Lilly's bebtelovimab receives Emergency Use Authorization for the treatment of mild-to-moderate COVID-19

February 11, 2022

FDA has authorized bebtelovimab for emergency use for certain non-hospitalized patients with mild-to-moderate COVID-19 at high risk of progression to severe disease for whom alternative COVID-19 treatment options approved or authorized by FDA are not accessible or clinically appropriate

Bebtelovimab neutralizes Omicron as demonstrated by pseudovirus and authentic virus data

INDIANAPOLIS, Feb. 11, 2022 /PRNewswire/ -- The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for bebtelovimab, an antibody that demonstrates neutralization against the Omicron variant, Eli Lilly and Company (NYSE: LLY) announced today.

Bebtelovimab can now be used for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options approved or authorized by FDA are not accessible or clinically appropriate. The authorized dose of bebtelovimab is 175 mg given as an intravenous injection over at least 30 seconds.

"As a global pharmaceutical company, Lilly has worked hard to fight this pandemic. Early in 2021, prior to the identification of the Omicron variant, Lilly scientists were already working to develop bebtelovimab as a broadly neutralizing antibody that could be used to fight a highly mutated variant, should one emerge," said Daniel Skovronsky, M.D., Ph.D., Lilly's chief scientific and medical officer, and president of Lilly Research Laboratories. "With the emergence of variants such as Omicron, treatment options remain limited. Lilly is pleased to provide another treatment option to help address the ongoing needs of patients and health care providers who continue to battle this pandemic."

The data supporting this EUA are primarily based on analyses from the Phase 2 BLAZE-4 trial (NCT04634409), treatment arms 9-14. This trial was a Phase 2, randomized, clinical trial evaluating treatment of non-hospitalized patients with mild-to-moderate COVID-19 who were treated with the authorized dose of bebtelovimab (175 mg) alone or together with 700 mg bamlanivimab and 1,400 mg of etesevimab. Pseudovirus and authentic virus testing demonstrate that bebtelovimab retains full neutralizing activity against Omicron – currently the predominant variant in the U.S. In addition, pseudovirus testing with bebtelovimab demonstrates that it retains neutralization against all other known variants of interest and concern, including BA.2.

As previously announced, Lilly has signed an agreement with the U.S. government to supply up to 600,000 doses of investigational drug bebtelovimab for at least $720 million.

For more information about the use of bebtelovimab to treat COVID-19, contact Lilly's 24-hour support line at 1-855-LillyC19 (1-855-545-5921).

Important Information about bebtelovimab

Bebtelovimab has not been approved, but has been authorized for emergency use by the FDA under an EUA, for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death and for whom alternative COVID-19 treatment options approved or authorized by FDA are not accessible or clinically appropriate.

The emergency use of bebtelovimab is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.

Healthcare providers should review the Fact Sheet for Healthcare Providers for information on the authorized use of bebtelovimab and mandatory requirements of the EUA. Please also see the FDA Letter of Authorization and the Fact Sheet for Patients, Parents and Caregivers on the authorized use of bebtelovimab.

Authorized Use and Important Safety Information

Bebtelovimab is authorized for use under Emergency Use Authorization (EUA) for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg):

- with positive results of direct SARS-CoV-2 viral testing, **and**
- who are at high risk[i] for progression to severe COVID-19, including hospitalization or death, **and**
- for whom alternate COVID-19 treatment options approved or authorized by FDA are not accessible or clinically appropriate.

LIMITATIONS OF AUTHORIZED USE

Bebtelovimab is not authorized for treatment of mild-to-moderate COVID-19 in geographic regions where infection is likely to have been caused by a non-susceptible SARS-CoV-2 variant based on available information including variant susceptibility to this drug and regional variant frequency.

- FDA will monitor conditions to determine whether use in a geographic region is consistent with this scope of authorization,

referring to available information, including information on variant susceptibility, and CDC regional variant frequency data available at: https://covid.cdc.gov/covid-data-tracker/#variant-proportions.
- FDA's determination and any updates will be available at: https://www/fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs

Bebtelovimab is not authorized for use in patients who:

- are hospitalized due to COVID-19, OR
- require oxygen therapy and/or respiratory support due to COVID-19, OR
- require an increase in baseline oxygen flow rate and/or respiratory support due to COVID-19 and are on chronic oxygen therapy and/or respiratory support due to underlying non-COVID-19 related comorbidity.

Treatment with bebtelovimab has not been studied in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bebtelovimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

Important Safety Information

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

WARNINGS

Hypersensitivity Including Anaphylaxis and Infusion-Related Reaction

Serious hypersensitivity reactions, including anaphylaxis, have been observed with administration of other SARS-CoV-2 monoclonal antibodies and could occur with administration of bebtelovimab. 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, which may occur up to 24 hours after the injection, have been observed in clinical trials of bebtelovimab when administered with other monoclonal antibodies and may occur with use of bebtelovimab alone. These reactions may be severe or life threatening. Signs and symptoms of infusion-related reactions may include:

- fever, difficulty breathing, reduced oxygen saturation, chills, fatigue, arrhythmia (e.g. atrial fibrillation, sinus tachycardia, bradycardia), chest pain or discomfort, weakness, altered mental status, nausea, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, vasovagal reactions (e.g. pre-syncope, syncope), dizziness, and diaphoresis.

Administer appropriate medications and/or supportive care if an infusion-related reaction occurs.

Hypersensitivity reactions occurring more than 24 hours after the injection have also been reported with the use of SARS-CoV-2 monoclonal antibodies under Emergency Use Authorization.

Clinical Worsening After Monoclonal Antibody Administration

Clinical worsening of COVID-19 after administration of SARS-CoV-2 monoclonal antibody treatment has been reported and may include signs or symptoms of fever, hypoxia or increased respiratory difficulty, arrhythmia (e.g., atrial fibrillation, sinus tachycardia, bradycardia), fatigue, and altered mental status. Some of these events required hospitalization. It is not known if these events were related to SARS-CoV-2 monoclonal antibody use or were due to progression of COVID-19.

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

Treatment with bebtelovimab has not been studied in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bebtelovimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high-flow oxygen or mechanical ventilation. See Limitations of Authorized Use.

Adverse Reactions

Adverse reactions observed in those who have received bebtelovimab alone or in combination with bamlanivimab and etesevimab, at the authorized dose or higher are infusion-related reactions (n=2, 0.3%), pruritus (n=2, 0.3%) and rash (n=5, 0.8%). The most common treatment-emergent adverse events observed in subjects treated with bebtelovimab, alone or in combination with bamlanivimab and etesevimab, at the authorized dose or higher included nausea (0.8%) and vomiting (0.7%).

USE IN SPECIFIC POPULATIONS

Pregnancy

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

Breastfeeding

There are no available data on the presence of bebtelovimab in human or animal milk, the effects on the breastfed infant, or the effects on milk production. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

About bebtelovimab

Bebtelovimab (LY-CoV1404; LY3853113) is a neutralizing IgG1 monoclonal antibody (mAb) directed against the spike protein of SARS-CoV-2 that maintains binding and neutralizing activity across currently known and reported variants of concern, including Omicron and BA.2. Bebtelovimab is being studied for the treatment of mild-to-moderate COVID-19 both as a monotherapy and together with other mAbs. Lilly has licensed and developed bebtelovimab after it was discovered by AbCellera and the scientists at the National Institute of Allergy and Infectious Diseases (NIAID) Vaccine Research Center.

About BLAZE-4

BLAZE-4 is a Phase 2, randomized clinical trial evaluating treatment of subjects with mild-to-moderate COVID-19 (subjects with COVID-19 symptoms who are not hospitalized).

The data supporting this EUA for treatment of mild-to-moderate COVID-19 are primarily based on analyses of data from the Phase 2 BLAZE-4 trial (NCT04634409), treatment arms 9-14. This trial evaluated the clinical safety and efficacy from subjects receiving 175 mg bebtelovimab, alone and together with 700 mg bamlanivimab and 1,400 mg of etesevimab. The authorized dosage of bebtelovimab is 175 mg given as an intravenous injection over at least 30 seconds.

Clinical data confirm the neutralizing ability of bebtelovimab. The trial enrolled subjects who were not hospitalized and had 1 or more COVID-19 symptoms that were at least mild in severity.

About Lilly's COVID-19 Efforts

Lilly has utilized the full force of its expertise to develop the first monoclonal antibody authorized for Emergency Use (EUA) by the U.S. Food and Drug Administration (FDA) – bamlanivimab, followed by the authorization of bamlanivimab with etesevimab and, most recently, bebtelovimab. The authorized dose of bebtelovimab is 175 mg given as an intravenous injection over at least 30 seconds.

While bamlanivimab together with etesevimab are not authorized for use in the U.S., at this time, the FDA will monitor conditions to determine whether use in a geographic region is medically appropriate, referring to available information, including information on variant susceptibility, and CDC regional variant frequency data available at: https://covid.cdc.gov/covid-data-tracker/#variant-proportions.

To date, over 700,000 patients have been treated with Lilly's monoclonal antibodies in the U.S., potentially preventing more than 35,000 hospitalizations and at least 14,000 deaths during the worst of the pandemic. Click here for resources related to Lilly's COVID-19 efforts.

About Eli Lilly and Company

Lilly is a global health care leader that unites caring with discovery to create medicines that make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at www.lilly.com and www.lilly.com/news. P-LLY

Lilly Cautionary Statement Regarding Forward-Looking Statements

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about bebtelovimab as a potential therapy for patients with COVID-19, the supply, distribution and contracts with governments relating to bebtelovimab, and Lilly's development plans, and reflects Lilly's current beliefs and expectations. However, as with any such undertaking, there are substantial risks and uncertainties in the process of drug research, development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with the results to date, that bebtelovimab will prove to be a safe and effective treatment for COVID-19, that bebtelovimab will receive regulatory approvals or additional authorizations, that patients will volunteer to participate in clinical trials or achieve positive outcomes, that Lilly will obtain any additional purchase orders or supply contracts, or that Lilly can provide an adequate supply of bebtelovimab in all circumstances. For a further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, please see Lilly's most recent Forms 10-K and 10-Q filed with the U.S. Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

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[i.] For information on medical conditions and factors associated with increased risk for progression to severe COVID-19, see the Centers for Disease Control and Prevention (CDC) website: *https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html*. Healthcare providers should consider the benefit-risk for an individual patient.

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