ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Beyfortus 50 mg solution for injection in pre-filled syringe
Beyfortus 100 mg solution for injection in pre-filled syringe

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Beyfortus 50 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 50 mg of nirsevimab in 0.5 mL (100 mg/mL).

Beyfortus 100 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 100 mg of nirsevimab in 1 mL (100 mg/mL).

Nirsevimab is a human immunoglobulin G1 kappa (IgG1κ) monoclonal antibody produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology.

Excipients with known effect

This medicine contains 0.1 mg of polysorbate 80 (E433) in each 50 mg (0.5 mL) dose and 0.2 mg in each 100 mg (1 mL) dose (see section 4.4).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection).

Clear to opalescent, colourless to yellow, pH 6.0 solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

i. Neonates and infants during their first RSV season.

ii. Children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season (see section 5.1).

Beyfortus should be used in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Infants during their first RSV season

The recommended dose is a single dose of 50 mg administered intramuscularly for infants with body weight <5 kg and a single dose of 100 mg administered intramuscularly for infants with body weight ≥5 kg.

Beyfortus should be administered from birth for infants born during the RSV season. For others born outside the season Beyfortus should be administered ideally prior to the RSV season.

Dosing in infants with a body weight from 1.0 kg to <1.6 kg is based on extrapolation, no clinical data are available. Exposure in infants <1 kg is anticipated to yield higher exposures than in those weighing more. The benefits and risks of nirsevimab use in infants <1 kg should be carefully considered.

There are limited data available in extremely preterm infants (Gestational Age [GA] <29 weeks) less than 8 weeks of age. No clinical data available in infants with a postmenstrual age (gestational age at birth plus chronological age) of less than 32 weeks (see section 5.1).

Children who remain vulnerable to severe RSV disease through their second RSV season

The recommended dose is a single dose of 200 mg given as two intramuscular injections (2 x 100 mg). Beyfortus should be administered ideally prior to the start of the second RSV season.

For individuals undergoing cardiac surgery with cardiopulmonary bypass, an additional dose may be administered as soon as the individual is stable after surgery to ensure adequate nirsevimab 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 could 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.

The safety and efficacy of nirsevimab in children aged 2 to 18 years have not been established. No data are available.

Method of administration

Beyfortus is for intramuscular injection only.

It is administered intramuscularly, preferably in the anterolateral aspect of the thigh. The gluteal muscle should not be used routinely as an injection site because of the risk of damage to the sciatic nerve. If two injections are required, different injection sites should be used.

For instructions on special handling requirements, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity including anaphylaxis

Serious hypersensitivity reactions have been reported following Beyfortus administration. Anaphylaxis has been observed with human immunoglobulin G1 (IgG1) monoclonal antibodies. If signs and symptoms of anaphylaxis or other clinically significant hypersensitivity reaction occur, immediately discontinue administration and initiate appropriate medicinal products and/or supportive therapy.

Clinically significant bleeding disorders

As with any other intramuscular injections, nirsevimab should be given with caution to individuals with thrombocytopenia or any coagulation disorder.

Immunocompromised children

In some immunocompromised children with protein-losing conditions, a high clearance of nirsevimab has been observed in clinical trials (see section 5.2), and nirsevimab may not provide the same level of protection in those individuals.

Polysorbate 80 (E433)

This medicine contains 0.1 mg of polysorbate 80 in each 50 mg (0.5 mL) dose and 0.2 mg in each 100 mg (1 mL) dose. Polysorbates may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed. Monoclonal antibodies do not typically have significant interaction potential, as they do not directly affect cytochrome P450 enzymes and are not substrates of hepatic or renal transporters. Indirect effects on cytochrome P450 enzymes are unlikely as the target of nirsevimab is an exogenous virus.

Nirsevimab 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.

Concomitant administration with vaccines

Since nirsevimab is a monoclonal antibody, a passive immunisation specific for RSV, it is not expected to interfere with the active immune response to co-administered vaccines.

There is limited experience of co-administration with vaccines. In clinical trials, when nirsevimab was given with routine childhood vaccines, the safety and reactogenicity profile of the co-administered regimen was similar to the childhood vaccines given alone. Nirsevimab can be given concomitantly with childhood vaccines.

Nirsevimab should not be mixed with any vaccine in the same syringe or vial (see section 6.2). When administered concomitantly with injectable vaccines, they should be given with separate syringes and at different injection sites.

4.6 Fertility, pregnancy and lactation

Not applicable.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Summary of the safety profile

The most frequent adverse reaction was rash (0.7%) occurring within 14 days post dose. The majority of cases were mild to moderate in intensity. Additionally, pyrexia and injection site reactions were reported at a rate of 0.5% and 0.3% within 7 days post dose, respectively. Injection site reactions were non-serious.

Tabulated list of adverse reactions

Table 1 presents the adverse reactions reported in 2 966 term and preterm infants (GA ≥29 weeks) who received nirsevimab in clinical trials, and in post-marketing setting (see section 4.4).

Adverse reactions reported from controlled clinical trials are classified by MedDRA System Organ Class (SOC). Within each SOC, preferred terms are arranged by decreasing frequency and then by decreasing seriousness. Frequencies of occurrence of adverse reactions are defined as: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1 000 to <1/100); rare (≥1/10 000 to <1/1 000); very rare (<1/10 000) and not known (cannot be estimated from available data).

Table 1: Adverse reactions

MedDRA SOC	MedDRA Preferred Term	Frequency
Immune system disorders	Hypersensitivity[a]	Not known
Skin and subcutaneous tissue disorders	Rash[b]	Uncommon
General disorders and administration site conditions	Injection site reaction[c]	Uncommon
	Pyrexia	Uncommon

[a] Adverse reaction from spontaneous reporting.
[b] Rash was defined by the following grouped preferred terms: rash, rash maculo-papular, rash macular.
[c] Injection site reaction was defined by the following grouped preferred terms: injection site reaction, injection site pain, injection site induration, injection site oedema, injection site swelling.

Infants at higher risk for severe RSV disease in their first season

Safety was evaluated in MEDLEY in 918 infants at higher risk for severe RSV disease, including 196 extremely preterm infants (GA <29 weeks) and 306 infants with chronic lung disease of prematurity, or haemodynamically significant congenital heart disease entering their first RSV season, who received nirsevimab (n=614) or palivizumab (n=304). The safety profile of nirsevimab in infants who received nirsevimab in their first RSV season was comparable to the palivizumab comparator and consistent with the safety profile of nirsevimab in term and preterm infants GA ≥29 weeks (D5290C00003 and MELODY).

Infants who remain vulnerable to severe RSV disease in their second season
Safety was evaluated in MEDLEY in 220 children with chronic lung disease of prematurity or haemodynamically significant congenital heart disease who received nirsevimab or palivizumab in their first RSV season and went on to receive nirsevimab entering their second RSV season (180 subjects received nirsevimab in both Season 1 and 2, 40 received palivizumab in Season 1 and nirsevimab in Season 2). The safety profile of nirsevimab in children who received nirsevimab in their second RSV season was consistent with the safety profile of nirsevimab in term and preterm infants GA ≥29 weeks (D5290C00003 and MELODY).

Safety was also evaluated in MUSIC, an open label, uncontrolled, single dose trial in 100 immunocompromised infants and children ≤24 months, who received nirsevimab in their first or second RSV season. This included subjects with at least one of the following conditions:

immunodeficiency (combined, antibody, or other etiology) (n=33); systemic high-dose corticosteroid therapy (n=29); organ or bone marrow transplantation (n=16); receiving immunosuppressive chemotherapy (n=20); other immunosuppressive therapy (n=15), and HIV infection (n=8). The safety profile of nirsevimab was consistent with that expected for a population of immunocompromised children and with the safety profile of nirsevimab in term and preterm infants GA ≥29 weeks (D5290C00003 and MELODY).

The safety profile of nirsevimab in children during their second RSV season was consistent with the safety profile of nirsevimab observed during their first RSV season.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immune sera and immunoglobulins, antiviral monoclonal antibodies, ATC code: J06BD08

Mechanism of action

Nirsevimab is a recombinant neutralising human IgG1κ long-acting monoclonal antibody to the prefusion conformation of the RSV F protein which has been modified with a triple amino acid substitution (YTE) in the Fc region to extend serum half-life. Nirsevimab binds to a highly conserved epitope in antigenic site Ø on the prefusion protein with dissociation constants K_D = 0.12 nM and K_D = 1.22 nM for RSV subtype A and B strains, respectively. Nirsevimab inhibits the essential membrane fusion step in the viral entry process, neutralising the virus and blocking cell-to-cell fusion.

Pharmacodynamic effects

Antiviral activity

The cell culture neutralisation activity of nirsevimab against RSV was measured in a dose-response model using cultured Hep-2 cells. Nirsevimab neutralised RSV A and RSV B isolates with median EC_{50} values of 3.2 ng/mL (range 0.48 to 15 ng/mL) and 2.9 ng/mL (range 0.3 to 59.7 ng/mL), respectively. The clinical RSV isolates (70 RSV A and 49 RSV B) were collected between 2003 and 2017 from subjects across the United States, Australia, Netherlands, Italy, China and Israel and encoded the most common RSV F sequence polymorphisms found among circulating strains.

Nirsevimab demonstrated *in vitro* binding to immobilised human FcγRs (FcγRI, FcγRIIA, FcγRIIB, and FcγRIII) and equivalent neutralising activity compared to parental monoclonal antibodies, IG7 and IG7-TM (Fc region modified to reduce FcR binding and effector function). In a cotton rat model of RSV infection, IG7 and IG7-TM exhibited comparable dose-dependent reduction in RSV

replication in the lungs and nasal turbinates, strongly suggesting that protection from RSV infection is dependent on nirsevimab neutralisation activity rather than Fc-mediated effector function.

Antiviral resistance

In cell culture

Escape variants were selected following three passages in cell culture of RSV A2 and B9320 strains in the presence of nirsevimab. Recombinant RSV A variants that showed reduced susceptibility to nirsevimab included those with identified substitutions N67I+N208Y (103-fold as compared to reference). Recombinant RSV B variants that showed reduced susceptibility to nirsevimab included those with identified substitutions N208D (>90,000-fold), N208S (>24,000-fold), K68N+N201S (>13,000-fold), or K68N+N208S (>90,000-fold). All resistance-associated substitutions identified among neutralisation escape variants were located in the nirsevimab binding site (amino acids 62-69 and 196-212) and were shown to reduce binding affinity to RSV F protein.

In clinical trials

In MELODY, MEDLEY and MUSIC, no subject with medically attended RSV lower respiratory tract infection (MA RSV LRTI) had an RSV isolate containing nirsevimab resistance-associated substitutions in any treatment group.

In D5290C00003 (subjects who received a single dose of 50 mg nirsevimab irrespective of weight at time of dosing), 2 of 40 subjects in the nirsevimab group with MA RSV LRTI had an RSV isolate containing nirsevimab resistance-associated substitutions. No subjects in the placebo group had an RSV isolate containing nirsevimab resistance-associated substitution. Recombinant RSV B variants harbouring the identified I64T+K68E+I206M+Q209R (>447.1-fold) or N208S (>386.6-fold) F protein sequence variations in the nirsevimab binding site conferred reduced susceptibility to nirsevimab neutralisation.

Nirsevimab retained activity against recombinant RSV harbouring palivizumab resistance-associated substitutions identified in molecular epidemiology studies and in neutralisation escape variants of palivizumab. It is possible that variants resistant to nirsevimab could have cross-resistance to other monoclonal antibodies targeting the F protein of RSV.

Immunogenicity

Anti-drug antibodies (ADA) were commonly detected.

The employed immunogenicity assay has limitations in detecting ADAs at early onset (prior to Day 361) in the presence of high concentrations of drug, therefore, the incidence of ADA might not have been conclusively determined. The impact on clearance of nirsevimab is uncertain. Subjects who were ADA positive at Day 361 had reduced nirsevimab concentrations at Day 361 compared to subjects who received nirsevimab and were ADA-negative.

The impact of ADA on the efficacy of nirsevimab has not been determined. No evidence of ADA impact on safety was observed.

Clinical efficacy

The efficacy and safety of nirsevimab were evaluated in two randomised, double-blind, placebo controlled multicentre trials (D5290C00003 [Phase IIb] and MELODY [Phase III]) for the prevention of MA RSV LRTI in term and preterm infants (GA ≥29 weeks) entering their first RSV season. Safety and pharmacokinetics of nirsevimab were also evaluated in a randomised, double-blind, palivizumab-controlled multicentre trial (MEDLEY [Phase II/III]) in infants GA <35 weeks at higher risk for severe RSV disease, including extremely preterm infants (GA <29 weeks) and infants with

chronic lung disease of prematurity, or haemodynamically significant congenital heart disease, entering their first RSV season and children with chronic lung disease of prematurity or haemodynamically significant congenital heart disease entering their second RSV season.
Safety and pharmacokinetics of nirsevimab were also evaluated in an open-label, uncontrolled, single dose multicentre trial (MUSIC [Phase II]) in immunocompromised infants and children ≤24 months of age.

Efficacy against MA RSV LRTI, MA RSV LRTI hospitalisation, and very severe MA RSV LRTI in term and preterm infants (D5290C00003 and MELODY)

D5290C00003 randomised a total of 1 453 very and moderately preterm infants (GA ≥29 to <35 weeks) entering their first RSV season (2:1) to receive a single intramuscular dose of 50 mg nirsevimab or placebo. At randomisation, 20.3% were GA ≥29 to <32 weeks; 79.7% were GA ≥32 to <35 weeks; 52.4% were male; 72.2% were White; 17.6% were of African origin; 1.0% were Asian; 59.5% weighed <5 kg (17.0% <2.5 kg); 17.3% of infants were ≤1.0 month of age, 35.9% were >1.0 to ≤3.0 months, 32.6% were >3.0 to ≤6.0 months, and 14.2% were >6.0 months.

MELODY (Primary cohort) randomised a total of 1 490 term and late preterm infants (GA ≥35 weeks) entering their first RSV season (2:1) to receive a single intramuscular dose of nirsevimab (50 mg nirsevimab if <5 kg weight or 100 mg nirsevimab if ≥5 kg weight at the time of dosing) or placebo. At randomisation, 14.0% were GA ≥35 to <37 weeks; 86.0% were GA ≥37 weeks; 51.6% were male; 53.5% were White; 28.4% were of African origin; 3.6% were Asian; 40.0% weighed <5 kg (2.5% <2.5 kg); 24.5% of infants were ≤1.0 month of age, 33.4% were >1.0 to ≤3.0 months, 32.1% were >3.0 to ≤6.0 months, and 10.0% were >6.0 months.

The trials excluded infants with a history of chronic lung disease of prematurity/bronchopulmonary dysplasia or haemodynamically significant congenital heart disease (except for infants with uncomplicated congenital heart disease). Demographic and baseline characteristics were comparable between the nirsevimab and placebo group in both trials.

The primary endpoint for D5290C00003 and MELODY (Primary cohort) was the incidence of medically attended lower respiratory tract infection (inclusive of hospitalisation) caused by RT-PCR-confirmed RSV (MA RSV LRTI), characterised predominantly as bronchiolitis or pneumonia, through 150 days after dosing. Signs of LRTI were defined by having one of the following findings at physical examination indicating lower respiratory tract involvement (e.g., rhonchi, rales, crackles, or wheeze); and at least one sign of clinical severity (increased respiratory rate, hypoxemia, acute hypoxic or ventilatory failure, new onset apnoea, nasal flaring, retractions, grunting, or dehydration due to respiratory distress). The secondary endpoint was the incidence of hospitalisation in infants with MA RSV LRTI. RSV hospitalisation was defined as hospitalisation for LRTI with a positive RSV test, or worsening of respiratory status and positive RSV test in an already hospitalised patient. Very severe MA RSV LRTI was also evaluated, defined as MA RSV LRTI with hospitalisation and requirement for supplemental oxygen or intravenous fluids.

The efficacy of nirsevimab in term and preterm infants (GA ≥29 weeks) entering their first RSV season against MA RSV LRTI, MA RSV LRTI with hospitalisation and very severe MA RSV LRTI are shown in Table 2.

Table 2: Efficacy in term and preterm infants against MA RSV LRTI, MA RSV LRTI with hospitalisation and very severe MA RSV LRTI through 150 days post dose, D5290C00003 and MELODY (Primary cohort)

Group	Treatment	N	Incidence % (n)	Efficacy[a] (95% CI)
Efficacy in infants against MA RSV LRTI through 150 days post dose				
Very and moderately preterm GA ≥29 to <35 weeks (D5290C00003)[b]	Nirsevimab	969	2.6 (25)	70.1% (52.3, 81.2)[c]
	Placebo	484	9.5 (46)	
Term and late preterm GA ≥35 weeks (MELODY Primary cohort)	Nirsevimab	994	1.2 (12)	74.5% (49.6, 87.1)[c]
	Placebo	496	5.0 (25)	
Efficacy in infants against MA RSV LRTI with hospitalisation through 150 days post dose				
Very and moderately preterm GA ≥29 to <35 weeks (D5290C00003)[b]	Nirsevimab	969	0.8 (8)	78.4% (51.9, 90.3)[c]
	Placebo	484	4.1 (20)	
Term and late preterm GA ≥35 weeks (MELODY Primary cohort)	Nirsevimab	994	0.6 (6)	62.1% (-8.6, 86.8)
	Placebo	496	1.6 (8)	
Efficacy in infants against very severe MA RSV LRTI through 150 days post dose				
Very and moderately preterm GA ≥29 to <35 weeks (D5290C00003)[b]	Nirsevimab	969	0.4 (4)	87.5% (62.9, 95.8)[d]
	Placebo	484	3.3 (16)	
Term and late preterm GA ≥35 weeks (MELODY Primary cohort)	Nirsevimab	994	0.5 (5)	64.2% (-12.1, 88.6)[d]
	Placebo	496	1.4 (7)	

[a] Based on relative risk reduction versus placebo.

[b] All subjects who received 50 mg irrespective of weight at the time of dosing.

[c] Prespecified multiplicity controlled; p-value =<0.001.

[d] Not multiplicity controlled.

Subgroup analyses of the primary efficacy endpoint by gestational age, gender, race and region showed results were consistent with the overall population.

The severity of breakthrough cases of subjects hospitalised for MA RSV LRTI was assessed. The percentage of subjects who required supplementary oxygen was 44.4% (4/9) vs. 81.0% (17/21), subjects who required continuous positive airway pressure [CPAP]/high flow nasal cannula [HFNC] was 11.1% (1/9) vs. 23.8% (5/21), and 0% (0/9) vs. 28.6% (6/21) subjects were admitted to intensive care unit, for nirsevimab vs. placebo, respectively.

MELODY continued to enrol infants following the primary analysis, and overall, 3 012 infants were randomised to receive Beyfortus (n=2 009) or placebo (n=1 003). Efficacy of nirsevimab against MA RSV LRTI, MA RSV LRTI with hospitalisation, and very severe MA RSV LRTI through 150 days post dose was a relative risk reduction of 76.4% (95% CI 62.3, 85.2), 76.8% (95% CI 49.4, 89.4) and 78.6% (95% CI 48.8, 91.0), respectively.

The rates of MA RSV LRTI events in the second season (day 361 to day 510 post-dose) were similar in both treatment groups [19 (1.0%) nirsevimab recipients and 10 (1.0%) placebo recipients].

Efficacy against MA RSV LRTI in infants at higher risk and children who remain vulnerable to severe RSV disease in their second season (MEDLEY and MUSIC)

MEDLEY randomised a total of 925 infants at higher risk for severe RSV disease including infants with chronic lung disease of prematurity or haemodynamically significant congenital heart disease and preterm infants GA <35 weeks, entering their first RSV season. Infants received a single intramuscular

dose (2:1) of nirsevimab (50 mg nirsevimab if <5 kg weight or 100 mg nirsevimab if ≥5 kg weight at the time of dosing), followed by 4 once-monthly intramuscular doses of placebo, or 5 once-monthly intramuscular doses of 15 mg/kg palivizumab. At randomisation, 21.6% were GA <29 weeks; 21.5% were GA≥29 to <32 weeks; 41.9% were GA ≥32 to <35 weeks; 14.9% were GA ≥35 weeks. Of these infants 23.5% had chronic lung disease of prematurity; 11.2% had haemodynamically significant congenital heart disease; 53.5% were male; 79.2% were White; 9.5% were of African origin; 5.4% were Asian; 56.5% weighed <5 kg (9.7% were <2.5 kg); 11.4% of infants were ≤1.0 month of age, 33.8% were >1.0 to ≤3.0 months 33.6% were >3.0 months to ≤6.0 months, and 21.2% were >6.0 months.

Children at higher risk of severe RSV disease with chronic lung disease of prematurity or haemodynamically significant congenital heart disease ≤24 months of age who remain vulnerable continued in the trial for a second RSV season. Subjects who received nirsevimab during their first RSV season received a second single dose of 200 mg nirsevimab entering their second RSV season (n=180) followed by 4 once-monthly intramuscular doses of placebo. Subjects who received palivizumab during their first RSV season were re-randomised 1:1 to either the nirsevimab or the palivizumab group entering their second RSV season. Subjects in the nirsevimab group (n=40) received a single fixed dose of 200 mg followed by 4 once-monthly intramuscular doses of placebo. Subjects in the palivizumab group (n=42) received 5 once-monthly intramuscular doses of 15 mg/kg palivizumab. Of these children 72.1% had chronic lung disease of prematurity, 30.9% had haemodynamically significant congenital heart disease; 57.6% were male; 85.9% were White; 4.6% were of African origin; 5.7% were Asian; and 2.3% weighed <7 kg. Demographic and baseline characteristics were comparable between the nirsevimab/nirsevimab, palivizumab/nirsevimab and palivizumab/palivizumab groups.

The efficacy of nirsevimab in infants at higher risk for severe RSV disease, including extremely preterm infants (GA <29 weeks) entering their first RSV season and children with chronic lung disease of prematurity or haemodynamically significant congenital heart disease ≤24 months of age entering their first or second RSV season, is established by extrapolation from the efficacy of nirsevimab in D5290C00003 and MELODY (Primary cohort) based on pharmacokinetic exposure (see section 5.2). In MEDLEY, the incidence of MA RSV LRTI through 150 days post dose was 0.6% (4/616) in the nirsevimab group and 1.0% (3/309) in the palivizumab group in the first RSV season. There were no cases of MA RSV LRTI through 150 days post dose in the second RSV season.

In MUSIC, the efficacy in 100 immunocompromised infants and children ≤24 months who received the recommended dose of nirsevimab is established by extrapolation from the efficacy of nirsevimab in D5290C00003 and MELODY (Primary cohort) based on pharmacokinetic exposure (see section 5.2). There were no cases of MA RSV LRTI through 150 days post dose.

Duration of protection

Based on clinical and pharmacokinetic data, the duration of protection afforded by nirsevimab is at least 5 months.

5.2 Pharmacokinetic properties

The pharmacokinetic properties of nirsevimab are based on data from individual studies and population pharmacokinetic analyses. The pharmacokinetics of nirsevimab were dose-proportional in children and adults following administration of clinically relevant intramuscular doses over a dose range of 25 mg to 300 mg.

Absorption

Following intramuscular administration, the maximum concentration was reached within 6 days (range 1 to 28 days) and the estimated absolute bioavailability was 84%.

Distribution

The estimated central and peripheral volume of distribution of nirsevimab were 216 mL and 261 mL, respectively, for an infant weighing 5 kg. The volume of distribution increases with increasing body weight.

Biotransformation

Nirsevimab is a human IgG1κ monoclonal antibody that is degraded by proteolytic enzymes widely distributed in the body and not metabolised by hepatic enzymes.

Elimination

As a typical monoclonal antibody, nirsevimab is eliminated by intracellular catabolism and there is no evidence of target-mediated clearance at the doses tested clinically.

The estimated clearance of nirsevimab was 3.42 mL/day for an infant weighing 5 kg and the terminal half-life was approximately 71 days. Nirsevimab clearance increases with increasing body weight.

Special populations

Race

There was no clinically relevant effect of race.

Renal impairment

As a typical IgG monoclonal antibody, nirsevimab is not cleared renally due to its large molecular weight, change in renal function is not expected to influence nirsevimab clearance. However, in one individual with nephrotic syndrome, an increased clearance of nirsevimab was observed in clinical trials.

Hepatic impairment

IgG monoclonal antibodies are not primarily cleared via the hepatic pathway. However, in some individuals with chronic liver disease which may be associated with protein loss, an increased clearance of nirsevimab was observed in clinical trials.

Infants at higher risk and children who remain vulnerable to severe RSV disease in their second season

There was no significant influence of chronic lung disease of prematurity or haemodynamically significant congenital heart disease on the pharmacokinetics of nirsevimab. Serum concentrations at day 151 in MEDLEY were comparable to those in MELODY.

In children with chronic lung disease of prematurity or haemodynamically significant congenital heart disease (MEDLEY) and those that are immunocompromised (MUSIC), receiving a 200 mg intramuscular dose of nirsevimab in their second season, nirsevimab serum exposures were slightly higher with substantial overlap compared to those in MELODY (see Table 3).

Table 3: Nirsevimab intramuscular dose exposures, mean (standard deviation) [range], derived based on individual population pharmacokinetic parameters

Study/Season	N (AUC)	$AUC_{0\text{-}365}$ mg*day/mL	$AUC_{baseline\ CL}$ mg*day/mL	N (Day 151 serum conc)	Day 151 serum conc µg/mL

MELODY (Primary cohort)	954	12.2 (3.5) [3.3-24.9]	21.3 (6.5) [5.2-48.7]	636	26.6 (11.1) [2.1-76.6]
MEDLEY/Season 1	591	12.3 (3.3) [4.1-23.4]	22.6 (6.2) [7-43.8]	457	27.8 (11.1) [2.1-66.2]
MEDLEY/Season 2	189	21.5 (5.5) [7.5-41.9]	23.6 (7.8) [8.2-56.4]	163	55.6 (22.8) [11.2-189.3]
MUSIC/Season 1	46	11.2 (4.3) [1.2-24.6]	16.7 (7.3) [3.1-43.4]	37	25.6 (13.4) [5.1-67.4]
MUSIC/Season 2	50	16 (6.3) [2.2-25.5]	21 (8.4) [5.6-35.5]	42	33.2 (19.3) [0.9-68.5]

AUC_{0-365}= area under the concentration time curve from 0-365 days post dose, $AUC_{baseline\ CL}$ = area under the serum concentration-time curve derived from post hoc clearance values at dosing, Day 151 serum conc = concentration at day 151, visit day 151 ± 14 days.

Pharmacokinetic/pharmacodynamic relationship(s)

In D5290C00003 and MELODY (Primary cohort) a positive correlation was observed between a serum AUC (Area Under the Curve), based on clearance at baseline, above 12.8 mg*day/mL and a lower incidence of MA RSV LRTI. The recommended dosing regimen consisting of a 50 mg or 100 mg intramuscular dose for infants in their first RSV season and a 200 mg intramuscular dose for children entering their second RSV season was selected on the basis of these results.

In MEDLEY, >80% of infants at higher risk for severe RSV disease, including infants born extremely preterm (GA <29 weeks) entering their first RSV season and infants/children with chronic lung disease of prematurity or haemodynamically significant congenital heart disease entering their first or second RSV season, achieved nirsevimab exposures associated with RSV protection (serum AUC above 12.8 mg*day/mL) following a single dose (see section 5.1).

In MUSIC, 75% (72/96) of immunocompromised infants/children entering their first or second RSV season achieved nirsevimab exposures associated with RSV protection. When excluding 14 children with increased clearance of nirsevimab, 87% (71/82) achieved nirsevimab exposures associated with RSV protection.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, repeated dose toxicity and tissue cross-reactivity studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

L-histidine
L-histidine hydrochloride
L-arginine hydrochloride
Sucrose
Polysorbate 80 (E433)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

3 years

Beyfortus may be kept at room temperature (20°C - 25°C) when protected from light for a maximum of 8 hours. After this time, the syringe must be discarded.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).
Do not freeze.
Do not shake or expose to direct heat.

Keep the pre-filled syringe in the outer carton in order to protect from light.

For storage conditions of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Siliconised Luer lock Type I glass pre-filled syringe with a FluroTec-coated plunger stopper.

Each pre-filled syringe contains 0.5 mL or 1 mL solution.

Pack sizes:

- 1 or 5 pre-filled syringe(s) without needles.
- 1 pre-filled syringe packaged with two separate needles of different sizes.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

This medicinal product should be administered by a trained healthcare professional using aseptic techniques to ensure sterility.

Visually inspect the medicinal product for particulate matter and discolouration prior to administration. The medicinal product is a clear to opalescent, colourless to yellow solution. Do not inject if the liquid is cloudy, discoloured, or it contains large particles or foreign particulate matter.

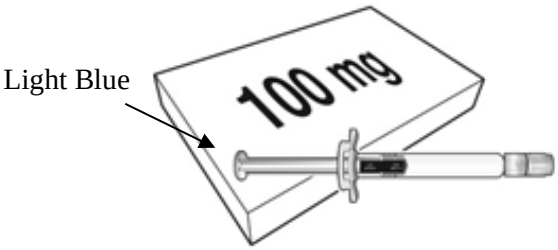
Do not use if the pre-filled syringe has been dropped or damaged or the security seal on the carton has been broken.

Instructions for administration

Beyfortus is available in a 50 mg and a 100 mg pre-filled syringe. Check the labels on the carton and pre-filled syringe to make sure you have selected the correct 50 mg or 100 mg presentation as required.

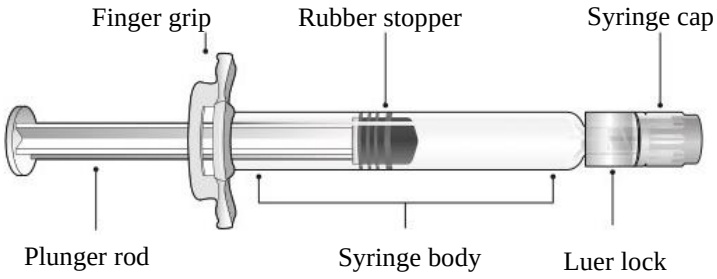
Beyfortus 50 mg (50 mg/0.5 mL) pre-filled syringe with a purple plunger rod.

Beyfortus 100 mg (100 mg/1 mL) pre-filled syringe with a light blue plunger rod.



Refer to Figure 1 for pre-filled syringe components.

Figure 1: Luer lock syringe components



Step 1: Holding the Luer lock in one hand (avoid holding the plunger rod or syringe body), unscrew the syringe cap by twisting it counter clockwise with the other hand.

Step 2: 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.

Step 3: 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 or 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.

Step 4: Administer the entire contents of the pre-filled syringe as an intramuscular injection, preferably in the anterolateral aspect of the thigh. The gluteal muscle should not be used routinely as an injection site because of the risk of damage to the sciatic nerve.

Step 5: Dispose of the used syringe immediately, together with the needle, in a sharps disposal container or in accordance with local requirements.

If two injections are required, repeat steps 1-5 in a different injection site.

<u>Disposal</u>

Each pre-filled syringe is for single-use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Sanofi Winthrop Industrie
82 avenue Raspail
94250 Gentilly
France

8. MARKETING AUTHORISATION NUMBER

EU/1/22/1689/001	50 mg, 1 single-use pre-filled syringe
EU/1/22/1689/002	50 mg, 1 single-use pre-filled syringe with needles
EU/1/22/1689/003	50 mg, 5 single-use pre-filled syringe
EU/1/22/1689/004	100 mg, 1 single-use pre-filled syringe
EU/1/22/1689/005	100 mg, 1 single-use pre-filled syringe with needles
EU/1/22/1689/006	100 mg, 5 single-use pre-filled syringe

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 31 October 2022

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

AstraZeneca Pharmaceuticals LP Frederick Manufacturing Center (FMC)
633 Research Court
Frederick, Maryland
21703
United States

Name and address of the manufacturer responsible for batch release

AstraZeneca AB
Gärtunavägen
SE-152 57 Södertälje
Sweden

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON PACK OF 1 OR 5 PRE-FILLED SYRINGES; WITH OR WITHOUT NEEDLES

1. NAME OF THE MEDICINAL PRODUCT

Beyfortus 50 mg solution for injection in pre-filled syringe
nirsevimab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 50 mg of nirsevimab in 0.5 mL (100 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: L-histidine, L-histidine hydrochloride, L-arginine hydrochloride, sucrose, polysorbate 80 (E433), water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe
1 pre-filled syringe with 2 needles
5 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze, shake or expose to direct heat.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Sanofi Winthrop Industrie
82 avenue Raspail
94250 Gentilly
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1689/001	1 pre-filled syringe without needles
EU/1/22/1689/002	1 pre-filled syringe with 2 needles
EU/1/22/1689/003	5 pre-filled syringes without needles

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Beyfortus 50 mg injection
nirsevimab
IM

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 mL

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON PACK OF 1 OR 5 PRE-FILLED SYRINGES; WITH OR WITHOUT NEEDLES

1. NAME OF THE MEDICINAL PRODUCT

Beyfortus 100 mg solution for injection in pre-filled syringe
nirsevimab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 100 mg of nirsevimab in 1 mL (100 mg/mL).

3. LIST OF EXCIPIENTS

Excipients: L-histidine, L-histidine hydrochloride, L-arginine hydrochloride, sucrose, polysorbate 80 (E433), water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe
1 pre-filled syringe with 2 needles
5 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze, shake or expose to direct heat.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Sanofi Winthrop Industrie
82 avenue Raspail
94250 Gentilly
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1689/004	1 pre-filled syringe without needles
EU/1/22/1689/005	1 pre-filled syringe with 2 needles
EU/1/22/1689/006	5 pre-filled syringes without needles

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Beyfortus 100 mg injection
nirsevimab
IM

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 mL

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Beyfortus 50 mg solution for injection in pre-filled syringe
Beyfortus 100 mg solution for injection in pre-filled syringe
nirsevimab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects your child may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before your child is given this medicine because it contains important information for you and your child.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If your child gets any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Beyfortus is and what it is used for

What Beyfortus is
Beyfortus is a medicine given as an injection to protect babies and children less than 2 years of age against *respiratory syncytial virus* (RSV). RSV is a common respiratory virus that usually causes mild symptoms comparable to the common cold. However, especially in babies, vulnerable children and older adults, RSV can cause severe illness, including bronchiolitis (inflammation of the small airways in the lung) and pneumonia (infection of the lungs) that may lead to hospitalisation or even death. The virus is usually more common during the winter.

Beyfortus contains the active ingredient nirsevimab which is an antibody (a protein designed to attach to a specific target) that attaches to a protein that RSV needs to infect the body. By attaching to this protein, Beyfortus blocks its action, thereby stopping the virus from entering and infecting human cells.

What Beyfortus is used for
Beyfortus is a medicine to protect your child from getting RSV disease.

2. What you need to know before your child is given Beyfortus

Your child should not use Beyfortus if he or she is allergic to nirsevimab or any of the other ingredients of this medicine (listed in section 6).
Inform your child's doctor, pharmacist or nurse if this applies to your child. If you are not sure**,** check with your child's doctor, pharmacist or nurse before the medicine is given.
If your child shows signs of a severe allergic reaction contact the doctor immediately.

Warnings and precautions
Tell your doctor or seek medical help immediately if you notice any signs of an **allergic reaction**, such as:

- difficulty breathing or swallowing
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps

Talk to your healthcare professional before your child is given Beyfortus if they have low numbers of blood platelets (which help blood clotting), a bleeding problem or bruise easily or if they are taking an anticoagulant (a medicine to prevent blood clots).

In certain chronic health conditions, where too much protein is lost via the urine or the gut, for example nephrotic syndrome and chronic liver disease, the level of protection of Beyfortus may be reduced.

Beyfortus contains 0.1 mg of polysorbate 80 in each 50 mg (0.5 mL) dose and 0.2 mg in each 100 mg (1 mL) dose. Polysorbates may cause allergic reactions. Tell your doctor if your child has any known allergies.

Children and adolescents
Do not give this medicine to children between the age of 2 and 18 years of age because it has not been studied in this group.

Other medicines and Beyfortus
Beyfortus is not known to interact with other medicines. However, tell your doctor, pharmacist or nurse if your child is taking, has recently taken or might take any other medicines.

Beyfortus may be given at the same time as vaccines that are part of the national immunisation program.

3. How and when Beyfortus is given

Beyfortus is given by a healthcare professional as an injection in the muscle. It is usually given in the outer part of the thigh.

The recommended dose is:
- 50 mg for children weighing less than 5 kg and 100 mg for children weighing 5 kg or more in their first RSV season.
- 200 mg for children who remain vulnerable to severe RSV disease in their second RSV season (given as 2 x 100 mg injections at separate sites).

Beyfortus should be given before the RSV season. The virus is usually more common during the winter (known as the RSV season). If your child is born during the winter, Beyfortus should be given after birth.

If your child is to have a heart operation (cardiac surgery), he or she may be given an extra dose of Beyfortus after the operation to ensure they have adequate protection over the remainder of the RSV season.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Side effects can include:

Uncommon (may affect up to 1 in 100 children)
- rash
- injection site reaction (i.e. redness, swelling, and pain where the injection is given)
- fever

Not known (cannot be estimated from available data)
- allergic reactions

Reporting of side effects
If your child gets any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Beyfortus

Your doctor, pharmacist or nurse is responsible for storing this medicine and disposing of any unused product correctly. The following information is intended for healthcare professionals.

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C). After removal from the refrigerator, Beyfortus must be protected from light and used within 8 hours or discarded.

Keep the pre-filled syringe in the outer carton in order to protect from light.

Do not freeze, shake or expose to direct heat.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

6. Contents of the pack and other information

What Beyfortus contains
- The active substance is nirsevimab.
  - One pre-filled syringe of 0.5 mL solution contains 50 mg nirsevimab.
  - One pre-filled syringe of 1 mL solution contains 100 mg nirsevimab.

- The other ingredients are L-histidine, L-histidine hydrochloride, L-arginine hydrochloride, sucrose, polysorbate 80 (E433), and water for injections.

What Beyfortus looks like and contents of the pack
Beyfortus is a colourless to yellow solution for injection.

Beyfortus is available as:
- 1 or 5 pre-filled syringe(s) without needles.
- 1 pre-filled syringe packaged with two separate needles of different sizes.

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Sanofi Winthrop Industrie

82 avenue Raspail
94250 Gentilly
France

Manufacturer
AstraZeneca AB
Gärtunavägen
SE-152 57 Södertälje
Sweden

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

The following information is intended for healthcare professionals only:

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Visually inspect Beyfortus for particulate matter and discolouration prior to administration. Beyfortus is a clear to opalescent, colourless to yellow solution. Do not inject Beyfortus if the liquid is cloudy, discoloured, or it contains large particles or foreign particulate matter.

Do not use if the Beyfortus pre-filled syringe has been dropped or damaged or the security seal on the carton has been broken.

Administer the entire contents of the pre-filled syringe as an intramuscular injection, preferably in the anterolateral aspect of the thigh. The gluteal muscle should not be used routinely as an injection site because of the risk of damage to the sciatic nerve.