Drug FAQs for Clinicians
FREQUENTLY ASKED QUESTIONS

Nirsevimab-alip (Beyfortus) for Prevention of Respiratory Syncytial Virus Disease

Nirsevimab is a long-acting monoclonal antibody approved by the U.S. Food and Drug Administration (FDA) to provide immediate protection against lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) in neonates and infants born during or entering their first RSV season, and in children up to age 24 months who remain at higher risk for severe RSV disease through their second RSV season.[1] RSV is the leading cause for hospitalizations for infants in the United States.[8]

What are the current treatment options for prevention of RSV-related LRTD in infants and young children?

- Passive immunization can be provided by monoclonal antibodies that are administered to infants and young children. These options provide immediate but short-term protection against RSV-associated LRTD.[3,11,13,14]
    - Nirsevimab (Beyfortus) is a long-acting monoclonal antibody recommended for infants below 8 months of age born during or entering their first RSV season. Infants born during the RSV season should receive nirsevimab during the first week of life. For certain infants and children aged 8 to 19 months who are at increased risk of severe RSV disease and are entering their second RSV season, it is recommended they receive nirsevimab regardless of maternal RSV vaccination.[13,14]
    - Palivizumab (Synagis) is another monoclonal antibody FDA-approved RSV-related LRTD and recommended only for high-risk infants and children up to age 24 months with certain underlying medical conditions. The American Academy of Pediatrics (AAP), however, recommends limited use of palivizumab for children with certain underlying medical conditions.[10,11]
    - Both nirsevimab and palivizumab are administered intramuscularly; however, palivizumab requires monthly dosing during the RSV season while nirsevimab is given as a single dose.[1,2]
- The maternal RSV vaccine (Abrysvo) is the only vaccine option. The U.S. Centers for Disease Control and Prevention (CDC) recommends the RSV vaccine for pregnant people during 32 weeks and 0 days through 36 weeks and 6 days gestation, using seasonal administration (typically September through January), to prevent LRTD in infants.[14] Refer to the Clinician FAQs and Member FAQs for Maternal RSV Vaccine.
- The CDC recommends to protect all infants against RSV-associated LRTI through use of either the maternal RSV vaccine or administration of nirsevimab to the infant.[14]
- Healthcare providers should present information on both the maternal RSV vaccine and nirsevimab for infant immunization and consider the patient's preferences when determining which product to administer.

	Advantages[14]	Disadvantages[14]
Maternal RSV Vaccine	• Provides protection immediately after birth • Might be more resistant to potential mutations in F protein*	• Potential reduced protection if fewer antibodies are produced or are transferred from pregnant person to baby (e.g., pregnant person is immunocompromised or infant born soon after vaccination) • Potential risk for preterm birth and hypertensive disorders of pregnancy
Nirsevimab	• Direct receipt of antibodies (i.e., does not rely on transplacental transfer) • No adverse pregnancy outcomes • Studies† of antibody levels suggest that protection might wane more slowly than protection from the maternal RSV vaccine • Can time the dose for when baby enters RSV season	• Potentially limited availability during 2023-2024 RSV season • Requires infant injection

*****Maternal RSV vaccination results in a polyclonal immune response, which is expected to be more resistant to potential mutations in the RSV F protein than a monoclonal antibody product

†No data are available directly comparing the efficacy of nirsevimab and maternal RSVpreF vaccine (Abrysvo).

Is nirsevimab a vaccine? What is the mechanism of action of nirsevimab?

- Nirsevimab is not a vaccine; it is a monoclonal antibody product that is a passive immunization. While not technically a "vaccine" in a traditional sense (i.e., active immunization), it is being used in a manner similar to routine childhood vaccines.[1]
- Nirsevimab targets the RSV F-protein, which blocks RSV from entering healthy cells, especially those in the lungs. This helps to prevent RSV infection.[1]
    - A single dose of nirsevimab provides protection through 5 months, the length of a typical RSV season.

Who should receive nirsevimab?

- The Centers for Disease Control and Prevention (CDC) is recommending immunization with nirsevimab in a **narrower population than the FDA-approved indication**:[1,6,7,8,13,14]
    - Infants below 8 months of age born during or entering their first RSV season.
    - Infants and children aged 8 to 19 months who are at increased risk of severe RSV disease and are entering their second RSV season. This includes children:
        - With chronic lung disease of prematurity who required medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) any time during the 6-month period before the start of the second RSV season
        - With severe immunocompromise
        - With cystic fibrosis who have either 1) manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the first year of life or abnormalities on chest imaging that persist when stable), or 2) weight-for-length <10th percentile
        - Who are American Indian or Alaska Native

Is nirsevimab needed for a newborn if the mother received the maternal RSV vaccine?[13,14]

- Nirsevimab is not needed for most infants born ≥14 days after maternal vaccination.
- If a baby is born <14 days after maternal vaccination, the infant is recommended to receive nirsevimab. This is because 14 days or more are likely needed for development and transplacental transfer of maternal antibodies to protect the infant after maternal vaccination.
- Nirsevimab may be considered in rare circumstances even though the mother received an RSV vaccine when, per the clinical judgment of the healthcare provider, the potential incremental benefit of administration is warranted:
    - Pregnant people who may not mount an adequate immune response to vaccination (e.g., people with immunocompromising conditions) or have conditions associated with reduced transplacental antibody transfer (e.g., people living with HIV infection)
    - Infants who have had cardiopulmonary bypass leading to loss of RSV antibodies
    - Infants with substantially increased risk for severe RSV disease (e.g., hemodynamically significant congenital heart disease, intensive care admission, and requiring oxygen at discharge)

What is the recommendation for babies born outside the RSV season (April to September)?

- Pregnant individuals who deliver their baby outside of the RSV season will not be vaccinated by the maternal RSV vaccine. Therefore, nirsevimab is recommended for these babies who are <8 months of age at the onset of their first RSV season.[14]

What is the evidence supporting FDA approval of nirsevimab?

- The FDA approval of nirsevimab was based on the Phase 2b MEDI8897 Ph2b trial (Trial 03; NCT02878330) and the Phase 3 MELODY trial (Trial 04; NCT03979313).[1-3] Supportive data have also been provided from the MEDLEY trial (Trial 05; NCT03959488).[1,5]
- Trial 03 was a phase 2b randomized double blind, placebo-controlled trial in preterm infants born at GA 29 weeks through 34 weeks and who were 1 year of age or younger entering their first RSV season. A total of 1,417 patients completed the trial (913 in the nirsevimab group which received 50 mg IM injection, and 454 in the placebo group).[1,3]
    - Primary endpoint was medically attended (MA) RSV lower respiratory tract infection (LRTI) through 150 days after treatment. MA RSV LRTI occurred in 25 (2.6%) patients in the nirsevimab group and in 46 (9.5%) patients in the placebo group, corresponding to a 70.1% relative risk reduction (95% CI, 52.3 – 81.2, p<0.001), 6.9% absolute risk reduction, and number needed to treat (NNT) of 15.
    - Secondary endpoint was hospitalization due to RSV LRTI through 150 days after treatment, hospitalization occurred in 8 (0.8%) patients in nirsevimab group and 20 (4.1%) patients in the placebo group, which is a 78.4% relative risk reduction, 3.3% absolute risk reduction, and NNT of 31.

- MELODY (Trial 04) was a phase 3 randomized, double-blind, placebo-controlled trial in late-preterm and term infants born at gestational age (GA) of at least 35 weeks and 1 year of age or younger entering their first RSV season. There was a total of 1,478 participants (987 received nirsevimab and 491 received placebo).[1,4]
  - Primary endpoint was MA RSV LRTI through 150 days after treatment, MA RSV occurred in 12 (1.2%) infants in the nirsevimab group and 25 (5%) infants in the placebo group, which is a relative risk reduction of 74.5% (95% CI, 49.6 to 87.1; p<0.001), absolute risk reduction of 3.8%, and NNT of 27.
  - Secondary endpoint was hospitalization for RSV-associated LRTI through 150 days after treatment. Which occurred in 6 infants (0.6%) in the nirsevimab group and in 8 infants (1.6%) in the placebo group. This difference was not statistically significant, but it was noted that the number of events was low.
- MEDLEY (Trial 05) is an ongoing Phase 2/3 randomized, double-blind, multicenter, international, palivizumab-controlled study to evaluate safety and tolerability in infants at high-risk for severe RSV infection who are eligible to receive palivizumab when entering their first or second RSV season.[1,5]
  - Primary objective was the safety and tolerability of nirsevimab versus palivizumab. Based on the limited data available, the safety profile of nirsevimab and palivizumab appear comparable.
  - Exploratory efficacy analysis found seven infants had MA RSV LRTI (4 of 616 infants [0.6%] receiving nirsevimab and 3 of 309 infants [1.0%] receiving palivizumab).
  - Secondary endpoint of ADA response at day 151 was low (occurring in 2 of 483 infants [0.4%] in the nirsevimab group and 9 of 251 infants in the palivizumab group [3.6%]).
  - Secondary endpoint of PK at day 151 showed mean serum nirsevimab levels were similar between pre-term infants (n=401) and infants with chronic lung disease and congenital heart disease (n=208).

What are the safety issues associated with nirsevimab?

- The most common side effects reported at a higher incidence rate than placebo included injection site reaction (0.3%) and rash (0.9%).[1]
- The product labeling for nirsevimab also warns of possible serious hypersensitivity reactions based on observations with other human immunoglobulin G1 monoclonal antibodies and risk of uncontrolled bleeding in predisposed patients (as with any intramuscular injection).[1]

How should adverse reactions that occur with nirsevimab be reported to the FDA?

- If an adverse reaction occurs after administration of nirsevimab alone, this should be reported to MedWatch online (https://www.fda.gov/medwatch), by fax, by mail, or by contacting FDA at 1-800-FDA-1088.
- If an adverse reaction occurs after coadministration of nirsevimab with a vaccine, this should be reported to the Vaccine Adverse Event Reporting System (VAERS) online (https://vaers.hhs.gov), by fax, or by mail. VAERS information is available by telephone (1-800-822-7967).

How is nirsevimab dosed?

- Nirsevimab dose is based on body weight and is administered as a single IM injection.[1]

Population	Recommended Dosage
First RSV Season Dosing	Less than 5 kg: 50 mg 5 kg and greater: 100 mg
Second RSV Season Dosing	200 mg (2 x 100 mg)
Children with cardiopulmonary bypass undergoing cardiac surgery	An additional dose is recommended as soon as the child is stable post-surgery. Refer to product labeling for first and second RSV season dosing details.

Should nirsevimab be administered to a healthy infant 8 months of age or older who presents to clinic at the start of RSV season?

- No. CDC recommends that only those healthy infants younger than 8 months of age at the time of administration receive nirsevimab.[1,7,13]

Should nirsevimab be administered to an infant who is born at the very end of the RSV season?

- Yes. Optimal timing for administration is within 1 week after birth during the RSV season. Administering nirsevimab to infants born through the end of the season is important because the risk of severe disease is highest during the first few months of life.[8,13]

Can both nirsevimab and palivizumab be used in the same RSV season?

- No. Palivizumab should not be administered to infants who have already received nirsevimab in the same RSV season.[1]
- Patients who received palivizumab during their first RSV season and who remain at higher risk for severe RSV disease are eligible to receive nirsevimab prior to or during the second RSV season.[1]
- There are no data regarding the substitution of nirsevimab for palivizumab once prophylaxis with palivizumab is initiated for the RSV season.[1]

Can nirsevimab be co-administered with other routine vaccines?

- Yes, following CDC general best practices for immunizations, nirsevimab may be co-administered with other age-appropriate vaccines. Per Best Practice Guidelines, providers may consider a 15-minute post-dose observation period particularly to monitor for syncopal episodes, but this is universal guidance (i.e., not specific to nirsevimab).[12]
- Nirsevimab is not expected to interfere with the immune response to other vaccines and based on limited data from clinical trials, had similar safety and reactogenicity profiles to vaccines administered without nirsevimab.[1,7]

Is there a lower gestation age limit to receive nirsevimab?

- No, nirsevimab does not have a minimum gestational age recommended for premature infants.[1,13]
- Trial 03 include otherwise healthy preterm infants and Trial 05 included preterm infants and infants with chronic lung disease of prematurity or congenital heart disease.[1,5]

When will supplies of nirsevimab be commercially available?

- The manufacturer expects to have limited supplies of nirsevimab during the 2023-2024 RSV season.
- Kaiser Permanente expects to have supply of nirsevimab late-October or November 2023 for use within the KP program for the RSV season.

What is the formulary status of nirsevimab?

- The Regional P&T Committee in each market has completed review of nirsevimab for their respective Commercial Formularies. Refer to your regional drug formulary for formulary status.

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