Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35
Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-1119

Prior Authorization Criteria Update: Respiratory Syncytial Virus (RSV) Prophylaxis

Plain Language Summary:

- This update highlight new treatments that can be used to prevent respiratory syncytial virus (RSV) in newborns, infants and children who are at high risk.
- In most parts of the U.S., 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.
- The medicine SYNAGIS (palivizumab) requires multiple monthly injections and has been the only treatment available for several years, but two other treatment options are also now available: a medicine called BEYFORTUS (nirsevimab) that requires a single dose, and a vaccine called ABRYSVO that is administered to the pregnant woman before the baby is born.
- SYNAGIS should not be given to infants who have already received a dose of BEYFORTUS in the same RSV season. If a mother received the ABRYSVO vaccine, the baby does not need SYNAGIS or BEYFORTUS to protect them from RSV.
- More than 5 doses of SYNAGIS may be considered for infants and vulnerable children if there are high levels of RSV infections, even if it is outside the normal RSV season.
- The Oregon Health Plan fee-for-service program will ensure that SYNAGIS and BEYFORTUS are not used together, and infants born to mothers who received ABRYSVO do not also get SYNAGIS.

Purpose of Update: To briefly summarize new therapies recently approved by the Food and Drug Administration (FDA) for prevention of lower respiratory tract disease from respiratory syncytial virus (RSV) and highlight current clinical practice guidelines for these therapies. BEYFORTUS is part of the Vaccines for Children (VFC) program and thus federally funded with open access to Oregon Health Plan (OHP) members, and therefore will not be extensively reviewed. An evidence review for AVRYSO was not performed because it is a vaccine and does not fall under the purview of the P and T committee.

Recommendation:

- Update the clinical prior authorization (PA) criteria for palivizumab to align with the Advisory Committee on Immunization Practices (ACIP) recommendations for combination use of prophylactic therapy. Prevention with more than one agent each RSV season is not currently recommended.

New Evidence:

<u>BEYFORTUS™ (nirsevimab):</u>

Nirsevimab was approved in July of 2023 and is a RSV F protein-directed fusion inhibitor that was approved by the FDA for the prevention of RSV lower respiratory tract disease (LRTD) in all neonates and infants born during or entering their first RSV season, or in children up to 24 months of age who remain

vulnerable to severe RSV disease through their second RSV season. Efficacy was based on 3 clinical trials in term and preterm infants; 2 phase 2 trials and one phase 3 trial.[1] Two studies were done in infants entering their first RSV season and the third trial was done in infants born at less than 35 weeks gestation with chronic lung disease (CLD) or chronic heart disease (CHD) entering their first RSV season and in those infants with CLD or CHD only entering their second RSV season. In the phase 3 trial, term and late preterm infants with a gestational age greater than or equal to 35 weeks entering their first RSV season were enrolled. The primary endpoint was the incidence of Medically Attended Respiratory Syncytial Virus Lower Respiratory Tract Infection (MA RSV LRTI) caused by a reverse transcription-polymerase chain reaction (RT-PCR)-confirmed RSV, characterized predominantly as bronchiolitis or pneumonia through 150 days after dosing. The number of medically attended RSV LRTD was 1.2% in the nirsevimab group compared to 5.0% in the placebo group (efficacy 74.9%; 95% CI, 50.6 to 87.3; p <0.001).[1] The most common adverse reaction was rash at the injection site.[1]

Palivizumab should not be given to infants who have already received nirsevimab in the same season because of lack of evidence. Nirsevimab may be given in the second RSV season to those infants who are up to 24 months of age who received palivizumab in the first RSV season.[1] Labeling provides instructions for co-administration of other immunoglobulin products.[1] There is no evidence to support the use of BEYFORTUS in a baby born to an individual immunized against RSV during their pregnancy.

ABRYSVO™ (RSV Vaccine):

In August 2023, the RSV vaccine ABRYSVO received an additional indication for active immunization of pregnant individuals at 32 through 36 weeks gestational age for the prevention of LRTD and severe LRTD caused by RSV) in infants from birth through 6 months of age.[2] One phase 3, double-blind, randomized controlled trial provided evidence for efficacy.[3] RSV-associated LRTD in infants was defined as a medically attended visit with a RT-PCR confirmed RSV illness with one or more of the following respiratory symptoms: tachypnea (respiratory rate ≥60 breaths/minute [<2 months of age], ≥50 breaths/minute [≥2 to 12 months of age], or ≥40 breaths/minute [≥12-24 months of age]); SpO2 measured in room air <95%; chest wall indrawing. RSV-associated severe LRTD was a subset defined as meeting the LRTD RSV criteria plus at least one of the following: tachypnea (respiratory rate ≥70 breaths per minute [<2 months of age], ≥60 breaths per minute [≥2 to 12 months of age], or ≥50 bpm [≥12 to 24 months of age]); SpO2 measured in room air <93%; high-flow nasal cannula or mechanical ventilation (invasive or noninvasive), ICU admission for >4 hours and/or failure to respond/unconscious.[3] Six infants born to individuals who received ABRYSVO experienced severe LRTD caused by RSV within 90 days of birth compared to 33 infants who received placebo (vaccine efficacy 81.8%; 99.5% CI, 40.6 to 96.3%).[3] At 180 days from birth, 19 infants born to individuals who received ABRYSVO experienced severe LRTD caused by RSV compared to 62 infants who received placebo (vaccine efficacy 69.4%; 97.58% CI, 44.3 to 84.1%).[3] There is no evidence to support use of palivizumab in infants born to individuals who received ABRYSVO.

American Academy of Pediatrics Recommendations

In November 2022, the American Academy of Pediatrics (AAP) updated recommendations for use of palivizumab for RSV prophylaxis.[4] These recommendations take into account the changes in RSV season onset and offset and inter-seasonal variability observed in the 2021-2022 RSV seasons due to precautions taken due to COVID-19 and interactions with SARS-CoV-2 virus and other viruses. The AAP now recommends that more than 5 consecutive doses of palivizumab be

considered for eligible infants or children if RSV activity persists at high levels within a given region.[4] Evidence of increased risk of adverse events with additional doses of palivizumab is currently insufficient.

The AAP updated their guidance in August 2023 after the approval of nirsevimab to recommend that a single dose of nirsevimab be used in all neonates and infants born during or entering their first RSV season, or in children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season. The AAP also recommends that palivizumab be used in those neonates, infants or children who are not able to access nirsevimab.[5]

Centers for Disease Control Recommendation

The Centers for Disease Control (CDC) Advisory Committee on Immunization Practices (ACIP) has recommended nirsevimab for all infants under 8 months and those older than 8 months with risk factors for severe respiratory illness due to RSV.[6]

Conclusion:
Palivizumab and nirsevimab are both monoclonal antibodies indicated for the prevention of RSV LRTD. There is currently insufficient evidence to use nirsevimab and palivizumab concomitantly in the same RSV season. Additionally, infants born to individuals who receive ABRYSVO receive passive immunity to RSV and there is no evidence to suggest palivizumab would offer additional protection in this population.

Database(s): **Ovid MEDLINEI ALL** 1946 to August 10, 2023
Search Strategy:

#	Searches	Results
1	Palivizumab/	874
2	limit 1 to 3nglish language and humans and ”r=”2022 -Current”)	51
3	limit 2 to (clinical trial, phase iii or meta analysis or practice guideline “r “systematic review”)	8

References:

1. Beyfortus (nirsevimab) [prescribing information]. Swiftwater, PA; Sanofi Pasteur, Inc. July 2023.
2. ABRYSVO™ (respiratory Syncytial Virus Vaccine)[prescribing information). New York NY; Pfizer, Inc. August 2023.
3. Kampmann B, Madhi SA, Munjal I, et al. Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants. *N Engl J Med*. 2023;388(16):1451-1464. doi:10.1056/NEJMoa2216480.

4. American Academy of Pediatrics. Updated Guidance: Use of Palivizumab Prophylaxis to Prevent Hospitalization From Severe Respiratory Syncytial Virus Infection During the 2022-2023 RSV Season. Available at: https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/interim-guidance-for-use-of-palivizumab-prophylaxis-to-prevent-hospitalization/. Accessed August 11, 2023.

5. ACIP and AAP Recommendations for Nirsevimab. Published online August 15, 2023. Available at: https://publications.aap.org/redbook/resources/25379/ACIP-and-AAP-Recommendations-for-Nirsevimab. Accessed August 22, 2023.

6. Centers for Disease Control and Prevention Newsroom. CDC Recommends a Powerful New Tool to Protect Infants from the Leading Cause of Hospitalization. August 3, 2023. Available at: https://www.cdc.gov/media/releases/2023/p-0803-new-tool-prevent-infant-hospitalization-.html. Accessed August 22, 2023.

Palivizumab (Synagis®)

Goal(s):

- Promote safe and effective use of palivizumab in high-risk infants and children. Prophylaxis against RSV should cover up to 5 months during high viral activity season, usually spanning from November through March in Oregon.

Length of Authorization:

- Based on individual factors; may extend up to 5 months (5 total doses)

Requires PA:

- Synagis (palivizumab) pharmacy and physician-administered claims

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code	
2. Has the patient been receiving monthly palivizumab prophylaxis and been hospitalized for a breakthrough RSV infection?	**Yes:** Pass to RPh; deny for medical appropriateness.	**No:** Go to #3
3. Is the request consistent with the current Advisory Committee on Immunization Practices (ACIP) recommendations for combination prophylactic agents (outlined here)? 2023 ACIP update: if the patient, or birth mother of the patient, has received other therapies for the prevention of RSV during or prior to the RSV season, palivizumab is not indicated	**Yes:** Go to #4	**No:** Pass to RPh; deny for medical appropriateness.
4. Is the request for RSV prophylaxis to be administered during the typical high viral activity season from November through March?	**Yes:** Go to #6	**No:** Go to #5

Approval Criteria		
5. Is the request for prophylaxis starting in October due to interseasonal increase in RSV activity with season onset designated by the OHA*? * Data provided by the Oregon's Weekly Respiratory Syncytial Virus Surveillance Report from the Oregon Public Health Division based on regions. Weekly updates are found at: https://public.health.oregon.gov/DiseasesConditions/DiseasesAZ/Pages/disease.aspx?did=40)	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness. Prophylaxis is indicated only during high viral activity.
6. Is the current age of the patient < 24 months at start of RSV season?	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness. Not recommended for patients ≥24 months old.
7. GROUP A Does the patient have the CLD (chronic lung disease) of prematurity ICD10 Q331through Q339 **and** in the past 6 months has required medical treatment with at least one of the following: a. diuretics b. chronic corticosteroid therapy c. supplemental oxygen therapy	**Yes:** Go to #19	**No:** Go to 8
8. GROUP B Has the patient received a cardiac transplant during the RSV season?	**Yes:** Go to #19	**No:** Go to #9
9. GROUP C Is the child profoundly immunocompromised during the RSV season (i.e. solid organ transplant or hematopoietic stem cell transplantation)?	**Yes:** Go to #19	**No:** Go to #10
10. GROUP D Does the infant have cystic fibrosis and manifestations of severe lung disease or weight or length less than the 10th percentile?	**Yes:** Go to #19	**No:** Go to #11

Approval Criteria		
11. **GROUP E** Is the request for a second season of palivizumab prophylaxis for a child born <32 weeks, 0 days gestation who required at least 28 days of oxygen, chronic systemic corticosteroid therapy, or bronchodilator therapy within 6 months of start of second RSV season?	**Yes:** Go to #19	**No:** Go to #12
12. Will the patient be <12 months at start of RSV season?	**Yes:** Go to #13	**No:** Pass to RPh. Deny; medical appropriateness.
13. **GROUP F** Was the infant born before 29 weeks, 0 days gestation?	**Yes:** Go to #19	**No:** Go to #14
14. **GROUP G** Does the infant have pulmonary abnormalities of the airway or neuromuscular disease compromising handling of secretions?	**Yes:** Go to #19	**No:** Go to #15
15. **GROUP H** Does the patient have hemodynamically significant congenital heart disease (CHD) ICD10: P293, Q209, Q220-Q223, Q225, Q229-Q234, Q238, Q240-Q246, Q248-Q249, Q250-Q256, Q278-Q279,Q282-Q283,Q288-Q289, Q2560-Q2565,Q2568-Q2569, Q2570-Q2572, Q2579,Q2731-Q2732 and at least one of the following: a. Acyanotic heart disease who are receiving treatment to control congestive heart failure and will require cardiac surgical procedures; OR b. Have moderate to severe pulmonary hypertension; OR c. History of lesions adequately corrected by surgery AND still requiring medication for congestive heart failure?	**Yes:** Go to #19	**No:** Go to #16

Approval Criteria		
16. **GROUP I** Does the patient have chronic lung disease (CLD) of prematurity defined as gestational age <32 weeks, 0 days and requirement for >21% oxygen for at least the first 28 days after birth?	**Yes:** Go to #19	**No:** Go to #17
17. **GROUP J** Does the patient have cyanotic heart defects and immunoprophylaxis is recommended?	**Yes:** Go to #19	**No:** Go to #18
18. **GROUP K** Does the patient have cystic fibrosis with clinical evidence of CLD and/or nutritional compromise?	**Yes:** Go to #19	**No:** Pass to RPh. Deny; medical appropriateness.
19. Is the request for more than 5 doses within the same RSV season or for dosing <28 days apart?	**Yes:** Pass to RPh. Deny; medical appropriateness. Prophylaxis is indicated for 5 months maximum and doses should be administered ≥28 days apart. May approve for the following on a case-by-case basis: a. >5 doses; b. Prophylaxis for a second / subsequent RSV season	**No:** Go to #20
20. Has the patient had a weight taken within the last 30 days?	**Yes:** Document weight and date and go to #21 Weight:_____ Date:_____	**No:** Pass to RPh. Obtain recent weight so accurate dose can be calculated.

Approval Criteria

21. Approve palivizumab for a dose of 15 mg/kg. Document number of doses received in hospital and total number approved according to month of birth (refer to Table 1):

Total number of doses approved for RSV season:_____
Number of doses received in the hospital:_____

Prior to each refill, the patient's parent/caregiver and prescriber must comply with all case management services, including obtaining current weight for accurate dosing purposes throughout the approved treatment period as required by the Oregon Health Authority.

Table 1. Maximum Number of Doses for Palivizumab for RSV Prophylaxis

MONTH	ALL GROUPS
April	5
May	5
June	5
July	5
August	5
September	5
October	5
November	5
December	4
January	3
February	2
March	1

* Infant may require less doses than listed based on age at the time of discharge from the hospital. Subtract number of doses given in hospital from total number of approved doses.

Notes:
- Dose: 15 mg/kg via intramuscular injection once monthly throughout RSV season.
- The start date for Synagis® is November 1 each year (or sooner when the Oregon Public Health Division has determined that RSV season onset has occurred) for a total of up to 5 doses.
- Approval for more than 5 doses or additional doses after March 31 will be considered on a case-by-case basis. Results from clinical trials indicate that Synagis® trough concentrations greater than 30 days after the 5th dose are well above the protective concentration. Therefore, 5 doses will provide more than 20 weeks of protection.

P&T/DUR Review: *8/23 (KS); 2/22 (KS); 11/16 (DE); 9/14; 5/11; 5/12*
Implementation: *11/1/23; 12/1/22; 4/1/22; 1/1/17; 3/30/12*