EVUSHELD™ (tixagevimab and cilgavimab) 
Information for Health-Care Providers

What is EVUSHELD?
EVUSHELD is a combination monoclonal antibody product containing two anti-spike SARS-CoV-2 monoclonal antibodies (tixagevimab and cilgavimab).

In Canada, tixagevimab/cilgavimab is approved for pre-exposure prophylaxis of COVID-19 in adults and adolescents (≥12 years of age, and weighing at least 40 kg), who have not had a known recent exposure to an individual infected with SARS-CoV-2 and:
- who are immune compromised and unlikely to mount an adequate immune response to COVID-19 vaccination, OR
- for whom COVID-19 vaccination is not recommended.1

Pre-exposure prophylaxis with tixagevimab/cilgavimab is not a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended.

Eligibility for Tixagevimab/Cilgavimab in Manitoba
Tixagevimab/cilgavimab may be considered as pre-exposure prophylaxis for COVID-19 on a case-by-case basis for severely immunocompromised individuals. These include:
- lung transplant recipients,
- individuals receiving other solid organ transplant within the past 6 months,
- individuals receiving anti-CD20 agents or B-cell depleting agents (e.g., rituximab, ocrelizumab, ofatumumab, obinutuzumab, blinatumomab, inotuzumab, ibrutinib, etc.) within the past 6 months,
- individuals receiving CAR-T therapy, hematopoietic stem cell transplantation, or induction chemotherapy for acute leukemia,
- individuals with significant primary immunodeficiencies, such as disorders affecting T-cells, immune dysregulation, or type 1 interferon defects.

In addition to the above, the patient must meet the following criteria:
- NO known cardiovascular disease (e.g. coronary artery disease, history of myocardial infarction or stroke, unstable angina, heart failure, congenital heart disease, or arrhythmias),
- other risk factors for cardiovascular disease should also be considered (e.g. hyperlipidemia, hypertension),
- age ≥12 years of age with weight of at least 40 kg,
- patients should be informed of the potential risks and limited evidence supporting the use of tixagevimab/cilgavimab.

Given the limited data regarding benefit, and the potential for harm Shared Health strongly encourages individualized assessment of each patient and consultation with an appropriate specialist prior to prescribing tixagevimab/cilgavimab.

Dosage and Administration
The dose of tixagevimab/cilgavimab that is approved by Health Canada for pre-exposure prophylaxis of COVID-19 is 300 mg (tixagevimab 150 mg and cilgavimab 150 mg) administered intramuscularly.1 See Table 1.

Table 1. Preparation and Administration of tixagevimab/cilgavimab 300 mg total dose.1
**Discard remainder of vial.**
**Administer tixagevimab and cilgavimab as separate injections.**

The SARS-CoV-2 viral variants that are currently circulating may be associated with resistance to monoclonal antibodies such as tixagevimab and cilgavimab. Healthcare providers should routinely review information regarding the resistance of circulating viral variants, as well as guidance from Shared Health. A higher dose of 600 mg (tixagevimab 300 mg and cilgavimab 300 mg) may be considered, based on currently circulating viral variants. See Table 2.

Table 2. Preparation and Administration of tixagevimab/cilgavimab 600 mg total dose.

<table>
<thead>
<tr>
<th>Cartons Required</th>
<th>Monoclonal antibody</th>
<th>Dose</th>
<th>No. vials required</th>
<th>Preparation</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>One carton</td>
<td>tixagevimab</td>
<td>150 mg</td>
<td>tixagevimab 150 mg/1.5 mL vial (dark grey cap) x 1</td>
<td>Withdraw 1.5 mL from vial into a syringe*</td>
<td>Inject tixagevimab intramuscularly (preferably gluteal muscle)**</td>
</tr>
<tr>
<td></td>
<td>cilgavimab</td>
<td>150 mg</td>
<td>cilgavimab 150 mg/1.5 mL vial (white cap) x 1</td>
<td>Withdraw 1.5 mL from vial into a syringe*</td>
<td>Inject cilgavimab intramuscularly (preferably gluteal muscle)**</td>
</tr>
</tbody>
</table>

| Two cartons      | tixagevimab         | 300 mg | tixagevimab 150 mg/1.5 mL vial (dark grey cap) x 2 | Withdraw 1.5 mL from each vial into a syringe for total volume 3 mL* | Inject tixagevimab intramuscularly (preferably gluteal muscle)** |
|                  | cilgavimab          | 300 mg | cilgavimab 150 mg/1.5 mL vial (white cap) x 2 | Withdraw 1.5 mL from each vial into a syringe for total volume 3 mL* | Inject cilgavimab intramuscularly (preferably gluteal muscle)** |

*Discard remainder of vial.
**Administer tixagevimab and cilgavimab as separate injections.

The current recommendation is that for appropriate patients, subsequent doses of tixagevimab/cilgavimab will be required every 6 months. Patients due for COVID vaccination should wait 14 days after vaccination before receiving tixagevimab/cilgavimab, or delay vaccination until 14 days after administration of tixagevimab/cilgavimab.

Tixagevimab/cilgavimab is preservative-free and, therefore, the prepared syringes should be administered immediately. If immediate administration is not possible, the total time from vial puncture to administration should not exceed 4 hours, with prepared syringes stored either refrigerated at 2ºC to 8ºC or at room temperature up to 25ºC.

**Contraindications**
Tixagevimab/cilgavimab is contraindicated in patients who are allergic to tixagevimab, cilgavimab, or ingredients contained in the tixagevimab/cilgavimab vial. For a list of ingredients, refer to the product monograph.

**Warning and Precautions**
In the PROVENT phase 3 clinical trial, there were a higher proportion of serious cardiac events reported in patients who received tixagevimab/cilgavimab, compared to the placebo group (0.7% vs 0.3%, respectively). The proportion of serious thromboembolic events reported was also greater in the
tixagevimab/cilgavimab group versus placebo (0.5% vs 0.2%, respectively). Most subjects had cardiac risk factors, and/or a history of cardiovascular disease. A causal relationship between tixagevimab/cilgavimab and adverse cardiac events has not been established.

**Adverse Reactions**¹²

Adverse effects with tixagevimab/cilgavimab were generally uncommon in clinical trials and were similar to the placebo arm. Hypersensitivity (rash and urticaria), and injection site reactions (erythema, pain, pruritis, induration) were the most commonly observed adverse events. See Table 3.

Anaphylaxis has been observed with other monoclonal antibodies; although data for tixagevimab/cilgavimab is limited, patients should be monitored for 1 hour following the injection, and recommend having epinephrine on hand for initial management of a serious hypersensitivity reaction.

Please see the “Manitoba Provincial Anaphylaxis Protocol: Community Health Immunization” for more guidance on preparation and management of anaphylaxis in community settings: [https://professionals.wrha.mb.ca/old/professionals/immunization/files/mb-anaphylaxis-protocol.pdf](https://professionals.wrha.mb.ca/old/professionals/immunization/files/mb-anaphylaxis-protocol.pdf)

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Description</th>
<th>Tixagevimab/cilgavimab 300 mg*</th>
<th>Placebo (n=2108)</th>
<th>Tixagevimab/cilgavimab 600 mg**</th>
<th>Placebo (n=451)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypersensitivity</td>
<td>rash and urticaria</td>
<td>1.0%</td>
<td>0.9%</td>
<td>0.4%</td>
<td>0.7</td>
</tr>
<tr>
<td>Injection site reactions</td>
<td>injection site pain, erythema, pruritus, or induration</td>
<td>1.3%</td>
<td>1.2%</td>
<td>2.4%</td>
<td>2.4%</td>
</tr>
</tbody>
</table>

*PROVENT and STORM CHASER trials; **TACKLE trial

**Supplied As**¹

Each carton/box of tixagevimab/cilgavimab contains two vials:
- 1 x tixagevimab vial for injection 150 mg (dark grey vial cap)
- 1 x cilgavimab vial for injection 150 mg (white vial cap)

**Storage Requirements**

Store tixagevimab/cilgavimab in the fridge at 2 to 8°C.¹

The authorized shelf life of tixagevimab/cilgavimab with Lot number “CAAN” was extended by Health Canada in a notice sent on July 15, 2022.³ The new expiry date is December 31, 2022, when stored at 2 to 8°C.³
- The expiration date for tixagevimab/cilgavimab vials can be accessed at astrazeneca.ca, or by scanning the QR code on the global English-only carton label to visit www.laab.azcovid-19.com.³

**Tixagevimab/Cilgavimab Clinical Trial**¹²

- In a phase 3 clinical trial (PROVENT) conducted between November 21, 2020, and March 22, 2021, tixagevimab/cilgavimab (AZD7442) was studied for pre-exposure prophylaxis of COVID-19.
Patients aged 18 years or older with an increased risk of inadequate response to COVID-19 vaccinations, or at increased risk of exposure to SARS-CoV-2 (e.g. occupation) were eligible for enrollment. Patients were required to have no prior COVID-19 infection (as determined by a negative SARS-CoV-2 serologic test).

- The investigators defined patients who were at increased risk for an inadequate response to COVID-19 vaccination as those who were: older (≥60 years of age), obese, immunocompromised, or unable to receive vaccines without adverse effects; or as having congestive heart failure, chronic obstructive pulmonary disease, chronic kidney disease, or chronic liver disease.

Using a 2:1 randomization, 3460 and 1737 patients were randomized to receive tixagevimab/cilgavimab or placebo, respectively. The SARS-CoV-2 variants of concern circulating during the study included alpha (B1.1.7_1), beta (B.1.351), and delta (B.1.617.2).

- The primary efficacy endpoint was the first episode of symptomatic COVID-19 confirmed by PCR between date of administration and up to or on day 183.
- Primary analysis at the data cut-off point found 8 of 3441 (0.2%) tixagevimab/cilgavimab recipients developed COVID-19 compared to 17 of 1731 (1.0%) placebo participants (relative risk reduction, 76.7%; 95% confidence interval [CI], 46.0 to 90.0; P<0.001).

**Tixagevimab/Cilgavimab Study Limitations**

- In vitro studies indicate the neutralizing activity of tixagevimab/cilgavimab is decreased against the SARS-CoV-2 Omicron variants of concern.4-6
- Tixagevimab/cilgavimab was evaluated only in patients without prior COVID-19 infection.
- The clinical effectiveness of tixagevimab/cilgavimab for pre-exposure prophylaxis in the immunocompromised population is not known, as only small number of immunocompromised patients were enrolled in the clinical trial.
- The clinical efficacy of tixagevimab/cilgavimab for pre-exposure prophylaxis of COVID-19 due to circulating SARS-CoV-2 variants of concern has not been studied.

**References**


