# Bebtelovimab

## NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

## BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

## DESCRIPTION

The intent of the bebtelovimab policy is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

Bebtelovimab is an investigational neutralizing immunoglobulin G1 (IgG1) mAb that works by binding to the spike protein of the SARS-CoV-2 virus. It is administered as a single intravenous injection.

FDA-Approved Indication
Bebtelovimab is not FDA-approved for any use, including for use as treatment of COVID-19.

Emergency Use Authorization (EUA)
The Food and Drug Administration issued an Emergency Use Authorization (EUA) for the emergency use of bebtelovimab for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in certain adults and pediatric patients who are at high-risk for progression to severe COVID-19, including hospitalization or death, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3).

The U.S. Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the emergency use of bebtelovimab 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 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.

Limitations

- 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-andresponse/mcm-legal-regulatory-and-policy-framework/emergencyuse-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 COVID19, 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-COVID19 related comorbidity.

National Institutes of Health (NIH) COVID-19 Treatment Guideline Recommendations

For nonhospitalized adults aged ≥18 years with mild to moderate COVID-19 who are at high risk of progressing to severe disease, NIH recommends using bebtelovimab 175 mg intravenous (IV) injection as an alternative therapy ONLY when both ritonavir-boosted nirmatrelvir (Paxlovid) and remdesivir are not available, feasible to use, or clinically appropriate. In the absence of sufficient clinical trial data on the treatment of children with COVID-19, NIH recommendations for the therapeutic management of nonhospitalized children are based largely on adult safety and efficacy data from clinical trials. NIH states there is insufficient evidence to recommend either for or against the use of bebtelovimab.

## POLICY

Criteria for Approval

I. Bebtelovimab may be considered **medically necessary** for for the treatment of COVID-19 when ALL of the following criteria are met:
    a. Member is 12 years of age or older and weighs at least 40kg
    b. Member is diagnosed with mild to moderate COVID-19 not requiring hospitalization or treatment with high-flow oxygen
    c. Member has a positive result of direct SARS-CoV-2 viral testing
    d. The requested medication will be administered within 7 days of symptom onset
    e. Member is at high risk for progressing to severe COVID-19, including hospitalization or death, as defined by the Centers for Disease Control and Prevention (see Appendix A)
    f. The current first-line COVID-19 treatments, Paxlovid (nirmatrelvir co-packaged with ritonavir) and Veklury (remdesivir), are are not accessible or clinically appropriate for the member (see Appendix B)

    **Approval** will be for **1 dose.**

Bebtelovimab is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

## APPENDIX

APPENDIX A: Established, probable, and possible risk factors (comorbidities that have been associated with severe COVID-19 in at least 1 meta-analysis or systematic review, in observational studies, or in case series):

- Age ≥65 years
- Asthma
- Cancer
- Cerebrovascular disease
- Children with certain underlying conditions
- Chronic kidney disease
- Chronic lung disease (interstitial lung disease, pulmonary embolism, pulmonary hypertension, bronchiectasis, COPD)
- Chronic liver disease (cirrhosis, non-alcoholic fatty liver disease, alcoholic liver disease, autoimmune hepatitis)
- Cystic fibrosis
- Diabetes mellitus, type 1 and type 2
- Disabilities (eg, ADHD, cerebral palsy, congenital malformations, limitations with self-care or activities of daily living, intellectual and developmental disabilities, learning disabilities, spinal cord injuries)
- Heart conditions (such as heart failure, coronary artery disease, or cardiomyopathies)
- HIV
- Mental health disorders (mood disorders including depression, schizophrenia spectrum disorders)
- Neurologic conditions (dementia)
- Obesity (BMI ≥30 kg/m$^2$) and overweight (BMI 25 to 29 kg/m$^2$), or ≥95$^{th}$ percentile in children
- Physical inactivity
- Pregnancy or recent pregnancy
- Primary immunodeficiencies
- Smoking (current and former)
- Sickle cell disease or thalassemia
- Solid organ or blood stem cell transplantation
- Substance use disorders
- Tuberculosis
- Use of corticosteroids or other immunosuppressive medications

For a list of risk factors, see the Center of Disease Control and Prevention (CDC) webpage Underlying Medical Conditions Associated With Higher Risk for Severe COVID-19.

APPENDIX B: Factors Affecting the Selection of COVID-19 Treatment

- Clinical efficacy of the treatment option against circulating variants
- Availability of the treatment option(s)
- Feasibility of administering parenteral medications (e.g., logistical constraints to administering remdesivir [Veklury] and bebtelovimab)

- The potential for significant drug-drug interactions (e.g., those associated with the use of ritonavir-boosted nirmatrelvir [Paxlovid])
- The regional prevalence of variants of concern (e.g., the regional prevalence of the Omicron BA.2 subvariant may affect which anti-SARS-CoV-2 monoclonal antibodies [mAbs] can be used for treatment)

*Note:* The convenience of receiving one injection of bebtelovimab versus a daily intravenous infusion of remdesivir for 3 consecutive days would not meet the definition of not accessible or clinically appropriate when the preferred treatment option(s) are available and there are no logistical or supply constraints.

For the rationale for the use of specific agents, see the National Institutes of Health (NIH) COVID-19 Treatment Guidelines: Therapeutic Management of Nonhospitalized Adults With COVID-19.

## CLINICAL RATIONALE

On February 11, 2022, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for bebtelovimab based on in vitro data that showed that bebtelovimab has activity against all circulating Omicron subvariants and clinical efficacy data from a small, Phase 2 clinical trial in individuals with mild to moderate COVID-19 who were at low risk of disease progression. The phase 2 trial showed no unexpected safety events, and patients who received bebtelovimab had more rapid viral decay than those who received the placebo. However, evidence supporting clinical efficacy is still limited and there are no Phase 3 clinical trial data for bebtelovimab at this time.

Although four anti-SARS-CoV-2 monoclonal antibody (mAb) products have received FDA Emergency Use Authorizations (EUAs) for the treatment of nonhospitalized adolescents aged ≥12 years and weighing ≥40 kg who are at high risk of severe COVID-19, only bebtelovimab is currently available for use, as it is the only anti-SARS-CoV-2 mAb with in vitro activity against the Omicron VOC and its subvariants (BA.1, BA1.1., BA.2, BA.4, BA.5).

There are insufficient data on hospitalization and mortality outcomes for patients with COVID-19 who are at high risk of disease progression and who receive bebtelovimab at this time. However, due to bebtelovimab having a mechanism of action that is similar to other anti-SARS-CoV-2 mAbs that have been shown to reduce rates of hospitalization or death among high-risk patients in Phase 3 trials with prior variants, the National Institutes of Health (NIH) COVID-19 Treatment Guidelines state the in vitro data and Phase 2 clinical trial data for bebtelovimab, coupled with the clinical efficacy data for other anti-SARS-CoV-2 mAbs, support the use of bebtelovimab in high-risk patients with COVID-19 when preferred treatment options are not available, feasible to use, or clinically appropriate.

## PROCEDURES AND BILLING CODES

**To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.**

- Q0222 - Injection, bebtelovimab, 175 mg

## REFERENCES


- US Food and Drug Administration. Letter of authorization: Emergency use authorization for use of Bebtelovimab. Dated February 11, 2022. From FDA website. Available at https://www.fda.gov/media/156151/download.

- US Food and Drug Administration. Fact sheet for health care providers (k): Emergency use authorization (EUA) of Bebtelovimab. Dated August 23, 2022. Available at https://www.fda.gov/media/156152/download.
- National Institutes of Health. COVID-19 Treatment Guidelines: Therapeutic Management of Nonhospitalized Adults With COVID-1. Dated August 18, 2022. Available at: https://files.covid19treatmentguidelines.nih.gov/guidelines/covid19treatmentguidelines.pdf.
- Dougan M, Azizad M, Chen P, et al. Bebtelovimab, alone or together with bamlanivimab and etesevimab, as a broadly neutralizing monoclonal antibody treatment for mild to moderate, ambulatory COVID-19. MedRxiv. 2022.
- US Centers for Disease Control and Prevention. Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Professionals. Updated June 15, 2022. Accessed September 9, 2022. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html.


## POLICY HISTORY

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