab is a large protein molecule. Discontinuation of breastfeeding may be considered. For management of pregnant and breastfeeding women with COVID-19, see [National COVID-19 Clinical Evidence Taskforce guidelines](#).
- **Paediatric population:** The safety and efficacy of sotrovimab has not been established in children <12 years of age or weighing <40 kg.

Drug Interactions¹:

No formal interaction studies have been conducted with sotrovimab. Sotrovimab is not renally excreted or metabolised by the CYP450 enzymes. (Sotrovimab is degraded by proteolytic enzymes widely distributed in the body and not restricted to hepatic tissue).

Contact the local pharmacy department or medicines information service for further advice.

Interaction with COVID-19 vaccination has not been determined. The US Centers for Disease Control and Prevention advises delaying COVID-19 vaccination until 90 days after administration of monoclonal antibodies for the treatment of COVID-19.⁹ This advice applies to those who have not received any vaccine dose as well as those who have received the first dose but not the second dose.⁹

Presentation and Storage^{1,10}:

- Available as a single use vial of 500 mg in 8 mL (62.5 mg/mL) concentrated injection solution for infusion (after diluting). The solution in the vial should be clear and colourless to yellow or brown.
- Store refrigerated at 2 - 8°C in original package. Protect from light. Do not freeze.

Dose^{1,2}:

The recommended dose is 500 mg as a single dose intravenous infusion over 30 minutes
No dose adjustments for renal or hepatic function or age are required.

Preparation and Administration^{1,2,10}:

- The occupational hazard of intermittent low dose exposure to sotrovimab is not known. Wear a mask and gloves when preparing the infusion to minimise exposure. Preparation in a cytotoxic hood/sterile environment is not required.
- It is recommended that the name and the batch number of the administered product is clearly recorded in the patient's medical record in order to improve traceability if the product is prepared outside of the pharmacy department.
- Preferably use immediately after dilution. If this is not possible, the diluted solution may be stored at room temperature for up to 6 hours (include infusion time) or stored in the refrigerator for up to 24 hours (include infusion time).
- Personnel and equipment to manage anaphylaxis must be present during infusion and for at least 60 minutes post-infusion.

Preparation Steps

1. Remove one vial containing 8 mL sotrovimab solution from refrigerator at least 15 minutes before preparation of the infusion.
2. Visually inspect vial to ensure no particulate matter is present or damage to the vial. (Discard if present).
3. Gently swirl the vial several times without creating air bubbles before using. (Do NOT shake vigorously).
4. Withdraw 8 mL from a 50 mL or 100 mL sodium chloride 0.9% infusion bag or glucose 5% infusion bag.
5. Withdraw 8 mL solution from the sotrovimab vial.
6. Slowly inject 8 mL of sotrovimab solution into selected infusion bag.
7. Prior to infusion, to mix, gently rock the infusion bag back and forth 3 to 5 times. Do NOT invert the bag. Avoid forming air bubbles.
8. Discard the vial including any unused solution, in line with local protocols for monoclonal antibody handling.

Administration Steps

1. Do not use the same IV line to administer other medications at the same time.
2. Attach an infusion set to the infusion bag using standard bore tubing. Information from the manufacturer states the additional use of a 0.2 micrometre in-line filter is recommended but not required; check local requirements regarding in-line filter use.¹³
3. Prime the infusion set with sotrovimab infusion and then infuse intravenously over 30 minutes (until the bag is finished) via a central or peripheral line.
4. After the sotrovimab infusion is completed, flush the giving set with at least 20 mL of 0.9% sodium chloride/ glucose 5% (at the same rate as the sotrovimab infusion).
5. **Observe the patient during the infusion and for 60 minutes after infusion cessation** in case of hypersensitivity reactions or anaphylaxis.

For use in paediatric patients (18 years of age and under) please follow paediatric monograph as per link provided – [ChAMP Guidelines for Use of Sotrovimab for COVID-19 Paediatric Patients.](#)

Monitoring Requirements^{1,5,6,10}:

Monitor the patient for adverse effects (see *Adverse Effects* section below).

Infusion reactions include fever, chills, dizziness, dyspnoea, pruritis and rash. For mild to moderate infusion reactions, slow or stop the infusion and treat accordingly¹⁰, noting that in the COMET-ICE trial, mild hypersensitivity reactions did not require pausing or discontinuation of the infusion.⁵

Anaphylactic reactions are rare but are a medical emergency. Stop the infusion and commence treatment immediately.

Adverse Effects^{1,5}:

It may be difficult to distinguish between adverse effects of sotrovimab and signs and symptoms of COVID-19. As the proposed use is for a provisionally approved medicine which has no relevant post-marketing data, it is important to document and report all (from possible to confirmed) adverse effects experienced by the patient during treatment to inform its safety profile and future use.

Refer to product information for complete list of possible adverse effects.

- **Common (>1%):**
Diarrhoea (1%), hypersensitivity reactions (includes rash (2%), infusion-related reaction, bronchospasm).
- **Rare:** Anaphylaxis.

Reporting⁴:

- As sotrovimab is a TGA provisionally registered medicine and only available through the National Medical Stockpile, prescribers must complete and submit a **WA Emergency COVID-19 Treatment Approval for Sotrivimab Form**, for approval for each patient they intend to treat with sotrovimab.
- This will enable appropriate medicines governance and ensure the collection and analysis of patient outcomes and systematic monitoring of medicines use. The prescribing clinician and health professional administering sotrovimab is responsible for reporting medication errors and adverse events occurring as a result of sotrovimab treatment.
- Adverse events related to medicines should be reported to the [TGA](#) & via the [Datix CIMS](#) (WA Health).

APPENDIX 1: Anaphylaxis Kits

An anaphylaxis response kit must always be readily available and easily accessible by health professional administering sotrovimab.

The recommended contents of these pre-prepared kits are based on the Australian Immunisation Handbook and the WA COVID-19 Vaccination Clinical Reference Group.

Item	Quantity per kit
Needle 23 Gauge x 25mm	10 per kit
1mL 'single use only' syringes (not insulin syringes)	10 per kit
Cotton wool swab	10 per kit
Manual resuscitator set Adult: Mask; Flow Diverter; 4.2m Oxygen tubing; single patient use.	1 per kit
Manual resuscitator set Paediatric: Mask; Flow Diverter; 4.2m Oxygen tubing; single patient use.	1 per kit
Adrenaline 1:1000	10 ampoules per kit
Guedel Airway - Adult	1 per kit
Guedel Airway - Paediatric	1 per kit
Mask – non-rebreather – Adult	1 per kit
Mask – non-rebreather - Paediatric	1 per kit
Laminated copy of 'Recognition and Treatment of Anaphylaxis' Australian Immunisation Handbook Table. Recognition and treatment of anaphylaxis The Australian Immunisation Handbook (health.gov.au)	1 per kit
Laminated copy of 'Doses of intramuscular 1:1000 adrenaline for anaphylaxis' – Australian Immunisation Handbook Doses of intramuscular 1:1000 adrenaline for anaphylaxis The Australian Immunisation Handbook (health.gov.au)	1 per kit
Documentation to record treatment of anaphylaxis	1 per kit
Address of venue	1 per kit
Digital Clock/Timer (for timing of adrenaline)	1 per kit
Pens	2 per kit
A4 notebook	1 per kit
Anaphylaxis Response Kit Storage (e.g. backpack)	1 per kit
Razor	1 per kit

APPENDIX 2: Guidelines for Safe Handling and Administration of Monoclonal Antibodies

(Adapted from WACHS [Safe Handling and Administration of Monoclonal Antibodies](#))

1. Guiding Principles

Monoclonal antibodies (MABs) are large protein drugs that have an affinity for a specific antigen. They are used in the management of cancer and non-cancer diseases. Administration is by injection or infusion and the route is usually subcutaneous or intravenous.¹¹

The action of MABs is different from traditional cytotoxic therapies and most are not inherently cytotoxic and do not need to be handled with cytotoxic precautions.^{11,12,13,14,15,16}

With the continuing development of new MABs, the advent of fixed dosing and expansion of indications for existing MABS, a universal approach is required when assessing the risk to healthcare workers as well as the management of these medications.

2. Guideline

This guideline has been developed to advise healthcare staff of the minimum level of personal protection required when preparing, handling, administering, and disposing of MABs. This guideline will also provide guidance and direction on the preparation of low risk MABs on site.

2.1 Risk Assessment of MABs

All MABs need to be risk assessed. The occupational health and safety risk of handling MABs is dependent on the risk of internal exposure as well as the toxicity and immunogenicity of the MAB.

Although each MAB is unique, the safe handling requirements of these agents can be considered as a class.^{11,12,13}

Cytotoxic MABs are not included in the scope of this document.

- Any MAB conjugated to a cytotoxic molecule must be handled with cytotoxic precautions and should only be prepared in a manufacturing unit.^{11,13,14,16}
- Current cytotoxic MABs available:
 - o Brentuximab vedotin (Adcetris®)
 - o Trastuzumab emtansine (Kadcyla®)

If unsure about specific handling for a MAB product, please contact your pharmacist.

2.1.1 Occupational exposure

Concerns over the handling of MABs arose due to the uncertainty over the effects of potential occupational exposure to this diverse group of drugs. Factors associated with the risk of occupational exposure include the actions of the drug, the methods used to prepare and administer the drug, staff experience, potential route of exposure and likely level of exposure.^{11,14,15}

Potential Routes of Exposure	Summary of literature
Inhaled	<ul style="list-style-type: none"> Animal models have shown that there can be systemic absorption of MABs through inhalation The generation of aerosolised particles are greatest during preparation or when dis/connecting lines, although the likelihood of producing a liquid aerosol in the clinical setting is low
Mucosal	<ul style="list-style-type: none"> Animal models have shown that there is the potential for local and systemic absorption from mucosal uptake (nasal and ocular) The generation of aerosolised particles are greatest during preparation or when dis/connecting lines, although the likelihood of producing a liquid aerosol in the clinical setting is low
Dermal	<ul style="list-style-type: none"> Due to the molecular size of most MABs dermal absorption is considered unlikely Healthcare workers with exposed damaged skin may be at an increased risk
Oral	<ul style="list-style-type: none"> Animal and human models have shown the oral route is a potential route of absorption Hand to mouth contamination is the most likely cause The level of occupational exposure is unlikely to cause toxicity

Table 1: Potential routes of occupational exposure of MABs ^{11,13,14,16}

2.2 Minimum personal protective equipment requirements during handling

Non-cytotoxic MABs do not need be handled with cytotoxic precautions; however, they do require greater handling precautions than other non-hazardous injectable medications. Table 2 has the recommended safeguards to minimise the risk to healthcare workers when MABs are handled outside of an aseptic manufacturing unit. ^{11,12,13,14,16}

Personal Protective Equipment	Recommendations
Gloves and effective hand hygiene	<ul style="list-style-type: none"> Use to minimise the risk of contamination and infection as part of good aseptic technique
Gowns	<ul style="list-style-type: none"> Not warranted for preparation or administration
Mask (N95)	<ul style="list-style-type: none"> Worn during dose preparation. Not mandated during administration but may be considered when dis/connecting administration lines during intravenous administration due to potential aerolisation risk
Protective Eyewear	<ul style="list-style-type: none"> Worn during dose preparation Not mandated during administration but may be considered when dis/connecting administration lines during intravenous administration due to potential aerolisation risk

Table 2: Minimum Personal Protective Equipment ^{11,12,13,14,16}

2.3 Preparation of low risk MABs

There may be occasions in regional areas that MABs are required to be prepared on site. Preparation is the process of preparing or being prepared for use and is different to the process of administration. Examples of these include subcutaneous MABs or if a prepared infusion has a short expiry. These should be prepared just before administration when the patient is ready to receive treatment. They should not be prepared in advance and stored in a refrigerator.

When determining the appropriate site of preparation of a MAB please refer to the occupational health and safety risk assessment in the [Australian consensus guidelines for the safe handling of monoclonal antibodies for cancer treatment by healthcare professionals](#) or regionally endorsed assessment form for non-cancer MABs. The risk assessment must be conducted with input from medical teams, nursing and regional pharmacist.¹¹

Nursing staff preparing and administering MABs should be competent in aseptic technique. Preparation should be undertaken in a dedicated area away from patients and carers. Pregnant or currently immunocompromised staff are not to be involved in the preparation of MABs for administration.^{11,12,13}

2.4 Disposal of waste, patient waste and spills

MABs should be disposed of in the same manner as other non-hazardous injectable medications. Exposure to waste products including waste and /or bodily fluids of patients should not present an additional occupational health and safety risk to healthcare workers. They should be disposed of in accordance with the disposal of clinical waste. Patients do not require additional contact precautions when receiving treatment with a MAB.^{11,13,14}

If a spill occurs during preparation, administration or disposal of a MAB, it is recommended that the spill clean-up procedure is managed in the same manner as other non-hazardous injectable medications.^{11,13,14}

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Version Control

Version	Date	Comments
1.0	2/2/2022	Guidelines endorsed by COVID-19 EAG and PSCQ ED

This guidance is correct at the time of publishing. However, as it is subject to updates, please use the hyperlinks to confirm the information is accurate.

WA guidance may be amended as additional federal guidance is finalised and/or further information becomes available.

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