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| Pre-exposure prophylactic treatment for COVID-19: tixagevimab and cilgavimab (EvusheldTM) – Frequently asked questions |
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| OFFICIAL |



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# Background:

A limited supply of tixagevimab and cilgavimab (EvusheldTM) is available in Victoria for use in high-risk people for **pre-exposure prophylaxis** of COVID-19.

Tixagevimab and cilgavimab (EvusheldTM) is currently available in Victoria for the following patient groups:

Eligible patient groups for tixagevimab and cilgavimab (Evusheld™) pre-exposure prophylaxis have been expanded and now include:

* heart/lung transplant recipients
* STEM Cell Transplant or CAR T-cell therapy recipients within 12 months OR STEM Cell recipients with GVHD OR still requiring significant ongoing immunosuppression for other reasons
* kidney, pancreas/islet cell or liver transplant recipients within 12 months OR requiring therapy for acute rejection OR still requiring significant ongoing suppression for other reasons
* individuals with primary immunodeficiency syndromes
* haematologic disorders that may affect B cell function eg. CLL, CMML, myelodysplastic syndrome, myeloma
* individuals unable to be immunised with COVID-19 vaccines due to genuine, severe allergy if ≥ 65 years old (≥ 50 years old if Aboriginal) and not recently infected with COVID-19 within 3 months
* individuals who have haematological malignancies and are receiving active therapy
* individuals with HIV who have a CD4 cell count < 50 cells/mm3
* individuals who within the last 12 months received:

- anti-CD20 antibodies (rituximab, obinutuzumab, ocrelizumab, ofatumumab)

- BTK inhibitors (ibrutinib, acalabrutinib, zanubrutinib)

- BLC2 inhibitor (venetoclax)

- anti-CD38 (daratumumab)

- anti-BCMA bi-specific antibody

- sphingosine 1- phosphate receptor modulators (fingolimod, siponimod)

- anti-CD52 antibodies (alemtuzumab)

- anti-complement antibodies (eculizumab)

- anti-thymocyte globulin

- high dose (> 1 g/m²) cyclophosphamide.

The purpose of this document is to address frequently asked questions (FAQs) to support clinicians in their use of tixagevimab and cilgavimab (EvusheldTM).

This document has been developed by an expert working group of Victorian clinicians.

# **What is the benefit of tixagevimab and cilgavimab (EvusheldTM)?**

### Tixagevimab and cilgavimab (EvusheldTM) are monoclonal antibodies designed to block viral attachment and entry into cells. A large ongoing Phase III, randomised, double-blind placebo-controlled clinical trial (PROVENT) in high-risk individuals showed an 83% reduction of symptomatic COVID-19 in the six months after administration. Please see [the Australian guidelines for the clinical care of people with COVID-19](https://app.magicapp.org/#/guideline/L4Q5An/section/j7Amwz) <[https://app.magicapp.org/#/guideline/L4Q5An/section/j7Amwz](https://app.magicapp.org/%23/guideline/L4Q5An/section/j7Amwz)> for further details about the benefits of tixagevimab and cilgavimab (EvusheldTM) as a pre-exposure prophylactic treatment for individuals at risk of severe disease from COVID-19.

# **What patients are able to receive tixagevimab and cilgavimab (EvusheldTM)?**

Patients who would benefit from tixagevimab and cilgavimab (EvusheldTM) include those with moderate to severe immune compromise that make it likely that they will not mount an adequate immune response to a COVID‐19 vaccination or for whom vaccination is not recommended due to a history of severe adverse reaction to a COVID‐19 vaccine/vaccine components.

Currently eligibility in Victoria is available at [Medications for patients with COVID-19](https://www.health.vic.gov.au/covid-19/vaccines-and-medications-in-patients-with-covid-19) <<https://www.health.vic.gov.au/covid-19/vaccines-and-medications-in-patients-with-covid-19>> on the Department of Health website. Eligibility has been restricted in the first instance due to limited supply from the National Medical Stockpile. Eligibility criteria will be expanded as additional supply becomes available. Updates will be communicated to health services and updated at the webpage above.

# **Is it necessary or desirable to check antibody status prior to administration?**

Serology testing is not required prior to administration of tixagevimab and cilgavimab (EvusheldTM).

# **Is the timing between a patient receiving a COVID-19 vaccine and being administered tixagevimab and cilgavimab (EvusheldTM) significant?**

Tixagevimab and cilgavimab (EvusheldTM) can impact the body's immune response to a COVID-19 vaccination. If the patient has recently received a COVID-19 vaccine, you should wait at least two weeks from the date of that vaccination to administer tixagevimab and cilgavimab (EvusheldTM).

# **Is the timing between a patient having a confirmed COVID-19 infection and being administered tixagevimab and cilgavimab (EvusheldTM) significant?**

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(EvusheldTM).

# **What is the recommended observation time for a patient after receiving tixagevimab and cilgavimab (EvusheldTM)?**

Currently, a minimum 15-minute observation time is recommended.

In the PROVENT clinical trial, observation time post administration of tixagevimab and cilgavimab (EvusheldTM) was 60 minutes. There were no anaphylactic reactions to the medication after 15 minutes in the PROVENT trial. Observation time should balance individual patient risk of a reaction with risk of the patient being exposed to COVID-19 or other viruses in the time spent in an indoor environment with other people.

# **Are patients required to obtain a negative PCR prior to receiving tixagevimab and cilgavimab (EvusheldTM)?**

The administration of tixagevimab and cilgavimab (EvusheldTM) does not require a negative PCR prior. However, patients should follow testing guidelines as per usual process. For example, getting tested if they have symptoms of COVID-19.

# **What is the implication of a patient having a past history of receiving COVID-19 medications such as sotrovimab (XevudyTM) or antivirals?**

Tixagevimab and cilgavimab(EvusheldTM) can still be given if a person has previously had sotrovimab or any other antivirals for the treatment of COVID-19. If the patient has had a previous COVID-19 infection which required treatment, it is suggested to wait 30 days from the start of the infection before administering tixagevimab and cilgavimab(EvusheldTM).

# **Are there any restrictions in the co-administration of tixagevimab and cilgavimab (EvusheldTM) with the administration of B cell depleting therapies?**

There are no current restrictions on timing of doses of tixagevimab and cilgavimab(EvusheldTM) relative to timing of other immunosuppressive therapies, including B cell depleting therapies.

# **Would you prescribe tixagevimab and cilgavimab (EvusheldTM) to people with a history of ischemic heart disease?**

In the PROVENT clinical trial which studied tixagevimab and cilgavimab(EvusheldTM) for prevention of severe illness from COVID-19 through pre-exposure prophylaxis treatment it was reported that when people had risk factors for cardiac events (including a history of ischaemic heart disease), more people (N=23, Exposure Adjusted Incidence (EAIR) 1.2) who received tixagevimab and cilgavimab(EvusheldTM) experienced cardiac complications than the placebo group (N=5, EAIR 0.5). In this trial comparing tixagevimab and cilgavimab(EvusheldTM) (N=3,461) to placebo (N=1,736), there was one intervention recipient (<0.1%) and one placebo recipient (<0.1%) who each had two serious cardiac adverse events. It is not known if this was related to the tixagevimab and cilgavimab(EvusheldTM) or to the person’s pre-existing medical conditions and is still under investigation.

# **What is the current recommended dose of tixagevimab and cilgavimab (EvusheldTM)?**

Currently the dose recommendation is 150 mg of tixagevimab and 150 mg of cilgavimab administered as separate sequential IM injections. See the [product information](https://www.tga.gov.au/sites/default/files/evusheld-pi.pdf) <<https://www.tga.gov.au/sites/default/files/evusheld-pi.pdf>> for further information. It is noted that the U.S. Food and Drug Administration (FDA) has recommended a higher dose in the United States due to circulating Omicron subvariants BA.1 and BA.1.1. The activity against BA. 2 which is the current circulating strain is not known to be reduced and in vitro activity against BA. 3, 4 and 5 are only slightly reduced. There is no current rationale to increase the dose in the Victorian context.

# **Can tixagevimab and cilgavimab (EvusheldTM) be given intravenously?**

Clinically significant bleeding disorders, such as thrombocytopenia and other coagulation disorders, are a precaution for intramuscular injections. For patients at high risk of bleeding, administration via an intravenous route may be an option. Seek specialist advice from a major health service regarding this.

# **Are there any medication related interactions with tixagevimab and cilgavimab (EvusheldTM)?**

Drug-drug interaction studies have not been performed. However, tixagevimab and cilgavimab (EvusheldTM) are not renally excreted or metabolized by cytochrome P450 (CYP) enzymes; therefore, interactions with concomitant medications that are renally excreted or that are substrates, inducers, or inhibitors of CYP enzymes are unlikely and can be co-administered. The University of [Liverpool COVID-19 Drug Interactions checker](https://www.covid19-druginteractions.org/) <<https://www.covid19-druginteractions.org/>> provides an interactive tool for COVID-19 therapies and is a recommend resource for updates.

# **Is tixagevimab and cilgavimab (EvusheldTM) being used in Paediatric populations?**

As the risk of severe COVID-19 is lower in children, tixagevimab and cilgavimab (EvusheldTM) is recommended to only be used in high-risk children who have significant immunosuppression in addition to another risk factor for severe disease. This should be discussed with a paediatric infectious diseases specialist and immunologist. Please see the [Product Information](https://www.tga.gov.au/sites/default/files/evusheld-pi.pdf) <<https://www.tga.gov.au/sites/default/files/evusheld-pi.pdf>> which outlines a summary of advice regarding administration of tixagevimab and cilgavimab(EvusheldTM) in paediatric cohorts. As per the Product Information, the recommended dosing regimens are expected to result in comparable serum exposures of tixagevimab and cilgavimab (EvusheldTM) in individuals 12 years of age and older and weighing at least 40 kg as observed in adults. The safety and efficacy of tixagevimab and cilgavimab (EvusheldTM) in children aged under 12 and less than 40 kg is still being investigated.

# **Is the dose of tixagevimab and cilgavimab (EvusheldTM) repeated after six months?**

Current evidence supports six-month efficacy with a single dose of tixagevimab and cilgavimab (EvusheldTM). The need for subsequent doses is under review.

# **What models of care are currently being used to deliver tixagevimab and cilgavimab (EvusheldTM) to eligible cohorts?**

Inpatient and outpatient models of care are being used currently to deliver EvusheldTM. This includes an opportunistic approach where patients are being offered treatment as part of a routine outpatient appointment or during an inpatient admission. Other successful models have included “blitz clinics”, outpatient weekend clinics where eligible patients have been invited to attend an appointment, to administer doses of the medication to larger eligible cohorts at a single point in time.

The Victorian Department of Health (the department) acknowledges current resourcing constraints and administration barriers within health services. The department continues to consult with sector representatives to improve access and prescribing pathways.

# **How is the data going to be managed?**

Health services administering tixagevimab and cilgavimab (EvusheldTM) will be responsible for patient record documentation as per standard process for all clinical treatment. Limited, deidentified patient information is collected as part of the request to access process which allows the department to monitor stock use and informs reporting obligations back to the Commonwealth. The department will not be developing a central register for information such as patient demographics, adverse events and other relevant clinical information for either early therapies treatment or pre-exposure prophylaxis for COVID-19. As per the [Product Information](https://www.tga.gov.au/sites/default/files/evusheld-pi.pdf) <<https://www.tga.gov.au/sites/default/files/evusheld-pi.pdf>>, healthcare professionals should report any suspected adverse reactions at [www.tga.gov.au/reporting-problems](http://www.tga.gov.au/reporting-problems).

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