

PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

^{Pr}Bamlanivimab for injection

Solution for infusion, 700 mg/20 mL (35 mg/mL)

Anti-SARS-CoV-2 spike protein monoclonal antibody

HEALTH CANADA HAS AUTHORIZED THE SALE OF THIS COVID-19 DRUG BASED ON LIMITED CLINICAL TESTING IN HUMANS AND/OR QUALITY INFORMATION

Bamlanivimab is indicated for:

The treatment of adults and pediatric patients 12 years of age or older with mild to moderate COVID-19 who weigh at least 40 kg and who are at high risk of progressing to severe COVID-19 illness and/or hospitalization.

The use of bamlanivimab is permitted under an interim authorization delivered in accordance with section 5 of the COVID-19 Interim order (IO)*, pending the results of trials to verify its clinical benefit. Patients should be advised of the nature of the authorization. The interim authorization is associated with Terms and Conditions that need to be met by the sponsor to ascertain the continued quality, safety and efficacy of the product. For further information on authorization under this pathway, please refer to Health Canada's IO Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19.

* <https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/interim-order-import-sale-advertising-drugs.html#a2.8>

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Bamlanivimab is indicated for the treatment of adults and pediatric patients 12 years of age or older with mild to moderate coronavirus disease 2019 (COVID-19), who weigh at least 40 kg and who are at high risk of progressing to severe COVID-19 illness and/or hospitalization.

High risk is defined as patients who meet at least one of the following criteria:

- Are \geq 65 years of age
- Have a body mass index (BMI) \geq 35 for patients \geq 18 years of age
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are \geq 55 years of age **AND have**
 - cardiovascular disease, OR
 - hypertension, OR
 - chronic obstructive pulmonary disease/other chronic respiratory disease
- Are 12-17 years of age **AND have**
 - BMI \geq 85th percentile for their age and gender, OR
 - Sickle cell disease, OR
 - Congenital or acquired heart disease, OR
 - Neurodevelopmental disorders, for example, cerebral palsy, OR
 - A medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
 - Asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

Bamlanivimab should not be used in patients hospitalized with severe COVID-19 respiratory disease as benefit of treatment has not been observed in this setting. Bamlanivimab, a monoclonal antibody, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Interim authorization is supported by a numerical reduction in hospitalization or emergency room visits in high risk patients treated with bamlanivimab compared to high risk patients treated with placebo (see **14 CLINICAL TRIALS**).

1.1 Pediatrics

Pediatrics: Based on the data submitted in this interim authorization and reviewed by Health Canada, the safety and efficacy of bamlanivimab in pediatric patients has not been established. However, because the mechanism of action of bamlanivimab, as a neutralizing IgG1 mAb against the spike (S) protein of SARS-CoV-2, is directed against the virus and not the host response to the viral infection, it is reasonable to anticipate similar function in adolescents compared to adults. In addition, considering the acceptable safety profile observed from the adult population who weigh at least 40 kg, treating physicians may consider the use of bamlanivimab for adolescents 12 years of age or older who weigh \geq 40 kg with high risk factors. Close monitoring in this patient population is highly recommended.

2 CONTRAINDICATIONS

Bamlanivimab is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Bamlanivimab should only be administered in settings in which health care providers have immediate access to medications to treat a severe reaction, such as severe infusion reaction or anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

Bamlanivimab should be administered to patients as soon as possible after a positive test for COVID-19 using a direct SARS-CoV-2 validated testing method. The drug should be administered within 10 days following the onset of clinical signs and symptoms of infection.

4.2 Recommended Dose and Dosage Adjustment

The recommended dose of bamlanivimab is a single intravenous infusion of 700 mg bamlanivimab.

Use in Specific Populations

- Bamlanivimab is not recommended for patients weighing less than 40 kg.

4.3 Reconstitution

No reconstitution of bamlanivimab is required.

4.4 Administration

Preparation

Bamlanivimab for injection should be prepared by a qualified healthcare professional using aseptic technique:

- Remove the bamlanivimab vial from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. **Do not expose to direct heat.**
- Inspect bamlanivimab visually for particulate matter and discoloration.
 - Bamlanivimab is a clear to opalescent and colorless to slightly yellow to slightly brown solution.
- Gently invert vial by hand approximately 10 times. **Do not shake.**

There are two options for preparation of the diluted solution (see Table 1):

Option 1: dilution using PREFILLED infusion bag containing 250 mL of 0.9% Sodium Chloride Injection, USP.

- Withdraw and discard required volume of 0.9% Sodium Chloride Injection from infusion bag.
- Withdraw required volume of bamlanivimab from the vial using an appropriately sized syringe.

- Transfer bamlanivimab to the 0.9% Sodium Chloride Injection infusion bag.

OR

Option 2: dilution using an EMPTY, sterile, infusion bag able to accommodate 200 mL solution.

- Add required volume of 0.9% Sodium Chloride Injection to an empty, sterile infusion bag.
- Withdraw required volume of bamlanivimab from the vial using an appropriately sized syringe.
- Transfer bamlanivimab to the sterile infusion bag.

Following completion of Option 1 **OR** Option 2:

- Discard any product remaining in the vial.
- Gently invert IV bag by hand approximately 10 times to mix. **Do not shake.**
- This product is preservative-free and therefore, the diluted infusion solution should be administered immediately. If immediate administration is not possible, store the diluted bamlanivimab infusion solution for up to 48 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) or up to 14 hours at room temperature (20°C to 25°C [68°F to 77°F]) including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature for approximately 20 minutes prior to administration.

Table 1: Recommended Dilution and Administration Instructions for Bamlanivimab

Drug	Number of Vials	Total Dose	Volume of 0.9% sodium chloride	Final Volume for IV Infusion	Maximum Infusion Rate	Minimum Infusion Time
Option 1: dilution using a PREFILLED infusion bag containing 250 mL of 0.9% Sodium Chloride Injection, USP						
Bamlanivimab (700 mg/20 mL)	1 Vial	700 mg/20 mL	Discard 70 mL 0.9% Sodium Chloride	200 mL	200 mL/hr	60 minutes
Option 2: dilution using an EMPTY, sterile infusion bag						
Bamlanivimab (700 mg/20 mL)	1 Vial	700 mg/20 mL	Add 180 mL 0.9% Sodium Chloride	200 mL	200 mL/hr	60 minutes

Administration

Bamlanivimab for injection should be administered by a qualified healthcare professional.

- Gather the recommended materials for infusion:
 - Polyvinylchloride (PVC) infusion set containing a 0.20/0.22 micron in-line polyethersulfone (PES) filter.
- Attach the infusion set to the IV bag.
- Prime the infusion set.
- Administer the infusion solution via pump or gravity over at least 60 minutes (see **Table 1**).

- Once infusion is complete, flush the infusion line to ensure delivery of the required dose.
- Discard unused product.
- Clinically monitor patients during administration and observe patients after infusion is complete according to standard practice.

5 OVERDOSAGE

In the case of overdose, use supportive therapy. There is no known antidote to bamlanivimab.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 2 - Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
intravenous infusion	Solution, 700 mg/20 mL (35 mg/mL)	<ul style="list-style-type: none"> • L-histidine • L-histidine hydrochloride monohydrate • sodium chloride • sucrose • polysorbate 80 • water for injection

7 WARNINGS AND PRECAUTIONS

General

The limited clinical data available for bamlanivimab are derived from single intravenous doses administered in the ongoing Phase 2 randomized, double-blind, placebo-controlled clinical study, BLAZE-1 (Study PYAB). Serious and unexpected adverse events may occur that have not been previously reported with bamlanivimab use.

Sensitivity

Hypersensitivity and Anaphylaxis

There is a potential for serious hypersensitivity and/or anaphylactic reactions with administration of bamlanivimab. If signs and symptoms of a clinically significant hypersensitivity or anaphylactic reaction occur, immediately discontinue administration and initiate appropriate medications and/or supportive care.

Infusion-related Reactions

Infusion-related reactions have been observed with administration of bamlanivimab.

- Signs and symptoms of infusion related reactions may include: dyspnea, fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, and dizziness.

If an infusion-related reaction occurs, consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.

7.1 Special Populations

7.1.1 Pregnant Women

There are insufficient data to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Bamlanivimab should only be used during pregnancy if the potential benefit outweighs the potential risk for the mother and the fetus.

Nonclinical reproductive toxicity studies have not been performed with bamlanivimab. Human immunoglobulin G1 (IgG1) antibodies are known to cross the placental barrier; therefore, bamlanivimab has the potential to be transferred from the mother to the developing fetus. It is unknown whether the potential transfer of bamlanivimab provides any treatment benefit or risk to the developing fetus.

7.1.2 Breast-feeding

There are no available data on the presence of bamlanivimab in human or animal milk, the effects on the breastfed infant, or the effects 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 bamlanivimab and any potential adverse effects on the breastfed child from bamlanivimab or from the underlying maternal condition. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

7.1.3 Pediatrics

The safety and efficacy of bamlanivimab in children have not been established, although as per above (see **1 INDICATIONS**) it is reasonable to consider a single intravenous dose of bamlanivimab in adolescents 12 years of age or older who weigh ≥ 40 kg and who are high risk of developing severe COVID-19 symptoms and/or hospitalization.

7.1.4 Geriatrics

Of the 309 patients receiving bamlanivimab in BLAZE-1, 11% were 65 years of age and older and 3% were 75 years of age and older. Based on preliminary population PK analyses, there is no difference in PK in geriatric patients compared to younger patients (see **10.3 Pharmacokinetics, Special Populations and Conditions**).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Clinical studies evaluating the safety of bamlanivimab are ongoing. See Warnings and Precautions for potential risks associated with bamlanivimab.

An acceptable safety profile of bamlanivimab was reported in patients with mild to moderate COVID-19 illness (N = 309) following single intravenous doses of bamlanivimab in the BLAZE-1 Phase II study (700 mg, 2800 mg and 7000 mg). Based on the data, after treatment, adverse events occurred in 23% bamlanivimab-treated patients and 26% of placebo-treated patients who were followed for at least 28

days. Serious adverse events occurred in 1 placebo-treated subject (1%) and in no bamlanivimab-treated subjects.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

TEAEs reported in $\geq 1\%$ of all participants in the BLAZE-1 Phase 2 study, following a single intravenous dose of placebo or 700 mg bamlanivimab are summarized in Table 3.

Table 3 - Treatment-emergent Adverse Events Reported in BLAZE-1

Adverse Event	Placebo N=156 n (%)	Bamlanivimab - 700 mg N=101 n (%)
Nausea	6 (3.8)	3 (3.0)
Dizziness	3 (1.9)	3 (3.0)
Headache	3 (1.9)	3 (3.0)
Pruritus	1 (0.6)	2 (2.0)
Diarrhoea	8 (5.1)	1 (1.0)
Vomiting	4 (2.6)	1 (1.0)

Hypersensitivity Including Anaphylaxis and Infusion-related Reactions:

One anaphylaxis reaction and one serious infusion-related reaction were reported during infusion of bamlanivimab in ongoing, blinded trials. The infusions were stopped. Both reactions required treatment, one required epinephrine. Both events resolved.

Immediate non-serious hypersensitivity events were noted for 2% of bamlanivimab treated subjects and 1% of placebo-treated subjects in BLAZE-1. Reported events of pruritus, flushing and hypersensitivity were mild with one case of face swelling which was moderate. All events resolved (see **7 WARNINGS AND PRECAUTIONS**).

8.2.1 Clinical Trial Adverse Reactions – Pediatrics

The BLAZE-1 Phase 2 study did not include patients who were less than 18 years of age.

8.3 Less Common Clinical Trial Adverse Reactions

There were no significant adverse reactions reported at $< 1\%$ in patients treated with bamlanivimab.

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data Clinical Trial Findings

There were no clinically significant abnormal laboratory findings with bamlanivimab.

8.5 Post-Market Adverse Reactions

There are no post-market adverse drug reactions reported for bamlanivimab.

9 DRUG INTERACTIONS

9.1 Serious Drug Interactions

No serious drug interactions have been reported for bamlanivimab.

9.2 Drug Interactions Overview

No drug interaction studies have been performed. Bamlanivimab is not renally excreted or metabolized by cytochrome P450 enzymes; therefore, interactions with concomitant medications that are renally excreted or that are substrates, inducers, or inhibitors of cytochrome P450 enzymes are unlikely.

9.3 Drug-Behavioural Interactions

Interactions with behaviour have not been established.

9.4 Drug-Drug Interactions

Interactions with other drugs have not been established.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Bamlanivimab is a neutralizing IgG1 monoclonal antibody (mAb) to the spike protein of SARS-CoV-2, which can block the spike protein attachment to human ACE2 receptors, thus preventing subsequent viral entry into human cells and viral replication.

10.2 Pharmacodynamics

A Phase 2 trial evaluated bamlanivimab over a dose range of 1 to 10 times the recommended dose (700 to 7000 mg) of bamlanivimab in patients with mild to moderate COVID-19. Based on preliminary population pharmacokinetic/pharmacodynamic modelling and simulation, a flat exposure-response relationship for viral load reduction was identified for bamlanivimab within this dose range. In addition, body weight had no clinically meaningful effect on viral load reduction in adults with COVID-19 over the body weight range of 41 kg to 173 kg.

10.3 Pharmacokinetics

The pharmacokinetic (PK) profile of bamlanivimab is expected to be consistent with the profile of other IgG1 monoclonal antibodies.

Special Populations and Conditions

The PK of bamlanivimab was not affected by age (18 to 86), sex, race, or disease severity based on a preliminary population PK analysis.

Hepatic Insufficiency:

No clinical studies have been conducted to evaluate the effect of hepatic impairment on the PK of bamlanivimab.

Renal Insufficiency:

No clinical studies have been conducted to evaluate the effect of renal impairment on the PK of bamlanivimab. Bamlanivimab is not expected to be eliminated intact in the urine, thus renal impairment is not expected to affect the exposure of bamlanivimab.

11 STORAGE, STABILITY AND DISPOSAL

Refrigerate unopened vials at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze or expose to direct heat.

This product is preservative free and therefore, the prepared solution should be administered immediately. If immediate administration is not possible, store diluted bamlanivimab solution for up to 48 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) or 14 hours at room temperature (20°C to 25°C [68°F to 77°F]).

12 SPECIAL HANDLING INSTRUCTIONS

Protect from direct heat and light. Do not shake.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: bamlanivimab for injection

Chemical name: bamlanivimab

Molecular mass: 146439 Da

Structural formula:

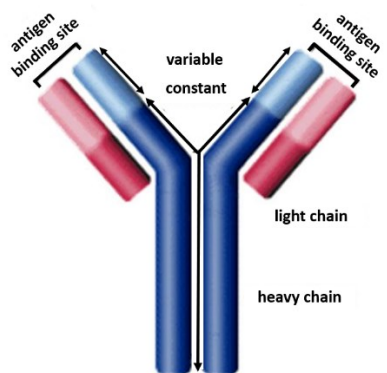


Figure 1: Structure of bamlanivimab

Product Characteristics:

Bamlanivimab is a fully human immunoglobulin G (IgG1 variant) mAb consisting of 2 identical light chain polypeptides composed of 214 amino acids each and 2 identical heavy chain polypeptides composed of 455 amino acids produced by a CHO cell line.

Bamlanivimab for injection is a sterile, preservative-free, clear to opalescent and colorless to slightly yellow to slightly brown solution in a single-dose vial for intravenous infusion after dilution.

Each mL contains 35 mg of bamlanivimab, and L-histidine (0.4 mg), L-histidine hydrochloride monohydrate (0.6 mg), sodium chloride (2.9 mg), sucrose (60 mg), polysorbate 80 (0.5 mg), and Water for Injection. The bamlanivimab solution has a pH range of 5.5-6.5.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

Mild to Moderate COVID-19 (BLAZE-1)

The data supporting this interim authorization are based on an interim analysis from Part A of BLAZE-1 that occurred after all enrolled subjects completed at least Day 29 of the trial. BLAZE-1 Part A is a Phase 2 randomized, double-blind, placebo-controlled clinical trial studying bamlanivimab for the treatment

of subjects with mild to moderate COVID-19 (subjects with COVID-19 symptoms who are not hospitalized). BLAZE-1 enrolled adult subjects who were not hospitalized and had at least 1 or more COVID-19 symptoms that were at least mild in severity. Treatment with bamlanivimab was initiated within 3 days of obtaining the clinical sample for the first positive SARS-CoV-2 viral infection determination. Subjects were treated with a single infusion of bamlanivimab (at doses of 700 mg [N=101], 2,800 mg [N=107], or 7,000 mg [N=101]) or placebo (N=156).

At baseline, median age was 45 years (with 12% of subjects aged 65 or older); 55% of subjects were female, 88% were White, 44% were Hispanic or Latino, and 6% were Black; 44% of subjects were considered high risk (as defined in Section 1, see **INDICATIONS**). Subjects had mild (76%) to moderate COVID-19 (24%); the mean duration of symptoms was 5 days; mean viral load by cycle threshold (CT) was 24 at baseline. The baseline demographics and disease characteristics were well balanced across bamlanivimab and placebo treatment groups.

14.2 Study Results

The pre-specified primary endpoint in the BLAZE-1 Phase 2 trial was change in viral load from baseline to Day 11 for bamlanivimab versus placebo. However, most subjects, including those receiving placebo, effectively cleared virus by Day 11 (not shown); therefore, no statistically significant reduction in viral load, as detected by viral RNA, was observed in subjects treated with bamlanivimab compared to subjects treated with placebo.

Evidence of the efficacy of bamlanivimab in subjects with mild to moderate COVID-19 related illness is limited to the predefined secondary endpoint of COVID-19-related hospitalizations or emergency room visits within 28 days after treatment. Numerically, a lower proportion of bamlanivimab-treated subjects progressed to COVID-19-related hospitalization or emergency room visits compared to placebo-treated subjects (Table 4). Results for this endpoint were suggestive of a relatively flat dose-response relationship.

Table 4 - Proportion of Subjects with Events of Hospitalization or Emergency Room Visits within 28 Days After Treatment

Treatment	N ^a	Events	Proportion of Subjects %
Placebo	156	9	5.8%
bamlanivimab 700 mg	101	1	1.0%
bamlanivimab 2800 mg	107	2	1.9%
bamlanivimab 7000 mg	101	2	2.0%
All bamlanivimab doses	309	5	1.6%

^a Abbreviations: N = number of treated patients in analysis.

The subgroup of subjects who met the risk criteria (see **1 INDICATIONS**) also experienced a numerical reduction in the proportion of subjects who required COVID-19 related hospitalisations or emergency room visits (Table 5).

Table 5 - Proportion of Subjects with Events of Hospitalization or Emergency Room Visits for Subjects at Higher Risk of Progression to Severe COVID-19 Illness^a

Treatment	N ^b	Events	Proportion of Subjects %
Placebo	69	7	10.1%
bamlanivimab 700 mg	46	1	2.2%
bamlanivimab 2800 mg	46	1	2.2%
bamlanivimab 7000 mg	44	2	4.5%
All bamlanivimab doses	136	4	2.9%

^a Higher risk for progression to severe COVID-19 illness as defined in section 1 **INDICATIONS**.

^b Abbreviations: N = number of treated patients in analysis.

The median time to symptom improvement as recorded in a trial specific daily symptom diary was 6 days for bamlanivimab-treated subjects, as compared with 8 days for placebo-treated subjects. Symptoms assessed were cough, shortness of breath, feeling feverish, fatigue, body aches and pains, sore throat, chills, and headache. Symptom improvement was defined as symptoms scored as moderate or severe at baseline being scored as mild or absent, and symptoms scored as mild or absent at baseline being scored as absent.

14.3 Immunogenicity

Immunogenicity has not yet been investigated. Samples for immunogenicity assessments have been collected and stored. Analysis will occur once validated anti-drug antibody assays are available.

15 MICROBIOLOGY

Antiviral Activity

The cell culture neutralization activity of bamlanivimab against SARS-CoV-2 was measured in a dose-response model using cultured Vero E6 cells. Bamlanivimab neutralized SARS-CoV-2 with an estimated EC50 value = 0.03 µg/mL and an estimated EC90 value = 0.09 µg/mL.

Bamlanivimab demonstrated antibody-dependent cell-mediated cytotoxicity on reporter Jurkat cells expressing FcγRIIIa following engagement with target cells expressing spike protein. Bamlanivimab did not elicit complement-dependent cytotoxicity activity in cell-based assays.

In Vivo Efficacy Pharmacology

Prophylactic administration of bamlanivimab to female Rhesus macaques (n=3 or 4 per group) resulted in 1 to 4 log₁₀ decreases in viral load (genomic RNA) and viral replication (sub-genomic RNA) in bronchoalveolar lavage samples relative to control animals, but less of an impact on viral RNA in throat and nasal swabs following SARS-CoV-2 inoculation. The applicability of these findings to a prophylaxis or treatment setting is not known.

Antiviral Resistance

There is a potential risk of treatment failure due to the development of viral variants that are resistant to bamlanivimab.

Non-clinical studies using serial passage of SARS-CoV-2 and directed evolution of the spike protein identified E484K, F490S, Q493R and S494P, amino acid substitutions in the spike protein receptor binding domain, which had reduced susceptibility to bamlanivimab as determined in neutralization assays using SARS-CoV-2 (F490S and S494P: > 485-fold and > 71-fold reduction, respectively) and/or vesicular stomatitis virus-based pseudovirus (all variants > 100-fold reduction).

In a preliminary genotypic analysis of a subset of patients with mild or moderate COVID-19 who were considered high risk for severe illness and/or hospitalization, SARS-CoV-2 variants, at positions associated with bamlanivimab resistance, were identified more frequently at $\geq 15\%$ and $\geq 50\%$ allele fractions in bamlanivimab treated patients (14% and 9.3%, respectively) compared to placebo treated patients (2.4% and 0%, respectively). Phenotypic analysis of the identified variations is in progress. The clinical relevance of these findings is not known.

Immune Response Attenuation

There is a theoretical risk that antibody administration may attenuate the endogenous immune response to SARS-CoV-2 and make patients more susceptible to re-infection.

16 NON-CLINICAL TOXICOLOGY

Carcinogenicity, Genotoxicity and Reproductive and Developmental Toxicology:

Not conducted.

General Toxicology:

Toxicology studies in the rat uncovered no adverse effects when bamlanivimab was administered intravenously. Non-adverse increases in neutrophils were observed.

Special Toxicology:

Antibody Dependent Enhancement (ADE) of Infection

The risk that bamlanivimab could mediate viral uptake and replication by immune cells was studied in THP-1 and Raji cell lines and primary human macrophages. This experiment did not demonstrate productive viral infection in immune cells exposed to SARS-CoV-2 at concentrations of bamlanivimab down to 100-fold below the EC50 value.

Tissue Cross-Reactivity

In tissue cross reactivity studies using human adult and fetal tissues, no binding of clinical concern was detected.

PATIENT MEDICATION INFORMATION

HEALTH CANADA HAS AUTHORIZED THE SALE OF THIS COVID-19 DRUG BASED ON LIMITED CLINICAL TESTING IN HUMANS AND/OR QUALITY INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr Bamlanivimab

Bamlanivimab for injection

Read this carefully before you start taking **bamlanivimab**. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **bamlanivimab**.

What is bamlanivimab used for?

Bamlanivimab is a medicine being studied for the treatment of COVID-19. Bamlanivimab may help limit the amount of virus in your body; this may help you get better faster. Bamlanivimab may be given if you or your child are 12 years of age or older who weigh at least 40 kg (kilograms) and are not already in the hospital. Bamlanivimab is only given to patients at high-risk of having the disease get worse. Your healthcare professional will decide if you or your child should take bamlanivimab.

How does bamlanivimab work?

COVID-19 is caused by a virus called a coronavirus. Bamlanivimab may help limit the amount of virus in your body, which may help you get better faster.

What are the ingredients in bamlanivimab?

Medicinal ingredients: bamlanivimab

Non-medicinal ingredients: L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, sodium chloride, sucrose, water for injection

Bamlanivimab comes in the following dosage forms:

Bamlanivimab solution, 700 mg/20 mL (35 mg/mL)

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take bamlanivimab. Talk about any health conditions or problems you may have, including if you:

- Have any allergies
- Are pregnant or plan to become pregnant
- Are breast-feeding a child

- Have any serious illnesses
- Are taking any medications (prescription, over-the-counter, vitamins, or herbal products)
- Have reactions during or after the infusion. Symptoms of a possible allergic reaction include:
 - Changes to blood pressure or heart rate, low oxygen level in the blood, high temperature, shortness of breath, wheezing, swelling of the face, lips, tongue, or throat, rash/hives/itching, feeling sick or nauseous, sweating, shivering, muscle soreness, dizziness, headache

Tell your doctor if you get any of these signs or symptoms.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

How to take bamlanivimab:

- Bamlanivimab will be given to you by a healthcare professional through a vein (intravenous or IV) for at least 1 hour.

Usual dose:

Bamlanivimab is given once. The recommended dose is 700 mg.

Overdose:

If you think you, or a person you are caring for, have taken too much bamlanivimab, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using bamlanivimab?

Possible side effects of bamlanivimab are:

- Allergic reactions. Allergic reactions can happen during and after infusion with bamlanivimab. Tell your healthcare provider right away if you get any of the following signs and symptoms of allergic reactions: fever, chills, nausea, headache, shortness of breath, low blood pressure, wheezing, swelling of your lips, face, or throat, rash including hives, itching, muscle aches, and dizziness.

The side effects of getting any medicine by vein may include brief pain, bleeding, bruising of the skin, soreness, swelling, and possible infection at the infusion site.

These are not all the possible side effects of bamlanivimab. Not a lot of people have been given bamlanivimab. Serious and unexpected side effects may happen. Bamlanivimab is still being studied so it is possible that all of the risks are not known at this time.

It is possible that bamlanivimab could interfere with your body's own ability to fight off a future infection of SARS-CoV-2. Similarly, bamlanivimab may reduce your body's immune response to a vaccine for SARS-CoV-2.

Specific studies have not been conducted to address these possible risks. Talk to your healthcare provider if you have any questions.

If you experience any side effects not listed here, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

If you want more information about bamlanivimab:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: <https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>; the manufacturer's website www.lilly.ca, or by calling 1-888-545-5972.

This leaflet was prepared by Eli Lilly Canada, Inc.

Last Revised: