Preventing RSV

(modified October 30, 2023)

--Please see the October 23, 2023 CDC Health Alert Network (HAN) Health Advisory for US recommendations to manage the limited supply of nirsevimab at https://emergency.cdc.gov/han/2023/han00499.asp.).--

RSV is a common virus that infects most children before the age of two years.[1,2] Infection does not confer long-term immunity, which leads to continual reinfection throughout a patient's lifetime.[1] This FAQ answers common questions about who's at risk of severe RSV infection and the products used to prevent it.

Question	Answer/Pertinent Information
What is **RSV**?	• Respiratory syncytial virus (RSV) typically causes mild, self-limiting (one to two weeks) cold-like symptoms.[3] • Serious RSV infections can cause respiratory distress, bronchiolitis, pneumonia, hospitalization, and death.[2,4] • The typical season for RSV is from fall through late winter (i.e., October/November to March/April).[2,5]

Who is at risk of **severe RSV disease**?	• Those at risk of severe RSV disease include:
	  • Infants and children less than two years.
	  ○ Up to 40% of first RSV infections in children under one year result in bronchiolitis.[4]
	  ○ RSV is a leading cause of hospitalization of infants in the US and Canada.[5,21,22]
	  • Children with lung disease (e.g., congenital airway anomalies, chronic lung disease of prematurity, cystic fibrosis), congenital heart disease, neuromuscular disorders, Down syndrome, immunosuppressive disorders, and some infants in remote communities (e.g., northern Inuit, American Indian, and Alaska Native children).[2,4,6-8]
	  • Older adults and patients with chronic lung disease, heart disease, or immunosuppressive disorders.[2]

How can RSV be **prevented**?	• RSV is transmitted via respiratory droplets (inhaled and from contact with contaminated surfaces).[5,9]
	  ○ Prevent transmission of RSV (and other respiratory illnesses) by:[9]
	  ▪ coughing or sneezing into a tissue or your shirt sleeve/elbow (not your hands).
	  ▪ washing hands with soap and water for at least 20 seconds.
	  ▪ avoiding close contact with people (i.e., stay at home) when you feel ill (i.e., cold-like symptoms).
	  ▪ cleaning frequently touched surfaces (e.g., doorknobs, mobile devices).
	• Monoclonal antibody formulations are available to prevent RSV in infants and young children (see below for details).
	  ○ Provide passive immunization.
	  ○ Protection wanes over time.
	  ○ Must be administered in a clinic or hospital.
	• RSV vaccines are available for pregnant patients (US only) and adults over 60 years (see below for more details).
	• Infants can be protected with either maternal immunization (US) OR monoclonal antibodies. **Most infants do not need both**.[21]

Question	Answer/Pertinent Information

Who should get the monoclonal antibody, **nirsevimab** (*Beyfortus*)?	• Nirsevimab is FDA- and Health Canada-indicated for the prevention of RSV infection in:[6,11]
	  o all infants born during or entering their first RSV season.
	  o children up to 24 months of age who are at risk of severe RSV disease during their second RSV season.
	• **US recommendations**: ACIP recommends nirsevimab for infants <8 months born during or entering their first RSV season and children aged 8 to 19 months who are at increased risk of severe RSV disease entering their second RSV season.[5,20,c]
	  o If RSV prevention has been initiated with palivizumab and less than five doses of palivizumab have been administered, the infant should receive one dose of nirsevimab. No further palivizumab should be administered.[20]
	  o Nirsevimab should be administered during season two (as indicated) regardless of which monoclonal antibody was administered during season one.
	• In **Canada**, NACI recommendations on the use of nirsevimab are pending as of the publication of this chart. The Public Health Agency of Canada (PHAC)'s requested CADTH report recommends: nirsevimab for infants entering their **first** RSV season, prioritized by risk of severe RSV disease:[19]
	  o Tier 1 (highest risk): infants with limited access to healthcare (e.g., rural or remote settings who would require air transport for hospitalization) AND <33 weeks gestational age OR one or more of these risk factors: chronic lung disease of prematurity or other severe chronic lung disease, hemodynamically significant heart disease, or moderately to severely immunocompromised.
	  o Tier 2 (high risk): <37 weeks gestational age who have limited access to healthcare, <33 weeks gestational age, OR one or more risk factors.
	  o Tier 3: limited access to healthcare.

Who should get the monoclonal antibody, **palivizumab** (*Synagis*)?	• Palivizumab is indicated for the prevention of RSV infection in **high-risk infants and toddlers**.[9,10,12]
	• In the **US**, palivizumab is recommended (per the high-risk indications below) if nirsevimab is not available or not feasible to administer.[20]
	• The American Academy of Pediatrics recommends palivizumab for patients:[12,23]
	  o born before 29 weeks gestation and younger than 12 months at the beginning of RSV season.
	  o with chronic lung disease of prematurity during the first year of life. During the second year of life, palivizumab can be considered if these children continue to require medical support during the six months prior to RSV season.
	  o palivizumab can also be considered for patients:[12,23]
	  ▪ younger than 24 months who are profoundly immunocompromised during RSV season.
	  ▪ with a pulmonary or neurological abnormality that impairs clearance of upper airway secretions and who are younger than 12 months.
	  ▪ who have hemodynamically significant congenital heart disease and who are 12 months or younger.

Question	**Answer/Pertinent Information**		
How do the available **RSV monoclonal antibodies compare**?		**Palivizumab (*Synagis*)**[9,10]	**Nirsevimab (*Beyfortus*)**[6,11]
	How Supplied	Single-dose vials: 50 mg/0.5 mL, 100 mg/1 mL	Single-dose prefilled syringes: 50 mg/0.5 mL, 100 mg/1 mL
	Storage	• Refrigerate (2°C to 8°C). • Opened vials may be kept (refrigerated) for up to 6 hours.[7] • Store in original packaging. • Do not shake.	• Refrigerate (2°C to 8°C). • May be kept at room temperature for up to 8 hours. • Store in original packaging to protect from light. • Do not shake.
	Dosing	• 15 mg/kg IM **monthly** throughout the RSV season. • Give an additional dose to children following cardiopulmonary bypass surgery (even if less than one month since last dose).[7,9] • It is recommended to stop monthly palivizumab if a child has an RSV hospitalization.[7,12] • Usual duration is four to five months.[7,9]	• **First RSV season**: o Less than 5 kg: 50 mg IM **x one dose** o 5 kg or more: 100 mg IM **x one dose** • **Second RSV season**: o 200 mg IM **x one dose** • Give an additional dose to children following cardiopulmonary bypass surgery. See footnote "b" for dosing.
	Adverse Effects	• Rash, fever, severe hypersensitivity reactions	• Rash, injection site reactions. • Potential for serious hypersensitivity reactions.
	Usual Admin Site	• Anterolateral thigh preferred. • Avoid the gluteal muscle.	• Anterolateral thigh preferred. • Avoid the gluteal muscle.
	Cost (US)[a]	$1,800/dose	$495/dose
Can monoclonal antibodies be **given with vaccines**?	• Nirsevimab can be given at the same time as routine childhood vaccines.[20] Give in separate syringes and at different injection sites.		

<table>
<tr><th>Question</th><th colspan="3">Answer/Pertinent Information</th></tr>
<tr><td>Who should get an RSV vaccine?</td><td colspan="3">• Recommendations for Abrysvo (US only):
o ACIP (US) recommends shared decision making to determine which patients 60 years and older are vaccinated.[16]
o ACIP (US) recommends the seasonal use (usually September through January) of Abrysvo in pregnant patients who are 32 weeks through 36 weeks gestation to prevent RSV disease in newborns.[21]
• Recommendations for Arexvy:
o ACIP (US) recommends shared clinical decision making to determine which patients (over 60 years) are vaccinated.[14]
o NACI (Canada) recommendations for the use of Arexvy are pending as of the publication date of this chart.[7]</td></tr>
<tr><td rowspan="8">How do the available RSV vaccines compare?</td><td></td><td>Abrysvo (US only)[13]</td><td>Arexvy[17,18]</td></tr>
<tr><td>Vaccine type</td><td>• non-adjuvanted</td><td>• adjuvanted (with AS01$_E$ to boost immunity).</td></tr>
<tr><td>Approved indications</td><td>• for the prevention of RSV in:
o pregnant women, 32 to 36 weeks gestation (to prevent RSV in newborns via placental transfer of antibodies).
o patients 60 years and older.</td><td>• for the prevention of RSV in in patients 60 years and older.</td></tr>
<tr><td>Dosing</td><td>• 0.5 mL IM x one dose</td><td>• 0.5 mL IM x one dose</td></tr>
<tr><td>Use in pregnant patients</td><td>• There is a potential risk of preterm birth with Abrysvo. To avoid this risk, do not administer Abrysvo prior to 32 weeks gestation. Patients at risk of preterm birth were generally excluded from the studies.</td><td>• There are no data on the administration of Arexvy in pregnant patients.</td></tr>
<tr><td>Storage</td><td>• Refrigerate (2°C to 8°C) in the original packaging.</td><td>• Refrigerate (2°C to 8°C) in the original packaging to protect from light.</td></tr>
<tr><td>Reconstitution and stability</td><td>• Reconstitute with the diluent provided. Use immediately or keep at room temperature (15°C to 30°C) and use within four hours.</td><td>• Reconstitute with the diluent provided. Use immediately or refrigerate (2°C to 8°C) and use within four hours.</td></tr>
<tr><td>Efficacy</td><td>• Data show moderate to high efficacy of one dose of Abrysvo in older adults for the prevention of RSV-associated symptomatic LRTD and medically attended LRTD over two RSV seasons [Evidence Level A-1].[14]
o Data on the prevention of hospitalization, severe illness, and death are lacking.[14]
• Infants born to pregnant patients who were given Abrysvo, had a significantly reduced risk of severe LRTD at both 90 days and 180 days after birth [Evidence Level A-1].[15]</td><td>• Data show moderate to high efficacy of one dose of Arexvy in older adults for the prevention of RSV-associated symptomatic LRTD and medically attended LRTD over two RSV seasons [Evidence Level A-1].[14]
o Data on the prevention of hospitalization, severe illness, and death are lacking.[14]</td></tr>
<tr><td>Cost (US)[a]</td><td>• $295/dose</td><td>• $280/dose</td></tr>
</table>

Abbreviations: ACIP = Advisory Committee on Immunization Practices; admin = administration; CADTH = Canada's Drug and Health Technology Agency; IM = intramuscular; LRTD = lower respiratory tract disease; NACI = National Advisory Committee on Immunization; RSV = respiratory syncytial virus.

a. Pricing based on wholesale acquisition cost (WAC). US medication pricing by Elsevier, accessed September 2023.
b. Once infants are stable following cardiopulmonary bypass surgery, administer an additional dose of **nirsevimab** to ensure adequate serum levels. If it is the child's **first RSV season** and within 90 days of the initial nirsevimab dose, give a weight-based dose (<5 kg: 50 mg; ≥5 kg: 100 mg). If it has been more than 90 days since the initial nirsevimab dose, give a 50 mg dose. If it is the child's **second RSV season** and within 90 days of the initial nirsevimab dose, give a 200 mg dose. If it has been more than 90 days since the initial nirsevimab dose, give a 100 mg dose.[6,11]
c. In the US, nirsevimab is recommended for children between the ages of 8 and 19 months, entering their second RSV season, with increased risk of severe RSV disease:[5]
    - chronic lung disease of prematurity, requiring medical support during the six months prior to RSV season.
    - severe immunocompromise.
    - cystic fibrosis with manifestations of severe lung disease OR abnormalities on chest imaging that persist when stable OR weight-for-length rate is less than the 10th percentile.
    - American Indian or Alaska Native children.

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	1. High-quality randomized controlled trial (RCT) 2. Systematic review (SR)/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician. 2004 Feb 1;69(3):548-56. https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html.]

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