Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy

CENTENE Corporation

Clinical Policy: Bebtelovimab (LY-CoV1404)

Reference Number: CP.PHAR.579
Effective Date: FDA Approval Date
Last Review Date: 05.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Bebtelovimab (LY-CoV1404) is a human immunoglobulin G-1 (IgG1 variant) monoclonal antibody.

EUA Approved Indication(s)

LY-CoV1404 is permitted by the FDA for emergency use 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.

Limitation(s) 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-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 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that LY-CoV1404 is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*
**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. COVID-19 (must meet all)**:**
1. Diagnosis of COVID-19 infection via a positive viral test for SARS-CoV-2 within the last 3 days;
2. Member has one or more mild or moderate COVID-19 symptoms;
3. Member is within 7 days of symptom onset;
4. Age ≥ 12 years;
5. Member's body weight is ≥ 40 kg;
6. At the time of request, member does not have any of the following EUA-specified limitations against used (a, b, c, or d):
   a. Member is hospitalized due to COVID-19;
   b. Member requires oxygen therapy due to COVID-19;
   c. Member is on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity and requires n increase in baseline oxygen flow rate due to COVID-19;
   d. Member is in a geographic region where infection is likely caused by non-susceptible COVID-19 variant based on variant susceptibility to this drug and regional variant frequency;
7. Bebtelovimab will be administered as a single intravenous injection;
8. Bebtelovimab will be administered to the member in a setting in which health care providers have immediate access to mediations to treat a severe infusion reaction, such as anaphylaxis, and the ability to active the emergency medical system, as necessary;
9. Dose does not exceed 175 mg (1 vial) one time.

Approval duration: One time

B. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy*
**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. COVID-19 (must meet all)**:**
1. Re-authorization is not permitted.

Approval duration: Not applicable

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
COVID-19: coronavirus disease 2019
EUA: Emergency Use Authorization
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable.

Appendix C: Contraindications/Boxed Warnings [Pending]

- Contraindication(s): No contraindications
- Boxed warning(s): pending

Appendix D: General Information

- The data supporting this EUA for treatment of mild-to-moderate COVID-19 are based on the Phase 2 portion of the BLAZE-4 trial (NCT04634409) that looked at both low-risk and high-risk subjects for treatment arms. This trial evaluated the clinical efficacy from subjects receiving 175 mg bebtelovimab alone and together with 700 mg bamlanivimab and 1,400 mg of etesevimab.
- BLAZE-4 is a Phase 1/2, randomized, single-dose clinical trial evaluating treatment of subjects with mild-to-moderate COVID-19 who were not hospitalized. Efficacy of bebtelovimab, alone and together with bamlanivimab and etesevimab, was evaluated in low-risk adults.
- In one placebo-controlled portion of the BLAZE-4 trial that looked at low risk subjects, adult subjects were treated with a single infusion of bamlanivimab 700 mg, etesevimab 1,400 mg, and bebtelovimab 175 mg, 175 mg bebtelovimab alone, or placebo. The majority of the subjects enrolled in these treatment arms did not meet the criteria for high-risk. The primary endpoint was the proportion of subjects with persistently high viral load (PHVL) by Day 7. PHVL occurred in 26 subjects treated with placebo (21%) as compared to 16 (13%) subjects treated with bamlanivimab 700 mg, etesevimab 1,400 mg, and bebtelovimab 175 mg together [p=0.098], and 17 (14%) subjects treated with bebtelovimab 175 mg alone [p=0.147], a 38% (95% CI: -9%, 65%) and 34% (95% CI: -

15%, 62%) relative reduction, respectively. For the secondary endpoint of COVID-19 related hospitalization (defined as ≥24 hours of acute care) or death; events occurred in 2 (1.6%) subjects treated with placebo as compared with 3 (2.4%) events in subjects treated with bamlanivimab 700 mg, etesevimab 1,400 mg, and bebtelovimab 175 mg together and 2 (1.6%) events in subjects treated with bebtelovimab 175 mg alone.

- In another randomized part of the BLAZE-4 trial that looked at high risk subjects, subjects were treated with a single infusion of bamlanivimab 700 mg, etesevimab 1,400 mg, and bebtelovimab 175 mg or 175 mg bebtelovimab alone. The majority of the subjects enrolled in these dose arms meet the criteria for high-risk. The primary endpoint for these treatment arms was safety profile of bebtelovimab 175 mg by evaluating adverse events and serious adverse events. The proportion of subjects with COVID-19 related hospitalization (defined as ≥24 hours of acute care) or death by any cause was assessed by Day 29. Events occurred in 2 (4%) subjects treated with bamlanivimab 700 mg, etesevimab 1,400 mg, and bebtelovimab 175 mg together and 3 (3%) subjects treated with bebtelovimab 175 mg alone. One subject treated with bebtelovimab 175 mg died on day 34.
- In the non-randomized open-label part of the BLAZE-4 trial that looked at high risk subjects, subjects were treated with a single infusion of bamlanivimab 700 mg, etesevimab 1,400 mg, and bebtelovimab 175 mg. The majority of the subjects enrolled met the criteria for high-risk. The primary endpoint for this treatment arm was to study the safety profile of bamlanivimab 700 mg, etesevimab 1,400 mg, and bebtelovimab 175 mg by evaluating adverse events and serious adverse events. The proportion of subjects with COVID-19 related hospitalization (defined as ≥24 hours of acute care) or death by any cause was assessed by Day 29; events occurred in 3 subjects (1.7%), and no subjects died.
- Per EUA for bebtelovimab, the agent may only be administered in settings in which health care providers have immediate access to mediations to treat a severe infusion reaction such as anaphylaxis, and the ability to active the emergency medical system, as necessary. Clinically monitor patients for possible infusion-related reactions during administration and observe patients for at least 1 hour after injection is complete.
- There is potential for serious hypersensitivity reactions that have been observed with other SARS-CoV-2 monoclonal antibodies and could occur with administration of bebtelovimab.
- Infusion-related reactions have been observed with other SARS-CoV-2 monoclonal antibodies and could occur with administration of bebtelovimab. Signs and symptoms include fever, difficulty breathing, reduced oxygen saturation, chills, fatigue, arrhythmia, chest pain or discomfort, weakness, altered mental status, nausea, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, vasovagal reactions, dizziness and diaphoresis.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
COVID-19 Infection	Bebtelovimab 175 mg administered as a single intravenous injection	Bebtelovimab 175 mg

VI. Product Availability

Single-dose vial: 175 mg/2 mL (87.5 mg/mL)

VII. References

1. Fact Sheet fore Healthcare Providers: Emergency Use Authorization for Bebtelovimab. August 2022. Available at: https://www.fda.gov/media/156152/download. Accessed August 10, 2022.
2. Bebtelovimab EUA letter of authorization. August 2022. Available at: https://www.fda.gov/media/156151/download. Accessed August 10, 2022.
3. ClinicalTrials.gov. A study of Immune System Proteins in Participants with Mild to Moderate COVID-19 Illness 9 (BLAZE-4). Available at: https://clinicaltrials.gov/ct2/show/NCT04634409. Accessed March 2, 2022.
4. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at: https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-bebtelovimab/. Accessed March 2, 2022.
5. IPD Analytics. HCPCS Code Update: New Codes for Billing and Administration of Bebtelovimab. Published February 11, 2022.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
Q0222	Injection, bebtelovimab, 175 mg
M0222	Intravenous injection, bebtelovimab, includes injection and post administration monitoring
M0223	Intravenous injection, bebtelovimab, includes injection and post administration monitoring in the home or residence; this includes a beneficiary's home that has been made provider-based to the hospital during the covid-19 public health emergency.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	03.01.22	05.22
RT4: added criteria to ensure that the member is not located in a geographic area where infection is likely to have been caused by a non-susceptible SARS-CoV-2 variant, per the EUA Limitations of Authorized Use.	08.10.22	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted

standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.