# Clinical Policy: Clesrovimab-cfor (Enflonsia)

Reference Number: CP.PHAR.741
Effective Date: 09.01.25
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Line of Business: Commercial, HIM, Medicaid

Revision Log

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

## Description

Clesrovimab-cfor (Enflonsia™) is a respiratory syncytial virus (RSV) F protein-directed fusion inhibitor.

## FDA Approved Indication(s)

Enflonsia is indicated for the prevention of RSV lower respiratory tract disease in neonates and infants who are born during or entering their first RSV season

## 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 Enflonsia is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Preterm, Late Preterm or Term Infant** (must meet all)**:**

1. Age at onset of RSV season ≤ 12 months;
2. Request is for RSV prophylaxis;
3. Medical justification supports requests for RSV prophylaxis outside the identified season* duration for the specific region (*see Appendix D*);
   **Requests for RSV prophylaxis outside of the typical season (e.g., September through May) by region may be considered. Traditionally RSV season onset was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity. Due to the increased use of PCR testing, alternative statistical methods are used to determine seasonality in real time. Local and State health departments should be consulted to determine the real-time RSV season. Additional information on RSV trends by state can be found by visiting: https://www.cdc.gov/nrevss/php/dashboard/index.html.*
4. Member has not previously received Enflonsia or other RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination (unless infant is born < 14 days after maternal RSV vaccination);
5. If member previously received Synagis® for the current RSV season, < 5 Synagis doses were administered;*
   **Synagis should no longer be administered following Enflonsia. Existing Synagis authorizations should be termed.*
6. Member has not been hospitalized or previously infected with RSV disease during the current RSV season;
7. Dose does not exceed a 105 mg single dose.

**Approval duration: 4 weeks (1 dose per lifetime)**

**B. Chronic Lung Disease of Prematurity** (must meet all)**:**

1. Diagnosis of chronic lung disease (CLD) of prematurity (i.e., bronchopulmonary dysplasia [BPD]) defined as both of the following (a and b):
   a. GA < 32 weeks;
   b. Requirement for > 21% oxygen for ≥ 28 days after birth;
2. Medical management (i.e., supplemental oxygen, bronchodilators, diuretics, or chronic corticosteroid therapy) of CLD was required within the previous 6 months;
3. Age at onset of RSV season ≤ 12 months;
4. Request is for RSV prophylaxis;
5. Medical justification supports requests for RSV prophylaxis outside the identified season* duration for the specific region (*see Appendix D*);
   **Requests for RSV prophylaxis outside of the typical season (e.g., September through May) by region may be considered. Traditionally RSV season onset was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity. Due to the increased use of PCR testing, alternative statistical methods are used to determine seasonality in real time. Local and State health departments should be consulted to determine the real-time RSV season. Additional information on RSV trends by state can be found by visiting: https://www.cdc.gov/nrevss/php/dashboard/index.html.*
6. Member has not previously received Enflonsia or other RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination (unless infant is born < 14 days after maternal RSV vaccination);
7. If member previously received Synagis for the current RSV season, < 5 Synagis doses were administered;*
   **Synagis should no longer be administered following Enflonsia. Existing Synagis authorizations should be termed.*
8. Member has not been hospitalized or previously infected with RSV disease during the current RSV season;
9. Dose does not exceed a 105 mg single dose.

**Approval duration: 4 weeks (1 dose per lifetime)**

**C. Congenital Heart Disease** (must meet all)**:**

1. Diagnosis of hemodynamically significant congenital heart disease (CHD) and one of the following (a or b):
   a. CHD is unoperated or partially corrected;
   b. Presence of acyanotic cardiac lesions and one of the following (i or ii):
      i. Pulmonary hypertension with ≥ 40 mmHg measured pressure in the pulmonary artery;
      ii. Requirement of daily medication therapy to manage CHD;
2. Age at onset of RSV season ≤ 12 months;
3. Request is for RSV prophylaxis;
4. Medical justification supports requests for RSV prophylaxis outside the identified season* duration for the specific region (*see Appendix D*);
   **Requests for RSV prophylaxis outside of the typical season (e.g., September through May) by region may be considered. Traditionally RSV season onset was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity. Due to the increased use of PCR testing, alternative statistical methods are used to determine seasonality in real time. Local and State health departments should be consulted to determine the real-time RSV season. Additional information on RSV trends by state can be found by visiting: https://www.cdc.gov/nrevss/php/dashboard/index.html.*

5. Member has not previously received another RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination (unless infant is born < 14 days after maternal RSV vaccination);
6. If member is undergoing cardiac surgery with cardiopulmonary bypass, member has not previously received ≥ 2 doses of Enflonsia;
7. If member previously received Synagis, one of the following (a or b):*
   a. Request for Enflonsia is not within the same RSV season in which Synagis was administered;
   b. < 5 Synagis doses were administered for the current RSV season;

   **Synagis should no longer be administered following Enflonsia. Existing Synagis authorizations should be termed.*
8. Member has not been hospitalized or previously infected with RSV disease during the current RSV season;
9. Dose does not exceed one of the following (a or b):
   a. 105 mg single dose;
   b. Member is undergoing cardiac surgery with cardiopulmonary bypass: an additional 105 mg dose (2 doses total).

**Approval duration:**
**Cardiac surgery with cardiopulmonary bypass –** 12 months (2 doses total per lifetime)
**All other requests –** 4 weeks (1 dose per lifetime)

**D. Anatomic Pulmonary Abnormalities, Neuromuscular Disorders, Infants Profoundly Immunocompromised (off-label)** (must meet all)**:**
1. Member has anatomic pulmonary abnormalities, neuromuscular disorders, or is profoundly immunocompromised;
2. Age and diagnosis at onset of RSV season ≤ 12 months;
3. Request is for RSV prophylaxis;
4. Medical justification supports requests for RSV prophylaxis outside the identified season* duration for the specific region (*see Appendix D*);

   **Requests for RSV prophylaxis outside of the typical season (e.g., September through May) by region may be considered. Traditionally RSV season onset was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity. Due to the increased use of PCR testing, alternative statistical methods are used to determine seasonality in real time. Local and State health departments should be consulted to determine the real-time RSV season. Additional information on RSV trends by state can be found by visiting: https://www.cdc.gov/nrevss/php/dashboard/index.html.*
5. Member has not previously received Enflonsia or other RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination (unless infant is born < 14 days after maternal RSV vaccination);
6. If member previously received Synagis for the current RSV season, < 5 Synagis doses were administered;*

   **Synagis should no longer be administered following Enflonsia. Existing Synagis authorizations should be termed.*
7. Member has not been hospitalized or previously infected with RSV disease during the current RSV season;
8. Dose does not exceed a 105 mg single dose.

**Approval duration: 4 weeks (1 dose per lifetime)**

**E. Cystic Fibrosis (off-label)** (must meet all)**:**
1. Diagnosis of cystic fibrosis and one of the following (a or b):
   a. Clinical evidence of nutritional compromise;
   b. Diagnosis of CLD of prematurity defined as both of the following (i and ii):
      i. GA < 32 weeks;
      ii. Requirement for > 21% oxygen for ≥ 28 days after birth;
2. Age at onset of RSV season ≤ 12 months;
3. Request is for RSV prophylaxis;
4. Medical justification supports requests for RSV prophylaxis outside the identified season* duration for the specific region (*see Appendix D*);
   **Requests for RSV prophylaxis outside of the typical season (e.g., September through May) by region may be considered. Traditionally RSV season onset was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity. Due to the increased use of PCR testing, alternative statistical methods are used to determine seasonality in real time. Local and State health departments should be consulted to determine the real-time RSV season. Additional information on RSV trends by state can be found by visiting: https://www.cdc.gov/nrevss/php/dashboard/index.html.*
5. Member has not previously received Enflonsia or other RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination (unless infant is born < 14 days after maternal RSV vaccination);
6. If member previously received Synagis for the current RSV season, < 5 Synagis doses were administered;*
   **Synagis should no longer be administered following Enflonsia. Existing Synagis authorizations should be termed.*
7. Member has not been hospitalized or previously infected with RSV disease during the current RSV season;
8. Dose does not exceed a 105 mg single dose.

**Approval duration: 4 weeks (1 dose per lifetime)**

**F. Alaska Native and Other American Indian Infants (off-label)** (must meet all):
1. Medical director consultation is required for requests relating to Alaska native and other American Indian infants that fall outside the criteria outlined above;
2. Alaska native infants: Eligibility for prophylaxis may differ from the remainder of the U.S. on the basis of epidemiology of RSV in Alaska, particularly in remote regions where the burden of RSV disease is significantly greater than in the general U.S. population;
3. Other American Indian infants: Limited information is available concerning the burden of RSV disease among American Indian populations. However, special consideration may be prudent for Navajo and White Mountain Apache infants.
4. Age at onset of RSV season ≤ 12 months;
5. Request is for RSV prophylaxis;
6. Medical justification supports requests for RSV prophylaxis outside the identified season* duration for the specific region (*see Appendix D*);
   **Requests for RSV prophylaxis outside of the typical season (e.g., September through May) by region may be considered. Traditionally RSV season onset was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity. Due to the increased use of PCR testing, alternative statistical methods are used to determine seasonality in real time. Local and State health departments should be consulted to determine the real-time RSV season. Additional information on RSV trends by state can be found by visiting: https://www.cdc.gov/nrevss/php/dashboard/index.html.*

7. Member has not previously received Enflonsia or other RSV monoclonal antibody or any RSV vaccine, including maternal RSV vaccination (unless infant is born < 14 days after maternal RSV vaccination);
8. If member previously received Synagis for the current RSV season, < 5 Synagis doses were administered;*
   **Synagis should no longer be administered following Enflonsia. Existing Synagis authorizations should be termed.*
9. Member has not been hospitalized or previously infected with RSV disease during the current RSV season;
10. Dose does not exceed a 105 mg single dose.

**Approval duration: 4 weeks (1 dose per lifetime)**

**G. 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

**A. All Indications in Section I**

1. Continued therapy will not be authorized as Enflonsia is indicated to be dosed once, unless member is undergoing cardiac surgery with cardiopulmonary bypass, in which case an additional dose may be administered (2 doses total per lifetime).

**Approval duration: Not applicable**

**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.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

BPD: bronchopulmonary dysplasia
CDC: Centers for Disease Control and Prevention
CHD: congenital heart disease
CLD: chronic lung disease
FDA: Food and Drug Administration
GA: gestational age
HHS: Health and Human Services
RSV: respiratory syncytial virus

*Appendix B: Therapeutic Alternatives*

Not applicable

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): infants with a history of serious hypersensitivity reactions, including anaphylaxis, to any component of Enflonsia
- Boxed warning(s): none reported

*Appendix D: RSV Seasonal Durations Across the United States - Initiation and Termination of RSV Prophylaxis*

- Historical 2014-2017 CDC data from the 10 U.S. Department of Health and Human Services (HHS) regions, with the exception of Florida, shows RSV seasons commencing as early as September in some regions and ending as late as May in others.
- Traditionally, the RSV season was defined by consecutive weeks when RSV antigen-based tests exceeded 10% positivity; however, since 2008, laboratories have shifted away from antigen-based RSV testing, and since 2014 the majority of tests and RSV detections among consistently reporting laboratories are determined by polymerase chain reaction (PCR). The method that consistently captured the highest percentage of PCR detections for retrospectively characterizing RSV seasons was determined to be the retrospective slope 10 (RS10) method. This method uses a centered 5-week moving average of RSV detections normalized to a season peak of 1,000 detections. The season onset was defined as the second of 2 consecutive weeks when the slope, or normalized 5-week moving average of RSV detections between subsequent weeks, exceeded 10. The season offset was the last week when the standardized (normalized) detections exceeded the

standardized detections at onset. The peak was the week with the most standardized detections. The season duration was the inclusive weeks between onset and offset. The RS10 method captures a high proportion of RSV PCR detections for retrospectively determining RSV seasonality, but cannot be used to determine seasonal onset and offset in real time, and can only be employed after the season ends. Alternative statistical methods, including the tenfold baseline or 3% threshold methods might be used to determine seasonality in real time or near real time.

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| Prophylaxis - first RSV season | Single IM injection of 105 mg<br><br>For infants undergoing cardiac surgery with cardiopulmonary bypass, an additional 105 mg dose administered as an IM injection is recommended as soon as the infant is stable after surgery to ensure adequate Enflonsia serum levels. | 1 dose per lifetime<br><br>Cardiopulmonary bypass: 2 doses per lifetime |

## VI. Product Availability

Single-dose pre-filled syringe: 105 mg/0.7 mL

## VII. References

1. Enflonsia Prescribing Information. Rahway, NJ: Merck Sharp & Dohme LLC. June 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761432s000lbl.pdf. Accessed June 18, 2025.
2. Respiratory syncytial virus infection (RSV): Surveillance of RSV. Centers for Disease Control and Prevention website. Available at https://www.cdc.gov/rsv/php/surveillance/index.html. Page last reviewed: August 30, 2024. Accessed May 20, 2025.
3. Rha B, Curns AT, Lively JY, et al. Respiratory Syncytial Virus-Associated Hospitalizations Among Young Children: 2015-2016. Pediatrics. 2020 Jul; 146(1): e20193611.
4. Rose EB, Wheatley A, Langley G, Gerber S, Haynes A. Respiratory Syncytial Virus Seasonality — United States, 2014–2017. MMWR Morb Mortal Wkly Rep 2018;67:71–76. DOI: http://dx.doi.org/10.15585/mmwr.mm6702a4.
5. ACIP and AAP Recommendations for the Prevention of RSV Disease in Infants and Children. February 21, 2024. Available at: https://publications.aap.org/redbook/resources/25379/AAP-Recommendations-for-the-Prevention-of-RSV. Accessed May 20, 2025.
6. CDC 2024-2025 Respiratory Disease Season Outlook. August 29, 2024. Available at: https://www.cdc.gov/cfa-qualitative-assessments/php/data-research/season-outlook24-25/index.html. Accessed May 20, 2025.
7. CDC: RSV Immunization Guidance for Infants and Young Children. August 30, 2024. Available at: https://www.cdc.gov/rsv/hcp/vaccine-clinical-guidance/infants-young-children.html. Accessed May 20, 2025.

8. Advisory Committee on Immunization Practices: Proposed clinical considerations for clesrovimab. April 16, 2025. Available at: https://www.cdc.gov/acip/downloads/slides-2025-04-15-16/03-jones-maternal-peds-rsv-508.pdf. Accessed July 1, 2025.

**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 |
|---|---|
| 90382 | Respiratory syncytial virus, monoclonal antibody, seasonal dose, 0.7 mL, for intramuscular use |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created | 06.23.25 | 08.25 |

**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.