

**FACT SHEET FOR HEALTH CARE PROVIDERS
EMERGENCY USE AUTHORIZATION (EUA) OF BAMLANIVIMAB**

AUTHORIZED USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product bamlanivimab for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

LIMITATIONS OF AUTHORIZED USE

- Bamlanivimab is not authorized for use in patients:
 - who are hospitalized due to COVID-19, OR
 - who require oxygen therapy due to COVID-19, OR
 - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
- Benefit of treatment with bamlanivimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Bamlanivimab has been authorized by FDA for the emergency uses described above. Bamlanivimab is not FDA-approved for these uses.

Bamlanivimab is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of bamlanivimab under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

This EUA is for the use of the unapproved product bamlanivimab for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization [see *Limitations of Authorized Use*].

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

- Have a body mass index (BMI) ≥ 35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥ 65 years of age

- Are ≥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 ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, 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 must be administered by intravenous (IV) infusion.

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

Health care providers must submit a report on all medication errors and **ALL SERIOUS ADVERSE EVENTS** potentially related to bamlanivimab. See Sections 8 and 9 of the Full EUA Prescribing Information for reporting instructions below.

- The authorized dosage for bamlanivimab is a single intravenous (IV) infusion of 700 mg administered as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset.
- Bamlanivimab is available as concentrated solution and must be diluted prior to administration.
- Administer bamlanivimab 700 mg via IV infusion over at least 60 minutes via pump or gravity.
- Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete.
- Patients treated with bamlanivimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect “high touch” surfaces, and frequent handwashing) according to CDC guidelines.

The authorized dosage may be updated as additional data from clinical trials becomes available.

For information on clinical trials that are testing the use of bamlanivimab in COVID-19, please see www.clinicaltrials.gov.

Contraindications

None.

Dosing

Patient Selection and Treatment Initiation

This section provides essential information on the unapproved product bamlanivimab for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization [see *Limitations of Authorized Use*].

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

- Have a body mass index (BMI) ≥ 35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥ 65 years of age
- Are ≥ 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 ≥ 85 th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, 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.

Dosage

The dosage of bamlanivimab in adults and pediatric patients 12 years of age and older weighing at least 40 kg is a single IV infusion of 700 mg bamlanivimab administered over at least 60 minutes. Bamlanivimab should be given as soon as possible after positive results of direct SARS-CoV-2 viral testing and within 10 days of symptom onset.

Dosage Adjustment in Specific Populations

No dosage adjustment is recommended based on age, sex, race, body weight, renal or mild hepatic impairment, during pregnancy or while lactating, or for disease severity or inflammation [see *Full EUA Prescribing Information, Use in Specific Populations (11)*].

Preparation and Administration

Preparation

Bamlanivimab solution for infusion 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. Do not shake the vial.**

- Inspect bamlanivimab visually for particulate matter and discoloration.
 - Bamlanivimab is a clear to opalescent and colorless to slightly yellow to slightly brown solution.
- Dilute bamlanivimab using a 250 mL prefilled 0.9% Sodium Chloride Injection bag for intravenous infusion according to **Table 1**.
 - Withdraw and discard 70 mL of 0.9% Sodium Chloride Injection from infusion bag.
 - Withdraw 20 mL of bamlanivimab from the vial using an appropriately sized syringe.
 - Transfer bamlanivimab to the 0.9% Sodium Chloride Injection infusion bag.
 - 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 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) or up to 7 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

Treatment	Dose/Volume of Bamlanivimab (# of vials)	Volume of 0.9% Sodium Chloride to Discard from a 250 mL IV bag	Total Volume for Infusion	Maximum Infusion Rate	Minimum Infusion Time
Bamlanivimab	700 mg/20 mL (1 vial)	70 mL	200 mL	200 mL/hr	60 minutes

Administration

Bamlanivimab infusion solution 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 for at least 1 hour after infusion is complete.

Storage

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, shake, or expose to direct light.

Warnings

There are limited clinical data available for bamlanivimab. Serious and unexpected adverse events may occur that have not been previously reported with bamlanivimab use.

Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions

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

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

Signs and symptoms of infusion related reactions may include:

- fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness.

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

Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19

Benefit of treatment with bamlanivimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation. Therefore, bamlanivimab is not authorized for use in patients *[see Limitations of Authorized Use]*:

- who are hospitalized due to COVID-19, OR
- who require oxygen therapy due to COVID-19, OR
- who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

Side Effects

Adverse events have been reported with bamlanivimab *[see Full EUA Prescribing Information, Clinical Trials Experience (6.1)]*.

Additional adverse events associated with the drug may become apparent with more widespread use.

INSTRUCTIONS FOR HEALTHCARE PROVIDERS

As the healthcare provider, you must communicate to your patient or parent/caregiver, as age appropriate, information consistent with the “Fact Sheet for Patients, Parents and Caregivers” (and provide a copy of the Fact Sheet) prior to the patient receiving bamlanivimab, including:

- FDA has authorized the emergency use of bamlanivimab for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at

least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization [see *Limitations of Authorized Use*].

- The patient or parent/caregiver has the option to accept or refuse bamlanivimab.
- The significant known and potential risks and benefits of bamlanivimab, and the extent to which such potential risks and benefits are unknown.
- Information on available alternative treatments and the risks and benefits of those alternatives, including clinical trials.
- Patients treated with bamlanivimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal items, clean and disinfect “high touch” surfaces, and frequent handwashing) according to CDC guidelines.

For information on clinical trials that are testing the use of bamlanivimab for COVID-19, please see www.clinicaltrials.gov.

MANDATORY REQUIREMENTS FOR BAMLANIVIMAB ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION:

In order to mitigate the risks of using this unapproved product under the EUA and to optimize the potential benefit of bamlanivimab, the following items are required. Use of bamlanivimab under this EUA is limited to the following (all requirements **must** be met):

1. Treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization [see *Limitations of Authorized Use*].
2. As the healthcare provider, communicate to your patient or parent/caregiver, as age appropriate, information consistent with the “Fact Sheet for Patients, Parents and Caregivers” prior to the patient receiving bamlanivimab. Healthcare providers (to the extent practicable given the circumstances of the emergency) must document in the patient’s medical record that the patient/caregiver has been:
 - a. Given the “Fact Sheet for Patients, Parents and Caregivers”,
 - b. Informed of alternatives to receiving authorized bamlanivimab, and
 - c. Informed that bamlanivimab is an unapproved drug that is authorized for use under this Emergency Use Authorization.
3. Patients with known hypersensitivity to any ingredient of bamlanivimab must not receive bamlanivimab.
4. The prescribing health care provider and/or the provider’s designee are/is responsible for mandatory reporting of all medication errors and serious adverse events* potentially related to bamlanivimab treatment within 7 calendar days from the onset of the event. The reports should include unique identifiers and the words “Bamlanivimab treatment under Emergency Use Authorization (EUA)” in the description section of the report.
 - Submit adverse event reports to FDA MedWatch using one of the following methods:
 - Complete and submit the report online: www.fda.gov/medwatch/report.htm, or

- By using a postage-paid Form FDA 3500 (available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf>) and returning by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787), or by fax (1-800-FDA-0178), or
- Call 1-800-FDA-1088 to request a reporting form
- Submitted reports should include in the field name, “Describe Event, Problem, or Product Use/Medication Error” the statement “Bamlanivimab treatment under Emergency Use Authorization (EUA)”

*Serious Adverse Events are defined as:

- death;
 - a life-threatening adverse event;
 - inpatient hospitalization or prolongation of existing hospitalization;
 - a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
 - a congenital anomaly/birth defect;
 - a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.
5. The prescribing health care provider and/or the provider’s designee are/is to provide mandatory responses to requests from FDA for information about adverse events and medication errors following receipt of bamlanivimab.

6. OTHER REPORTING REQUIREMENTS

In addition, please provide a copy of all FDA MedWatch forms to:

Eli Lilly and Company, Global Patient Safety

Fax: 1-317-277-0853

E-mail: mailindata_gsmtindy@lilly.com

Or call Eli Lilly and Company at 1-855-LillyC19 (1-855-545-5921) to report adverse events.

APPROVED AVAILABLE ALTERNATIVES

There is no adequate, approved and available alternative to bamlanivimab for patients who have mild to moderate COVID-19 who are at high risk for progressing to severe COVID-19 and/or hospitalization. Additional information on COVID-19 treatments can be found at <https://www.cdc.gov/coronavirus/2019-ncov/index.html>. The health care provider should visit <https://clinicaltrials.gov/> to determine whether the patient may be eligible for enrollment in a clinical trial.

AUTHORITY FOR ISSUANCE OF THE EUA

The Secretary of the Department of Health and Human Services (HHS) has declared a public health emergency that justifies the emergency use of drugs and biological products during the COVID-19 pandemic. FDA has issued this EUA, requested by Eli Lilly and Company for the unapproved product bamlanivimab for the treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who

are at high risk for progressing to severe COVID-19 and/or hospitalization.¹ As a health care provider, you must comply with the mandatory requirements of the EUA (see above).

Although limited scientific information is available, based on the totality of the scientific evidence available to date, it is reasonable to believe that bamlanivimab may be effective for the treatment of mild to moderate COVID-19 in certain high-risk patients as specified in this Fact Sheet. You may be contacted and asked to provide information to help with the assessment of the use of the product during this emergency.

This EUA for bamlanivimab will end when the Secretary determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

CONTACT INFORMATION

For additional information visit
www.bamlanivimab.com

If you have questions, please contact
1-855-LillyC19 (1-855-545-5921)

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¹ The health care provider should visit clinicaltrials.gov to determine whether there is an active clinical trial for the product in this disease/condition and whether enrollment of the patient(s) in a clinical trial is more appropriate than product use under this EUA.

FULL EUA PRESCRIBING INFORMATION

FULL EUA PRESCRIBING INFORMATION: CONTENTS*

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* Sections or subsections omitted from the full prescribing information are not listed.

1 AUTHORIZED USE

Bamlanivimab is authorized for use under an EUA for treatment of mild to moderate COVID-19 in adults and pediatric patients with positive results of direct SARS-CoV-2 viral testing who are 12 years of age and older weighing at least 40 kg, and who are at high risk for progressing to severe COVID-19 and/or hospitalization.

LIMITATIONS OF AUTHORIZED USE

- Bamlanivimab is not authorized for use in patients:
 - who are hospitalized due to COVID-19, OR
 - who require oxygen therapy due to COVID-19, OR
 - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
- Benefit of treatment with bamlanivimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation [see *Warnings and Precautions (5.2)*].

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Bamlanivimab should be administered as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset in adults and pediatric patients 12

years of age and older weighing at least 40 kg who are at high risk for progressing to severe COVID-19 and/or hospitalization.

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

- Have a body mass index (BMI) ≥ 35
- Have chronic kidney disease
- Have diabetes
- Have immunosuppressive disease
- Are currently receiving immunosuppressive treatment
- Are ≥ 65 years of age
- Are ≥ 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 ≥ 85 th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, 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.

2.2 Dosage

The dosage of bamlanivimab in adults and pediatric patients 12 years of age and older weighing at least 40 kg is a single intravenous (IV) infusion of 700 mg bamlanivimab administered over at least 60 minutes. Bamlanivimab should be administered as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset.

2.3 Dosage Adjustment in Specific Populations

Pregnancy or Lactation

No dosage adjustment is recommended in pregnant or lactating women [see *Use in Specific Populations (11.1, 11.2)*].

Pediatric Use

No dosage adjustment is recommended in pediatric patients who weigh at least 40 kg. Bamlanivimab is not authorized for patients weighing less than 40 kg [see *Use in Specific Populations (11.3)*].

Geriatric Use

No dosage adjustment is recommended in geriatric patients [see *Use in Specific Populations (11.4)*].

Renal Impairment

No dosage adjustment is recommended in patients with renal impairment [see *Use in Specific Populations (11.5)*].

Hepatic Impairment

No dosage adjustment is recommended in patients with mild hepatic impairment. Bamlanivimab has not been studied in patients with moderate or severe hepatic impairment [see *Use in Specific Populations (11.6)*].

2.4 Dose Preparation and Administration

Preparation

Bamlanivimab infusion solution should be prepared by a qualified healthcare professional using aseptic technique:

- Remove bamlanivimab vial from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. **Do not expose to direct heat. Do not shake the vial.**
- Inspect bamlanivimab visually for particulate matter and discoloration.
 - Bamlanivimab is a clear to opalescent and colorless to slightly yellow to slightly brown solution.
- Dilute bamlanivimab using a 250 mL prefilled 0.9% Sodium Chloride Injection bag for intravenous infusion according to **Table 1**.
 - Withdraw and discard 70 mL of 0.9% Sodium Chloride Injection from the infusion bag.
 - Withdraw 20 mL of bamlanivimab from the vial using an appropriately sized syringe.
 - Transfer bamlanivimab to the 0.9% Sodium Chloride Injection infusion bag.
 - 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 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) or up to 7 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

Treatment	Dose/Volume of Bamlanivimab (# of vials)	Volume of 0.9% Sodium Chloride to Discard from a 250 mL IV bag	Total Volume for Infusion	Maximum Infusion Rate	Minimum Infusion Time
Bamlanivimab	700 mg/20 mL (1 vial)	70 mL	200 mL	200 mL/hr	60 minutes

Administration

Bamlanivimab solution 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 for at least 1 hour after infusion is complete.

Storage

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 solution for up to 24 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]) or up to 7 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.

3 DOSAGE FORMS AND STRENGTHS

Injection: 700 mg/20 mL (35 mg/mL) as a sterile, preservative-free, clear to opalescent and colorless to slightly yellow to slightly brown solution in a single-dose vial.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

There are limited clinical data available for bamlanivimab. Serious and unexpected adverse events may occur that have not been previously reported with bamlanivimab use.

5.1 Hypersensitivity Including Anaphylaxis and Infusion-Related Reactions

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

Infusion-related reactions have been observed with administration of bamlanivimab. Signs and symptoms of infusion related reactions may include:

- fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, dizziness.

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

5.2 Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19

Benefit of treatment with bamlanivimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation. Therefore, bamlanivimab is not authorized for use in patients [*see Limitations of Authorized Use*]:

- who are hospitalized due to COVID-19, OR
- who require oxygen therapy due to COVID-19, OR
- who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.

6 OVERALL SAFETY SUMMARY

Over 1350 subjects have been exposed to bamlanivimab in clinical trials in both hospitalized and non-hospitalized patients.

6.1 Clinical Trials Experience

The safety of bamlanivimab is based on interim data from one Phase 2 trial of 465 ambulatory (non-hospitalized) subjects with COVID-19.

BLAZE-1 is a randomized, double-blind, placebo-controlled clinical trial in ambulatory adults with mild to moderate COVID-19 symptoms who had sample collection for the first positive SARS-CoV-2 viral infection determination within 3 days prior to the start of the infusion. 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).

Based on data from 309 bamlanivimab-treated subjects followed for at least 28 days after treatment, adverse events occurred in 23% bamlanivimab-treated subjects and 26% of placebo-treated subjects. Serious adverse events occurred in 1 placebo-treated subject (1%) and in no bamlanivimab-treated subjects.

The most commonly reported adverse event was nausea. Table 2 shows adverse events reported in at least 1% of patients in any treatment group. Bamlanivimab is not authorized at doses of 2,800 mg or 7,000 mg.

Table 2: Treatment-emergent Adverse Events Reported in at Least 1% of All Subjects in BLAZE-1

Preferred term	Placebo N=156 %	Bamlanivimab			
		700 mg N=101 %	2,800 mg N=107 %	7,000 mg N=101 %	Total N=309 %
Nausea	4%	3%	4%	5%	4%
Diarrhea	5%	1%	2%	7%	3%
Dizziness	2%	3%	3%	3%	3%
Headache	2%	3%	2%	0%	2%
Pruritus	1%	2%	3%	0%	2%
Vomiting	3%	1%	3%	1%	2%

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 *Warnings and Precautions (5.1)*].

7 PATIENT MONITORING RECOMMENDATIONS

Clinically monitor patients during administration and observe patients for at least 1 hour after infusion is complete [see *Warnings and Precautions (5.1) and Clinical Trials Experience (6.1)*].

8 ADVERSE REACTIONS AND MEDICATION ERRORS REPORTING REQUIREMENTS AND INSTRUCTIONS

Clinical trials evaluating the safety of bamlanivimab are ongoing [see *Overall Safety Summary (6)*].

Completion of FDA MedWatch Form to report all medication errors and serious adverse events is mandatory. The prescribing healthcare provider and/or the provider’s designee are/is responsible for the mandatory reporting of all medication errors and the following serious adverse events occurring during bamlanivimab use and considered to be potentially related to bamlanivimab. These adverse events must be reported within 7 calendar days from the onset of the event:

- death;
- a life-threatening adverse event;
- inpatient hospitalization or prolongation of existing hospitalization;
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- a congenital anomaly/birth defect;
- a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

If a serious and unexpected adverse event occurs and appears to be associated with the use of bamlanivimab, the prescribing healthcare provider and/or the provider's designee should complete and submit a MedWatch form to FDA using one of the following methods:

- Complete and submit the report online: www.fda.gov/medwatch/report.htm, or
- Use a postage-paid Form FDA 3500 (available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf>) and returning by mail (MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787), or by fax (1-800-FDA- 0178), or
- Call 1-800-FDA-1088 to request a reporting form

IMPORTANT: When reporting adverse events or medication errors to MedWatch, please complete the entire form with detailed information. It is important that the information reported to FDA be as detailed and complete as possible. Information to include:

- Patient demographics (e.g., patient initials, date of birth)
- Pertinent medical history
- Pertinent details regarding adverse events and course of illness
- Concomitant medications
- Timing of adverse event(s) in relationship to administration of bamlanivimab
- Pertinent laboratory and virology information
- Outcome of the event and any additional follow-up information if it is available at the time of the MedWatch report. Subsequent reporting of follow-up information should be completed if additional details become available.

The following steps are highlighted to provide the necessary information for safety tracking:

- In section A, box 1, provide the patient's initials in the Patient Identifier
- In section A, box 2, provide the patient's date of birth
- In section B, box 5, description of the event:
 - Write "Bamlanivimab treatment under Emergency Use Authorization (EUA)" as the first line
 - Provide a detailed report of medication error and/or adverse event. It is important to provide detailed information regarding the patient and adverse event/medication error for ongoing safety evaluation of this unapproved drug. Please see information to include listed above.
- In section G, box 1, name and address:
 - Provide the name and contact information of the prescribing healthcare provider or institutional designee who is responsible for the report.
 - Provide the address of the treating institution (NOT the healthcare provider's office address).

9 OTHER REPORTING REQUIREMENTS

In addition, please provide a copy of all FDA MedWatch forms to:

Eli Lilly and Company, Global Patient Safety

Fax: 1-317-277-0853

E-mail: mailindata_gsmtindy@lilly.com

Or call Eli Lilly and Company at 1-855-LillyC19 (1-855-545-5921) to report adverse events.

10 DRUG INTERACTIONS

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.

11 USE IN SPECIFIC POPULATIONS

11.1 Pregnancy

Risk Summary

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. In a tissue cross reactivity study with bamlanivimab using human fetal tissues, no binding of clinical concern was detected. 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.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

11.2 Lactation

Risk Summary

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.

11.3 Pediatric Use

The safety and effectiveness of bamlanivimab have not been assessed in pediatric patients. The recommended dosing regimen is expected to result in comparable serum exposures of bamlanivimab in patients 12 years of age and older and weighing at least 40 kg as observed in adults, based on a pharmacokinetic (PK) modeling approach which accounted for effect of body weight changes associated with age on clearance and volume of distribution.

11.4 Geriatric Use

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 population PK analyses, there is no difference in PK in geriatric patients compared to younger patients.

11.5 Renal Impairment

Bamlanivimab is not eliminated intact in the urine, thus renal impairment is not expected to affect the exposure of bamlanivimab.

11.6 Hepatic Impairment

Based on population PK analysis, patients with mild hepatic impairment had approximately 20% higher clearance than patients with normal hepatic function. This effect is statistically significant, but not clinically meaningful. Bamlanivimab has not been studied in patients with moderate or severe hepatic impairment.

11.7 Other Specific Populations

Based on population PK analysis, the PK of bamlanivimab was not affected by sex, race, and disease severity or inflammation. Body weight had no clinically relevant effect on the PK of bamlanivimab in adults with COVID-19 over the body weight range of 41 kg to 173 kg.

12 OVERDOSAGE

Doses up to 7,000 mg (10 times the recommended dose) have been administered in clinical trials without dose-limiting toxicity. Treatment of overdose with bamlanivimab should consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient. There is no specific antidote for overdose with bamlanivimab.

13 DESCRIPTION

Bamlanivimab is a human immunoglobulin G-1 (IgG1 variant) monoclonal antibody 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 Chinese Hamster Ovary (CHO) cell line and molecular weight of 146 kDa.

Bamlanivimab 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 PHARMACOLOGY

14.1 Mechanism of Action

Bamlanivimab is a recombinant neutralizing human IgG1k monoclonal antibody (mAb) to the spike protein of SARS-CoV-2, and is unmodified in the Fc region. Bamlanivimab binds to spike protein with a dissociation constant $K_D = 0.071$ nM and blocks spike protein attachment to the human ACE2 receptor with an IC_{50} value of 0.025 μ g/mL.

14.2 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. A flat exposure-response relationship for efficacy was identified for bamlanivimab within this dose range, based on viral load and clinical outcomes.

14.3 Pharmacokinetics

Pharmacokinetic profile of bamlanivimab is expected to be consistent with the profile of other IgG1 monoclonal antibodies.

Special Populations:

The PK of bamlanivimab was not affected by age, sex, race, disease severity or inflammation based on a population PK analysis. Body weight had no clinically relevant effect on the PK of bamlanivimab in adults with COVID-19 over the body weight range of 41 kg to 173 kg [see *Use in Specific Populations (11.4, 11.7)*].

Pediatric population

The PK of bamlanivimab in pediatric patients have not been evaluated.

Using modeling and simulation, the recommended dosing regimen is expected to result in comparable plasma exposures of bamlanivimab in pediatric patients ages 12 years of age or older who weigh at least 40 kg as observed in adult patients [see *Use in Specific Populations (11.3)*].

Patients with renal impairment

Bamlanivimab is not eliminated intact in the urine, thus renal impairment is not expected to affect the exposure of bamlanivimab [see *Use in Specific Populations (11.5)*].

Patients with hepatic impairment

Based on population PK analysis, patients with mild hepatic impairment had approximately 20% higher clearance than patients with normal hepatic function. This effect is statistically significant, but not clinically meaningful. Bamlanivimab has not been studied in patients with moderate or severe hepatic impairment [see *Use in Specific Populations (11.6)*].

Drug interactions:

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 [see *Drug Interactions (10)*].

15 MICROBIOLOGY/RESISTANCE INFORMATION

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.

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.

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, that 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).

Genotypic and phenotypic testing are ongoing to monitor for potential bamlanivimab-resistance-associated spike variations in clinical trials. Known bamlanivimab-resistant variants at baseline were observed at a frequency of 0.27% (1/375) in Part A of clinical trial BLAZE-1. In the same trial, treatment-emergent variants were detected at spike protein amino acid positions E484, F490 and S494, and included E484A/D/G/K/Q/V, F490L/S/V and S494L/P; only E484K/Q, F490S and S494P have been assessed phenotypically to date. Considering all variants detected at positions E484, F490 and S494, 9.2% (9/98) and 6.1% (6/98) of participants in the 700 mg bamlanivimab arm harbored such a variant post-baseline at ≥15% and ≥50% allele fractions, respectively, compared with 8.2% (8/97) and 4.1% (4/97), respectively, of participants in the placebo arm. Most of these variants were first detected on Day 7 following treatment initiation and many were detected only at a single time point (700 mg arm: 5/9 and 2/6 at ≥15% and ≥50% allele fractions, respectively; placebo arm: 8/8 and 4/4, respectively). For the 700 mg bamlanivimab arm, these variants were detected more frequently in high-risk participants (14.0% [6/43] and 9.3% [4/43] at ≥15% and ≥50% allele fractions, respectively, vs 2.4% [1/41] and 0% [0/41], respectively, in the placebo arm). The clinical relevance of these findings is not known.

It is possible that bamlanivimab resistance-associated variants could have cross-resistance to other mAbs targeting the receptor binding domain of SARS-CoV-2. The clinical impact 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 NONCLINICAL TOXICOLOGY

Carcinogenesis, mutagenesis, and reproductive toxicology studies with bamlanivimab have not been conducted.

In toxicology studies in rats, bamlanivimab had no adverse effects when administered intravenously. Non-adverse increases in neutrophils were observed.

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

17 ANIMAL PHARMACOLOGIC AND EFFICACY DATA

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.

18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA

18.1 Mild to Moderate COVID-19 (BLAZE-1)

The data supporting this EUA 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 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 patients who were not hospitalized and had at least 1 or more COVID-19 symptoms that were at least mild in severity. Treatment 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 2). 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.

The pre-specified primary endpoint in this Phase 2 trial was change in viral load from baseline to Day 11 for bamlanivimab versus placebo. Most subjects, including those receiving placebo, effectively cleared virus by Day 11 (Figure 1).

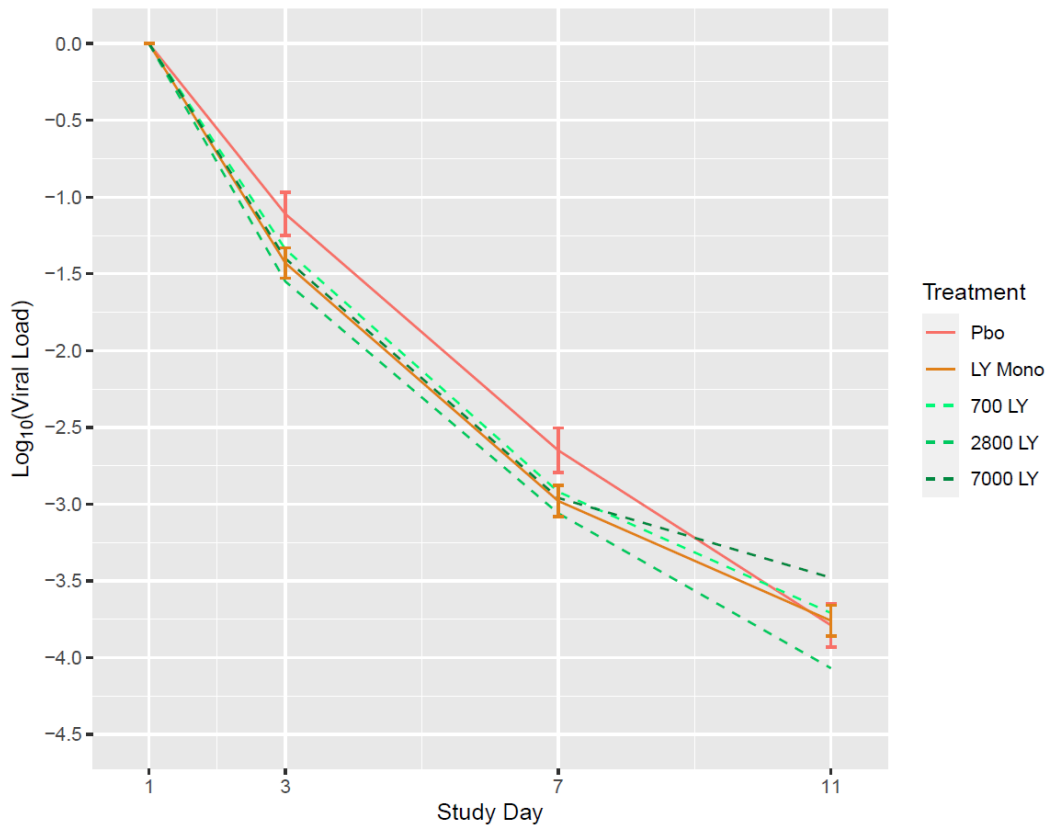


Figure 1: SARS-CoV-2 viral load change from baseline by visit.

While viral load was used to define the primary endpoint in this Phase 2 trial, the most important evidence that bamlanivimab may be effective came from the predefined secondary endpoint of COVID-19-related hospitalizations or emergency room visits within 28 days after treatment. A lower proportion of bamlanivimab-treated subjects progressed to COVID-19-related hospitalization or emergency room visits compared to placebo-treated subjects (Table 3). Results for this endpoint were suggestive of a relatively flat dose-response relationship.

Table 3: 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	6%
bamlanivimab 700 mg	101	1	1%
bamlanivimab 2800 mg	107	2	2%
bamlanivimab 7000 mg	101	2	2%
All bamlanivimab doses	309	5	2%

^a N = number of treated patients in analysis.

The absolute risk reduction for bamlanivimab compared to placebo is greater in subjects at higher risk of hospitalization according to the high risk criteria (Table 4).

Table 4: Proportion of Subjects with Events of Hospitalization or Emergency Room Visits for Subjects at Higher Risk of Hospitalization

Treatment	N ^a	Events	Proportion of Subjects %
Placebo	69	7	10%
bamlanivimab 700 mg	46	1	2%
bamlanivimab 2800 mg	46	1	2%
bamlanivimab 7000 mg	44	2	5%
All bamlanivimab doses	136	4	3%

^a 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.

19 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Bamlanivimab injection, 700 mg/20 mL (35 mg/mL), is a sterile, preservative-free clear to opalescent and colorless to slightly yellow to slightly brown solution supplied as one single-dose vial per carton.

NDC 0002-7910-01

Storage and Handling

Bamlanivimab is preservative-free. Discard unused portion.

Store unopened vials in a refrigerator at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light.

DO NOT FREEZE, SHAKE, OR EXPOSE TO DIRECT LIGHT.

Solution in vial requires dilution prior to administration. The prepared infusion solution is intended to be used immediately. If immediate administration is not possible, store diluted bamlanivimab infusion solution in the refrigerator at 2°C to 8°C (36°F to 46°F) for up to 24 hours or at room temperature (20°C to 25°C [68°F to 77°F]) for up to 7 hours, including infusion time. If refrigerated, allow the infusion solution to equilibrate to room temperature prior to administration.

20 PATIENT COUNSELING INFORMATION

Patients treated with bamlanivimab should continue to self-isolate and use infection control measures (e.g., wear mask, isolate, social distance, avoid sharing personal

items, clean and disinfect “high touch” surfaces, and frequent handwashing) according to CDC guidelines. Also see Fact Sheet for Patients, Parents and Caregivers.

21 CONTACT INFORMATION

For additional information visit:

www.bamlanivimab.com

If you have questions, please contact:

1-855-LillyC19 (1-855-545-5921)

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