SA Health

COVID-19: Pre-Exposure Prophylaxis (PrEP) with Tixagevimab plus Cilgavimab (Evusheld®)

Statewide Clinical Guideline - Adoption of CALHN Guideline

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Government of South Australia | Health
Central Adelaide Local Health Network

GUIDELINE

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Title	COVID-19: Pre-Exposure Prophylaxis (PrEP) with Tixagevimab plus Cilgavimab (Evusheld®)			
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Risk rating	☐ Extreme	☐ High	☒ Medium	☐ Low
Monitoring/audit	☒ Scheduled for audit		☐ Not scheduled for audit	
Title and reference of parent SA Health Policy	N/A			
Summary (three sentences maximum)	This guideline addresses the use of the medications tixagevimab and cilgavimab to prevent COVID-19 infection in patients at high risk of severe illness who have not been exposed to COVID-19 (pre-exposure prophylaxis).			
Keywords (five to eight)	COVID-19, prophylaxis, tixagevimab, cilgavimab, PrEP, Evusheld.			

Clinical Governance	Partnering with Consumers	Preventing and Controlling Healthcare Associated Infections	Medication Safety	Comprehensive Care	Communicating for Safety	Blood Management	Recognising and Responding to Acute Deterioration
☒	☐	☒	☒	☐	☐	☐	☐

Version	Change summary	Next scheduled review
5.0	Non-scheduled review. Changed in recommendations. No longer recommended for routine use as PrEP as per SA Health recommendations. Link to new SA Health recommendations memo.	February 2026
4.0	Non-scheduled review. Recommended dose increased to 600mg as per TGA recommendations. Updated information regarding dosing schedule and administration instructions.	December 2025
3.0	Non-scheduled review, Second dose now permitted for Tier 1 patients. Additional text regarding uncertainty of efficacy vs new and emerging variants.	December 2025
2.1	Non-scheduled review. Addition of sphingosine 1-phosphate receptor modulator medications to those included in Tier 2.	December 2025

Government of South Australia | Health Central Adelaide Local Health Network

Title	COVID-19: Pre-Exposure Prophylaxis (PrEP) with Tixagevimab plus Cilgavimab				
Reference	CALHN-GDE05871	Version	5.0	Approved	16 February 2023

GUIDELINE

COVID-19: Pre-Exposure Prophylaxis (PrEP) with Tixagevimab plus Cilgavimab

Introduction

- Since the emergence of COVID-19, there have been significant developments in the antiviral and immunomodulatory medications available for both the prevention and treatment of COVID-19 infection.
- This guideline addresses the use of tixagevimab plus cilgavimab (Evusheld®) to prevent COVID-19 infection in patients who are unlikely to be protected from COVID-19 vaccination due to immunosuppression from underlying medical conditions, or medications which suppress the immune system. This guideline is for those patients who have NOT been exposed to COVID-19 (pre-exposure prophylaxis).
- This guideline **DOES NOT:**
  - provide guidance for the overall care for patients with COVID-19
  - provide advice regarding supportive therapies recommended for COVID-19
  - provide advice regarding post exposure prophylaxis for COVID-19
  - provide advice regarding disease-modifying therapies recommended for patients with mild illness or those hospitalised with COVID-19
- For information related to the management and care of patients with COVID-19 please refer to:
  - COVID–19 (SARS–COV–2) – Management Guide (CALHN–PRC05409)
  - CALHN COVID–19 internet page
  - COVID-19 Disease-modifying treatment recommendations for hospitalised adult patients (CALHN-GDE05778)
  - COVID-19: Medication Management of Mild Illness in the Outpatient Setting (CALHN-GDE05808)
- Medication recommendations for COVID-19 can change rapidly due to medication shortages, ongoing research and as novel agents are discovered. For the most up to date Australian guidelines and recommendations refer to:
  - National COVID-19 Clinical Evidence Taskforce (The Australian Living Guidelines)

Updated recommendations on the use of tixagevimab plus cilgavimab January 2023

SA Health no longer recommends the routine use of Evusheld® for pre-exposure prophylaxis in any patient group.

Recent evidence indicates that Evusheld® may be ineffective against multiple subvariants of Omicron that are currently circulating in South Australia (including BQ.1, BQ.1.1., XBB, XBF and the BA.2.75 sub lineage). These variants are now believed to comprise the majority of the circulating variants in South Australia and the prevalence of such variants is expected to continue to rise

Antiviral medications for the early treatment of COVID-19 infection are available for all patients eligible for PrEP with tixagevimab plus cilgavimab. **ALL** patients receiving tixagevimab plus cilgavimab should be counselled on the need for early testing for COVID-19 infection if they become symptomatic even after administration of tixagevimab plus cilgavimab and the importance of having a treatment plan for COVID-19 infection should they test positive. The decision to use Evusheld should NOT delay or impact the decision to use available antiviral medications as treatment for COVID-19 infection

For more information see updated SA Health recommendation on the use of Evusheld® (tixagevimab plus cilgavimab) January 2023 here.

Indications for use of tixagevimab plus cilgavimab

A small supply of tixagevimab plus cilgavimab is available from the Commonwealth's National Medical Stockpile. Whilst it is not recommended for routine use as PrEP, in exceptional circumstances where the health care provider and patient have determined that the potential benefits outweigh the risks, its use may be considered (i.e. Tier 1 patients) via the IPU process.

Prevention of COVID-19 infection in adults and adolescents (aged ≥ 12 years and weighing ≥ 40 kg) who have NOT been exposed to COVID-19 and who:

- have a medical condition making them unlikely to respond to or be protected by vaccination (i.e. are moderately to severely immunosuppressed)
  OR
- are not recommended to have vaccination against COVID-19 by an authorised person/department such as the vaccination clinic or immunologist due to a history of severe adverse reaction to a COVID-19 vaccine or COVID-19 vaccine component

Rationale for pre-exposure prophylaxis (PrEP) for COVID-19

- Vaccination is the most important tool in preventing hospitalisations from COVID-19 infection.
- Patients who are significantly immunosuppressed may not be able to produce an adequate immune response to COVID-19 vaccination, and therefore are still at a high risk of hospitalisation or death if exposed to the virus.
- Tixagevimab plus cilgavimab is a combination of two monoclonal antibodies which mimic the body's natural antibody response.
- PrEP is not a substitute for vaccination but may be an option for those with proven allergies to COVID-19 vaccinations.

Prioritised patient cohorts for PrEP with tixagevimab plus cilgavimab

Tier 1: Not recommended for routine use. IPU required for all patients (including those who have already had an initial dose in the previous 3 to 6 months): Severely immunocompromised individuals regardless of vaccination status who are not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to underlying conditions.

Patients with **haematological malignancies** on the following therapy or with the following conditions:

- Allogenic stem cell transplant within the last 12 months
- Extensive chronic graft vs host disease requiring multiple immunosuppressants or severe lung chronic GVHD
- Autologous stem cell transplantation within 6 months
- B-cell depleting therapy within the last 12 months (rituximab, alemtuzumab)
- BITE antibodies within the last 6 months
- Bruton tyrosine kinase inhibitors in patients with risk factors for severe COVID-19 (appendix 3) within 12 months
- Chimeric antigen receptor T (CAR-T) cell recipients within 12 months
- Anti-thymocyte globulin (ATG) within the last 12 months
- Patients on active therapy for T-NHL in the last 6 months
- Patients on active therapy for ALL, AML, CLL

Solid organ transplant recipients who:

- Are heart and/or lung transplant recipients regardless of time from transplant with:
  - Recurrent infections with significant respiratory or systemic compromise
  - Prospectively receiving T-cell depletion therapy
  - Prospectively or receiving B-cell depletion therapy in last 6 months
  - Children in same household under 11 years of age
  - BOS 3, on home oxygen or listed for redo lung transplantation
- Are within 1 year of receiving a solid-organ transplant (other than lung transplant), OR
- Are on belatacept regardless of time from transplant OR
- Received treatment for acute rejection with T or B cell depleting agents within the last 12 months

Patients with the following congenital or acquired i**mmunodeficiency** disorders:

- Patients receiving T or B cell depleting agents within the last 12 months (e.g. rituximab, ocrelizumab, ofatumumab) + high dose steroids (> 20mg prednisolone daily) at time of vaccination
- Patients with an autoimmune disorder (e.g. vasculitis) receiving cyclophosphamide and high dose steroids (≥ 20mg of prednisolone or equivalent)
- Combined immunodeficiency syndromes including transplanted SCID where immunoglobulin replacement is required
- HIV positive with a CD4 < 50 cells/mm^3 or not on treatment

Tier 2 Not currently eligible : To be offered when > 80% of eligible Tier 1 patients have received treatment or when there is enough supply to ensure Tier 1 patients will have access even if available to Tier 2 patients.

- Patients with **haematological malignancies** on the following **immunosuppressive** therapy or with the following conditions:
  - Allogenic stem cell transplantation > 12 months and on immunosuppressive therapy
  - Autologous stem cell transplantation > 6 months and on immunosuppressive therapy
  - Multiple myeloma on active treatment with 2 or more agents including and not limited to proteosome inhibitors, immunomodulators, CD138 targeted therapies +/- high dose steroids
  - Lymphoma on therapy
  - Patients with ALL or AML who have completed treatment within the previous 12 months
  - Other chronic leukaemias (e.g. CML or CLL) receiving treatment except those receiving first or second line *BCR::ABL1* directed tyrosine kinase inhibitors
  - Aplastic Anaemia on active therapy
  - Myeloproliferative neoplasms especially those on JAK2 inhibitors
- **Solid organ transplant** recipients who:
  - Are more than 12 months since transplant AND aged 70 or older
  - Are heart or lung transplant recipients regardless of time from transplant
- Patients with **solid tumour malignancies** who are receiving the following treatments with a curative intent:
  - Lung cancer on active chemotherapy +/- immunotherapy in the last 3-6 months
  - Patients receiving moderate intensity chemotherapy within the past 2 weeks (defined as chemotherapy with a high risk of severe neutropenia (neutrophils <0.5*10^9/L) for 3-5 days duration post-chemotherapy)
  - Whole body radiotherapy within the last 6 months
- Patients with the following congenital or acquired **immunodeficiency disorders**:
  - Primary immunodeficiency associated with impaired type I interferon signalling
  - Good's syndrome (thymoma plus B-cell deficiency)
  - X-linked agammaglobulinaemia (and other primary agammaglobulinaemias)
  - Any patient with a secondary immunodeficiency receiving, or eligible for, immunoglobulin replacement therapy
  - Common variable immunodeficiency (CVID)
  - Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig)
  - Hyper-IgM syndromes
  - Autoimmune polyglandular syndromes /autoimmunepolyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)
- Patients at high risk of reduced immunogenic response to COVID-19 vaccine:
  - Taking high dose steroids (≥ 20mg prednisolone daily for ≥ 2 weeks) and/or abatacept or mycophenolate mofetil at the time of vaccination

- Patients with Castleman's Disease on therapy or paroxysmal nocturnal haemoglobinuria (PNH) on complement inhibitors (i.e. eculuzimab/ravaluzimab)
- Patients who are within a year of receiving T or B cell-depleting therapies (e.g. rituximab, ocrelizumab, ofatumumab, alemtuzumab)
- Patients with an autoimmune disorder (e.g. vasculitis) receiving cyclophosphamide
- Patients on sphingosine 1-phosphate receptor modulators (e.g. fingolimod, siponimod and ozanimod) for multiple sclerosis

- Immunocompetent individuals aged > 60 years with a contraindication to COVID-19 vaccination as determined by a specialist immunologist AND with ONE or more risk factors for progressing to severe COVID-19 illness (see appendix 3)

Tier 3: Not currently eligible

- **Haematological malignancies:**
  - Any patient with a haematological malignancy not already included in tier 1 and 2
- **Solid organ transplant** recipients:
  - Any SOT recipient not included in tier 1 and 2
- Patients with **solid tumour malignancies** who:
  - Have received cytotoxic chemotherapy within the past 6 months
- Patients with the following **congenital or acquired immunodeficiency** disorders:
  - HIV positive with a CD4 < 250 cells/mm3 or those with a higher CD4 count unable to be established on effective antiretroviral therapy
  - On active treatment with any immunosuppressive or immunomodulatory therapy listed in table 2 and not already included in tier 1 or 2
  - Most specific Ab deficiency patients
  - Most selective IgA deficiency patients
  - Complement deficiencies
- Immunocompetent individuals with a contraindication to COVID-19 vaccination as determined by a specialist immunologist AND with ONE or more risk factors for progressing to severe COVID-19 illness

Tier 4: Not currently eligible

- Immunocompetent individuals with a contraindication to/for whom COVID-19 vaccination is not recommended due to a history of severe adverse reaction to a COVID-19 vaccine as determined by a specialist immunologist.

Tixagevimab plus cilgavimab drug monograph for PrEP

Tixagevimab plus Cilgavimab (Evusheld®)

IPU and patient consent required (verbal or written)

For more detailed information on the use of Tixagevimab and Cilgavimab in patients with COVID-19 visit the product information available on the TGA website

Drug Class	• Tixagevimab and cilgavimab are long-acting monoclonal antibodies. They bind to non-overlapping portions of the SARS-CoV-2 spike protein preventing the virus from interacting with the human ACE2 receptor.

Indications	**No longer recommended for routine use as PrEP in any patient group. Use requires an IPU**
	• Prevention of COVID-19 infection in adults and adolescents (aged ≥ 12 years and weighing ≥ 40kg) who have NOT been exposed to COVID-19 and who:
	  ○ have a medical condition making them unlikely to respond to or be protected by vaccination (i.e. are severely immunosuppressed)
	  OR
	  ○ are not recommended to have vaccination against COVID-19 by an authorised person/department such as the vaccination clinic/immunologist due to a history of severe adverse reaction to a COVID-19 vaccine or COVID-19 vaccine component
	
	Tixagevimab plus cilgavimab is not recommended as a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended.

Contra-indications	• Hypersensitivity to tixagevimab or cilgavimab or any of the excipients in the product

Precautions	• **Current or recent COVID-19 infection:** ALL patients should have a negative COVID-19 RAT or PCR test 24-48 hours prior to tixagevimab plus cilgavimab
	  ○ If the patient recently had a confirmed COVID-19 infection, it is suggested to wait 30 days from the start of the infection before administering tixagevimab and cilgavimab (Evusheld®). Consideration can be given to administering prior to 30 days on a case-by-case basis – discussion with Infectious Diseases for these patients is recommended
	• **Serious hypersensitivity reactions:** Exercise caution in patients with a history of anaphylaxis to other medicines. Serious hypersensitivity reactions have been observed with Evusheld®. Administration of Evusheld® should be done under the supervision of a healthcare provider with appropriate medical support to manage severe hypersensitivity reactions.
	• **Previous severe hypersensitivity reaction to COVID-19 vaccine:** For individuals with a history of a severe hypersensitivity reaction to a COVID-19 vaccine, consider consultation with an immunologist prior to Evusheld® administration. Evusheld® contains polysorbate 80, which is in some COVID-19 vaccines and is structurally similar to polyethylene glycol (PEG), an ingredient in other COVID-19 vaccines.
	  ○ Consider referral to SA COVID-19 Specialist Immunisation Clinic for patients with any history of allergic reactions to previous vaccinations or PEG.
	• **Clinically significant bleeding disorders** such as thrombocytopenia or coagulation disorders due to administration by intramuscular injection.
	• **Cardiovascular and thrombotic events**: In the PROVENT trial, a higher proportion of patients who received tixagevimab plus cilgavimab compared to placebo reported myocardial infarction and cardiac failure. All patients with events had cardiac risk factors and/or a prior history of cardiovascular disease, and there was no clear temporal pattern.

	A causal relationship between tixagevimab plus cilgavimab and these events has not been established. Consider the risks and benefits prior to initiating tixagevimab plus cilgavimab in individuals at high risk for cardiovascular or thromboembolic events, and advise individuals to seek immediate medical attention if they experience any signs or symptoms suggestive of a cardiovascular event.
	• **Pregnancy**: There are insufficient data to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal or foetal outcomes. Tixagevimab plus cilgavimab should only be used during pregnancy if the potential benefit outweighs the potential risk for the mother and the foetus.
	• **Breastfeeding**: There are no available data on the presence of tixagevimab or cilgavimab in human milk or animal milk, the effects on the breastfed infant, or the effects of the drug on milk production. Maternal IgG is known to be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for tixagevimab plus cilgavimab and any potential adverse effects on the breastfed infant from tixagevimab plus cilgavimab.
	• **Paediatric patients:** only approved for use in patients aged 12 years or older AND who weigh at least 40kg however the safety and efficacy of tixagevimab plus cilgavimab in children <18 years have not been established and no data are available.
	• **Renal impairment**: Tixagevimab plus cilgavimab are not eliminated intact in the urine, renal impairment is not expected to affect the exposure of tixagevimab plus cilgavimab. Similarly, dialysis is not expected to impact the pharmacokinetics of tixagevimab plus cilgavimab.
	• **Hepatic impairment**: The effect of hepatic impairment on the pharmacokinetics of tixagevimab plus cilgavimab is unknown.
	• **COVID-19 vaccinations**:
	  ○ Tixagevimab plus cilgavimab should not be administered within 2 weeks after administration of a COVID-19 vaccine.
	  ○ COVID-19 vaccinations can be given at any interval following administration of tixagevimab plus cilgavimab

Drug Interactions	• Drug-drug interactions have not been studied. • For a full list of drug interactions, check the University of Liverpool COVID-19 resource page.
Preparation and storage	• Supplied as cartons which contain one 150mg/1.5mL vial of tixagevimab and one 150mg/1.5mL vial of cilgavimab. Tixagevimab and cilgavimab are clear to opalescent, colourless to slightly yellow solutions. Discard the vials if the solution is cloudy, discoloured or visible particles are observed. • Store refrigerated at 2 - 8^{O}C in original package. Protect from light. Do not freeze. • Tixagevimab and cilgavimab are both preservative-free and therefore, the prepared syringes should be administered immediately. • If immediate administration is not possible, and the prepared tixagevimab and cilgavimab syringes need to be stored, the total time from vial puncture to administration must not exceed 4 hours at < 25 ^{O}C.
Dose	• **Initial dose:** 300mg of tixagevimab and 300mg cilgavimab each by separate intramuscular injections as a single dose (total dose of 600mg Evusheld®) **Repeat doses (For tier 1 patients only)** • **If initial dose was 150mg of tixagevimab plus 150mg cilgavimab:** A repeat dose of 300mg tixagevimab and 300mg cilgavimab may be considered for patients **THREE** months after the initial dose

	• **If initial dose was 300mg of tixagevimab plus 300mg cilgavimab:** A repeat dose of 300mg tixagevimab and 300mg cilgavimab may be considered for patients **SIX** months after the initial dose. The decision to offer a second dose to patients in tier 1 should be based on clinical judgement guided by ongoing immune compromise, circulating COVID-19 variants and after discussion with the patient.

Administration	• Tixagevimab and cilgavimab are each supplied in individual 150mg vials.
	• Administer as TWO separate, consecutive intramuscular (IM) injections, 1 injection each of tixagevimab and cilgavimab. To do this:
	  ○ Withdraw 300mg (3mL) of tixagevimab solution into ONE syringe AND 300mg (3mL) of cilgavimab solution into a different syringe. Discard unused portion in vials
	  ○ Administer as TWO separate consecutive IM injections at different injection sites, one in each of the gluteal muscles.
	  ○ If discomfort due to the volume of the IM injections is a concern then the dose can be administered as 4 separate consecutive injections: TWO separate consecutive injections of 150mg (1.5mL) of tixagevimab and TWO separate consecutive injections of 150mg (1.5mL) cilgavimab.

Monitoring	• Patients should be monitored for signs of a reaction for 15 minutes after administration
Adverse Effects	• It may be difficult to distinguish between adverse effects of tixagevimab and cilgavimab and the signs and symptoms of COVID-19. • As new medications, adverse reactions to tixagevimab and/or cilgavimab continue to be investigated. Refer to the product information for a complete list of possible adverse effects. To date reactions include: ○ Common (>1%): fatigue, headache, cough • Suspected or confirmed adverse reactions should be reported via Safety Learning System and also via the Therapeutic Goods Administrations adverse effects online form: TGA adverse event reporting • Consider referral to SA COVID-19 Specialist Immunisation Clinic (SACSIC) for any patient with allergic reactions to previous vaccinations and/or PEG.
Patient Information and consent forms	• Tixagevimab plus cilgavimab patient information leaflets can be found here • Examples of generic patient consent forms can be found here **Tixagevimab plus cilgavimab is not recommended as a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended.**

ACRONYMS/ABBREVIATIONS

BMI	Body Mass Index
DMARD	Disease-Modifying Anti-Rheumatic Drug
eGFR	estimated Glomerular Filtration Rate
ID	Infectious Diseases
IM	Intra-muscular
PrEP	Pre-exposure Prophylaxis
NMS	National Medical Stockpile

RESOURCES AND FORMS

- National COVID-19 Clinical Evidence Taskforce (The Australian Living Guidelines)
- Clinical Excellence Commission: Medication Safety Updates
- COVID–19 (SARS–COV–2) – Management Guide (CALHN–PRC05409)
- Anaphylaxis: Management Guidelines (CALHN-OWI04038)
- CALHN COVID–19 internet page
- World Health Organisation. Therapeutics and COVID-19: Living Guideline
- Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. 2020.
- SA Health Updated recommendations on the use of Evusheld (tixagevimab plus cilgavimab) Jan 2023

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Appendix 1: COVID-19 Pre-Exposure Prophylaxis Prioritisation Criteria

Introduction

The rapid development and production of medications active against SARS-CoV-2 has been key in reducing the morbidity and mortality associated with the COVID-19 illness. These new therapeutics have given health care workers not just the ability to treat patients who are unwell and in hospital but also the ability to treat patients with mild disease, thereby preventing hospitalisation and the associated burden on the healthcare system.

Casirivimab plus imdevimab was the first monoclonal antibody provisionally registered in Australia by the Therapeutic Goods Administration (TGA) for not just the treatment of COVID-19 illness but also post exposure prophylaxis for patients with weakened immune systems unlikely to be able to mount an appropriate response to the virus. Unfortunately, the rapid progression of the Omicron Variant of SARS-CoV-2 in South Australian meant that casirivimab plus imdevimab has been of little use in this patient group.

In early March 2022 the Therapeutics Good Association (TGA) announced the provisional registration of tixagevimab and cilgavimab. Unlike other COVID-19 treatments provisionally registered by the TGA, tixagevimab/cilgavimab is a combination of two long-acting monoclonal antibodies designed for use as pre-exposure prophylactic (PrEP) in patients who are either unable to mount an adequate immune response to COVID-19 vaccination or are unable to get a COVID-19 vaccine due to concern for severe adverse reactions. It is not a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended.

Rationale

All of the medications currently available in Australia for the prophylaxis and treatment of mild to moderate COVID-19, except molnupiravir, are accessed via the National Medical Stockpile (NMS). Medication supply and availability through the NMS may vary significantly according to regional outbreaks, supply constraints from manufacturers, changes in evidence and practice and new variants.

Studies have demonstrated that the medications available for prophylaxis (both PrEP and post exposure prophylaxis) from SARS-CoV-2 infection are most likely to benefit those who are unable to mount a significant immune response to the virus. As the anticipated demand for tixagevimab plus cilgavimab is expected to exceed the available supply, it is essential that it is provided in a fair and equal manner to those patients determined to be at the highest risk if they were to be infected by SARS-CoV-2.

Medication Access and Allocation

The core elements for allocation of tixagevimab plus cilgavimab while supplies are limited include:

- Establishment of prioritisation criteria to stratify risk based on a tiering system determined by a multi-disciplinary group of clinicians
- Identification of eligible patients based on prioritisation tiers
- Selection of eligible patients for treatment based on a fair and ethical allocation process
    - This process will determine the order in which patients will receive tixagevimab plus cilgavimab based on initial and ongoing supplies
- Provision of counselling on potential risks and benefits to patients selected for therapy and obtaining consent for treatment to go ahead

To assure fair and timely access of this medication healthcare systems should quickly put in place processes for the selection of and administration to qualifying patients based on prioritisation criteria. These criteria have been developed by a multi-disciplinary team comprising of Infectious Diseases, Haematology, Renal, Respiratory, Rheumatology and Immunology clinicians. Patient selection should involve a process in which Tier 1 patients receive the medication prior to those in the Tier 2 category. As 80% or more of eligible Tier 1 patients have received tixagevimab plus cilgavimab expansion to Tier 2 may occur. Depending on ongoing access to tixagevimab plus cilgavimab further stratification of risk within Tier 2 may be needed.

Appendix 2: Classification of Immune suppression

Table 1: Medical conditions associated with reduced immune response

Haematological disease and stem cell transplant recipients	• Allogenic haematopoietic stem cell transplant (HSCT) recipients in the last 12 months
	• Active graft vs host disease regardless of time from transplant (including HSCT for non-malignant diseases)
	• Autologous HSCT recipients in the last 12 months (including HSCT for non-malignant diseases)
	• Individuals with haematological malignancies who have:
	  ○ Received chimaeric antigen receptor (CAR)-T therapy within the last 2 years OR
	  ○ Radiotherapy in the last 6 months
	• Individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months except:
	  ○ patients with chronic phase chronic myeloid leukaemia (CML) in molecular response OR
	  ○ first or second line tyrosine kinase inhibitors (TKI) – see medications section below for more information
	• All patients with myeloma (excluding MGUS) or chronic B-cell lymphoproliferative disorders (e.g. chronic lymphocytic leukaemia, follicular lymphoma) or myelodysplastic syndrome (MDS) who do not fit the criteria above
	• Individuals with non-malignant haematological disorder (e.g. aplastic anaemia or paroxysmal nocturnal haemoglobinuria) receiving B-cell depleting systemic treatment (see medication section below) within the last 12 months

Patients with non-haematological malignancies	Active metastatic cancer and active solid cancers where patients have received: • Lung cancer on active chemotherapy +/- immunotherapy within 3-6 months • Moderate intensity chemotherapy within the past 2 weeks (see medications below) • Radiotherapy within the last 6 months
Solid organ transplant	All solid organ transplant patients receiving immunosuppressive therapy
HIV/AIDS	Advanced or untreated HIV with CD4 counts < 250/μL or those with a higher CD4 count unable to be established on effective antiretroviral therapy.
Primary immune deficiencies	• Primary immunodeficiency associated with impaired type I interferon signalling • Good's syndrome (thymoma plus B-cell deficiency) • X-linked agammaglobulinaemia (and other primary agammaglobulinaemias) • Any patient with a secondary immunodeficiency receiving, or eligible for, immunoglobulin replacement therapy • Common variable immunodeficiency (CVID) • Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig) • Hyper-IgM syndromes • Severe Combined Immunodeficiency (SCID) syndromes • Autoimmune polyglandular syndromes /autoimmunepolyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome) • Aplastic anaemia on active therapy

Table 2: Medications associated with a reduced immune response to COVID-19 vaccination

Clinicians may use their judgement for medications which are not listed

Corticosteroids	High dose corticosteroid treatment equivalent to ≥ 20mg/day of prednisone for ≥ 14 days in a month, or pulse corticosteroid therapy.
Selected conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDS)	• mycophenolate • methotrexate (≥ 10 mg/week) • leflunomide • azathioprine (≥ 1mg/kg day) • 6-mercaptopurine (≥ 0.5mg/kg/day), • alkylating agents (e.g. cyclophosphamide, chlorambucil) • systemic calcineurin inhibitors (e.g. cyclosporin, tacrolimus)
Moderate intensity chemotherapy agents	Agents with a high risk of severe neutropenia (neutrophils <0.5*10^9/L) for 3-5 days duration post-chemotherapy)
Biologic and targeted therapies including	Anti-CD20 antibodies • rituximab, obintuzumab, ocrelizumab, ofatumumab within 6 months BTK inhibitors • ibrutinib, acalabrutinib, zanubrutinib within 6 months JAK inhibitors • tofacitinib, baricitinib, ruxolitinib, upadacitinib Sphingosine 1-phosphate receptor modulators • fingolimod, siponimod Anti-CD52 antibodies • Alemtuzumab within 6 months Anti-complement antibodies • eculizumab Anti-thymocyte globulin (ATG) • anti-thymocyte globulin (e.g. ATGAM®, Thymoglobuline®, ATG-Grafalon®) Pyrimidine and purine synthesis inhibitors • teriflunamide, cladribine Other agents • abatacept, belimumab, blinatumomab, dimethyl fumarate, venetoclax, daratumumab
Multiple immune-suppressants or combination immunosuppression	Combination therapy where the cumulative effect is severely immunosuppressive (for examples see

Medications not associated with a reduced response to COVID-19 vaccination

The following therapies, when **not** given in combination with other immunosuppressive therapies, are likely to have a minimal effect on COVID-19 vaccine response. Patients prescribed these therapies are **not** eligible for monoclonal antibody or oral antiviral therapy for treatment of mild COVID-19 illness:

- Anti-TNF-α antibodies (e.g. infliximab, adalimumab, etanercept, golimumab, certolizumab)
- Anti-IL1 antibodies (e.g. anakinra)
- Anti-IL6 antibodies (e.g. siltuximab, tocilizumab and sarilumab)
- Anti-IL17 antibodies (e.g. apremilast, secukinumab, ixekizumab)
- Anti-IL4 antibodies (e.g. dupilumab)
- Anti-IL23 antibodies (e.g. guselkumab, risankizumab, tildrakizumab, ustekinumab)
- Immune checkpoint inhibitors (e.g. atezolizumab, durvalamab, ipilimumab, nivolumab, pembrolizumab)
- Integrin receptor inhibitors (e.g. natazilumab, vedolizumab)
- Interferons
- Glatiramer
- VEGF, EGFR and HER2 blockers (e.g. cetuximab, panitumumab, pertuzumab, traztuzumab, bevacizumab)

Appendix 3: Risk factors for progressing to severe illness

- Immunosuppression
- Renal impairment (eGFR < 60mL/min or equivalent renal impairment for pregnant women)
- Age ≥ 50 years or age ≥ 30 years if Aboriginal and/or Torres Strait Islander*
- Diabetes (requiring medication) or gestational diabetes (requiring medication) in pregnant women
- Obesity (BMI > 30 kg/m^2 or > 40 kg/m^2 for pregnant patients)
- Chronic liver disease (cirrhosis)
- Respiratory compromise including:
    - history of chronic bronchitis, bronchiectasis, chronic obstructive pulmonary disease (COPD)or moderate-to-severe asthma requiring an inhaled steroid to control symptoms or caused by neurological or musculoskeletal disease
- Neurological conditions including stroke, dementia and demyelinating conditions
- Coronary artery disease
- Heart failure or cardiomyopathies
- Residing in residential aged care
- Disability with multiple comorbidities and/or frailty
- Reduced, or lack of, access to higher level healthcare and lives in an area of geographic remoteness classified by the Modified Monash Model as Category 5 or above
- Pregnancy (see page 11)
- Down Syndrome
- Cerebral Palsy
- Congenital heart disease
- Thalassemia
- Sickle cell disease
- Other haemoglobinopathies not already listed

Studies have demonstrated that the risk of severe COVID-19 increases with age and number of comorbidities.

Supplies of medications from the National Medical Stockpile (NMS) can vary according to outbreaks and demand and in the setting of limited supply certain risk factors or patients with greater than 1 risk factor may be prioritised for treatment of mild disease.