Ontario

Ministry of Health

Infant and High-risk Children Respiratory Syncytial Virus (RSV) Prevention Program Guidance for Health Care Providers – Beyfortus® (Nirsevimab)

Version 1.0 – August 8, 2024

This guidance document for health care professionals provides basic information only. It is not intended to provide or replace medical advice, diagnosis, or treatment. For more details on the monoclonal antibody (mAb), Beyfortus® (nirsevimab), please refer to the product monograph authorized by Health Canada.

1. RSV Prevention Products Available in Canada

Health Canada has authorized three safe and effective products to help prevent respiratory syncytial virus (RSV) lower respiratory tract infections in infants:

- a vaccine (Abrysvo™) given during pregnancy, and
- two monoclonal antibody immunizing agents (Beyfortus® or Synagis®) given to infants just prior to or during RSV season.

Administration of both the vaccine to the pregnant individual and a monoclonal antibody to the infant is not needed except under specific circumstances (e.g., high-risk infant born to a pregnant person who received the vaccine per recommended timing).

The National Advisory Committee on Immunization (NACI) advises prioritizing the use of the mAb Beyfortus® for infant protection due to its effectiveness, long-lasting protection, and positive safety profile over vaccinating pregnant individuals. Therefore, Beyfortus® is the preferred method for safeguarding infants. Health care providers caring for pregnant people should provide information on vaccination and monoclonal antibody products.

a) Monoclonal Antibodies

Two injectable mAb products, nirsevimab (Beyfortus®) and palivizumab (Synagis®), are authorized by Health Canada to help protect infants and young children from lower respiratory tract infections caused by RSV.

For the 2024/25 RSV season, Beyfortus® will be the publicly funded product for eligible infants.

Sanofi Pasteur Limited received Health Canada authorization on April 19, 2023, for their injectable RSV mAb, Beyfortus®. Beyfortus® helps prevent severe RSV disease in infants and young children. Monoclonal antibodies do not activate the immune system, as would occur with infection or vaccination (active immunization). Instead, the injected antibodies provide direct and immediate protection against disease (passive immunization).

Since Beyfortus® is a mAb, protection wanes over time as the antibodies degrade. Therefore, it is most effective for six months after it is given. Beyfortus® does not provide long-term immunity to RSV disease but helps to protect infants when they are most at risk of getting severe RSV disease. As children get older, they are less likely to get severe symptoms from RSV infection.

b) RSV Vaccine for Pregnant People

Abrysvo™ received Health Canada authorization in December 2023. Abrysvo™ is authorized for pregnant persons who are 32-36 weeks pregnant and will deliver during the RSV season. Abrysvo™ is used to actively immunize pregnant individuals, providing infants with passive maternal antibodies that help protect them from severe RSV illness from birth to approximately six months of age as the protection wanes (i.e., antibodies degrade). While the parent who received Abrysvo™ will have multi-year protection, it does not provide the infant with long-term immunity.

2. Infant Monoclonal Antibody Eligibility

NACI recommends Beyfortus for any infant less than 8 months of age entering or born during their first RSV season. For the 2024/25 RSV season, Beyfortus®, is publicly funded for infants and children who are residents of Ontario and meet any of the following criteria:

- Born in 2024 prior to the RSV season
- Born during the 2024/25 RSV season
- Children up to 24 months of age who remain vulnerable from severe RSV disease through their second RSV season with:
    - Chronic lung disease (CLD), including bronchopulmonary dysplasia, requiring ongoing assisted ventilation, oxygen therapy or chronic medical therapy in the six months prior to the start of RSV season
        - Note: Children who were < 12 months of age and approved for coverage in the previous RSV season for chronic lung disease and bronchopulmonary dysplasia remain eligible.

- Hemodynamically significant congenital heart disease (CHD) requiring corrective surgery or are on cardiac medication for congestive heart failure or diagnosed with moderate to severe pulmonary hypertension
- Severe immunodeficiency
- Down syndrome/Trisomy 21
- Cystic fibrosis with respiratory involvement and/or growth delay
- Neuromuscular disease impairing clearing of respiratory secretions
- Severe congenital airway anomalies impairing the clearing of respiratory secretions

3. RSV Season Start and End

Due to the seasonality of the RSV virus, Beyfortus® should be administered shortly before and during the active RSV season. The RSV season is generally from November to April, peaking in December, with variations in various regions in Ontario and between years. For those infants born during the RSV season, Beyfortus® should be administered before hospital discharge.

The Ministry will communicate the start date and declare the end of the RSV season to inform Beyfortus® use.

4. Administration Schedule

a) Timing

Beyfortus® is available for infants born in 2024 prior to the RSV season or those born during the RSV season, and high-risk children (as per eligibility criteria above) entering their second RSV season.

NACI specifically recommends that infants eight months of age or less be immunized.

For infants born before or are entering their first RSV season (typically fall through spring), Beyfortus® should be offered if:

- The pregnant individual did not receive the RSV vaccine during pregnancy.
- The pregnant individual's RSV vaccination status is unknown.
- The infant was born within 14 days of RSV vaccination.

While the onset and duration of RSV season may vary, Beyfortus® should be administered shortly before or during the RSV season. The Ministry will communicate the start date and declare the end of the RSV season to inform use of Beyfortus®.

Although the optimal administration time is just before the start of the RSV season (e.g., October) for those entering their first season (i.e., born before the start of the season), Beyfortus® should also be offered to infants born during the RSV season before discharge from care/hospital.

For the following infants whose parent received Abrysvo™, Beyfortus® should be administered to:

- Infants born less than 14 days after administration of Abrysvo™ or
- Infants who meet the medical criteria for increased risk from severe RSV disease:
    - Chronic lung disease (CLD), including bronchopulmonary dysplasia, requiring ongoing assisted ventilation, oxygen therapy or chronic medical therapy in the six months prior to the start of RSV season
    - Hemodynamically significant congenital heart disease (CHD) requiring corrective surgery or are on cardiac medication for congestive heart failure or diagnosed with moderate to severe pulmonary hypertension
        - Severe immunodeficiency
    - Down syndrome/Trisomy 21
    - Cystic fibrosis with respiratory involvement and/or growth delay
    - Neuromuscular disease impairing clearing of respiratory secretions
    - Severe congenital airway anomalies impairing the clearing of respiratory secretions.

b) Route

Beyfortus® is administered intramuscularly. The preferred site of administration depends on the age of the child. For infants under 12 months of age, the preferred site is the anterolateral thigh region. For children over 12 months of age, the preferred administration site is the upper arm's deltoid region. Do not administer Beyfortus® intravenously, intradermally, or subcutaneously.

c) Number and Timing of Doses

Beyfortus® should be administered shortly before or during the RSV season (see Tables 1 and 2).

i) **Infants born during RSV season:** A single dose of Beyfortus® is administered based on the infant's weight at the time of administration.

- Infants < 5kg: 50 mg in 0.5 mL (100 mg/mL)
- Infants ≥ 5kg: 100 mg in 1 mL (100 mg/mL)

The dose can be administered in the hospital after delivery prior to discharge or a primary care provider clinic.

Infants with prolonged hospitalization (e.g., preterm infants) should ideally be immunized shortly before discharge or immediately after if Beyfortus® is not available prior to discharge. Administration information is limited for extremely preterm infants (gestational age under 29 weeks) who are less than 8 weeks old, and no clinical data

exist for infants with a postmenstrual age (gestational age at birth plus chronological age) of 32 weeks.

ii) Infants born outside of RSV season (includes those infants born in 2024 prior to RSV season, recommended for those 8 months of age and less): A single dose of Beyfortus® is recommended based on the infant's weight at the time of administration.

- Infants < 5 kg: 50 mg in 0.5 mL (100 mg/mL)
- Infants ≥ 5 kg: 100 mg in 1.0 mL (100 mg/mL)

Administration should be targeted shortly before the start of RSV season but can continue to be administered during the season.

iii) Children at continued high-risk entering their second RSV season: Administration of a one-time 200 mg dose given as two 1.0 mL intramuscular injections of 100 mg/mL of Beyfortus® administered in two separate injection sites should be targeted shortly before the start of their second RSV season but can continue to be administered during the season.

iv) Children undergoing cardiac surgery with cardiopulmonary bypass: An additional dose should be administered as soon as the individual is stable after surgery to ensure adequate Beyfortus® serum levels. If **within 90 days after receiving the first dose** of Beyfortus®, the additional dose during the first RSV season should be 50 mg or 100 mg according to body weight or 200 mg during the second RSV season. If **more than 90 days** have elapsed since the first dose, the additional dose should be a single dose of 50 mg regardless of body weight during the first RSV season or 100 mg during the second RSV season to cover the remainder of the RSV season.

Table 1: Beyfortus® Administration Guidelines for Infants and Children

Category	Weight	Dose	Timing
Infants born during the 2024/25 RSV season	< 5 kg	50 mg in 0.5 mL (100 mg/mL)	Administered from birth
	≥ 5 kg	100 mg in 1 mL (100 mg/mL)	Administered from birth
Infants born outside of the 2024/25 RSV season	< 5 kg	50 mg in 0.5 mL (100 mg/mL)	Shortly before the start of the RSV season
	≥ 5 kg	100 mg in 1 mL (100 mg/mL)	Shortly before the start of the RSV season
Children at continued high-risk from RSV infection entering their second season	N/A	200 mg (two 1 mL injections of 100 mg/mL)	Shortly before the start of their second RSV season

Table 2: Beyfortus® Administration Guidelines for Children Undergoing Cardiac Surgery with Cardiopulmonary Bypass*

Time Since First Dose	Weight	Dose
< 90 days after the first dose		
• First season	< 5 kg	50 mg
	≥ 5 kg	100 mg
• Second season	Any weight†	200 mg
≥ 90 days after the first dose		
• First season	Any weight	50 mg
• Second season	Any weight	100 mg

*Dosing applies to infants who have already received their dose of Beyfortus® for the season and then undergo cardiac surgery with cardiopulmonary bypass. The surgical procedure would cause a drop in serum concentration. All doses should be administered as soon as the individual is stable post-surgery.

†If a child weighs less than 10 kg entering their second RSV season, consideration can be given to administering a single dose of 100 mg at clinical discretion.

d) Co-administration with vaccine products

Beyfortus® can be administered on the same day or any time before or after routine childhood vaccines, including influenza. No interval between Beyfortus® and live vaccines (such as MMR and Varicella) is necessary.

Co-administration of Beyfortus® and vaccine products is not expected to interfere with the immune response to vaccine products. In clinical trials, when Beyfortus® was given concomitantly with routine childhood vaccines, the safety and reactogenicity profile was similar to when the childhood vaccines were given alone.

5. Contraindications and Precautions

Beyfortus® should not be given to those with known hypersensitivity or a history of a severe allergic reaction (e.g., anaphylaxis) to any product ingredients, including non-medicinal ingredients or materials in the product's packaging.

Caution should be exercised when administering Beyfortus® to individuals with bleeding disorders.

Individuals who have a moderate or severe acute illness, with or without fever, do not need to wait until they have recovered before receiving Beyfortus®.

Please refer to the Beyfortus® product monograph for detailed information on contraindications and precautions.

6. Efficacy

Efficacy was assessed in infants under eight months old who were either born during or entering their first RSV season, with evaluations conducted up to 150 days post-injection. Results from the combined phase 2 and 3 clinical trials revealed the following efficacy rates:

- 79.0% in preventing medically attended RSV-associated lower respiratory tract infection (LRTI).
- 80.6% in preventing RSV-associated LRTI requiring hospitalization.
- 90.0% in preventing RSV-associated LRTI leading to admission to an intensive care unit (ICU).

Data from real-world utilization during the 2023/2024 RSV season globally demonstrated similar effectiveness results:

- 82% - 90% in preventing RSV-associated LRTI requiring hospitalization
- 75.9% - 90.1% in preventing RSV-associated Intensive Care Unit admissions
- 69% - 90% overall reduction in RSV-associated hospitalizations compared to the previous season

7. Adverse Events

Like vaccines or medications, Beyfortus® may have some side effects, which are mild and last only a few days.

Common side effects for Beyfortus® are mild or moderate, including local reactions such as redness, swelling, and pain at the injection site. The most frequent adverse reactions in clinical trials were:

- Rash (0.7% vs. 0.3% placebo)
- Pyrexia (0.5% vs. 0.6% placebo)
- Injection site reactions (0.3% vs. 0% placebo) within seven days

Some participants experienced systemic adverse events, such as:

- RSV bronchiolitis (1.3% vs. 2.6% placebo)
- RSV pneumonia (0.7% vs. 0.9% placebo)
- RSV bronchitis (0.5% vs. 1.0% placebo)

As Beyfortus® is a new drug product, its safety and tolerability will continue to be monitored in post-market safety surveillance.

8. Reporting Side Effects Post-Administration

Those administering Beyfortus® should ensure that parents and guardians know the need to report side effects to their child's health care provider immediately. Parents and guardians should be advised to go to the nearest emergency department if their child develops severe reactions after receiving Beyfortus®, including the following:

- Hives
- Swelling of the mouth or throat
- Trouble breathing, hoarseness or wheezing
- High fever (over 40°C or 104°F)
- Seizures
- Other serious reactions

As Beyfortus® is a mAb and not a vaccine, s.38 of the *Health Protection and Promotion Act* requiring the follow-up and reporting of suspected adverse events following

immunization does not apply to providers administering this product. As such, these incidents do not need to be reported to the local public health unit and should be managed as per practices and organizational policies for other medicines and therapeutics.

Where no organizational policy exists, it is recommended that organizations, providers, and/or parents/guardians report all suspected side effects to Health Canada, especially those that are:

- Unexpected, regardless of their severity (i.e., not consistent with product information or labelling
- Serious, whether expected or not
- Reactions to health products on the market less than five years, regardless of their nature or severity.

To report a side effect of Beyfortus®, please see the Health Canada, *Side Effect Reporting Form*. This form may be completed online, downloaded, faxed, or mailed using the information on their website.

9. Health Care Professionals Eligible to Administer Beyfortus®

Physicians, nurse practitioners, registered nurses (RNs), and registered practical nurses (RPNs) can administer the publicly funded mAb product, Beyfortus®.

Midwives must have a direct order, medical directive or delegation to administer Beyfortus® as specified in O. Reg. 188/24 under the *Midwifery Act, 1991*.

Before administering a mAb product, including Beyfortus®, health care professionals should discuss with their employer. Also, prior to administering Beyfortus®, a health care professional must ensure they have the required authority, such as a direct order, medical directive or delegation, and the competency, to administer it.

10. Administration After RSV Infection

Beyfortus® is generally not necessary or recommended for an infant who has had a confirmed RSV infection during the current RSV season. The additional benefit of administering Beyfortus® after recovery from RSV is unknown and expected to be low, as the risk of rehospitalization in the same season is very low. However, consideration may be given to severely immunocompromised infants who may not mount an adequate immune response to the RSV infection.

No specific interval is recommended between RSV infection and receipt of Beyfortus®.

11. Observation Post-administration

Recipients should be observed for at least 15 minutes after immunization. A 30-minute observation period is preferred should concerns regarding possible allergies arise.

12. Preparing Beyfortus® for Administration

Each Beyfortus® pre-filled syringe is for single use only.

Prior to administration, perform the following:

a) Visually inspect the syringe for particulate matter and discolouration before administration. Beyfortus® is a clear to opalescent, colourless to yellow solution.
   - Do not use it if the liquid is cloudy, discoloured, or contains large particles or foreign particulate matter.
   - Do not use if the syringe has been dropped or damaged, the security seal on the carton has been broken, or the expiry date has passed.

b) Check the labels on the carton and pre-filled syringe to make sure you have selected the correct 50 mg (for infants < 5 kg), or 100 mg (for infants ≥ 5 kg) presentation as

c) required. See Figure 1 below.

Figure 1: Pre-filled syringe markings for 50 mg and 100 mg syringes

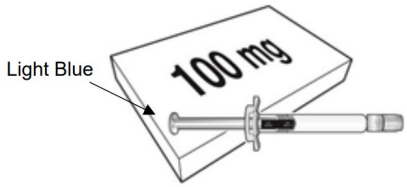
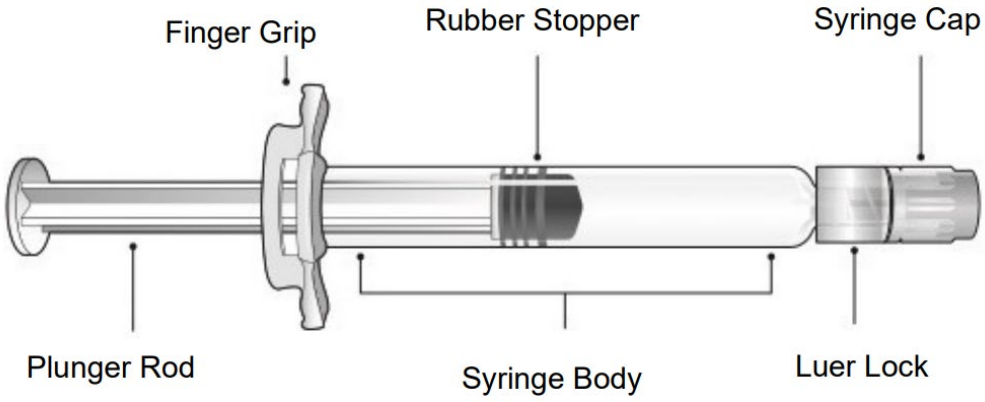
Beyfortus® 50 mg (50mg/0.5 mL) prefilled syringe with a purple plunger rod.	Beyfortus® 100 mg (100 mg/mL) prefilled syringe with a light blue plunger rod
	

Figure 2: Luer lock syringe components



d) Holding the Luer lock in one hand (avoid holding the plunger rod or syringe body), unscrew the syringe cap by twisting it counterclockwise with the other hand. See Figure 2 for Luer lock syringe components.

e) Attach a Luer lock needle to the pre-filled syringe by gently twisting the needle clockwise onto the pre-filled syringe until slight resistance is felt.

f) Hold the syringe body with one hand and carefully pull the needle cover straight off with the other hand. Do not hold the plunger rod while removing the needle cover; the rubber stopper may move. Do not touch the needle or let it touch any surface. Do not recap the needle or detach it from the syringe.

g) Administer all the contents of the pre-filled syringe as an intramuscular injection. The preferred site for infants under 12 months of age is the anterolateral thigh region. The preferred administration site for children over 12 months of age is the upper arm's deltoid region. The gluteal muscle should not be used routinely as an injection site because of the risk of damage to the sciatic nerve.

h) Repeat these steps in a different injection site if two injections are required.

13. Beyfortus® Packaging

Beyfortus® is a sterile, preservative-free product packaged in either a 5-pack or 1-pack carton. Each 5-pack includes five single-dose prefilled syringes without a needle, and each 1-pack includes a one-single dose prefilled syringe without a needle.

Each single-use, pre-filled syringe consists of a siliconized Luer lock Type I glass pre-filled syringe with a FluroTec-coated plunger stopper.

Product dimensions (L x W x H) for Beyfortus® are as follows (product version availability cannot be guaranteed):

- 5-pack (in millimetres): 140 x 108 x 24 (both 50 mg and 100 mg doses)
- 1-pack (in millimetres): 144 x 51 x 24 (both 50 mg and 100 mg doses)

14. Cold Chain Requirements

To ensure optimal protection, Beyfortus® must be maintained at a temperature between +2°C and +8°C and stored in the original outer carton until administration to protect it from light. It cannot be frozen, shaken, or exposed to heat. Once removed from the refrigerator, Beyfortus® should be administered immediately.

Beyfortus® may be kept at room temperature (+20°C and +25°C) for a maximum of eight hours, then discarded if not used. It cannot be returned to the refrigerator once removed and must be used within 8 hours or discarded. Please refer to the product monograph for more Beyfortus® storage and handling information.

For additional information, please refer to the Vaccine Storage and Handling Guidelines which have been developed to facilitate proper storage and handling of publicly funded vaccines and minimize vaccine wastage as well as promote vaccine safety and effectiveness.

15. Ordering Information

Health care providers should order Beyfortus® from their usual vaccine source (i.e., Public Health Unit or the OGPMSS).

16. Reducing Product Wastage

Please refer to the Vaccine Storage and Handling Guidelines for information on waste reduction best practices.

17. Additional Information and Resources

Health care providers looking for more information about RSV, the mAb product, the RSV vaccine, or the province's RSV prevention program can refer to the ministry's RSV website and the appropriate product monograph.