COVID-19 Therapies - tixagevimab/cilgavimab (EVUSHELD™)

Guidance for healthcare providers August 5, 2022

Recently, Health Canada approved tixagevimab/cilgavimab (Evusheld™), a long-acting monoclonal antibody, for prevention of COVID-19 in individuals who are expected to have a reduced response to vaccination or who cannot receive a COVID-19 vaccine.

Please see the full guide developed by the B.C. COVID Therapeutics Committee for more information:
Clinical Practice Guide for the Use of Tixagevimab/Cilgavimab

What are the current recommendations for tixagevimab/cilgavimab in BC?

Refer to: Clinical Practice Guide for the Use of Tixagevimab/Cilgavimab

Tixagevimab/cilgavimab is **NOT RECOMMENDED** for pre-exposure prophylaxis, including in severely immunocompromised patients (CEV1).

This recommendation is based on the following rationale:

- Tixagevimab is inactive against the currently predominating BA 4/5 variants of concern and cilgavimab has greatly reduced neutralization activity against these variants according to in-vitro studies.
- The activity of tixagevimab/cilgavimab against BA 4/5 has not been evaluated against live virus or in vivo. According to limited real world data, the reduction in binding likely leads to lower serological and clinical activity that cannot be fully overcome by a dose increase.
- Currently, there is a lack of high-quality evidence demonstrating a benefit of tixagevimab/ cilgavimab (EVUSHELD™) in preventing hospitalization or mortality from COVID-19 in general.
- Tixagevimab/cilgavimab was evaluated in unvaccinated non-immunocompromised individuals to prevent symptomatic infection with wild-type, Alpha and Delta virus; its role within the present vaccine and therapeutic landscape, especially in immunocompromised individuals who lacked adequate representation in the randomized clinical trial, is unclear and has not been properly evaluated.
- Retrospective observational studies show that it results in unpredictable antibody levels and is likely of minimal additive value in preventing hospitalizations in the current vaccine and treatment landscape.
- Further, any theoretical benefit may not outweigh by the potential risk of cardiac serious adverse events (SAEs). Further research and real-world evaluation are urgently needed.

Tixagevimab/cilgavimab is not a replacement for vaccination or proven therapies for treatment of COVID-19. Patients should be encouraged to receive scheduled booster doses and be offered therapy if they have symptomatic COVID-19.

The following guidance is for transparency and is not a recommendation to give Evusheld™

THERAPY DOSE: **tixagevimab/cilgavimab (EVUSHELD™)** - monoclonal antibody administered by gluteal intramuscular injection 300mg IM (150mg=1.5mL each tixagevimab and cilgavimab) every 6 months

COVID-19 Treatment

Health Care Provider Information

BC Centre for Disease Control
Provincial Health Services Authority

Administration considerations:

- The currently approved dose of 300mg is unlikely to effectively neutralize the BA 4/5 Variants of Concern.
- Health Canada has not provided guidance regarding dosing against BA 4/5.
- The US Monograph recommends a double dose of 600mg; however, it also states that the pharmacokinetic target attainment with this dose at 6 months is only 61%.
- Tixagevimab/cilgavimab should not be used if the patient has active COVID-19 or has been recently exposed to COVID-19 as tixagevimab/cilgavimab will not prevent the infection or be as effective as treatment compared to currently available therapies.

Tixagevimab/cilgavimab prescriptions should be faxed to **604-941-0532.** Special Authority is not required.

Injections are delivered through:

- physician clinics (couriered to the location where it will be administered to the patient) OR
- hospital inpatient or a hospital-based clinic (where the order is processed through the hospital pharmacy).

Tixagevimab/cilgavimab is provided free of charge to patients.

Contraindications and Cautions

Hypersensitivity reactions and infusion **reactions are rare**.

- Monoclonal antibodies have been shown to be associated with injection reactions and hypersensitivity reactions including anaphylaxis at rates similar to COVID-19 vaccines.
- Patients receiving tixagevimab/cilgavimab should be observed for 15 minutes after their injections.
- Tixagevimab/cilgavimab should not be given to patients allergic to mRNA vaccines due to cross reactivity of Polyethylene Glycol with polysorbate 80

Pediatrics: Tixagevimab/cilgavimab has been approved for children 12 years and over weighing 40 kg or more. There were no individuals < 18 years in clinical studies; dosing and safety has been inferred from pharmacokinetic and animal studies.

Renal and liver disease: There are no dose adjustments or contraindications with renal or liver disease.

Laboratory Monitoring

Drug-to-Drug Interactions

Possesses **no significant drug-drug interactions.**

Tixagevimab/cilgavimab should not delay **COVID-19 vaccinations**.

- Patients should have their vaccines up to date and should wait at least 14 days from their last COVID-19 vaccine dose before receiving tixagevimab/cilgavimab.

Side Effects

General side effects from tixagevimab/cilgavimab are mild and resolve quickly. As with vaccinations, patients can experience **pain at the injection site, headache, malaise and fatigue**.

Cardiovascular Serious Adverse Effects: Patients taking tixagevimab/cilgavimab experienced more cardiovascular serious adverse events (SAEs) than those taking placebo (22 vs. 5).

- All patients who experienced cardiac-related hospitalization or death who received

This document provides guidance only; patients defined above are those who may benefit from treatment. Case-by-case assessment is still required, and the totality of risk factors needs to be considered when offering treatment. Expert consultation can assist with additional risk assessments.

There is **no laboratory monitoring** required before or after the dose. Serology testing is not routinely recommended as it is not a useful predictor of clinical outcomes such as hospitalization from COVID-19 in vaccinated individuals.	tixagevimab/cilgavimab had cardiovascular risk factors; however not all had known cardiovascular disease. • The absolute risk of cardiovascular SAEs is low (approximately 0.56%); however, as the benefit of this drug in preventing hospitalization from COVID-19 is theoretical, the risk of tixagevimab/cilgavimab in those with cardiovascular diseases may not outweighed by this benefit.

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