-->

aetna™

(https://www.aetna.com/)

Nirsevimab-alip (Beyfortus)

Clinical Policy Bulletins Medical Clinical Policy Bulletins

Number: 1038

Table Of Contents

Policy History

Effective:

09/12/2023

Next Review: 07/27/2024

Definitions

Policy

I. Criteria for Approval

Aetna considers a single intramuscular (IM) nirsevimab-alip (Beyfortus) injection medically necessary for prevention of respiratory syncytial virus (RSV) lower respiratory tract disease when *any* of the following criteria is met:

Additional Information

Clinical Policy Bulletin Notes

A. For all infants (birth up to 12 months of age) who are born during or entering their first RSV season and have not previously received a nirsevimab-alip or palivizumab dose; *or*
B. For children up to 24 months of age who remain vulnerable to severe RSV disease prior to or during the second RSV season and have not received palivizumab in the same season. Beyfortus may be administered if palivizumab was received in the member's first RSV season. **Note:** a single 200 mg dose for this age group is administered as two IM injections [2 x 100 mg]; *or*
C. For children undergoing cardiac surgery with cardiopulmonary bypass, an additional dose of Beyfortus may be administered soon as the child is stable after surgery to ensure adequate nirsevimab-alip serum levels and when the following criteria is met:

    1. First RSV season:

        a. Surgery is within 90 days after receiving initial Beyfortus dose; *or*
        b. More than 90 days have elapsed since receiving initial Beyfortus dose; *or*

    2. Second RSV season:

        a. Surgery is within 90 days after receiving second Beyfortus dose; *or*
        b. More than 90 days have elapsed since receiving second Beyfortus dose.

Aetna considers all other indications as experimental and investigational.

II. **Related Policies**

- CPB 0155 - Ribavirin (Virazole) Inhalation (../100_199/0155.html)
- CPB 0318 - Palivizumab (Synagis) (../300_399/0318.html)
- CPB 1027 - Respiratory Syncytial Virus (RSV) Vaccine (1027.html)

Dosage and Administration

Beyfortus is a sterile, preservative-free, solution which contains nirsevimab-alip, a RSV F protein-directed fusion inhibitor, for intramuscular (IM) injection. It is supplied in a single-dose siliconized Luer lock Type I glass pre-filled syringe with a FluroTec coated plunger stopper. Beyfortus is available as:

- 50 mg/0.5 mL in a single-dose pre-filled syringe
- 100 mg/mL in a single-dose pre-filled syringe.

Beyfortus IM injection is to be administered by a healthcare provider. Below contains the FDA-approved dosage recommendations.

Neonates and Infants: First RSV Season

For neonates and infants born during or entering the RSV season, Beyfortus is administered starting from birth. For infants born outside the RSV season, Beyfortus is to be administered once prior to the start of the RSV season considering duration of protection provided by Beyfortus.

The recommended dosage for neonates and infants born

during or entering their first RSV season is based on body weight (see Table 1) and is administered as a single IM injection.

Table: Dosage Recommendations for Neonates and Infants Born During or Entering Their First RSV Season

Body Weight at Time of Dosing	Recommended Dosage
Less than 5 kg	50 mg by IM injection
5 kg and greater	100 mg by IM injection

Children Who Remain at Increased Risk for Severe RSV Disease: Second RSV Season

For children up to 24 months of age who remain at increased risk for severe RSV disease in their second RSV season, the recommended dosage of Beyfortus is a single 200 mg dose administered as two IM injections (2 x 100 mg).

Children Undergoing Cardiac Surgery with Cardiopulmonary Bypass

For children undergoing cardiac surgery with cardiopulmonary bypass, an additional dose of Beyfortus is recommended as soon as the child is stable after surgery to ensure adequate nirsevimab-alip serum levels. The recommended dosage is administered as an IM injection.

- First RSV season:
    - If surgery is within 90 days after receiving Beyfortus, the additional dose should be based on body weight at the time of the additional dose. Refer to Table 1 for

weight-based dosing.

- If more than 90 days have elapsed since receiving Beyfortus, the additional dose should be 50 mg regardless of body weight.

- Second RSV season:

  - If surgery is within 90 days after receiving Beyfortus, the additional dose should be 200 mg, regardless of body weight.
  - If more than 90 days have elapsed since receiving Beyfortus, the additional dose should be 100 mg, regardless of body weight.

Note: There is no information regarding co-administration of Beyfortus with other immunoglobulin products. Palivizumab should not be administered to infants who have already received Beyfortus in the same season. There are no data regarding substitution of Beyfortus for palivizumab once prophylaxis treatment is initiated with palivizumab for the RSV season. Beyfortus may be administered prior to or during the second RSV season to children up to 24 months of age who remain vulnerable to severe RSV disease, and who received palivizumab in their first RSV season.

Source: Sanofi Pasteur, 2023

CPT Codes / HCPCS Codes / ICD-

10 Codes

CPT codes covered if selection criteria are met:

Code	Code Description
90380	Respiratory syncytial virus, monoclonal antibody, seasonal dose; 0.5 mL dosage, for intramuscular use
90381	1 mL dosage, for intramuscular use
Other CPT codes related to the CPB:	
96372	Therapeutic, prophylactic or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
ICD-10 codes covered if selection criteria are met:	
B97.4	Respiratory syncytial virus as the cause of diseases classified elsewhere
Z23	Encounter for immunization

Background

U.S. Food and Drug Administration (FDA)-Approved Indications

- Beyfortus is a respiratory syncytial virus (RSV) F protein-directed fusion inhibitor indicated for the prevention of RSV lower respiratory tract disease in:
  - Neonates and infants born during or entering their first RSV season
  - Children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season.

Respiratory syncytial virus (RSV) is an enveloped single-stranded, negative-sense ribonucleic acid (RNA) virus of the *Pneumovirdae* family that can cause acute respiratory tract illness in persons of all ages. RSV is considered a common respiratory pathogen typically resulting in self-limited, mild, cold-like symptoms that can last around one to two weeks. However, for some people, the virus can lead to an infection that spreads to the lower respiratory tract, causing bronchiolitis or pneumonia, resulting in a severe or life-threatening illness. Those who are most vulnerable for severe infection include infants (especially premature infants), older adults (especially those 65 years and older), people with certain comorbid conditions (e.g., cardiac and pulmonary disease), and those who are immunocompromised. In most parts of the United States, RSV circulation is seasonal, typically starting during the fall and peaking in the winter. It is transmitted from person to person through close contact with someone who is infected.

Currently, there is not a "vaccine" readily available to prevent RSV in infants and children less than 2 years of age. However, since 1998, palivizumab, a humanized monoclonal antibody against the RSV F glycoprotein, has been available for the prevention of serious RSV lower respiratory tract disease in children, but only for those at high risk of RSV disease, and is only administered during RSV season. In July 2023, the FDA approved nirsevimab-alip (Beyfortus) (Sanofi Pasteur and AstraZeneca), a monoclonal antibody against the RSV F glycoprotein with an extended half-life, to protect all infants through their first RSV season. Approval also included use for children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season. Palivizumab and nirsevimab are classified as an immunoprophylactic drug, not a vaccine. They act similarly to a

vaccine; however, instead of prompting the immune system to develop antibodies to the virus (considered active immunization), they deliver the antibodies directly to the bloodstream (considered passive immunization).

FDA approval for Beyfortus is based on three multicenter, placebo-controlled randomized trials of otherwise healthy infants born at 29 weeks gestation or more, in which a single injection of nirsevimab was evaluated during the 150 days after administration and found to be safe and effective in preventing RSV lower respiratory tract infection that requires medical attention (e.g., emergency department or clinic/office visit) and RSV-associated hospitalization.

Griffin et al (2020) evaluated single-dose nirsevimab for the prevention of RSV in preterm infants. The study randomly assigned 1453 healthy infants who had been born preterm (29 weeks 0 days to 34 weeks 6 days of gestation) in a 2:1 ratio to receive nirsevimab (n=969), at a dose of 50 mg in a single intramuscular injection, or placebo (n=484) at the start of an RSV season. The primary end point was medically attended RSV-associated lower respiratory tract infection through 150 days after administration of the dose. The secondary efficacy end point was hospitalization for RSV-associated lower respiratory tract infection through 150 days after administration of the dose. The authors found that the incidence of medically attended RSV-associated lower respiratory tract infection was 70.1% lower with nirsevimab prophylaxis than with placebo ($p<0.001$), and that the incidence of hospitalization for RSV-associated lower respiratory tract infection was 78.4% lower with nirsevimab than with placebo ($p<0.001$). These differences were consistent throughout the 150-day period after the dose was administered and across geographic

locations and RSV subtypes. Adverse events were similar in the two trial groups, with no notable hypersensitivity reactions. The authors concluded that a single injection of nirsevimab resulted in fewer medically attended RSV-associated lower respiratory tract infections and hospitalizations than placebo throughout the RSV season in healthy preterm infants (ClinicalTrials.gov Identifier: NCT02878330).

Hammitt et al (2022) evaluated nirsevimab for prevention of RSV in healthy late-preterm and term infants. The authors randomly assigned, in a 2:1 ratio, 1490 infants who had been born at a gestational age of at least 35 weeks to receive a single intramuscular injection of nirsevimab (n=994) or placebo (n=496) before the start of an RSV season. The primary efficacy end point was medically attended RSV-associated lower respiratory tract infection through 150 days after the injection. The secondary efficacy end point was hospitalization for RSV-associated lower respiratory tract infection through 150 days after the injection. The authors found that medically attended RSV-associated lower respiratory tract infection occurred in 12 infants (1.2%) in the nirsevimab group and in 25 infants (5.0%) in the placebo group, which correspond to an efficacy of 74.5% ($p<0.001$) for nirsevimab. Hospitalization for RSV-associated lower respiratory tract infection occurred in 6 infants (0.6%) in the nirsevimab group and in 8 infants (1.6%) in the placebo group (efficacy, $p = 0.07$). Among infants with data available to day 361, antidrug antibodies after baseline were detected in 58 of 951 (6.1%) in the nirsevimab group and in 5 of 473 (1.1%) in the placebo group. Serious adverse events were reported in 67 of 987 infants (6.8%) who received nirsevimab and in 36 of 491 infants (7.3%) who received placebo. The authors concluded that a single injection of nirsevimab administered before the RSV season protected healthy late-preterm and term infants from medically attended RSV-associated lower respiratory tract

infection (ClinicalTrials.gov Identifier: NCT03979313).

Domachowske et al (2022) conducted a phase 2/3 randomized, double-blind, palivizumab-controlled, multicenter study that evaluated the safety and pharmacokinetics (PK) of nirsevimab in preterm infants born less than 35 weeks gestational age (GA) and infants with chronic lung disease (CLD) of prematurity or hemodynamically significant congenital heart disease (CHD). This trial was not powered for efficacy, but efficacy was assessed as a secondary endpoint. The efficacy of nirsevimab in preterm infants during their first RSV season and in pediatric subjects up to 24 months of age with CLD or CHD during their first and second RSV season was established by extrapolation of efficacy from prior trials based on similar nirsevimab exposures. For RSV season one, a total of 925 infants were randomized 2:1 in each of the preterm (n=615) and CLD/CHD (n=310) cohorts to receive nirsevimab or palivizumab. Infants received a single IM dose of nirsevimab (50 mg if less than 5 kg body weight or 100 mg if greater than 5 kg body weight at the time of dosing), followed by 4 once-monthly intramuscular (IM) doses of placebo, or 5 once-monthly IM doses of 15 mg/kg palivizumab, respectively. In the first RSV season, the incidence of medically attended RSV-associated lower respiratory tract infection through 150 days post dose was 0.6% (4/616) in the nirsevimab group and 1.0% (3/309) in the palivizumab group. Pediatric subjects with CLD of prematurity or hemodynamically significant CHD up to 24 months of age continued in the trial for a second RSV season (n=262). Subjects who received nirsevimab during their first RSV season also received a single dose of 200 mg nirsevimab entering their second RSV season followed by 4 once-monthly IM doses of placebo (n=180). Subjects who received palivizumab during their first RSV season were re-randomized 1:1 to either receive nirsevimab or palivizumab entering their second RSV season. Forty subjects who received palivizumab

in the first RSV season received a single IM dose of nirsevimab followed by 4 once-monthly IM doses of placebo in their second RSV season; and 42 subjects received palivizumab (5 once-monthly IM doses of 15 mg/kg palivizumab) in both first and second RSV seasons. In the second RSV season of trial, there were no cases of medically attended RSV-associated lower respiratory tract infection through Day 150 post-dose in subjects who received either nirsevimab or palivizumab (ClinicalTrials.gov Identifier: NCT03959488).

Beyfortus is a single-dose long-acting monoclonal antibody which is administered intramuscularly by a healthcare provider, and can be given concomitantly with childhood vaccines. It is contraindicated in infants and children with a history of serious hypersensitivity reactions, including anaphylaxis, to nirsevimab-alip or to any of the excipients. Labeled warnings and precautions include serious hypersensitivity reactions, including anaphylaxis, which have been observed with other human IgG1 monoclonal antibodies. The most common adverse reactions were rash (0.9%) and injection site reactions (0.3%). The safety and effectiveness of Beyfortus in children older than 24 months of age have not been established.

On August 3, 2023, the Centers for Disease Control and Prevention's (CDC's) Advisory Committee on Immunization Practices (ACIP) voted unanimously to recommend routine use of Beyfortus for: (i) newborns and infants below 8 months of age born during or entering their first RSV season, and (ii) children aged 8 to 19 months who are at increased risk of severe RSV disease and entering their second RSV season. In addition, the ACIP voted unanimously to include Beyfortus in the Vaccines for Children program. "The official recommendations will be published in the CDC's Morbidity and Mortality Weekly Report (MMWR). Once approved, routine use

of Beyfortus would be included in the CDC's Child and Adolescent Immunization Schedule" (CDC, 2023a).

RSV Seasonality

RSV epidemic in the U.S. typically follows a seasonal pattern. The RSV seasonality, which can vary by geographical region, usually occurs from October to April, peaking in December or January. Disruption of the typical seasonal pattern may result in off-season outbreaks, which was the case during the 2020-2022 seasons due to the coronavirus disease 2019 (COVID-19) pandemic. The CDC's RSV circulation data for the 2022-2023 RSV season in the U.S. indicates a return to pre-COVID-19 pandemic seasonality. However, the CDC's ACIP cautions that although an eventual return to pre-

pandemic RSV seasonality is expected, clinicians should be aware that off-season (atypical) RSV circulation might continue (Hamid et al, 2023).

References

The above policy is based on the following references:

1. American Academy of Pediatrics (AAP). FDA approves nirsevimab to prevent RSV in infants. AAP News [internet]. Jenco M, ed. July 17, 2023. Available at: https://publications.aap.org/aapnews/news/25085/FDA-approves-nirsevimab-to-prevent-RSV-in-infants?autologincheck=redirected. Accessed July 20, 2023.
2. Barr FE, Graham BS. Respiratory syncytial virus

infection: Clinical features and diagnosis. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed May 2023a.

3. Barr FE, Graham BS. Respiratory syncytial virus infection: Prevention in infants and children. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed July 2023b.
4. Centers for Disease Control and Prevention (CDC). Press Release: U.S. CDC Advisory Committee unanimously recommends routine use of Beyfortus (nirsevimab-alip) to protect infants against RSV disease. Press Release. August 3, 2023. Available at: https://www.bloomberg.com/press-releases/2023-08-03/press-release-u-s-cdc-advisory-committee-unanimously-recommends-routine-use-of-beyfortus-nirsevimab-alip-to-protect. Accessed August 7, 2023.
5. Centers for Disease Control and Prevention (CDC). Respiratory syncytial virus infection (RSV). Atlanta, GA: CDC; reviewed October 28, 2022. Available at: https://www.cdc.gov/rsv/index.html. Accessed July 20, 2023.
6. Domachowske J, Madhi SA, Simões EAF, et al. Safety of nirsevimab for RSV in infants with heart or lung disease or prematurity. N Engl J Med. 2022;386(9):892-894.
7. Griffin MP, Yuan Y, Takas T, et al. Single-dose nirsevimab for prevention of RSV in preterm infants [published correction appears in N Engl J Med. 2020 Aug 13;383(7):698]. N Engl J Med. 2020;383(5):415-425.
8. Hamid S, Winn A, Parikh R, et al. Seasonality of respiratory syncytial virus - United States, 2017-2023. MMWR Morb Mortal Wkly Rep. 2023;72(14):355-361.
9. Hammitt LL, Dagan R, Yuan Y, et al. Nirsevimab for prevention of RSV in healthy late-preterm and term infants. N Engl J Med. 2022;386(9):837-846.

10. Sanofi Pasteur, Inc. Beyfortus (nirsevimab-alip) injection, for intramuscular use. Prescribing Information. Swiftwater, PA: Sanofi Pasteur; revised July 2023a.
11. Sanofi Pasteur, Inc. Press release: FDA approves Beyfortus (nirsevimab-alip) to protect infants against RSV. Press Release. Swiftwater, PA: Sanofi Pasteur; July 17, 2023b.
12. U.S. Food and Drug Administration (FDA). FDA approves new drug to prevent RSV in babies and toddlers. FDA News Release. Silver Spring, MD; FDA; July 17, 2023.

Language services can be provided by calling the number on your member ID card. For additional language assistance: Español | 中文 | Tiếng Việt | _____ | Tagalog | Русский | العربية | Kreyòl | Français | Polski | Português | Italiano | Deutsch | _____ | فارسی | Other Languages... | (http://www.aetna.com/individuals-families/contact-aetna/information-in-other-languages.html)