Proposed Clinical Consideration Updates for Nirsevimab

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Timing of nirsevimab

- Providers should target administration[1]:
  - In the first week of life for infants born shortly before and during the season
  - Shortly before the start of the RSV season for infants aged <8 months
  - Shortly before the start of the RSV season for children aged 8–19 months who are at increased risk of severe RSV disease
- Based on pre-pandemic patterns, this means nirsevimab could be administered in most of the continental United States from October through the end of March
- Because timing of the onset, peak, and decline of RSV activity may vary, providers can adjust administration schedules based on local epidemiology

[1] While optimal timing for nirsevimab administration is shortly before the season, nirsevimab may be given at any time during the RSV season for age-eligible infants and children who have not yet received a dose

Timing of nirsevimab for infants born shortly before or during RSV season

- Nirsevimab should be administered within 1 week of birth.
  - Administration can be during the birth hospitalization or in the outpatient setting
- Infants with prolonged birth hospitalizations due to prematurity or other causes should receive nirsevimab shortly before or promptly after discharge

Tropical climates and Alaska

- Tropical climates may have seasonality that differs from most of the continental United States or is unpredictable
  - May include southern Florida, Hawaii, Guam, Puerto Rico, U.S. Virgin Islands, and U.S.-Affiliated Pacific Islands
- In Alaska, RSV seasonality is less predictable, and the duration of RSV seasons is often longer than the national average
- Providers in these jurisdictions should consult state, local, or territorial guidance on timing of nirsevimab administration

Coadministration with routine childhood vaccines

- In accordance with CDC's general best practices for immunizations, simultaneous administration of nirsevimab with age-appropriate vaccines is recommended
- In clinical trials, when nirsevimab was given concomitantly with routine childhood vaccines, the safety and reactogenicity profile of the coadministered regimen was similar to the childhood vaccines given alone[1]
- When coadministered, nirsevimab is not expected to interfere with the immune response to vaccines[2]

[1]FDA label for nirsevimab ; [2]Espocito Front Immunol. 2021 Aug 11;12:708939.

Children aged 8–19 months recommended to receive nirsevimab when entering their second RSV season because of increased risk of severe disease

- 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
- Children with severe immunocompromise
- Children with cystic fibrosis who have 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 weight-for-length <10th percentile
- American Indian and Alaska Native children

Nirsevimab recommendations for infants and children at increased risk of severe RSV

- Nirsevimab is recommended for infants aged <8 months born during or entering their first RSV season, including those recommended to receive palivizumab by AAP[1]
- Nirsevimab is recommended for children aged 8–19 months who are at increased risk of severe RSV disease and entering their second RSV season, including those recommended to receive palivizumab by AAP[1]
- Per FDA label, children who have received nirsevimab should not receive palivizumab for the same RSV season[2]

[1]American Academy of Pediatrics. Committee on Infectious Diseases [Respiratory Syncytial Virus.] In: Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH, eds. Red Book : 2021 Report of the Committee on Infectious Diseases. Itasca, IL: American Academy of Pediatrics, 2021.

[2]FDA label for nirsevimab

Precautions and Contraindications

- Providers administering nirsevimab should follow ACIP's general best practice guidelines for immunization[1]

- Nirsevimab should not be administered to persons with a history of severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a product component (contraindication)

[1] For immunization information systems, state or local guidance should be followed

Consumers and health care providers reporting suspected adverse reactions for nirsevimab

- Report suspect adverse reactions following the administration of nirsevimab without coadministration with any vaccine to MedWatch
  - Reports can be submitted to MedWatch online at www.fda.gov/medwatch or by phone at 1-800-FDA-1088
- Report suspect adverse reactions following co-administration of nirsevimab with any vaccine to the Vaccine Adverse Event Reporting System (VAERS)
  - Please specify that the patient received nirsevimab on the VAERS form, specifically, in Section 9: ‘Prescriptions, over-the-counter medications, dietary supplements, or herbal remedies being taken at the time of vaccination’

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1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Workgroup Considerations and Voting Language for Nirsevimab

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Safety monitoring for nirsevimab

- FDA will monitor safety reports submitted by patients, providers, and the manufacturer to the FDA Adverse Event Reporting System (FAERS) and Vaccine Adverse Event Reporting System (VAERS)
- FDA will monitor other data sources, including the scientific literature, applicant's periodic safety reports, ongoing clinical studies, and potentially other sources (e.g., medical billing and electronic health records)
- CDC will monitor reports submitted to VAERS that involve simultaneous administration of nirsevimab with childhood vaccines and will also monitor the safety of nirsevimab in the Vaccine Safety Datalink (VSD)

Effectiveness monitoring for nirsevimab

- CDC will leverage existing COVID-19 vaccine effectiveness (VE) platforms
- New Vaccine Surveillance Network (NVSN)
  - Active surveillance network for acute respiratory infection at 7 pediatric medical centers that can assess effectiveness against outpatient and emergency department visits and hospitalization
  - Capture nirsevimab receipt through parent interview, medical record review at the primary care provider and birth hospital, and state immunization information systems (IIS)
- Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network (VISION)
  - Multi-site, electronic healthcare record-based network that can assess effectiveness against emergency department/urgent care visits, hospitalization, and critical illness
  - Nirsevimab effectiveness analyses will be limited to integrated healthcare system sites that will have more complete capture of nirsevimab receipt (i.e., through IIS linkage and claims data)
- CDC will monitor nirsevimab effectiveness throughout the season, but end of season estimates will likely be most accurate. Power to estimate effectiveness depends on uptake and RSV incidence

RSV genomic surveillance

- Mutations resulting in nirsevimab resistance have been rarely reported[1,2]
- Sanofi and AstraZeneca sponsoring INFORM-RSV, a global genomic surveillance study in children aged < 5 years to monitor evolution of RSV strains, F protein antigenic sites, and their relationships with clinical features of RSV disease[3]
- CDC planning genomic RSV surveillance of pediatric and adult RSV specimens, including whole genomic surveillance
  - Will monitor for changes in F protein that might result in nirsevimab resistance

[1]Ahani et al. Nat Comm 2023 14:4347; [2]Wilkins et al. Lancet Infect Dis 2023; 23: 856–66; [3]Tabor 2020 Dec 17;59(1):e01828-20.

Work Group considerations for infants aged <8 months born during or entering RSV season

- Nirsevimab is safe and effective in reducing the risk of RSV disease, including hospitalization due to RSV
- Shared concerns as outlined in implementation considerations presentation
- Use of nirsevimab would be a reasonable and efficient allocation of resources
  - Many work group members prefer lower cost per dose

Work Group considerations for children aged 8–19 months who are at increased risk of severe RSV disease and entering their second RSV season

- Limited efficacy and safety data for the use of nirsevimab for children in their second RSV season
- Limited data on the burden of severe disease in the second RSV season for children with chronic conditions
- Support recommendation of nirsevimab being given to children aged 8–19 months who are entering their second RSV season for those who are recommended for palivizumab by American Academy of Pediatrics in their second RSV season and for American Indian and Alaska Native children

Proposed ACIP Voting Language

- Infants aged <8 months born during or entering their first RSV season are recommended to receive one dose of nirsevimab (50 mg for infants <5 kg and 100 mg for infants ≥5 kg)

- Children aged 8–19 months who are at increased risk of severe RSV disease and entering their second RSV season are recommended to receive one dose of nirsevimab (200 mg)

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