Overview of RSV Lower Respiratory Tract Disease in Infants

RSV, respiratory syncytial virus.

RSV Symptoms Are Typically Mild But Can Progress to Severe Disease in Infants[1–4]

- Initial symptoms of RSV infections are typically mild and cold-like[3,4]
- **20–30%** of infants develop **lower respiratory tract (LRT) disease** with first infection[5]
- LRT disease can occur **2–3 days** after onset of mild symptoms[2,6]

LRI caused by RSV manifests as bronchiolitis and/or pneumonia, with signs and symptoms that may vary in presence and intensity[1,2,5]

Signs and symptoms of RSV LRT disease include[1,2,5]:

- wheezing
- crackles
- retractions
- hypoxemia
- tachypnea
- dehydration

Risk for hospitalization for severe RSV-related illness is highest during the first few months of life[7,8]

Additional risk factors for severe disease include[1,4]:

- Preterm birth
- Chronic lung disease of prematurity
- Congenital heart disease

LRI, lower respiratory infection; LRT, lower respiratory tract; RSV, respiratory syncytial virus.
1. Walsh EE, Englund JA. In: Bennett JE et al, eds. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. 10th ed., Vol. 1. Philadelphia, PA: Elsevier Inc, 2025:2074–2084.e6. **2.** Kaler J, et al. *Cureus*. 2023;15(3):e36342. **3.** Centers for Disease Control and Prevention (CDC). About RSV. Last reviewed July 8, 2025. Accessed July 22, 2025. cdc.gov/rsv/about/index.html **4.** CDC. RSV in infants and young children. Last reviewed August 30, 2024. Accessed February 27, 2025. cdc.gov/rsv/infants-young-children/index.html **5.** Committee on Infectious Diseases, American Academy of Pediatrics (AAP), Kimberlin DW, et al. In: *Red Book: 2024–2027 Report of the Committee on Infection Diseases*. 33rd Edition. American Academy of Pediatrics; 2024:713–721. **6.** Black CP. *Respir Care*. 2003;48(3):209–231; discussion 231–233. **7.** Curns AT, et al. *Pediatrics.* 2024;153(3):e2023062574. **8.** Rha B, et al. *Pediatrics*. 2020;146(1):e20193611.

Most Infant RSV Cases Are Outpatient, But RSV Disease in Some Infants Can Progress Unpredictably, Potentially Leading to Hospitalization[1,2]

Based on a population-based estimate of medically attended RSV infections in a US cohort of privately insured infants <1 year of age[2,a]:

~81% of RSV-associated health care interactions
were outpatient visits for lower respiratory infection

RSV has been shown to be the leading cause of hospitalization in infants[3,4] and it is estimated that 1–3% of infants are hospitalized with severe RSV LRT disease in the first 12 months of life[5]

[a]The study estimated the annual incidence of RSV infections in a US cohort of privately insured children <5 years of age (N=6,767,107) between 2011–2019. Results were stratified by age. Medical encounters captured and evaluated in the MarketScan Commercial Claims and Encounters Database included inpatient, ICU, outpatient, and emergency department visits.

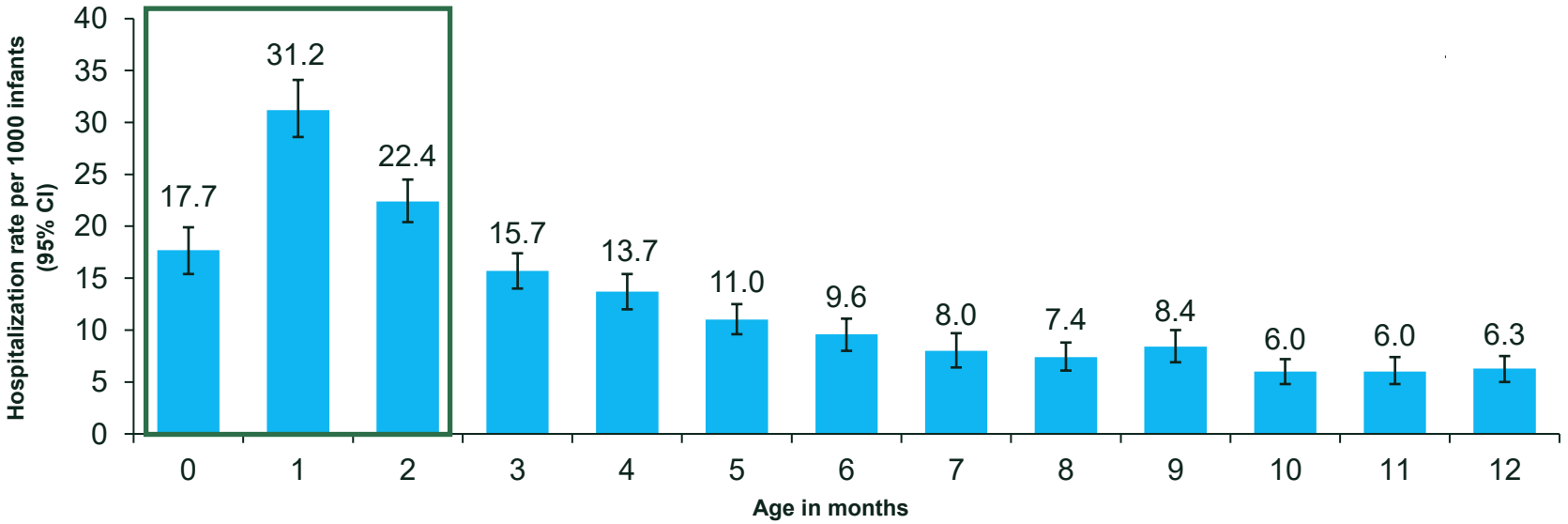
ICU, intensive care unit; LRT, lower respiratory tract; RSV, respiratory syncytial virus; US, United States.

1. Centers for Disease Control and Prevention (CDC). Clinical overview of RSV. Last reviewed August 18, 2025. Accessed October 27, 2025. cdc.gov/rsv/hcp/clinical-overview/index.html **2.** Nduaguba SO, et al. *Influenza Other Respir Viruses*. 2025;19(4):e70094. **3.** CDC. RSV in infants and young children. Last reviewed August 30, 2024. Accessed February 27, 2025. cdc.gov/rsv/infants-young-children/index.html **4.** Suh M, et al. *J Infect Dis*. 2022;226(S2):S154–S163. **5**. Committee on Infectious Diseases, American Academy of Pediatrics (AAP), Kimberlin DW, et al. In: *Red Book: 2024–2027 Report of the Committee on Infection Diseases*. 33rd Edition. American Academy of Pediatrics; 2024:713–721.

The Highest Rates of RSV-Associated Hospitalization in Infants <1 Year of Age Occurred During the First Few Months of Life[1,a]

The risk of RSV-associated hospitalization peaked at 1 month of age[1,a]

RSV-associated hospitalization rates, New Vaccine Surveillance Network — December 2016–September 2020[1,a]



[a]Based on active, prospective NVSN surveillance established by CDC for 13,524 children aged <5 years hospitalized with acute respiratory illness between December 1, 2016 to September 30, 2020 at 7 pediatric hospitals across the US who were tested for RSV with conclusive results.

CDC, Centers for Disease Control and Prevention; CI, confidence interval; NVSN, New Vaccine Surveillance Network; RSV, respiratory syncytial virus; US, United States.

1. Curns AT, et al. *Pediatrics.* 2024;153(3):e2023062574.

Disparities in the Risk of RSV-associated Hospitalization Across Race and Ethnicity Have Been Reported[1,2]

RSV-associated hospitalizations in infants aged <1 year by race and ethnicity, January 2009–December 2019[1,a]

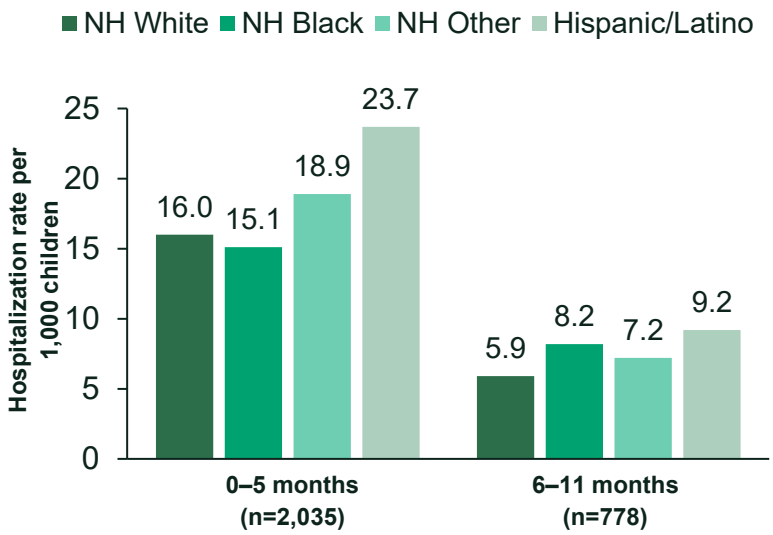
Hospitalizations were highest among

- **Non-Hispanic White**,
- **Hispanic**, and
- **American Indian/Alaskan Native** infants,

representing:

10.0% (95% CI, 9.7, 10.4)
to 11.1% (95% CI, 9.9, 12.2)[b] of
total infant hospitalizations

RSV-associated hospitalization rates by race, NVSN — December 2016–September 2020[2,c]



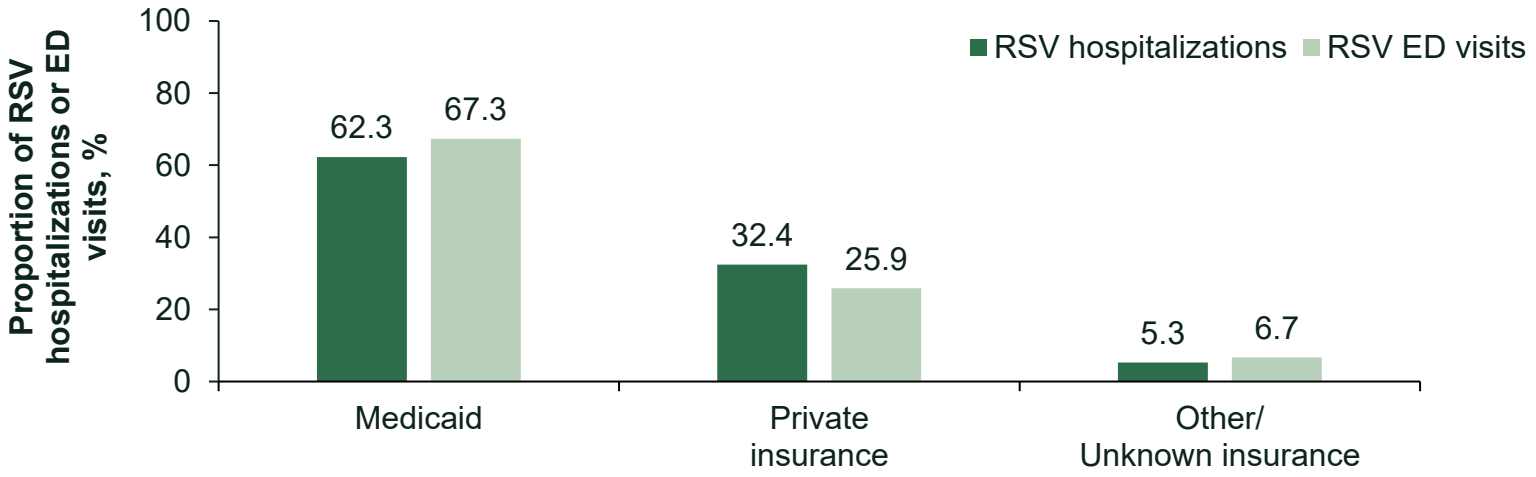
[a]Based on a retrospective study utilizing HCUP's inpatient hospital discharge datasets from the Agency for Healthcare Research and Quality to determine the leading causes of hospitalizations from January 2009 to December 2019 among >4.5 million US infants aged <1 year. RSV hospitalization was identified by a primary diagnosis of RSV, pneumonia due to RSV, acute bronchiolitis due to RSV, or acute bronchitis due to RSV using ICD-9 and ICD-10 codes. In sociodemographic analyses, denominator was the % of total infant hospitalizations in each group. [b]Hospitalizations due to acute bronchiolitis from RSV. [c]Based on active, prospective NVSN surveillance for children aged <5 years hospitalized with acute respiratory illness between December 1, 2016 and September 30, 2020, at 7 pediatric hospitals across the US.

CI, confidence interval; HCUP, Healthcare Cost and Utilization; ICD-9, International Classification of Diseases and Related Health Problems-9th revision; ICD-10, International Classification of Diseases and Related Health Problems-10th Revision; NH, non-Hispanic; NVSN, New Vaccine Surveillance Network; RSV, respiratory syncytial virus; US, United States.

1. Suh M, et al. *J Infect Dis*. 2022;226(Suppl 2):S154–S163. **2.** Curns AT, et al. *Pediatrics*. 2024;153(3):e2023062574.

Medicaid-insured Infants Had the Highest RSV-associated Hospitalization and Mortality Burden[1,2]

Retrospective, nationally representative data showing RSV-associated hospitalizations and ED visits in infants aged <1 year by insurance type KID, NIS, and NEDS — 2011–2019[1,2,a]



From 2011 through 2019,

59,927 RSV hospitalizations and **131,999 ED visits**

were estimated to occur annually in infants aged <1 year[1]

[a]Other/unknown insurance included Medicare, self-pay, no charge, other, and unknown payers.

CI, confidence interval; ED, emergency department; HCUP, Healthcare Cost and Utilization; ICD-9, International Classification of Diseases and Related Health Problems-9th revision; ICD-10, International Classification of Diseases and Related Health Problems-10th Revision; KID, Kids' Inpatient Database; NEDS, Nationwide Emergency Department Sample; NIS, National (Nationwide) Inpatient Sample; RSV, respiratory syncytial virus; US, United States.

1. Suh M, et al. *J Infect Dis.* 2022;226(Suppl 2):S184–S194. **2.** Suh M, et al. *J Infect Dis.* 2022;226(Suppl 2):S184–S194 (Suppl. Appendix).

RSV Disease Burden in Healthy Full-Term Infants

Full-Term Infants Without Underlying Conditions Accounted for the Majority of Medically Attended RSV Cases[1–3]

In a retrospective[a] analyses of US insurance claims data (N=2,129,828) including infants born between 2016 and 2020[1]:

75–80%

of medically attended RSV lower respiratory infection events[b] during infant's first RSV season occurred among full-term infants **without known comorbidities**

Based on prospective NVSN surveillance in RSV-positive children from 2016 to 2020 at 7 pediatric hospitals across the US[2,c]:

74%

of infants (n=2,813) hospitalized with RSV infection had **no history of premature birth or chronic comorbid conditions**

Of infants aged <1 year from the RSV-PIC public health prospective surveillance registry admitted to the ICU for RSV-related illness (N=600) in the 2022 RSV season[3,d]:

81.2%

had no underlying health conditions[e] (n=487)

71.1%

were full term (n=416)

The denominator for infants with documented prematurity status was 585; 15 infants were not accounted for in the data reporting term status

[a]Based on commercial insurance and Medicaid claims data from 3 separate retrospective birth cohorts of infants born between April 1, 2016 and February 29, 2020. [b]Medically attended RSV LRI events included outpatient, emergency department, and inpatient events identified based on ICD-10-CM diagnosis codes for RSV or for unspecified bronchiolitis. [c]Based on a prospective surveillance study in RSV-positive children <5 years old (n=4,243) with acute respiratory illness conducted from December 2016 through September 2020 at seven pediatric medical centers across the US. Of these, 2,813 were infants <12 months of age. [d]Based on a cross-sectional study of 600 infants <1 year of age admitted between October 17 and December 16, 2022 from the RSV-PIC public health prospective surveillance registry in 39 pediatric hospitals across 27 states in the US. Inclusion in the RSV-PIC registry required admission to the ICU or high acuity unit for 24 or more hours for RSV-related illness, symptom onset of less than 10 days before hospitalization, and evidence of laboratory-confirmed RSV before or within 72 hours after hospitalization. [e]Underlying conditions included: nonrespiratory, noncardiac; cardiac, nonrespiratory; respiratory; neurologic conditions; chronic lung disease; and Trisomy 21.

ICD-10-CM; International Classification of Diseases-Tenth Revision-Clinical Modification; ICU, intensive care unit; LRI, lower respiratory infection; NVSN, New Vaccine Surveillance Network; PIC, pediatric intensive care; RSV, respiratory syncytial virus; US, United States.

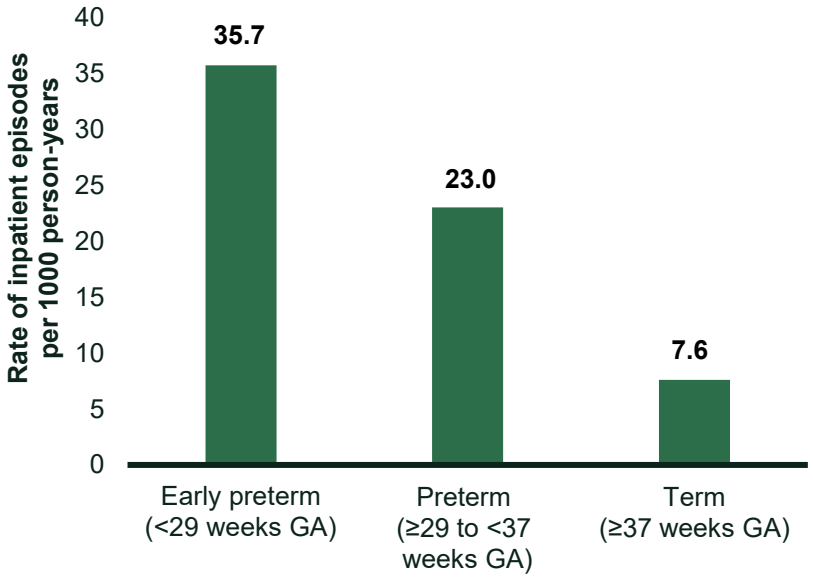
1. Gantenberg JR, et al. *J Infect Dis*. 2022;226(Suppl 2):S164–S174. **2.** Curns AT, et al. *Pediatrics.* 2024;153(3):e2023062574. **3.** Halasa N, et al. *JAMA Netw Open*. 2023;6(8):e2328950.

RSV Disease Burden in Infants at Increased Risk of Severe RSV Disease

Preterm Infants and Those With Underlying Health Conditions Are at Increased Risk of Severe RSV Disease[1,2]

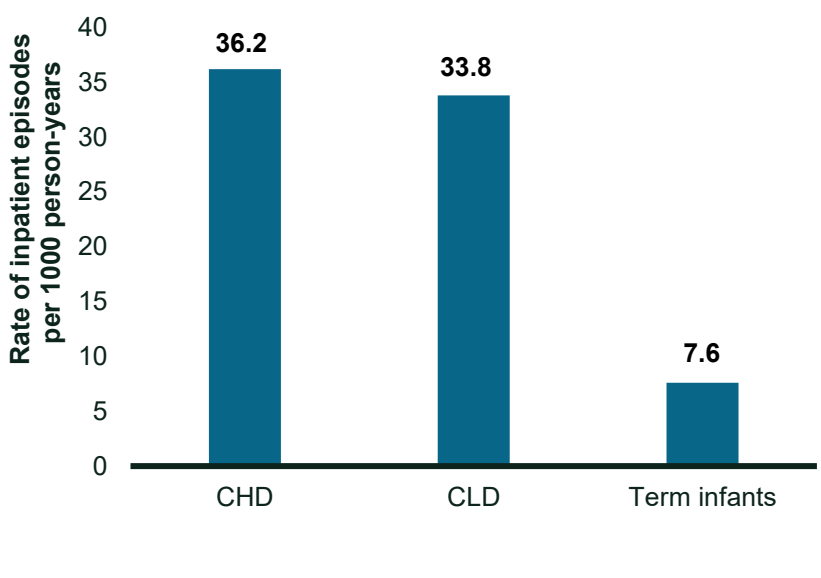
Incidence of RSV-LRTI inpatient episodes were ~3 to 5× higher among preterm children <1 year of age[1,2]

MarketScan, US – 2011 to 2019[1,a]



Incidence of RSV-LRTI inpatient episodes were ~4 to 5× higher among infants with underlying heart/lung conditions[1,2]

MarketScan, US – 2011 to 2019[1,a]



[a]The study estimated the annual incidence of RSV infections in a US cohort of privately insured children <5 years of age (N=6,767,107) between 2011–2019. Results were stratified by age. Medical encounters captured and evaluated in the MarketScan Commercial Claims and Encounters Database included inpatient, ICU, outpatient, and emergency department visits.

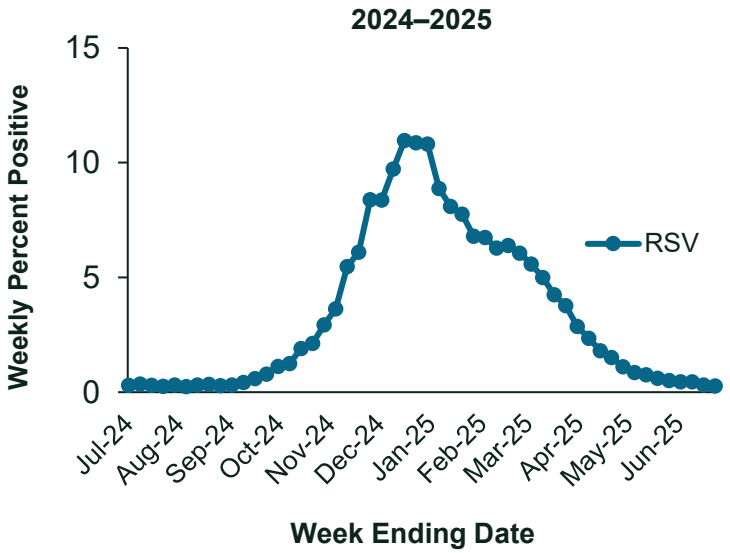
CHD, congenital heart disease; CI, confidence interval; CLD, chronic lung disease; GA, gestational age; ICU, intensive care unit; LRTI, lower respiratory tract infection; RSV, respiratory syncytial virus; US, United States.

1. Nduaguba SO, et al. *Influenza Other Respir Viruses.* 2025;19(4):e70094. **2.** Nduaguba SO, et al. Workbook: RSV Incidence. Accessed June 24, 2025. https://public.tableau.com/views/RSVIncidence/eTable3_Proportion?%3Alanguage=en-US&publish=yes&%3Adisplay_count=n&%3Aorigin=viz_share_

RSV Season in the US

RSV Season Generally Starts in the Fall and Peaks in the Winter in Most of the US[1,2]

Weekly percent positive tests for RSV — NREVSS, US[3,a]



Timing of RSV seasons can vary regionally in the US.[1,3] In 2024–2025, these patterns were observed in certain HHS regions[3–5,]:

- RSV season started in November 2024 at the national level
- RSV season started **3 to 5 weeks earlier in the Southeast and Southern regions**[a]
- RSV season started **3 to 5 weeks later in the Midwest, West, and Northern regions**[b]

RSV seasonality was disrupted by the COVID-19 pandemic[4]; post-pandemic seasonality in 2024–2025 resembled pre-pandemic seasonality based on NREVSS and RESP-NET[6–8]

[a]Southeast (HHS4): Atlanta, Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee; Southern (HHS6): Dallas, Arkansas, Louisiana, New Mexico, Oklahoma, and Texas. [b]Midwest (HHS7): Kansas City, Iowa, Kansas, Missouri, and Nebraska; Northern (HHS8): Denver, Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming; West (HHS10): Seattle, Alaska, Idaho, Oregon, and Washington.

HHS, US Department of Health and Human Services; NREVSS, National Respiratory and Enteric Virus Surveillance System; RESP-NET, Respiratory Virus Hospitalization Surveillance Network; RSV, respiratory syncytial virus; US, United States. **1.** Centers for Disease Control and Prevention (CDC). How RSV spreads. Last reviewed July 8, 2025. Accessed July 23, 2025. cdc.gov/rsv/causes/index.html **2.** CDC. About RSV. Last reviewed July 8, 2025. Accessed July 22, 2025. cdc.gov/rsv/about/index.html **3.** CDC. The National Respiratory and Enteric Virus Surveillance System (NREVSS). Accessed October 10, 2025. cdc.gov/nrevss/php/dashboard/index.html **4.** Hamid S, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72(14):355–361.**5.** U.S. Department of Health and Human Services (HHS). HHS Regional Offices. Last reviewed August 14, 2024. Accessed May 21, 2025. hhs.gov/about/agencies/iea/regional-offices/index.html **6.** CDC. NREVSS. 2019–2020. Last updated June 6, 2025. Accessed June 6, 2025. cdc.gov/nrevss/php/dashboard/index.html **7.** CDC. NREVSS. 2024–2025. Last updated September 26, 2025. Accessed October 9, 2025. cdc.gov/nrevss/php/dashboard/index.html **8.** CDC. Respiratory Virus Hospitalization Surveillance Network (RESP-NET). Last updated January 30, 2026. Accessed February 5, 2026. cdc.gov/resp-net/dashboard/index.html

ENFLONSIA™
(clesrovimab-cfor) 105 mg injection

Introducing: ENFLONSIA

MERCK

Indications and Usage

ENFLONSIA™ (clesrovimab-cfor) 105 mg injection

Not shown actual size.

ENFLONSIA is indicated for the prevention of respiratory syncytial virus (RSV) lower respiratory tract disease in neonates and infants who are born during or entering their first RSV season.

RSV, respiratory syncytial virus.

Dosage and Administration

ENFLONSIA™ (clesrovimab-cfor) 105 mg injection

Same dose

regardless of weight[a]

The recommended dose is 105 mg administered as a single IM injection.

[a]For infants undergoing cardiac surgery with cardiopulmonary bypass during or entering their first RSV season, an additional 105 mg dose is recommended as soon as the infant is stable after surgery to ensure adequate clesrovimab-cfor serum levels.

For neonates and infants born during the RSV season, administer ENFLONSIA once starting from birth.

For infants born outside the RSV season, administer ENFLONSIA once prior to the start of their first RSV season considering 5 months duration of protection provided by ENFLONSIA.

IM, intramuscular; RSV, respiratory syncytial virus.

Coadministration With Childhood Vaccines

ENFLONSIA™ (clesrovimab-cfor) 105 mg injection

In clinical trials, when ENFLONSIA was given concomitantly with routine childhood vaccines, the safety profile of the co-administered regimen was generally comparable to the safety profile when ENFLONSIA and childhood vaccines were administered alone.

Storage and Handling[1]

ENFLONSIA™ (clesrovimab-cfor) 105 mg injection

ENFLONSIA has a 30-month shelf life, which may enhance efficiency and inventory management.[1]

ENFLONSIA may be kept at room temperature for a maximum of 48 hours; if not used within the 48 hours, ENFLONSIA must be discarded.

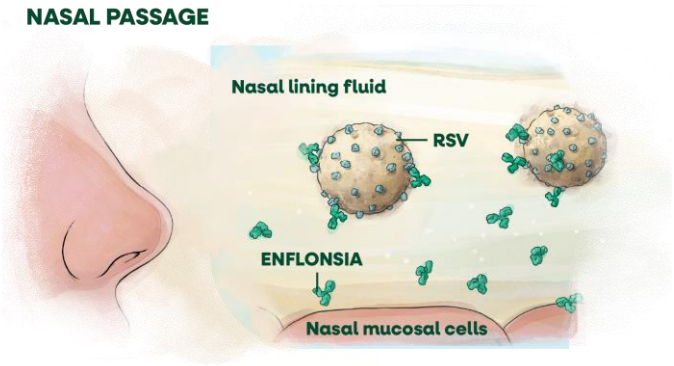
1. US Food & Drug Administration Center for Drug Evaluation and Research. BLA Approval Letter. Published June 9, 2025. Accessed October 21, 2025. accessdata.fda.gov/drugsatfda_docs/nda/2025/761432Orig1s000Approv.pdf

Designed to Rapidly Provide Antibodies to Help Protect Infants Entering Their First RSV Season

ENFLONSIA™ (clesrovimab-cfor) 105 mg injection

RSV infects cells along the respiratory tract from the nose to the lungs, causing a wide spectrum of respiratory disease, including lower respiratory tract infection[1]

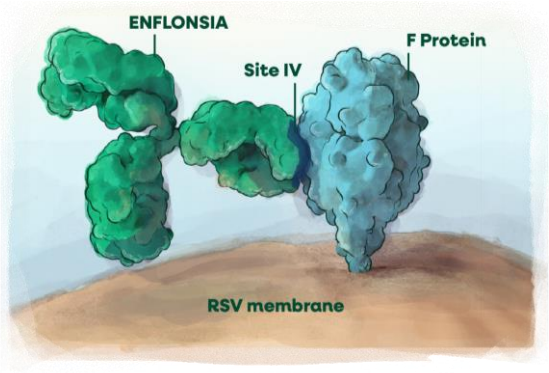
NASAL PASSAGE



ENFLONSIA has been detected in the lining fluid of the nasal mucosal cells in adults—an important point of viral entry into the body[2,3]

RSV neutralizing antibody titers in serum were estimated to be **~7 times higher than baseline levels at 4 hours** following administration

RSV MEMBRANE: A CLOSER LOOK



ENFLONSIA:

- binds to antigenic site IV (**highly conserved** in 99.8% of RSV strains)[a]
- is a fully human mAb modified for **extended serum half-life**[b]

[a]In sequences reported in GenBank database (accessed 4/2024). [b]Modified with a triple amino acid substitution (YTE) in the Fc region.

Fc, fragment crystallizable; mAb, monoclonal antibody; RSV, respiratory syncytial virus.

1. World Health Organization. Respiratory syncytial virus (RSV). March 25, 2025. Accessed April 16, 2025. who.int/news-room/fact-sheets/detail/respiratory-syncytial-virus-(rsv)# **2.** Centers for Disease Control and Prevention. How RSV spreads. Last reviewed July 8, 2025. Accessed July 23, 2025. cdc.gov/rsv/causes/index.html **3**. Phuah JU, et al. *Biomed Pharmacother*. 2023;169:115851. doi:10.1016/j.biopha.2023.115851

ENFLONSIA™
(clesrovimab-cfor) 105 mg injection

CLEVER (Trial 004)[1]

A Phase 2b/3 Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Clesrovimab in Healthy Preterm and Full-Term Infants

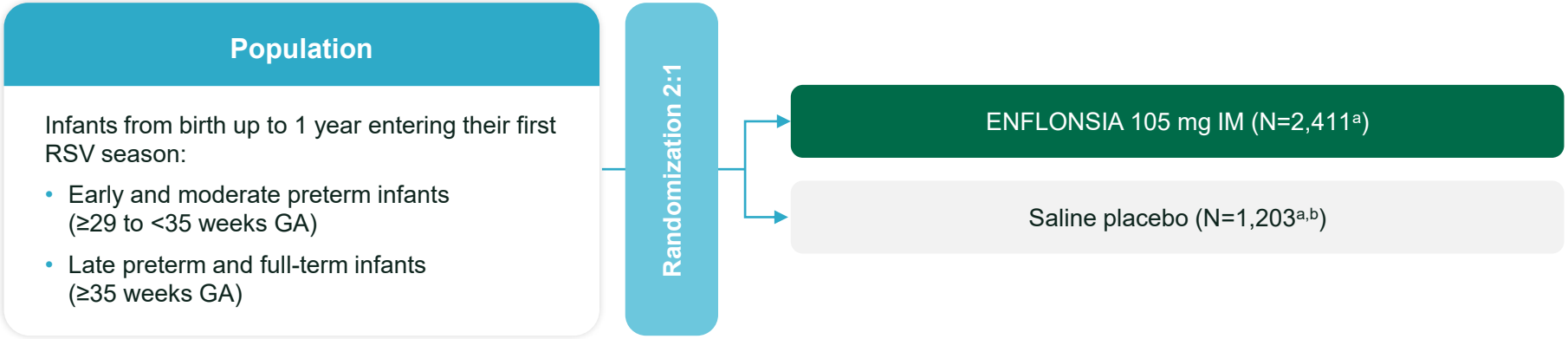
1. Zar HJ, et al. *N Engl J Med*. 2025;393(13):1292–1303.

MERCK

CLEVER (Trial 004) Study Design[1]: Phase 2b/3, Randomized, Double-Blind, Placebo-Controlled, Multi-Site trial

ENFLONSIA™ (clesrovimab-cfor) 105 mg injection

CLEVER was conducted in 22 countries from the Northern and Southern Hemispheres[1]



[a]Participants randomized and treated. [b]1 participant was randomized to placebo but received ENFLONSIA.

GA, gestational age; IM, intramuscular; RSV, respiratory syncytial virus.

1. Zar HJ, et al. *N Engl J Med*. 2025;393(13):1292–1303.

CLEVER (Trial 004)[1]: Select Baseline Characteristics

ENFLONSIA™ (clesrovimab-cfor) 105 mg injection

Age	
Median age	3.1 months (range: 0–12 months)
<6 months	80%
≥6 to <9 months	16%
≥9 months	4%

Gestational age	
≥29 to <35 weeks	18%
≥35 weeks	82%

Sex	
Male	51%

Race/Ethnicity	
White	45%
Asian	27%
Black or African American	14%
Multi-racial	12%
American Indian or Alaska Native	2%
Hispanic or Latino	28%

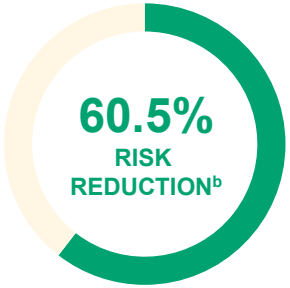
1. Zar HJ, et al. *N Engl J Med*. 2025;393(13):1292–1303.

CLEVER (Trial 004)[1]: Proven to Help Provide Robust RSV LRT Disease Protection

ENFLONSIA (n=2,411) vs placebo (n=1,203) efficacy data through 5 months

ENFLONSIA™ (clesrovimab-cfor) 105 mg injection

PRIMARY ENDPOINT



(95% CI[c]: 44.2, 72.0; *P*<0.001)

Incidence rates (# of cases)
ENFLONSIA: 0.026 (60)
Placebo: 0.065 (74)

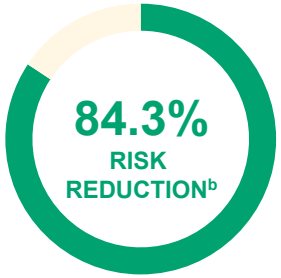
RSV-associated Medically Attended[a] LRI

through 5 months after administration

Endpoint definition:

RSV-positive RT-PCR NP sample, cough or difficulty breathing
AND
≥1 indicator of LRI:
Wheezing, rales/crackles
OR
≥1 indicator of severity:
Chest wall in-drawing/retractions, hypoxemia, tachypnea, dehydration due to respiratory symptoms

KEY SECONDARY ENDPOINT



(95% CI[c]: 66.7, 92.6; *P*<0.001)

Incidence rates (# of cases)
ENFLONSIA: 0.004 (9)
Placebo: 0.024 (28)

RSV-associated Hospitalization

through 5 months after administration

Endpoint definition:

RSV-positive RT-PCR NP sample
AND
Admitted for respiratory illness[2]

Increasing disease severity →

n=Number of participants eligible for inclusion in the full analysis set population.
[a]Medically attended (MA) includes all healthcare provider visits in settings such as outpatient clinic, clinical study site, emergency department, urgent care center, and/or hospital. [b]Efficacy for MALRI (requiring ≥1 indicator of LRI or severity) and hospitalization based on relative risk reduction against placebo adjusted for hemisphere at randomization, gestational age group, and age group at randomization. [c]Estimate and 95% of CI efficacy were estimated from the modified Poisson regression with robust variance method.

CI, confidence interval; LRI, lower respiratory infection; LRT, lower respiratory tract; MALRI, medically attended lower respiratory infection; NP, nasopharyngeal; RSV, respiratory syncytial virus; RT-PCR, reverse transcriptase polymerase chain reaction.

1. Zar HJ, et al. *N Engl J Med*. 2025;393(13):1292–1303. **2.** Zar HJ, et al. *N Engl J Med*. 2025;393(13):1292–1303 (Suppl. Appendix).

CLEVER (Trial 004)[1]: Safety Profile in Healthy Preterm and Full-Term Infants Was Generally Comparable to Placebo

ENFLONSIA™ (clesrovimab-cfor) 105 mg injection

Adverse Reactions Reported at an Incidence Higher Than Placebo (CLEVER Trial 004[1])

Adverse Reaction[a]	ENFLONSIA (N=2,412)[a]	Placebo (N=1,202)[a]
Injection-site erythema[b] (occurring within 5 days post-dose)	3.8%	3.3%
Injection-site swelling[b] (occurring within 5 days post-dose)	2.7%	2.6%
Rash[c] (occurring within 14 days post-dose)	2.3%	1.9%

Most (≥97%) of the adverse reactions were toxicity grade 1 (mild) or grade 2 (moderate).

These were the most commonly reported adverse reactions.
[a]Sample size reflects the number of participants included in the safety analysis population. [b]Solicited on Day 1 through Day 5 post-dose using an electronic diary device. [c]Defined by the following grouped preferred terms: rash, rash erythematous, rash macular, rash papular, rash maculo-papular, rash vesicular, rash exfoliative, dermatitis allergic, drug eruption and toxic skin eruption.

1. Zar HJ, et al. *N Engl J Med*. 2025;393(13):1292–1303.

Additional Data From CLEVER[1]: Incidence of RSV-Associated Disease in Infants Born at ≥29 Weeks GA Days 1 Through 150 Post-Dose[1,a]

ENFLONSIA™ (clesrovimab-cfor) 105 mg injection

Endpoints[1,2,b]	Criteria[1,2]	Incidence rate (# of cases)[1,2]		Observed efficacy[c] per exploratory endpoints[1,2] (95% CI)
		ENFLONSIA (N=2,398)	Placebo (N=1,201)	
Exploratory endpoint **LRI Hospitalization**	• **Admitted for respiratory illness,** and • **Cough/difficulty breathing,** and • **≥1 indicator of LRI** (wheezing, rales/crackles), or • **≥1 indicator of severity** (chest wall in-drawing/retractions, hypoxemia, tachypnea, and dehydration due to respiratory symptoms)	**0.002 (5)**	**0.023 (27)**	**90.9% (76.2, 96.5)**
Exploratory endpoint **Severe medically attended LRI**	• **Cough/difficulty breathing,** and • **Severe disease** (severe hypoxemia or the need for supplemental oxygen or mechanical ventilatory support)	**0.001 (2)**	**0.010 (12)**	**91.7% (62.9, 98.1)**

Limitations[1,3]: **No formal statistical testing was planned for the prespecified exploratory endpoints. No conclusions can be drawn from these results and they should be interpreted with caution.**

N=Number of participants eligible for inclusion in the full analysis set population.
[a]Results presented reflect those within the CLEVER 004 Clinical Study. The denominators of these results, which reflect total evaluated participants for the exploratory endpoints, differ slightly from the denominators reflected in the Prescribing Information, which inform the primary and key secondary endpoints. [b]Endpoints evaluated required an RSV-positive RT-PCR NP sample. [c]Estimate and 95% CI of observed efficacy were estimated from the modified Poisson regression with robust variance method.

CI, confidence interval; GA, gestational age; LRI, lower respiratory infection; NP, nasopharyngeal; RSV, respiratory syncytial virus; RT-PCR, reverse transcriptase polymerase chain reaction.

1. Zar HJ, et al. *N Engl J Med*. 2025;393(13):1292–1303. **2.** Zar HJ, et al. *N Engl J Med*. 2025;393(13):1292–1303 (Suppl. Appendix). **3.** Multiple endpoints in clinical trials: guidance for industry. U.S. Food and Drug Administration. October 2022. Accessed March 21, 2025. fda.gov/regulatory-information/search-fda-guidance-documents/multiple-endpoints-clinical-trials

Additional Data From CLEVER[1]: Incidence of RSV-Associated Disease in Infants Born at ≥29 Weeks GA Days 1 Through 150 Post-Dose[1,a]

ENFLONSIA™ (clesrovimab-cfor) 105 mg injection

Endpoint[1,2,b]	Criteria[1,2]	Incidence rate (# of cases)[1,2]		Observed efficacy[c] per analysis[1,2] (95% CI)
		ENFLONSIA (N=2,398)	Placebo (N=1,201)	
Post-hoc analysis **Medically attended LRI (requiring ≥2 indicators of LRI/severity)**	**≥1 indicator of LRI** (wheezing, rales/crackles, rhonchi), **and** **≥1 indicator of severity** (chest wall in-drawing/retractions, hypoxemia, tachypnea, and dehydration due to respiratory symptoms)	**0.004 (10)**	**0.035 (41)**	**88.0% (76.1, 94.0)**

Limitations[1,3,4]: **The post-hoc analysis was not prespecified in the statistical analysis plan; therefore, no conclusions can be drawn and results should be interpreted with caution.**

N=Number of participants eligible for inclusion in the full analysis set population.
[a]Results presented reflect those within the CLEVER 004 Clinical Study. The denominators of these results, which reflect total evaluated participants for the post-hoc analysis, differ slightly from the denominators reflected in the Prescribing Information, which inform the primary and key secondary endpoints. [b]Endpoints evaluated required an RSV-positive RT-PCR NP sample. [c]Estimate and 95% CI of observed efficacy were estimated from the modified Poisson regression with robust variance method.

CI, confidence interval; GA, gestational age; LRI, lower respiratory infection; NP, nasopharyngeal; RSV, respiratory syncytial virus; RT-PCR, reverse transcriptase polymerase chain reaction.

1. Zar HJ, et al. *N Engl J Med*. 2025;393(13):1292–1303. **2.** Zar HJ, et al. *N Engl J Med*. 2025;393(13):1292–1303 (Suppl. Appendix). **3.** Multiple endpoints in clinical trials: guidance for industry. U.S. Food and Drug Administration. October 2022. Accessed March 21, 2025. fda.gov/regulatory-information/search-fda-guidance-documents/multiple-endpoints-clinical-trials **4.** Andrade C. *Indian J Psychol Med*. 2023;45(6):640–641.

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SMART (Trial 007)[1]

A Phase 3, Multicenter, Randomized, Partially Blinded, Palivizumab-controlled Study to Evaluate the Safety, Efficacy, and Pharmacokinetics of Clesrovimab in Infants at Increased Risk for Severe RSV Disease

RSV, respiratory syncytial virus.

1. Sinha A, et al. *Contemp Clin Trials*. 2025;157:107995.

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SMART (Trial 007) Study Design[1]: Phase 3, Randomized, Partially-Blind, Palivizumab-Controlled, Multi-Site Trial in Infants at Increased Risk of Severe RSV Disease

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SMART was conducted in 27 countries from the Northern and Southern Hemispheres

Population

Infants from birth up to 1 year entering their first RSV season:

- Early (<29 weeks GA) or moderate (≥29 to ≤35 weeks GA) preterm infants
- Infants with chronic lung disease of prematurity or congenital heart disease of any GA

Randomization 1:1

- 1 dose ENFLONSIA 105 mg IM + 1 dose placebo one month later (N=446[a])
- 3–5 monthly doses of palivizumab 15 mg/kg IM (N=450)

Serious adverse events were monitored for up to 365 days post-dose

[a]176 had CLD of prematurity or CHD and 270 were early or moderate preterm infants (≤35 weeks GA) without CLD of prematurity or CHD.

CHD, congenital heart disease; CLD, chronic lung disease; GA, gestational age; IM, intramuscular; RSV, respiratory syncytial virus.

1. Sinha A, et al. *Contemp Clin Trials*. 2025;157:107995.

SMART (Trial 007)[1]: Select Baseline Characteristics

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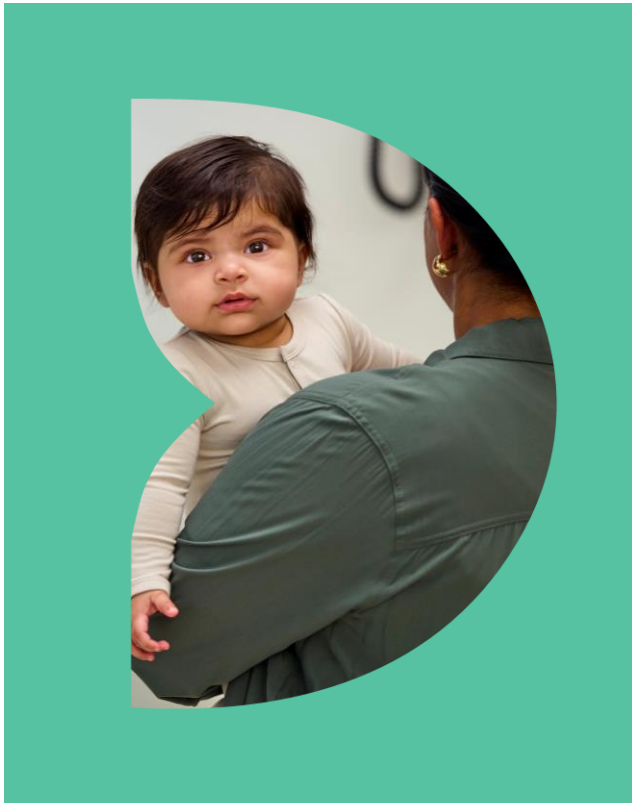
Age	
Median age	2.5 months (range: 0–12 months)
<6 months	89%
≥6 to <9 months	9%
≥9 months	2%

Gestational age and CLD/CHD status	
CLD	28%
CHD	11%
<29 weeks without CLD or CHD	6%
≥29 to ≤35 weeks without CLD or CHD	55%

Sex	
Male	50%

Race/Ethnicity	
White	52%
Asian	18%
Black or African American	15%
Multi-racial	12%
American Indian or Alaska Native	1%
Hispanic or Latino	32%



CHD, congenital heart disease; CLD, chronic lung disease.

1. Sinha A, et al. *Contemp Clin Trials*. 2025;157:107995.

SMART (Trial 007)[1]: Outcomes in Infants at Increased Risk for Severe RSV Disease

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Primary endpoints[1]: The safety profile of ENFLONSIA in infants at increased risk of severe RSV disease entering their first season was similar to palivizumab and consistent with the safety profile of ENFLONSIA in infants in CLEVER (Trial 004).[2]

There were no primary efficacy endpoints.[1] The efficacy of ENFLONSIA in infants at increased risk for severe RSV disease was established by extrapolation of efficacy of ENFLONSIA from CLEVER to SMART based on similar pharmacokinetic exposure.[1,2]

Secondary endpoints[1]	Incidence rate through 150 days after dosing (95% CI)	
	ENFLONSIA	Palivizumab
Medically attended[a] lower respiratory infection requiring ≥1 indicator of LRI/severity	3.6% (2.0, 6.0)	2.9% (1.5, 5.2)
Hospitalization	1.3% (0.4, 2.9)	1.5% (0.5, 3.2)

[a]Medically attended includes all healthcare provider visits in settings such as outpatient clinic, clinical study site, emergency department, urgent care center, and/or hospital.

CI, confidence interval; LRI, lower respiratory infection; RSV, respiratory syncytial virus.

1. Sinha A, et al. *Contemp Clin Trials*. 2025;157:107995. **2.** Zar HJ, et al. *N Engl J Med*. 2025;393(13):1292–1303.

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Infant RSV Passive Immunization Recommendations and Practical Considerations

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Current Recommendation for Preventive mAbs in Appropriate Infants

RSV Passive Immunization Guidance for Infants

American Academy of Pediatrics recommends the use of mAbs as an option for the prevention of RSV LRT disease in infants younger than 8 months of age born during or entering their first RSV season who meet AAP policy guidelines[1]

- Clesrovimab (a mAb) is included as an option in the AAP Recommended Child Adolescent Immunization Schedule[2]

Clesrovimab is available through the Vaccines for Children Program (VFC)[3] for children who qualify. Check with your state or local VFC Program to learn more.

Clesrovimab is the generic name for ENFLONSIA™ (clesrovimab-cfor).

AAP, American Academy of Pediatrics; LRT, lower respiratory tract; mAb, monoclonal antibody; RSV, respiratory syncytial virus.

1. Committee on Infectious Diseases. *Pediatrics*. 2025;156(5):e2025073923. **2.** American Academy of Pediatrics. Recommended child and adolescent immunization schedule for ages 18 years or younger. Updated February 5, 2026. Accessed February 10, 2026. downloads.aap.org/AAP/PDF/AAP-Immunization-Schedule.pdf **3.** Centers for Disease Control and Prevention (CDC). Pediatric/VFC vaccine price list. Accessed February 12, 2026. cdc.gov/vaccines-for-children/media/pdfs/2026/01/Pediatric-VFC-Vaccine-Price-List-01-26-26.pdf

RSV Passive Immunization Timing for Infants

In Season

Eligible infants born during the seasonal administration window for an RSV mAb **(from October through the end of March in most of the continental US)** should receive the RSV antibody dose within 1 week after birth, ideally during the birth hospitalization[1,2]

Out of Season

Eligible infants born outside the seasonal administration window **(ie, April–September in most of the continental US)** should receive an RSV mAb shortly before or during the RSV season[1,2]

The timing of the onset, peak, and decline of RSV activity vary geographically.[1,2]

For regions with unpredictable RSV circulation patterns, consult with local health authorities.[1–3]

mAb, monoclonal antibody; RSV, respiratory syncytial virus; US, United States.

1. Committee on Infectious Diseases. *Pediatrics*. 2025;156(5):e2025073923. **2.** American Academy of Pediatrics. Recommended child and adolescent immunization schedule for ages 18 years or younger. Updated February 5, 2026. Accessed February 10, 2026. downloads.aap.org/AAP/PDF/AAP-Immunization-Schedule.pdf **3.** American Academy of Pediatrics. RSV immunization frequently asked questions. Updated December 17, 2025. Accessed January 8, 2026. aap.org/en/patient-care/respiratory-syncytial-virus-rsv-prevention/rsv-frequently-asked-questions/

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Summary

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Summary

ENFLONSIA™ (clesrovimab-cfor) 105 mg injection

For infants born during or entering their first RSV season

1. Although usually mild, RSV disease can progress unpredictably and potentially lead to hospitalization[1]
2. ENFLONSIA is the first and only preventive option for RSV LRT disease administered to infants without the need for weight-based dosing[2,3]
3. ENFLONSIA has a 30-month shelf life and may be kept at room temperature for 48 hours; if not used within the 48 hours, ENFLONSIA must be discarded[4]

CDC, Centers for Disease Control and Prevention; RSV, respiratory syncytial virus.

1. Centers for Disease Control and Prevention (CDC). Clinical overview of RSV. Last reviewed August 18, 2025. Accessed October 27, 2025. cdc.gov/rsv/hcp/clinical-overview/index.html **2.** Beyfortus. Prescribing Information. Sanofi; 2025. **3.** Synagis. Prescribing and Patient information. Sobi Inc; 2021. **4.** US Food & Drug Administration Center for Drug Evaluation and Research. BLA Approval Letter. Published June 9, 2025. Accessed October 21, 2025. accessdata.fda.gov/drugsatfda_docs/nda/2025/761432Orig1s000Approv.pdf

Summary (*continued*)

ENFLONSIA™ (clesrovimab-cfor) 105 mg injection

For infants born during or entering their first RSV season

4. ENFLONSIA has a consistent safety profile across infant populations[1]

5. ENFLONSIA is indicated for the prevention of RSV LRT disease in infants born during or entering their first RSV season

LRT, lower respiratory tract; RSV, respiratory syncytial virus.

1. Zar HJ, et al. *N Engl J Med*. 2025;393(13):1292–1303.

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Before administering ENFLONSIA™ (clesrovimab-cfor), please read the accompanying Prescribing Information. The Patient Information also is available.

Thank you

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