BEYFORTUS is indicated for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in:

- Neonates and infants born during or entering their first RSV season. (1)
- Children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season. (1)

**CONTRAINDICATIONS**

BEYFORTUS is contraindicated in infants and children with a history of serious hypersensitivity reactions, including anaphylaxis, to nirsevimab-alip or to any of the excipients. (4)

**WARNINGS AND PRECAUTIONS**

Hypersensitivity Including Anaphylaxis: Serious hypersensitivity reactions, including anaphylaxis, have been observed with other human IgG1 monoclonal antibodies. Initiate appropriate medications and/or supportive therapy. (5.1)

**ADVERSE REACTIONS**

Most common adverse reactions were rash (0.9%) and injection site reactions (0.3%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Sanofi at 1-855-239-3678 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**USE IN SPECIFIC POPULATIONS**

The safety and effectiveness of BEYFORTUS in children older than 24 months of age have not been established. (8.4)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 07/2023

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**Table 1 Recommended Dosage of BEYFORTUS in Neonates and Infants Born During or Entering Their First RSV Season**

<table>
<thead>
<tr>
<th>Body Weight at Time of Dosing</th>
<th>Recommended Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 5 kg</td>
<td>50 mg by IM injection</td>
</tr>
<tr>
<td>5 kg and greater</td>
<td>100 mg by IM injection</td>
</tr>
</tbody>
</table>

Children Who Remain at Increased Risk for Severe RSV Disease: Second RSV Season

For children up to 24 months of age who remain at increased risk for severe RSV disease in their second RSV season, the recommended dosage of BEYFORTUS is a single 200 mg dose administered as two IM injections (2 x 100 mg).

**Children Undergoing Cardiac Surgery with Cardiopulmonary Bypass**

For children undergoing cardiac surgery with cardiopulmonary bypass, an additional dose of BEYFORTUS is recommended as soon as the child is stable after surgery to ensure adequate nirsevimab-alip serum levels. The recommended dosage of BEYFORTUS is administered as an IM injection.

**First RSV season:**

- If surgery is within 90 days after receiving BEYFORTUS, the additional dose should be based on body weight at the time of the additional dose. Refer to Table 1 for weight-based dosing.
- If more than 90 days have elapsed since receiving BEYFORTUS, the additional dose should be 50 mg regardless of body weight.

**Second RSV season:**

- If surgery is within 90 days after receiving BEYFORTUS, the additional dose should be 200 mg, regardless of body weight.
- If more than 90 days have elapsed since receiving BEYFORTUS, the additional dose should be 100 mg, regardless of body weight.

**Administration Instructions**

BEYFORTUS must be administered by a healthcare provider. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. BEYFORTUS is a clear to opalescent, colorless to yellow solution. Do not inject BEYFORTUS if the liquid is cloudy, discolored, or it contains large particles or foreign particulate matter.
Administration Instructions for Single-Dose Pre-filled Syringe

Co-administration with Childhood Vaccines and Immunoglobulin Products

BEYFORTUS can be given concomitantly with childhood vaccines [see Clinical Pharmacology (12.3)]. When administered concomitantly with injectable vaccines, they should be given with separate syringes and at different injection sites. Do not mix BEYFORTUS with any vaccines or medications in the same syringe or vial.

There is no information regarding co-administration of BEYFORTUS with other immunoglobulin products. Palivizumab should not be administered to infants who have already received BEYFORTUS in the same season. There are no data regarding substitution of BEYFORTUS for palivizumab once prophylaxis treatment is initiated with palivizumab for the RSV season. BEYFORTUS may be administered prior to or during the second RSV season to children up to 24 months of age who remain vulnerable to severe RSV disease, and who received palivizumab in their first RSV season [see Adverse Reactions (6.1) and Clinical Studies (14.3)].

Precautions

Adverse Reactions

Adverse reactions reported among Trial 05 subjects who received BEYFORTUS in their first RSV season were similar to those reported in subjects who received BEYFORTUS and infants weighing greater than or equal to 5 kg received a single 100 mg IM dose of BEYFORTUS and infants weighing greater than or equal to 5 kg received a single 100 mg IM dose.

Infants who received the recommended dose in Trial 03 and infants in Trial 04 were pooled to evaluate the safety of BEYFORTUS (N=2,570) compared to placebo (N=1,284). At randomization, in this pooled Safety Population from Trials 03 and 04 cohorts, 22% of infants were born at less than 35 weeks GA, 10% of infants were GA greater than or equal to 35 weeks and less than 37 weeks; 68% were GA greater than or equal to 37 weeks; 52% were male; 57% were White; 15% were Black; 4% were American Indian/Alaskan native; 4% were Asian; 1% were Pacific Islander; and 19% were Other or Mixed Race; 30% were Hispanic or Latino; 73% were from Northern Hemisphere; and 53% weighed less than or equal to 3 kg; 66% were less than or equal to 6 months of age; 74% were female; and 86% were less than or equal to 6 months of age. (Refer to Sections 14.2 and 14.3, Clinical Studies, for a description of the efficacy populations in Trials 03 and 04). In both trials, infants received a single dose of IM BEYFORTUS or placebo on Study Day 1 and were monitored for at least 60 minutes post-dose. Subjects were followed for 360 days post-dose to assess safety. Adverse reactions were reported in 1.2% of subjects who received BEYFORTUS; most (97%) of adverse reactions were mild to moderate in intensity.

Table 2 summarizes the adverse reactions that occurred in Trial 03 and Trial 04 (Safety Population) in subjects who received the recommended dose of BEYFORTUS.

Table 2 Adverse Reactions Reported at an Incidence Higher Than Placebo in the Safety Population (Trials 03 and 04)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>BEYFORTUS</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash*</td>
<td>N=2,570</td>
<td>N=1,284</td>
</tr>
<tr>
<td>Injection site reaction†</td>
<td>0.9</td>
<td>0.6</td>
</tr>
<tr>
<td>Injection site reaction‡</td>
<td>0.3</td>
<td>0.0</td>
</tr>
</tbody>
</table>

*The Safety Population includes all subjects who received the recommended dose of BEYFORTUS in Trials 03 and 04. Primary and Safety cohorts from Trial 04; infants who weighed less than 5 kg and who received the recommended dose of BEYFORTUS (single 50 mg IM dose) in Trial 03.
†Rash was defined by the following grouped preferred terms: rash, maculopapular, rash macular, rash papular.
‡Injection site reaction was defined by the following grouped preferred terms: injection site reaction, injection site pain, injection site induration, injection site edema, injection site swelling.

Infants Born at <35 Weeks Gestational Age and Infants and Children with CLD of Prematurity or Hemodynamically Significant CHD (Trial 05)

RSV Season One

The safety of BEYFORTUS was evaluated in Trial 05, a randomized, double-blind, palivizumab-controlled multicenter trial in infants at high risk for severe RSV disease. These 355 infants were randomized 2:1 to receive BEYFORTUS (N=230) or palivizumab (N=304) by IM injection. The 614 infants who received BEYFORTUS included 128 preterm infants born GA less than 29 weeks, 390 preterm infants who were born at 29 weeks or older to less than 35 weeks GA, and 96 late preterm and term infants born at 35 weeks GA or older. Among infants born at GA less than 29 weeks, 390 preterm infants who were born at 29 weeks or older to less than 35 weeks GA, and 96 late preterm and term infants born at 35 weeks GA or older, 52% were male; 57% were White; 15% were Black; 4% were American Indian/Alaskan native; 4% were Asian; 1% were Pacific Islander; and 19% were Other or Mixed Race; 30% were Hispanic or Latino; 73% were from Northern Hemisphere; and 53% weighed less than or equal to 3 kg; 66% were less than or equal to 6 months of age; 74% were female; and 86% were less than or equal to 6 months of age.

Adverse reactions reported in children and infants with CHD of prematurity or hemodynamically significant CHD were reported in 355 (90%) of subjects who received BEYFORTUS. Most (97%) of adverse reactions were mild to moderate in intensity.
in the second RSV season (N=180). Subjects who received palivizumab in the first RSV season were re-randomized to receive BEYFORTUS (N=40) or palivizumab (N=42) in the second RSV season. Safety data were available for 150 days after dosing in children with CLD or CHD who received BEYFORTUS (N=220) or palivizumab (N=42) in their second RSV season. The safety profile of BEYFORTUS in these children during their second RSV season was consistent with the safety profile of BEYFORTUS observed during their first RSV season.

7 DRUG INTERACTIONS

7.1 Interference with RT-PCR or Rapid Antigen Detection RSV Diagnostic Assays

Nirsevimab-alip does not interfere with reverse transcriptase polymerase chain reaction (RT-PCR) or rapid antigen detection RSV diagnostic assays that employ commercially available antibodies targeting antigenic site I, II, or IV on the RSV fusion (F) protein. For immunological assay results which are negative when clinical observations are consistent with RSV infection, it is recommended to confirm using an RT-PCR-based assay.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

BEYFORTUS is not indicated for use in females of reproductive potential.

8.2 Lactation

BEYFORTUS is not indicated for use in females of reproductive potential.

8.4 Pediatric Use

The safety and effectiveness of BEYFORTUS have been established for the prevention of RSV lower respiratory tract disease in neonates and infants born during or entering their first RSV season and in children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season. The safety and efficacy of BEYFORTUS for this indication and populations are discussed throughout the labeling.

Use of BEYFORTUS for this indication is supported by evidence from adequate and well-controlled studies in neonates and infants from birth up to 12 months of age with additional pharmacokinetic and safety data in children up to 24 months of age (see Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14)). The safety and effectiveness of BEYFORTUS have not been established in children older than 24 months of age.

10 OVERDOSE

There is limited experience of overdose with BEYFORTUS. There is no specific treatment for an overdose with BEYFORTUS. In the event of an overdose, the individual should be monitored for the occurrence of adverse reactions and provided with symptomatic treatment as appropriate.

11 DESCRIPTION

Nirsevimab-alip, a respiratory syncytial virus F protein-directed fusion inhibitor, is a human immunoglobulin G1 kappa (IgG1κ) monoclonal antibody produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology. The molecular weight is approximately 146,500 Da.

BEYFORTUS (nirsevimab-alip) injection is a sterile, preservative-free, clear to opalescent, colorless to yellow solution for intramuscular injection. It is supplied in a single-dose siliconized Luer lock Type I glass pre-filled syringe with a FluroTec coated plunger stopper. Each 0.5 mL contains 50 mg nirsevimab-alip, arginine hydrochloride (8 mg), histidine (1.1 mg), L-histidine hydrochloride monohydrate (3.3 mg), polysorbate 80 (0.2 mg), sucrose (41 mg), and water for injection (USP). The pH is 6.0.

Each 1 mL contains 100 mg nirsevimab-alip, arginine hydrochloride (17 mg), histidine (2.2 mg), L-histidine hydrochloride monohydrate (3.3 mg), polysorbate 80 (0.2 mg), sucrose (21 mg), and water for injection (USP). The pH is 6.0.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

BEYFORTUS is a human IgG1κ monoclonal antibody with anti-RSV activity [see Microbiology (12.4)].

12.2 Pharmacodynamics

There is a positive correlation between a serum nirsevimab-alip AUC (based on clearance at baseline) above 12.8 mg·day/mL, and a lower incidence of medically attended RSV lower respiratory tract infection (MA RSV LRTI). Following IM administration of nirsevimab-alip in adults, RSV neutralizing antibody levels in serum were approximately 4 times higher than baseline at 8 hours after nirsevimab-alip dosing, and maximum levels were reached at 11 DESCRIPTION

Each 0.5 mL contains 50 mg nirsevimab-alip, arginine hydrochloride (8 mg), histidine (1.1 mg), L-histidine hydrochloride monohydrate (3.3 mg), polysorbate 80 (0.2 mg), sucrose (41 mg), and water for injection (USP). The pH is 6.0.

Each 1 mL contains 100 mg nirsevimab-alip, arginine hydrochloride (17 mg), histidine (2.2 mg), L-histidine hydrochloride monohydrate (3.3 mg), polysorbate 80 (0.2 mg), sucrose (21 mg), and water for injection (USP). The pH is 6.0.

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Duration of Protection

Based on clinical data, the duration of protection offered by a single dose of BEYFORTUS extends through 5 months.

12.3 Pharmacokinetics

The PK of nirsevimab-alip is dose-proportional following a single IM administration of doses ranging from 25 mg (0.5 times the lowest approved recommended dosage) to 200 mg in pediatric subjects. Following the recommended dose, the nirsevimab-alip serum exposures were similar in neonates and infants born during or entering their first RSV season (Trials 03 and 04), and in neonates and infants born at less than 35 weeks GA (including less than 29 weeks GA) in their first RSV season (Trial 05), and in pediatric subjects up to 24 months of age with CLD or CHD in their first and second RSV season (Trial 05).

Absorption

The estimated nirsevimab-alip absolute bioavailability is 84% and the median time (range) to maximum concentration is 6 (1, 28) days.

Distribution

The estimated nirsevimab-alip total volume of distribution is 477 mL for an infant weighing 5 kg.

Elimination

The nirsevimab-alip terminal half-life is approximately 71 days and the estimated clearance is 3.42 mL/day for an infant weighing 5 kg.

Metabolism

Nirsevimab-alip is degraded into small peptides by catalytic pathways.

Specific Populations

No clinically significant differences in the pharmacokinetics of nirsevimab-alip were observed based on race or vulnerability to severe RSV disease (i.e., CLD, CHD, GA <29 weeks, or immunocompromised states). An effect of renal or hepatic impairment on nirsevimab-alip pharmacokinetics is not expected.
In Trial 04, 7% (55/830) of subjects were ADA-positive on Day 361, of whom 22% (12/55) had neutralizing antibodies and 96% (53/55) had ADA against YTE. In Trial 03, the efficacy of BEYFORTUS against MA RSV LRTI with hospitalization in infants born at GA greater than or equal to 35 weeks and less than 29 weeks, who received a single dose of BEYFORTUS, based on the relative risk reduction was 78.4% (95% CI 51.9, 90.3; p=0.0002), through 150 days post dose.

14.4 Prevention of MA RSV LRTI in Infants Born at ≤35 Weeks Gestational Age (Trial 05)

Trial 05 enrolled infants at higher risk for severe RSV disease entering their first RSV season into one of two cohorts: preterm infants (GA less than 35 weeks) and infants with CLD of prematurity or hemodynamically significant CHD. A total of 925 infants were randomized 2:1 in each of the preterm (n=615) and CLD/CHD (n=310) cohorts to receive BEYFORTUS or palivizumab. Infants received a single IM dose of BEYFORTUS (50 mg if less than 5 kg body weight or 100 mg if greater than or equal to 5 kg body weight at the time of dosing), or placebo (N=496). At randomization, 14% were GA greater than or equal to 35 weeks and less than 29 weeks; 86% were GA greater than or equal to 37 weeks; 52% were male; 53% were White; 28% were Black; 6% were American Indian/Alaskan native; 4% were Asian; 1% were Pacific Islander; and 8% were Other or Mixed Race; 10% had Hispanic or Latino; and 69% were from Northern Hemisphere; and 40% weighed less than 5 kg. The median age was 2.6 months (range: 0.03 to 11.10 months); 32% were greater than 3 to less than or equal to 6 months; and 10% were greater than 6 months of age.

In Trial 04, the endpoint was the incidence of MA RSV LRTI caused by RTP-PCR-confirmed RSV, as defined in Trial 03. Incidence of RSV LRTI with hospitalization was a prespecified secondary endpoint. RSV hospitalization was defined as hospitalization for LRTI with a positive RSV test. Table 5 displays the primary efficacy result from Trial 04.

Table 5 Incidence of MA RSV LRTI in Infants Born at ≤35 Weeks Gestational Age and with CLD of Prematurity or Hemodynamically Significant CHD (Trial 05)

<table>
<thead>
<tr>
<th>N</th>
<th>Incidence % (n)</th>
<th>Efficacy* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BEYFORTUS</td>
<td>994</td>
<td>1.2% (12)</td>
</tr>
<tr>
<td>Palivizumab</td>
<td>496</td>
<td>5.0% (25)</td>
</tr>
</tbody>
</table>

*The primary efficacy analysis for Trial 04 is based on subjects from the Primary Cohort. †Efficacy for MA RSV LRTI based on relative risk reduction against placebo adjusted for age at randomization.

†‡p-value =< 0.001.

In Trial 04, the efficacy of BEYFORTUS against MA RSV LRTI with hospitalization in infants born at GA greater than or equal to 35 weeks who received a single IM 50 mg or 100 mg dose for those who weigh less than 5 kg greater than or equal to 5 kg, respectively, based on the relative risk reduction was 60.2% (95% CI -14.6, 86.2; p=0.09), through 150 days post dose.

14.5 Prevention of MA RSV LRTI in Infants Born at ≤35 Weeks Gestational Age and with CLD of Prematurity or Hemodynamically Significant CHD (Trial 05)

The safety and PK of BEYFORTUS were evaluated in a Phase 2/3 randomized, double-blind, palivizumab-controlled multicenter trial (Trial 05) in pediatric subjects born less than 35 weeks GA and infants with CLD of prematurity or hemodynamically significant CHD. This trial was not powered for efficacy, but efficacy was assessed as secondary endpoint. The efficacy of BEYFORTUS in preterm infants (GA less than 35 weeks) during their first RSV season and in pediatric subjects up to 24 months of age with CLD or CHD during their first and second RSV season was established by extrapolation of efficacy of BEYFORTUS from Trials 03 and 04 to the population enrolled in Trial 05 based on similar nirsevimab-alip exposures among subjects enrolled in Trial 04 and 05 [see Clinical Pharmacology (12.3)].

Table 6 Incidence of MA RSV LRTI in Infants Born at ≤35 Weeks Gestational Age and with CLD of Prematurity or Hemodynamically Significant CHD (Trial 05)

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†‡p-value =< 0.001.

In Trial 04, the efficacy of BEYFORTUS against MA RSV LRTI caused by RTP-PCR-confirmed RSV, as defined in Trial 03. Incidence of RSV LRTI with hospitalization was a prespecified secondary endpoint. RSV hospitalization was defined as hospitalization for LRTI with a positive RSV test. Table 5 displays the primary efficacy result from Trial 04.

Table 5 Incidence of MA RSV LRTI in Infants Born at ≤35 Weeks Gestational Age and with CLD of Prematurity or Hemodynamically Significant CHD (Trial 05)

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</tbody>
</table>

*The primary efficacy analysis for Trial 04 is based on subjects from the Primary Cohort. †Efficacy for MA RSV LRTI based on relative risk reduction against placebo adjusted for age at randomization.

†‡p-value =< 0.001.
**Before your child receives BEYFORTUS, tell your healthcare provider about all of your child’s medical conditions, including if your child:**

- has ever had a reaction to BEYFORTUS.
- has bleeding or bruising problems. If your child has a problem with bleeding or bruises easily, an injection could cause a problem.

**Tell your child’s healthcare provider about all the medicines your child takes,** including prescription and over-the-counter medicines, vitamins, and herbal supplements. Your infant should not receive a medicine called palivizumab if they have already received BEYFORTUS in the same RSV season.

**How is BEYFORTUS given?**

- BEYFORTUS is given as an injection, usually in the thigh (leg) muscle, by your child’s healthcare provider.
- Your child should receive BEYFORTUS before or during the RSV season. RSV season is the time of year when RSV infections are most common, usually occurring fall through spring. Your healthcare provider can tell you when the RSV season starts in your area.
- Your child may still get RSV disease after receiving BEYFORTUS. Talk to your child’s healthcare provider about what symptoms to look for.
- If your child has heart surgery, your child’s healthcare provider may need to give your child an additional BEYFORTUS injection soon after surgery.

**What are the possible side effects of BEYFORTUS?**

- **Serious allergic reactions** have happened with other medicines like BEYFORTUS. Get medical help right away if your child has any of the following signs or symptoms of a serious allergic reaction.
  - swelling of the face, mouth or tongue
  - difficulty swallowing or breathing
  - severe rash, hives or itching
  - bluish color of skin, lips or under fingernails
  - muscle weakness
  - severe pain, swelling or hardening at the site of your child’s injection.

**The most common side effects of BEYFORTUS include rash, and pain, swelling or hardness at the site of your child’s injection.** These are not all of the possible side effects of BEYFORTUS. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**General information about the safe and effective use of BEYFORTUS.**

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about BEYFORTUS that is written for health professionals.

**What are the ingredients in BEYFORTUS?**

**Active ingredient:** nirsevimab-alip

**Inactive ingredients:** arginine hydrochloride, histidine, L-histidine hydrochloride monohydrate, polysorbate 80, sucrose and water for injection.

Manufactured by: AstraZeneca AB, Södertälje, Sweden SE-15185

US License No. 2059

Distributed by: Sanofi Pasteur, Inc., Swiftwater, PA 18370 USA

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**PATIENT INFORMATION**

**BEYFORTUS™ (Bay for tus)**

(nirsevimab-alip) injection, for intramuscular use

**What is BEYFORTUS?**

BEYFORTUS is a prescription medicine that is used to help prevent a serious lung disease caused by Respiratory Syncytial Virus (RSV) in:

- newborns and babies under 1 year of age born during or entering their first RSV season.
- children up to 24 months of age who remain at risk of severe RSV disease through their second RSV season.

BEYFORTUS is an antibody that contains nirsevimab-alip which is used to help prevent RSV disease for 5 months.

It is not known if BEYFORTUS is safe and effective in children older than 24 months of age.

**Your child should not receive BEYFORTUS if your child has a history of serious allergic reactions to nirsevimab-alip or any of the ingredients in BEYFORTUS. See the end of this Patient Information leaflet for a complete list of ingredients in BEYFORTUS.”**