Evusheld™ (tixagevimab and cilgavimab) for Pre-Exposure Prophylaxis Clinical Practice Guideline

Evusheld™ is a combination of tixagevimab and cilgavimab, which are recombinant monoclonal antibodies (mAbs) that bind to the spike protein receptor binding domain of SARS-CoV-2 and block it from attaching to the human ACE2 receptor.[1,2] Monoclonal antibodies are produced in a lab and are designed to restore, enhance, or mimic the immune system. Several other mAbs have been developed to target the spike protein of SARS-CoV-2 and used in the treatment of COVID-19. Effectiveness of some mAbs has been limited due to the emergence of new SARS-CoV-2 variants and development of resistance.

Evusheld™ is approved by Health Canada to prevent COVID-19 infection in individuals at high risk. Evusheld™ may provide additional protection to these individuals, but it is not a substitute for vaccination. Vaccination remains the primary defense against COVID-19 infection and is well supported by evidence.

Evusheld™ was developed at a time when vaccines and therapeutic options for COVID-19 were widely unavailable, and the clinical trial for pre-exposure prophylaxis with Evusheld™ evaluated unvaccinated individuals when wild-type, Alpha, and Delta variants were circulating. The benefit of Evusheld™ for preventing meaningful outcomes (hospitalization and death) in vulnerable individuals with the current circulating variants is unknown. Further, the risks, including treatment failure due to resistance and cardiac serious adverse effects (SAEs), may outweigh any potential benefit.

Although approved by Health Canada, **the Saskatchewan Health Authority's Therapeutics Expert Group is not recommending the use of Evusheld™ at this time (Briefing Note – May 20, 2022).** If Evusheld™ is being considered for use for **prophylaxis**, it should be on a case-by-case basis where the potential benefit is expected to outweigh any potential risk. Evusheld™ should only be offered to those who are immunocompromised, are unlikely to mount an adequate response to vaccination, and who are at a high risk of severe outcomes from COVID-19 infection.

This Clinical Practice Guideline provides a summary of use and available evidence to aid in shared decision making between health care providers and patients. Information provided in this Guideline represents evidence and information available on the date of publication and is subject to change.

medSask respectfully acknowledges the work of the BC Centre for Disease Control which was used to help guide the creation of this Clinical Practice Guideline.

Therapeutic Options that Have Been Considered for COVID-19[3-5]

	Therapeutic options:	No longer recommended:	Not recommended:
Prevention and Prophylaxis	COVID-19 vaccine: Vaxzevria™, Comirnaty™, Janssen, Covifenz®, Spikevax™, Nuvaxovid™	bamlanivimab^/etesevimab*^, casirivimab^/imdevimab^	ivermectin* convalescent plasma* IVIG* hydroxycholorquine* ribavirin* interferon* lopinavir/ritonavir* azithromycin* vitamin D*
	tixagevimab^/cilgavimab^ (Evusheld™)@		
Treatment of Mild to Moderate Illness	nirmatrelvir$/ritonavir (Paxlovid™) remdesivir$ (Veklury®)	sotrovimab^ - inadequate activity versus BA.2 variant	
	inhaled corticosteroid#* fluvoxamine#* colchicine#*		
Treatment of Moderate to Severe Illness	tocilizumab*^ dexamethasone* baricitinib* sarilumab*^	bamlanivimab^/etesevimab*^ casirivimab^/imdevimab^	

@= limited evidence; uncertain benefit relative to harm; # = uncertainty/low certainty of evidence; * = not authorized by Health Canada for prevention or treatment of COVID-19; ^ = monoclonal antibody; $ = antiviral

Evusheld™ Indications

Evusheld™ is officially indicated in Canada for the **pre-exposure prophylaxis** of COVID-19 in adults and adolescents (≥12 years old weighing at least 40 kg) who have NOT had a recent exposure to an individual with COVID-19 and:

- are immunocompromised and not likely to mount an adequate immune response to COVID-19 vaccination OR
- for whom COVID-19 vaccination is not recommended.[1]

OCT 2022 UPDATE: Evusheld™ is officially indicated in Canada for the **treatment** of mild to moderate COVID-19 in adults and adolescents (≥12 years old weighing at least 40 kg). This guideline does not include information about the use of Evusheld™ for treatment of COVID-19.

Evusheld™ is:

- NOT a substitution for vaccination.
- NOT currently indicated for post-exposure prophylaxis of COVID-19 in people who have been exposed to COVID-19.

Eligibility

In Saskatchewan, the case-by-case use of Evusheld™ for pre-exposure prophylaxis should be limited to patients who:

- are severely immunocompromised. This includes:
  - solid organ transplant recipients;
  - individuals with malignant hematologic conditions (e.g., leukemia, lymphoma, or myeloma), who have received active treatment within the last year with chemotherapy, targeted therapies including CAR—T, and immunotherapy);
  - individuals who have received a bone marrow or stem cell transplant within the last 2 years;
  - individuals who are taking immunosuppressant medications for graft vs. host disease;
  - individuals who have taken anti-CD20 agents or B-cell depleting agents (e.g., rituximab, ocrelizumab, ofatumumab, obinotuzimab, blinatumomab, inotuzumab, ibrutinib, etc.) within the last 6 months;
  - individuals with significant primary immunodeficiency affecting T-cells, immune dysregulation, or type 1 interferon defects;

AND

- have additional risk factors or exceptional circumstances that correlate with an extremely high risk of poor outcomes from COVID-19 (i.e.: unable to receive COVID-19 vaccination, unable to complete COVID-19 vaccination course, treatment of COVID-19 is contraindicated, or severe graft vs. host disease).

Other risk factors may exist and should be considered on a case-by-case basis as per the prescribing clinician's discretion.

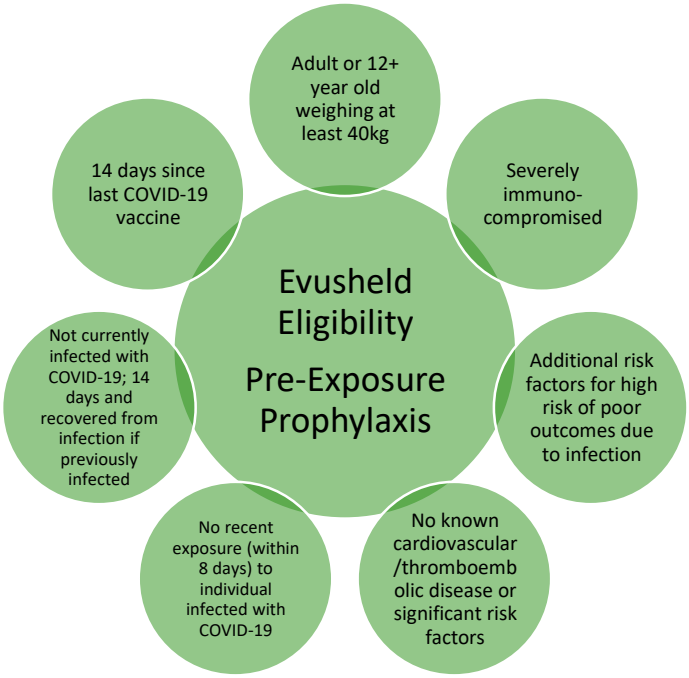
IN ADDITION,

- The individual must NOT have known cardiovascular disease (CVD) (i.e.: coronary artery disease, history of myocardial infarction (MI) or stroke, unstable angina, heart failure, congenital heart disease, or arrhythmias).

It is NOT recommended that Evusheld™ be administered to individuals who are severely immunocompromised but <u>without</u> additional risk factors for hospitalization from COVID-19.

There may be case-by-case exceptions for use of Evusheld™ for non-immunocompromised individuals with an absolute contraindication to receiving COVID-19 vaccine where benefits of pre-exposure prophylaxis with Evusheld™ may outweigh the risk of treatment.

Summary of Eligibility in Saskatchewan for Pre-exposure Prophylaxis ONLY:



Dosing

NOV 2022 UPDATE:

- As per Canadian monograph, the **recommended dose of Evusheld™ for pre-exposure prophylaxis is 600 mg** administered as two separate 3.0 mL sequential intramuscular (IM) injections of:
  - 300 mg of tixagevimab
  - 300 mg of cilgavimab
- There are no dose adjustments required for kidney or liver disease.

Dosing Considerations:

- Evusheld™ was originally authorized as a 300 mg dose which was established in the PROVENT trial when Alpha, Beta, Gamma, and Delta variants were circulating.
- There are limited data available with repeat dosing. The duration of protection demonstrated in the PROVENT clinical trial was 6 months. The duration of protection may vary with emerging variants.
- Consider giving individuals that originally received Evusheld™ 300 mg for pre-exposure prophylaxis an additional dose of 600 mg as the 300 mg dose is not likely to be effective.
- The product monograph recommends repeat doses of 600 mg every 6 months. Recommendations regarding repeat dosing may need to be reconsidered due to emerging SARS-CoV-2 variants and variability in activity against variants.

Cautions and Contraindications

- Evusheld™ is contraindicated in individuals who have history of severe hypersensitivity/anaphylaxis to the drug or any ingredient in the formulation. See Ingredients below for additional information.
- Evusheld™ is not currently recommended in individuals with known cardiovascular disease or at high risk for cardiovascular or thromboembolic events due to potential cardiac adverse events. Per Saskatchewan eligibility criteria, individuals must NOT have known cardiovascular disease (i.e.: coronary artery disease, history of myocardial infarction or stroke, unstable angina, heart failure, congenital heart disease, or arrhythmias).
- Use caution in individuals with thrombocytopenia, coagulation disorders, or other clinically significant bleeding disorders as Evusheld™ is an IM injection and any IM injection can potentially result in formation of intramuscular hematoma and further complications.
- Use caution in adolescent patients. Evusheld™ is approved for adults and adolescents ≥12 years of age and weighing 40 kg or more, however clinical trials only included individuals 18 years and older. Safety and efficacy in <18 years have not been established, and dosing was determined based on pharmacokinetic modeling data.
- Insufficient data in pregnancy; no data on lactation or fertility.

Ingredients

Evusheld™ contains:

- tixagevimab – monoclonal antibody
- cilgavimab – monoclonal antibody
- l-histidine, l-histidine hydrocholoride monohydrate – amino acid used to stabilize pH
- polysorbate 80 – emulsifier and surfactant to hold ingredients together
- sucrose
- water for injection

Evusheld™ does contain polysorbate 80 which is structurally similar to polyethylene glycol (PEG). Polysorbate 80 may cause anaphylaxis and may cross-react with PEG although at least one trial has demonstrated that cross-reactivity does not occur when vaccines containing polysorbate 80 are given to individuals with PEG allergy.[12]

Adverse Effects

- Adverse reactions reported in clinical trials were mild to moderate and include:
    - headache (6%)
    - fatigue (4%)
    - cough (3%)
    - injection site reaction (2.4%) = pain, redness, itching, swelling where injection given
    - hypersensitivity (1%) = rash, hives
    - insomnia (1%)
    - dizziness (1%)
    - anaphylaxis (<0.1%)
    - injection related reaction = headache, chills

- Although not a safety outcome that was assessed during clinical trials, injection site pain is commonly reported with IM injections.[13]
- Cardiac harm: In the clinical trials for Evusheld™, a signal for adverse cardiac events emerged. A causal relationship has not been established.
    - In the PROVENT trial, 23 cardiac SAEs – including MI, angina, increased troponin, arrythmia, and cardiac failure - were reported. Cardiac adverse events were infrequent, but participants taking tixagevimab/cilgavimab experienced more cardiovascular adverse events than those taking placebo (23/3461 [0.66%] versus 5/1736 [0.28%]). The number needed to harm (NNH) for cardiac SAEs in individuals taking Evusheld™ was 263 over 6 months.
        - It is important to note that most participants who experienced cardiac related adverse events who received Evusheld™ had cardiovascular risk factors and/or a prior history of CVD.
        - No clear temporal pattern was established; cardiac events were reported within hours of administration through to the end of study follow-up period.
    - No cardiac SAEs were reported in the STORM CHASER trial. Participants in STORM CHASER were noted to be younger and had fewer baseline cardiac risk factors than in PROVENT.
    - 4 cardiac SAEs were reported in the TACKLE trial (n=903). Acute MI was reported for 2 people who received EVUSHELD™ (1 of whom experienced cardiac failure leading to death) and 1 case of sudden cardiac death. 1 person who received placebo reported arrhythmia. All individuals had cardiac risk factors and/or history of CVD.

Interactions

Drugs:

- No known significant drug-drug interactions.

Vaccines:

- Wait at least 14 days from last COVID-19 vaccine dose before administering Evusheld™.
- The National Advisory Committee on Immunization (NACI) cautions that giving monoclonal antibodies and vaccines administered close together may result in decreased effectiveness because the monoclonal antibodies have high affinity for the spike protein expressed by the vaccines, which could prevent the production of antibodies stimulated by the vaccine.[14] A study of bamlanivimab and vaccine administration showed a slight decrease in antibody titres that was considered clinically insignificant.[15]

Storage/Dose Preparation

- Evusheld™ is supplied as two vials per carton – tixagevimab solution for injection and cilgavimab solution for injection. Two cartons (total of 2 vials of tixagevimab and 2 vials of cilgavimab) will be needed for total 600 mg dose.
    - Dark grey vial cap vial: tixagevimab solution 150 mg/1.5 ml
    - White vial cap vial: cilgavimab solution 150 mg/1.5 ml
- Drug vials need to be stored in a refrigerator (2°C - 8°C) and the cold chain must always be maintained, including during transport. Do not freeze Evusheld™.
- No reconstitution or dilution is required prior to administration. Do not shake Evusheld™.

- Two vials of each of tixagevimab and cilgavimab will be used to draw up the total dose. Both the tixagevimab and cilgavimab vials are single dose but contain overfill – ensure the proper dose of each vial is drawn up (1.5 mL per vial) and discard unused portion. Use separate syringes for tixagevimab and cilgavimab – do not mix tixagevimab and cilgavimab. Each syringe for administration should contain 3.0 ml.
- The tixagevimab and cilgavimab solutions for injection are preservative-free, and drug that has been drawn into a syringe should be administered immediately. If not able to give immediately, pre-drawn syringes can be stored between 2°C and 25°C for up to 4 hours.

Evusheld™ 600 mg = tixagevimab 300 mg (3.0 ml) IM injection + cilgavimab 300 mg (3.0 ml) IM injection

Prescribing/Administration

- Evusheld™ is approved and licensed under the Health Canada Food and Drug Regulations. Evusheld™ is available by prescription only. In Saskatchewan, Evusheld™ can be prescribed by licensed physicians and nurse practitioners. Individuals do not need to be referred to 811 nor do they need to be referred to the SHA Early COVID Therapeutics Team.
- Evusheld™ is given as an IM injection. IM injections can be done in a prescriber office, clinic space, or community pharmacy that is able to safely provide IM gluteal injections. Though administration at the prescriber's office is recommended, community pharmacists with Advanced Methods Certification can administer Evusheld®.
- The ventrogluteal site is preferred; health care providers need to follow best practice for IM gluteal injections.
- Administration does not require additional or specialized monitoring beyond the usual practise for IM gluteal injections.
- At time of administration, confirm individual:
    - is COVID-19 negative.
    - has had no known exposure to an individual infected with COVID-19 in last 8 days.
    - has not been infected with COVID-19 within past 14 days and has recovered from infection if previously infected.
    - has not received COVID-19 vaccine within past 14 days.
    - has no allergies to ingredients in Evusheld™.
- Evusheld™ is given as two separate, sequential intramuscular injections [300 mg (3.0 ml) tixagevimab and 300 mg (3.0 ml) cilgavimab] at different injection sites, preferably one in each of the gluteal muscles.
- Individuals that receive Evusheld™ should be observed for potential reactions for 15 minutes following injection.
- For more detailed product details and administration, see Product Monograph.

Distribution

- Evusheld™ is free of charge to eligible individuals, similar to COVID-19 vaccines and antivirals.
- Evusheld™ is available through McKesson. A McKesson account is required for ordering, therefore, supply will primarily be ordered and distributed through community pharmacies.
- Coordination will be required between prescribers, community pharmacies, and individuals receiving Evusheld™ to ensure continuity between prescribing, obtaining supply, and administration.

- Evusheld™ needs to be refrigerated - the cold chain must always be maintained, including during transport.
- At this time, Evusheld™ is not being provided in SHA acute care facilities or SHA COVID-19 Vaccine Clinics.
- Community Pharmacies: For more information about distribution and billing, refer to the Drug Plan and Extended Benefits Pharmacy Information Bulletin.

Monitoring

- No additional laboratory monitoring is required before or after administration.
- Prior to administration:
  - Ensure individual is COVID-19 negative.
- Following administration:
  - Individuals should be monitored for hypersensitivity/anaphylaxis for 15 minutes.
  - Monitor for treatment adverse effects and potential cardiovascular effects.
  - Patient counselling: consider vaccination if not fully vaccinated and boosted, maintain other preventative measures against COVID-19, monitor for potential COVID-19 symptoms, monitor for symptoms of cardiac events (chest pain or pressure, shortness of breath, feeling fatigued, swelling in lower legs), report any concerning symptoms.

Evidence

The primary source of evidence for the approval of Evusheld™ for pre-exposure prophylaxis is the PROVENT trial - an ongoing, manufacturer sponsored, multi-centre, double-blinded randomized controlled trial.

The Evusheld™ clinical development program includes the following Phase 3 Clinical Trials:

- PROVENT = pre-exposure prophylaxis
- STORM CHASER = post-exposure prophylaxis
- TACKLE = treatment of mild COVID-19
- ACTIV-3 = treatment of hospitalized patients

An observational study from the U.S. National Veterans Affairs Electronic Data provides some real-world evidence for Evusheld™. The study was done during the Omicron surge and findings support an association of Evusheld™ with reduced infection, hospitalization, and death. The findings were observed in those who were vaccinated, immunocompromised and older, providing some reassurance regarding use in these important patient groups.

PROVENT

Participants	• 5197 COVID-19 negative outpatients. Participants were screened between November 2020 and March 2021; last injection administered March 2021 • 73% white, 17% black, 3% Asian, 0.6% American Indian or Alaska Native, ~6% other • 18 years of age and older, ~70% over the age of 60 • 73.3% at risk of inadequate response to COVID-19 vaccine: ≥ 60yo, obese (BMI ≥30), congestive heart failure, chronic obstructive pulmonary disease, chronic kidney disease, chronic liver disease, immunocompromised, intolerant to vaccines

	• 52.5% at high risk of exposure (healthcare worker, military, industrial workers, students in dorms, close proximity living) • Only 3.3% of participants immunosuppressed due to medications, 0.5% of participants were immunosuppressed because of disease • Excluded people with previous/current COVID-19 infection, people that had previously received a COVID-19 vaccine
Intervention	300 mg IM dose of tixagevimab/cilgavimab
Comparator	placebo
Outcome	Primary: first case of symptomatic RT-PCR positive COVID-19 Other outcomes reported: severe or critical COVID-19, ER visit for symptoms, antibody response, serum drug concentrations. Also looked at incidence of adverse events. Post hoc analyses: primary endpoint within 3 months compared to 3-6 months, hospitalization at 6-month follow-up

Results:

- Many participants (~40%) chose to become unblinded to receive vaccination during the trial
- Maximum duration of follow up = 182 days, median = 83 days. Duration of safety follow up = 15 months.
- Primary outcome analysis at 3 months:

	Relative risk reduction:	Absolute risk reduction:	Number Needed to Treat:
Symptomatic infection:	77 (95% CI = 46%-90%)	0.75	133 to prevent one additional **symptomatic infection** at 3 months versus placebo

- Secondary outcome analysis at 6 months:
  - Symptomatic infection: 82.8% relative risk reduction (RRR) in symptomatic infections (CI = 66-96), absolute risk reduction (ARR) 1.5%, number needed to treat (NNT) = 68
  - Rate of COVID-19 hospitalization: no comparative analysis; reported 0 hospitalizations in tixagevimab/cilgavimab group and 7 hospitalizations (0.4%) in placebo group.
  - COVID-19 related mortality: no comparative analysis; reported 0 deaths in tixagevimab/cilgavimab group 2 deaths (0.1%) in placebo group.

Safety:

- Most adverse effects were mild or moderate in intensity
- Injection site reaction common (2.4%); injection site pain not reported
- Anaphylaxis rare – 1 case reported. No COVID-19 related deaths in tixagevimab/cilgavimab group, 2 COVID-19 related deaths in placebo group.
- An increase in cardiac disorders noted in the supplementary data.
  - total of 23/3461 events reported in tixagevimab/cilgavimab group -> NNH = 263. 5/1736 events reported in placebo group.
  - reported cardiac adverse events included acute left ventricular failure, angina pectoris, arrhythmia, arteriosclerosis, atrial fibrillation, cardiac failure, cardiomegaly, cardiomyopathy, cardio-respiratory arrest, congestive cardiac failure, coronary artery disease, myocardial infarction, and paroxysmal atrioventricular block.
- An increase in nervous system disorders also noted in the supplementary data.

- total of 18/3461 events reported in tixagevimab/cilgavimab group compared to 5/1736 in reported in placebo group.
- reported nervous system events include Bell's palsy, cerebrovascular accident, complex regional pain syndrome, metabolic encephalopathy, migraine, partial seizure, syncope, and transient ischemic attack.

PROVENT Study Appraisal:

RxFiles, CADTH

- Well-designed trial but may not be generalizable/applicable given the current landscape of COVID-19
  - participants unvaccinated, no previous history of COVID-19 and many individuals today have had exposure to vaccine and/or infection
  - primary outcome of symptomatic infection may not be clinically relevant; hospitalizations and death are more meaningful outcomes
  - different variants circulating; newer variants may emerge
- Immunocompromised participants, adults over the age of 75 not well represented
- Low number of overall events, particularly in subgroups
- Many participants chose to become unblinded which may have impacted outcomes

STORM CHASER

Participants	1,121 unvaccinated participants with recent (≤ 8 days) exposure to an individual with laboratory-confirmed COVID-19
Intervention	300 mg IM dose of tixagevimab/cilgavimab
Comparator	placebo
Outcome	prevention of PCR-confirmed symptomatic COVID-19 up to day 183 post treatment; participants were followed for 15 months

Results: **not published**; non-significant reduction in the absolute risk of symptomatic COVID-19 by 1.5% (RRR = 33%, 95% CI, 26%-65%) in the treatment arm compared to placebo (rates were 3% [23/749] and 4.6% [17/372], respectively).

TACKLE

Participants	• 903 non-hospitalized adults ≥18 years old with mild or moderate symptomatic COVID-19 at high risk of progression to severe disease. Participants enrolled between Jan-Jul 2021 • Excluded people that had previously received a COVID-19 vaccine, people that previously received mAb or biologic indicated for prevention/treatment of COVID-19
Intervention	600 mg IM dose of tixagevimab/cilgavimab
Comparator	placebo
Outcome	Primary: progression to severe COVID-19 disease or death to day 29 post dose Other: incidence of respiratory failure, hospitalization (exploratory)

Results: Severe COVID-19 or death occurred in 18/407 (4%) participants in the tixagevimab–cilgavimab group versus 37/415 (9%) participants in the placebo group (RRR 50.5%, 95% CI 14.6–71.3). The absolute risk reduction was 4.5% (95% CI 1.1–8.0).

- In post-hoc exploratory outcome, there were fewer hospitalizations for COVID-19 in treatment group than placebo: 17/413 (4.1%) versus 40/421 (9.5%).
- Viral sequencing in participants indicated that Alpha B.1.1.7 was most prevalent at day 29, followed by Gamma P.1, Delta B.1.617.2, Lambda, Mu, Two, and Beta.

Safety: Most adverse effects were mild to moderate. There were two deaths reported due to cardiac events (MI, sudden cardiac death), 2/452 SAE related to cardiac disorders reported in treatment group and 1/451 SAE related to cardiac disorders reported in placebo, and Injection site pain and reactions were reported by ~2% of participants.

Resistance concerns

UPDATE NOV 2022:

- There is a risk of resistance and loss of efficacy of Evusheld™ due to the development of variants. Prescribers should be aware of circulating variants and review available resistance information when considering Evusheld™.
- Resistance to Evusheld™ has already been demonstrated. It is not known how *in vitro* neutralization data correlate with clinical outcome, but *in vitro* studies of tixagevimab and cilgavimab in combination demonstrated:
  - 12-183 fold decreased neutralization activity against Omicron BA.1
  - 3.2-5.4 fold decreased neutralization activity against Omicron BA.2 but clinical efficacy expected to be retained
  - 33-65 fold decreased neutralization activity against Omicron BA.4
  - 2.8-65 fold decreased neutralization activity against Omicron BA.5
- Resistance surveillance is ongoing. Stanford University offers an excellent database of antivirals and resistance to COVID-19 variants.
- Circulating variants in Saskatchewan can be found on the bi-weekly COVID-19 Situation Reports.
- Health Canada issued a warning on the use of Evusheld™ and potential resistance in October 2022:
  - Evusheld™ may not be effective against certain SARS-CoV-2 Omicron subvariants.
  - Healthcare providers are advised to:
    - consider local epidemiology and individual exposure to circulating SARS-CoV-2 viral variants when making decisions regarding the use of Evusheld™.
    - inform patients who receive Evusheld™ about the potential for a lack of effectiveness against certain SARS-CoV-2 viral variants.
    - instruct patients who receive Evusheld™ to seek medical advice if signs or symptoms of COVID-19 occur, persist, or worsen.
- It is possible that variants resistant to Evusheld™ could have cross-resistance to other monoclonal antibodies targeting the receptor binding domain of SARS-CoV-2 thus limiting other treatment options.

Clinical decision making

Considerations to make when considering Evusheld™ for pre-exposure prophylaxis include:

- patient likelihood of responding to vaccination (i.e.: immune status), risk of progressing to severe illness, risk of exposure to COVID-19
- limited benefit demonstrated in clinical trials; primary outcome demonstrated in clinical trials may not be relevant given current COVID-19 landscape
- uncertainty in people under 18, pregnant/lactating individuals, vaccinated individuals, immunocompromised individuals
- risk of potential adverse effects with Evusheld™
- emerging concerns with resistance to variants

- unknown effect of repeated administration
- unknown impact on COVID-19 vaccination and other COVID-19 therapeutics – use may affect future eligibility for COVID-19 therapies until additional evidence available
- individual patient values and preferences

Helpful Resources

Health Canada Consumer Information
Health Canada Professional Information
Product Monograph

9 June 2022
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Thank you to the Saskatchewan Ministry of Health Drug Plan and Extended Benefits Branch for their contribution and review.

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