Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy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

Reference Number: CP.PHAR.571
Effective Date: FDA Approval Date
Last Review Date: 02.23
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

Tixagevimab and cilgavimab (Evusheld™) are recombinant human IgG1 monoclonal antibodies that target the receptor binding domain of the spike protein of SARS-CoV-2.

EUA Approved Indication(s)

Evusheld (tixagevimab and cilgavimab) is authorized for emergency use for the pre-exposure prophylaxis of coronavirus disease 2019 (COVID-19) in adults and pediatric individuals (12 years of age and older weighing at least 40 kg) who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to an individual infected with SARS-CoV-2 and:

- Who have moderate to severe immune compromise due to a medical condition or receipt of immunosuppressive medications or treatments **and** may not mount an adequate immune response to COVID-19 vaccination **or**
- For whom vaccination with any available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended due to a history of severe adverse reaction (e.g., severe allergic reaction) to a COVID-19 vaccine(s) and/or COVID-19 vaccine component(s).

Limitations of use:

- Evusheld is not authorized for use in individuals:
  - For the treatment of COVID-19, or
  - For post-exposure prophylaxis of COVID-19 in individuals who have been exposed to someone infected with SARS-CoV-2.
- Pre-exposure prophylaxis with Evusheld is not a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended. Individuals for whom COVID-19 vaccination is recommended, including individuals with moderate to severe immune compromise who may derive benefit from COVID-19 vaccination, should receive COVID-19 vaccination.
- In individuals who have received a COVID-19 vaccine, Evusheld should be administered at least two weeks after vaccination.

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 Evusheld 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. Pre-exposure Prophylaxis of COVID-19 (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Member has moderate to severe immune compromise due to a medical condition or receipt of immunosuppressive medications or treatments **and** may not mount an adequate immune response to COVID-19 vaccination (*see Appendix E*);
   b. Member for whom vaccination with any available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended due to a history of severe adverse reaction (e.g., severe allergic reaction) to a COVID-19 vaccine(s) and/or COVID-19 vaccine component(s);
2. Age ≥ 12 years;
3. Member's body weight is ≥ 40 kg;
4. Member is not currently infected with SARS-CoV-2;
5. Member has not had a known recent exposure to an individual infected with SARS-CoV-2;
6. If eligible for COVID-19 vaccination, member has received COVID-19 vaccine according to the approved or authorized schedule ≥ 2 weeks prior;
7. Dose does not exceed tixagevimab 300 mg (2 vials) and cilgavimab 300 mg (2 vials) as two separate, consecutive injections.

   Approval duration: 6 months (one dose each only)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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. Pre-exposure Prophylaxis of COVID-19 (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*

2. For member without a history of severe adverse reaction to a COVID-19 vaccine and/or its component(s), member continues to have moderate to severe immune compromise due to a medical condition or receipt of immunosuppressive medications or treatments (*see Appendix E*);
3. Member is not currently infected with SARS-CoV-2;
4. Member has not had a known recent exposure to an individual infected with SARS-CoV-2;
5. Six or more months have elapsed since the last Evusheld treatment;
6. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. Initial dose administered ≤ 3 months prior: tixagevimab 150 mg (1 vial) and cilgavimab 150 mg (1 vial) as two separate consecutive injections;
   b. Initial dose administered > 3 months prior: tixagevimab 300 mg (2 vials) and cilgavimab 300 mg (2 vials) as two separate consecutive injections.

Approval duration: 6 months (one dose each only)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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;
B. Treatment of COVID-19 infection;
C. Post-exposure prophylaxis in those who have been exposed to someone infected with SARS-CoV-2.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

COVID-19: coronavirus disease 2019
EUA: Emergency Use Authorization
FDA: Food and Drug Administration
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Pfizer-BioNTech COVID-19 Vaccine, mRNA (Comirnaty®)	Varies	0.3 mL
Moderna COVID-19 Vaccine*	Varies	0.5 mL
Janssen COVID-19 Vaccine*	Varies	0.5 mL

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Product has been issued an EUA but is not yet FDA-approved.*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): previous severe hypersensitivity reactions, including anaphylaxis, to any component of Evusheld
- Boxed warning(s): none

Appendix D: General Information

- The data supporting the EUA for Evusheld is based on the PROVENT (NCT04625725) study, a phase 3, randomized (2:1), double-blind, placebo-controlled clinical trial studying Evusheld for the pre-exposure prophylaxis of COVID-19 in adults ≥ 18 years of age. All subjects were either ≥ 60 years of age, had a pre-specified co-morbidity (obesity, congestive heart failure, chronic obstructive pulmonary disease, chronic kidney disease, chronic liver disease, immunocompromised state, or previous history of severe or serious adverse event after receiving any approved vaccine), or were at increased risk of SARS-CoV-2 infection due to their living situation or occupation. Subjects could not have previously received a COVID-19 vaccine. The study excluded subjects with a history of laboratory-confirmed SARS-CoV-2 infection or SARS-CoV-2 antibody positivity at screening. The primary analysis included 5,172 subjects who were SARS-CoV-2 negative at baseline, of which 3,441 received Evusheld and 1,731 received placebo. A single dose (administered as two IM injections) of Evusheld or placebo was administered. The primary efficacy endpoint was the incidence of the first case of SARS-CoV-2 positive symptomatic illness. A subject was defined as a COVID-19 case if their first case of SARS-CoV-2 positive symptomatic illness occurred after administration and prior to Day 183. Evusheld receipt resulted in a statistically significant 77% reduction in incidence of COVID-19 when compared to placebo (p-value < 0.001). Among subjects who received Evusheld, there were no severe/critical COVID-19 events (defined as SARS-CoV-2 positive symptomatic illness characterized by a minimum of either

pneumonia or hypoxemia and a WHO Clinical Progression Scale score of 5 or higher) compared to one event (0.1%) among subjects who received placebo.
- Under the terms of the EUA, Evusheld can be redosed every 6 months. Longer term data from the study PROVENT indicate that Evusheld may be effective for pre-exposure prophylaxis for 6 months post-administration. Evusheld has only been studied in single-dose studies. There are currently no safety and efficacy data available with repeat dosing. The recommendation for repeat dosing is based on the totality of the scientific evidence including clinical pharmacology data and clinical trial data.
- Although patients < 18 years old were not included in the Evusheld clinical trials to date, the dosing regimen is expected to result in comparable serum exposures of tixagevimab and cilgavimab in individuals 12 years of age and older and weighing at least 40 kg as observed in adults.
- The most commonly observed adverse events (all grades, incidence ≥ 3%) are headache, fatigue, and cough. Serious cardiac adverse events were infrequent in PROVENT. However, more trial participants had serious cardiac adverse events (such as myocardial infarctions, one of which resulted in death, and heart failure) after receiving Evusheld compared to placebo. These participants all had risk factors for cardiac disease or a history of cardiovascular disease before participating in the clinical trial. It is not clear if Evusheld caused these cardiac adverse events.

Appendix E: *Medical conditions or treatments that may result in moderate to severe immune compromise and an inadequate immune response to COVID-19 vaccination include but are not limited to (found at* https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#considerations-covid19-vax-immunocopromised*)*
- Active treatment for solid tumor and hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection (people with HIV and CD4 cell counts < 200/mm3, history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV)
- Active treatment with high-dose corticosteroids (i.e., ≥ 20 mg prednisone or equivalent per day when administered for ≥ 2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory (e.g., B-cell depleting agents)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Pre-exposure prophylaxis of COVID-19	300 mg of tixagevimab and 3000 mg of cilgavimab administered as two separate consecutive intramuscular injections	300 mg of tixagevimab and 300 mg of cilgavimab per administration

VI. Product Availability

Single-dose vials: tixagevimab 150 mg/1.5 mL, cilgavimab 150 mg/1.5 mL

VII. References

1. Fact Sheet for Healthcare Providers: Emergency Use Authorization for Evusheld. Wilmington, DE: AstraZeneca Pharmaceuticals LP; November 2022. Available at: https://www.fda.gov/media/154701/download. Accessed November 18, 2022.
2. ClinicalTrials.gov. Phase III Double-blind, Placebo-controlled Study of AZD7442 for Pre-exposure Prophylaxis of COVID-19 in Adult (PROVENT). Available at: https://clinicaltrials.gov/ct2/show/NCT04625725. Accessed November 18, 2022.
3. Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Approved or Authorized in the United States. Centers for Disease Control; October 19, 2022. Available at: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html. Accessed November 18, 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
Q0220	Injection, tixagevimab and cilgavimab, 300 mg
M0220	Injection, tixagevimab and cilgavimab, includes injection and post administration monitoring
M0221	Injection, tixagevimab and cilgavimab, 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	01.01.22	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.07.22	
1Q 2023 annual review: updated initial criteria's dosing regimen from tixagevimab 150 mg (1 vial) and cilgavimab 150 mg to tixagevimab 300 mg (2 vials) and cilgavimab 300 mg (2 vials) and provided further clarification for continued therapy dosing: if prior dose was administered ≤ 3 months then repeat dose of tixagevimab 150 mg (1 vial) and cilgavimab 150 mg (1 vial) vs if prior dose was administered > 3 months then repeat dose of tixagevimab 300 mg (2 vials) and cilgavimab 300 mg (2 vials) per updated EUA; references reviewed and updated.	11.18.22	02.23

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.