ABRYSVO™

Respiratory Syncytial Virus Stabilized Prefusion F Subunit Vaccine

Lyophilized Powder for Solution, 120 mcg RSV stabilized prefusion F protein per 0.5 mL,

Reconstituted Solution for Intramuscular Injection

Active Immunizing Agent

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

ABRYSVO (Respiratory Syncytial Virus Stabilized Prefusion F Subunit Vaccine) is a bivalent vaccine indicated for:

- Active immunization of pregnant individuals from 32 through 36 weeks gestational age for the prevention of lower respiratory tract disease (LRTD) and severe LRTD caused by respiratory syncytial virus (RSV) in infants from birth through 6 months of age.

- the prevention of lower respiratory tract disease caused by RSV in individuals 60 years of age and older by active immunization.

1.1 Pediatrics

The safety and efficacy of Abrysvo in individuals younger than 18 years of age have not been established. Limited data are available in pregnant adolescents and their infants.

1.2 Geriatrics

Clinical studies include participants 65 years of age and older and their data contribute to the overall assessment of safety and efficacy of Abrysvo (see **8 ADVERSE REACTIONS** and **14 CLINICAL TRIALS**).

2 CONTRAINDICATIONS

Abrysvo is contraindicated in individuals who are hypersensitive to the active substance or to any component of the vaccine. For a complete listing, see **6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.**

4 DOSAGE AND ADMINISTRATION

4.2 Recommended Dose and Dosage Adjustment

Pregnant individuals

Abrysvo is administered intramuscularly as a single dose (0.5 mL) in the third trimester of pregnancy (from 32 through 36 weeks gestation).

Individuals 60 years of age and older

Abrysvo is administered intramuscularly as a single dose (0.5 mL).

4.3 Reconstitution

Parenteral Products:

To form Abrysvo, the lyophilized vaccine must be reconstituted using the vial adapter and only with the diluent provided.

Table 1 - Reconstitution

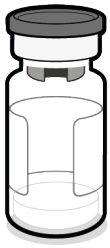
Vial Size	Volume of Diluent to be Added to Vial	Approximate Available Volume[1]	Concentration per mL[2]
2 mL	0.65 mL	0.68 mL	120 mcg per 0.5 mL

[1] Total volume in vial after reconstitution with 0.65 mL Sterile Water diluent

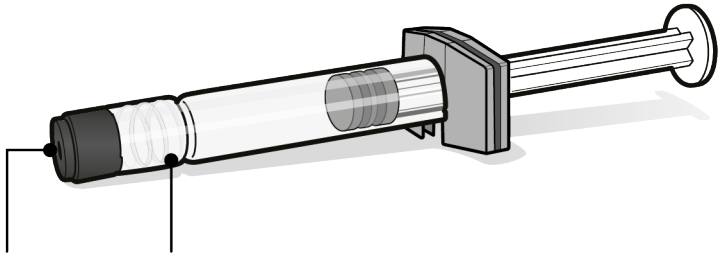
[2] Label Claim Volume of Total RSV Antigen Dose

Preparation for administration

Vial containing lyophilized RSVpreF vaccine



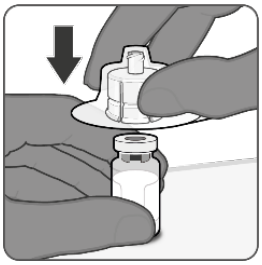
Syringe containing diluent



Vial adapter

Syringe cap **Luer lock adapter**

To form Abrysvo, reconstitute the Lyophilized Antigen Component with the accompanying Sterile Water Diluent Component as described in the panels below.

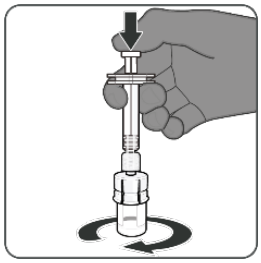


Step 1. Attach vial adapter

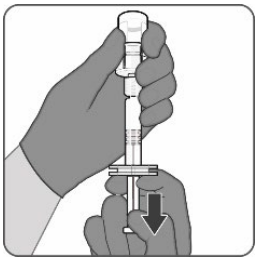
- Peel off the top cover from the vial adapter packaging and remove the flip off cap from the vial.
- While keeping the vial adapter in its packaging, centre over the vial's stopper and connect with a straight downward push. Do not push the vial adapter in at an angle as it may result in leaking. Remove the packaging.

Step 2. Reconstitute lyophilized vaccine component to form Abrysvo

- For all syringe assembly steps, hold the syringe only by the Luer lock adapter. This will prevent the Luer lock adapter from detaching during use.



- Twist to remove the syringe cap, then twist to connect the syringe to the vial adapter. Stop turning when you feel resistance.
- Inject the entire contents of the syringe into the vial. Hold the plunger rod down and gently swirl the vial until the powder is completely dissolved (less than 1 minute). Do not shake.



Step 3. Withdraw reconstituted vaccine

- Invert the vial completely and slowly withdraw the entire contents into the syringe to ensure a 0.5 mL dose of Abrysvo.
- Twist to disconnect the syringe from the vial adapter.
- Attach a sterile needle suitable for intramuscular injection.

4.4 Administration

For intramuscular use only. Do not administer Abrysvo intravascularly, intradermally or subcutaneously.

Each 0.5 mL dose is to be injected intramuscularly, into the deltoid muscle, with care to avoid injection into or near nerves and blood vessels.

Different injectable vaccines should always be given at different vaccination sites.

Do not mix Abrysvo with any other vaccines or products in the same syringe.

5 OVERDOSAGE

In the event of an overdose, the individual should be monitored and provided with symptomatic treatment as appropriate.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of vaccines for patient immunization record-keeping as well as safety monitoring, health professionals should record the time and date of administration, quantity of administered dose (if applicable), anatomical site and route of administration, brand name and generic name of the vaccine, the product lot number and expiry date.

Abrysvo is a sterile solution for injection supplied as a single dose vial of lyophilized powder containing 120 micrograms (mcg) of RSV stabilized prefusion F protein (60 mcg Subgroup A and 60 mcg Subgroup B antigens) that is reconstituted with sterile water (diluent) provided in a prefilled syringe.

A single dose after reconstitution is 0.5 mL.

Abrysvo is available in:

- a carton containing 1 vial of powder, 1 pre-filled syringe of diluent and 1 vial adapter;
- a carton containing 5 vials of powder, 5 pre-filled syringes of diluent and 5 vial adapters;
- a carton containing 10 vials of powder, 10 pre-filled syringes of diluent and 10 vial adapters.

The vial stopper, the tip cap and plunger stopper of the pre-filled syringe are not made with natural rubber latex.

Table 2 - Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form/ Strength/Composition	Non-medicinal Ingredients
Intramuscular	Lyophilized Powder for Solution (0.5 mL, single dose) 120 mcg of total lyophilized RSV stabilized prefusion F protein	Powder: Mannitol, polysorbate 80, sodium chloride, sucrose, tromethamine, trometamol hydrochloride. Diluent: Sterile Water for injection

Each 0.5 mL dose of the reconstituted Abrysvo includes the following ingredients: 60 mcg of each stabilized RSV prefusion F antigens (A and B), 22.5 mg mannitol, 0.08 mg polysorbate 80, 1.1 mg sodium chloride, 11.3 mg sucrose, 0.11 mg tromethamine, 1.04 mg trometamol hydrochloride, and sterile water as the diluent.

7 WARNINGS AND PRECAUTIONS

General

As with all injectable vaccines, appropriate medical treatment and supervision must always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

Syncope (fainting) may occur in association with administration of injectable vaccines, including Abrysvo. Procedures should be in place to avoid injury from fainting.

As with other vaccines, the administration of Abrysvo may not protect all vaccine recipients.

Concurrent illness

Vaccination with Abrysvo should be postponed in individuals suffering from an acute febrile illness. However, the presence of a minor infection, such as a cold, should not result in the deferral of vaccination.

Driving and Operating Machinery

Abrysvo is unlikely to affect your ability to drive or use machines.

Hematologic

As with other vaccines administered intramuscularly, Abrysvo must be administered with caution to individuals with thrombocytopenia or a coagulation disorder since bleeding may occur following an intramuscular administration.

Hypersensitivity and Anaphylaxis

Medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of Abrysvo (see **2 CONTRAINDICATIONS**).

Immune

Immunocompromised individuals, including those receiving immunosuppressive therapy, may have a diminished immune response to Abrysvo.

Reproductive Health: Female and Male Potential

No human data on the effect of Abrysvo on fertility are available. Animal studies do not indicate direct or indirect harmful effects with respect to female fertility (see **16 NON-CLINICAL TOXICOLOGY**).

7.1 Special Populations

7.1.1 Pregnant Women

Abrysvo has been studied in pregnant individuals from 24 weeks through 36 weeks of gestation.

7.1.2 Breast-feeding

There are no data on the excretion of Abrysvo in human or animal milk.

7.1.3 Pediatrics

The safety and efficacy of Abrysvo in non-pregnant individuals younger than 18 years of age have not been established.

7.1.4 Geriatrics

Abrysvo has been studied in the geriatric population (see **14 CLINICAL TRIALS**).

7.1.5 Immunocompromised individuals

There are no data on the use of Abrysvo in immunocompromised individuals. Immunocompromised individuals, including individuals receiving immunosuppressant therapy, may have a diminished immune response to Abrysvo.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The safety profile of Abrysvo presented below for pregnant individuals ≤49 years of age is based on data generated after a second interim efficacy analysis, a primary safety analysis of the ongoing pivotal Phase III randomized, placebo-controlled, double-blind, multicentre clinical trial (C3671008, NCT04424316) was performed. The trial was conducted in the Northern Hemisphere (United States, Japan, Taiwan, Spain, Gambia, Netherlands, Finland, Mexico, Philippines, Denmark, Canada, and South Korea) and Southern Hemisphere (South Africa, Argentina, Chile, New Zealand, Brazil, and Australia) involving 7,357 maternal participants who received Abrysvo (n = 3,682) or placebo (n = 3,675) and their corresponding 7,126 infant participants passively exposed to maternal antibodies following vaccination with Abrysvo (n = 3,568) or placebo (n = 3,558). Maternal participants were followed for 6 months postpartum; the infant participants in the first year of the study were planned to be followed for up to 24 months while those in the second year of the study were planned to be followed for up to 12 months.

Supportive safety data were generated from the Phase IIb randomized, placebo-controlled, observer-blind multicentre clinical trial (C3671003, NCT04032093) conducted in the Northern Hemisphere (United States) and Southern Hemisphere (Argentina, Chile and South Africa) involving 232 maternal participants who received Abrysvo (n = 115) or placebo (n = 117) and their corresponding 230 infant participants passively exposed to maternal antibodies following vaccination with Abrysvo (n = 114) or placebo (n = 116). Maternal and infant participants were followed for up to 12 months postpartum.

The safety profile for Abrysvo presented below for adult participants 60 years of age and older is based on data generated from interim safety analysis of the ongoing pivotal Phase III randomized, placebo-controlled, double-blind, muticentre clinical trial (C3671013, NCT05035212) conducted in the Northern Hemisphere (United States, Japan, Netherlands, Canada and Finland) and Southern Hemisphere

(Argentina and South Africa) involving 34,284 adult participants who received Abrysvo (n = 17,215) or placebo (n = 17,069). Study participants were planned to be followed for up to 25 months.

The following adverse reactions have been identified from Studies C3671008 and C3671013.

Adverse reactions are listed according to the following frequency categories: 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).

Adverse reactions reported are listed, in **Table 3**, per system organ class, in decreasing order of seriousness.

Table 3 - Adverse reactions following administration of Abrysvo

	Adverse Drug Reactions Study C3671008 Pregnant individuals ≤49 years N=3,682	**Adverse Drug Reactions Study C3671013 Individuals ≥60 years N=17,215**
Immune system disorders		
Hypersensitivity	---	Very rare
Nervous system disorders		
Headache	Very common	---
Musculoskeletal and connective tissue disorders		
Myalgia	Very common	---
General disorders and administration site conditions		
Vaccination site pain	Very common	Very common
Vaccination site redness	Common	Common
Vaccination site swelling	Common	Common

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials, therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

Infants from birth through 6 months of age by active immunization of pregnant individuals

Of the maternal participants in the pivotal Study C3671008, 65% were White, 20% were Black or African American, 13% were Asian, and 29% were Hispanic/Latino. The median maternal age at the time of study vaccination was 29 years (range 14 to 47 years). The median gestational age at vaccination was 31 weeks and 2 days (range 24-36.9 weeks).

The median infant gestational age at birth was 39 weeks and 1 day (range 27 weeks and 3 days to 44 weeks and 2 days).

Among maternal participants, the most frequently reported adverse reactions in Study C3671008 were vaccination site pain, fatigue, headache and myalgia.

Solicited Adverse Reactions

Maternal Participants

In Study C3671008, all maternal participants were monitored for solicited local and systemic adverse reactions using e-diary during the 7 days following administration of Abrysvo or placebo. Solicited local and systemic reactions reported within 7 days after vaccination in Study C3671008 are presented in **Tables 4** and **5**.

The majority of solicited local and systemic reactions in maternal participants were mild to moderate in severity and resolved within 2-3 days of onset.

Table 4: Percentage of Maternal Participants with Solicited Local Adverse Reactions within 7 Days after Vaccination – Safety Population (Study C3671008)[a]

Local Reactions	**ABRYSVO N=3,663[b] n (%)**	**PLACEBO N=3,639[b] n (%)**
Injection site pain[c]		
Any[d]	1488 (40.6)	369 (10.1)
Mild	1321 (36.1)	337 (9.3)
Moderate	163 (4.4)	32 (0.9)
Severe	4 (0.1)	0 (0)
Redness[e]		
Any[d]	264 (7.2)	8 (0.2)
Mild	182 (5.0)	4 (0.1)
Moderate	77 (2.1)	4 (0.1)
Severe	5 (0.1)	0 (0)
Swelling[e]		
Any[d]	227 (6.2)	8 (0.2)
Mild	150 (4.1)	5 (0.1)
Moderate	74 (2.0)	3 (<0.1)
Severe	3 (<0.1)	0 (0)

[a] NCT04424316 (C3671008)

[b] N = number of participants who provided e-diary data for a specific reaction after vaccination.

[c] Mild: does not interfere with activity; moderate: interferes with activity; severe: prevents daily activity.

[d] Any includes all participants who reported a reaction as mild, moderate, or severe during Day 1 to Day 7 after vaccination.

[e] Mild: >2 cm to 5 cm; moderate: >5 cm to 10 cm; severe: >10 cm.

Table 5: Percentage of Maternal Participants with Solicited Systemic Adverse Reactions within 7 Days after Vaccination – Safety Population (Study C3671008)[a]

Systemic Reactions	ABRYSVO N=3,663[b] n (%)	PLACEBO N=3,638-3,639[b] n (%)
Fever (≥38.0°C)		
≥38.0°C	94 (2.6)	107 (2.9)
≥38.0°C to 38.4°C	61 (1.7)	55 (1.5)
>38.5°C to 38.9°C	29 (0.8)	42 (1.2)
>39.0°C to 40.0°C	1 (<0.1)	5 (0.1)
>40.0°C	3 (<0.1)	5 (0.1)
Fatigue[c]		
Any[d]	1688 (46.1)	1594 (43.8)
Mild	856 (23.4)	828 (22.8)
Moderate	783 (21.4)	714 (19.6)
Severe	49 (1.3)	52 (1.4)
Headache[c]		
Any[d]	1134 (31.0)	1004 (27.6)
Mild	739 (20.2)	651 (17.9)
Moderate	380 (10.4)	340 (9.3)
Severe	15 (0.4)	13 (0.4)
Muscle pain[c]		
Any[d]	972 (26.5)	623 (17.1)
Mild	644 (17.6)	363 (10.0)
Moderate	314 (8.6)	248 (6.8)
Severe	14 (0.4)	12 (0.3)
Nausea[c]		
Any[d]	732 (20.0)	700 (19.2)
Mild	527 (14.4)	502 (13.8)
Moderate	197 (5.4)	190 (5.2)
Severe	8 (0.2)	8 (0.2)
Joint pain[c]		

Systemic Reactions	ABRYSVO N=3,663[b] n (%)	PLACEBO N=3,638-3,639[b] n (%)
Any[d]	424 (11.6)	382 (10.5)
Mild	238 (6.5)	218 (6.0)
Moderate	180 (4.9)	161 (4.4)
Severe	6 (0.2)	3 (<0.1)
Diarrhea[e]		
Any	412 (11.2)	417 (11.5)
Mild	335 (9.1)	343 (9.4)
Moderate	73 (2.0)	68 (1.9)
Severe	4 (0.1)	6 (0.2)
Vomiting[f]		
Any	287 (7.8)	254 (7.0)
Mild	233 (6.4)	196 (5.4)
Moderate	47 (1.3)	56 (1.5)
Severe	7 (0.2)	2 (<0.1)

[a] NCT04424316 (C3671008)

[b] N = number of participants who provided e-diary data for a specific reaction after vaccination.

[c] Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily routine activity.

[d] Any includes all participants who reported a reaction as mild, moderate, or severe during Day 1 to Day 7 after vaccination. [e] Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours.

[f] Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration.

Infant Participants

In Study C3671008, solicited local and systemic adverse reactions were not studied in infant participants, who were not directly vaccinated but received passive immunity from their actively immunized parents prior to delivery.

Unsolicited Adverse Events

Maternal Participants

All maternal participants were monitored for unsolicited adverse events during the 28 days following administration of Abrysvo or placebo. Unsolicited adverse events reported within 1 month after vaccination by maternal participants were 13. 8% (n = 507) in the Abrysvo group and 13.1% (n = 483) in the placebo group. The most commonly reported adverse event was premature delivery (2.1% [n = 79] in the Abrysvo group and 1.9% [n = 70] in the placebo group). Severe adverse events were reported in 1.7% (n = 63) of the Abrysvo group and 1.3% (n = 48) of the placebo group.

Infant Participants

All infant participants were monitored for unsolicited adverse events during the 28 days following delivery as a newborn of a maternal participant administered of Abrysvo or placebo between 24 to 36 weeks gestation. Unsolicited adverse events in infants from birth to 1 month of age were observed in 37.1% (n = 1324) in the Abrysvo group compared to 34.5% (n = 1229) in the placebo group. The adverse event of Neonatal jaundice was observed in 7.2% (n = 257) in the Abrysvo group versus 6.7% (n = 240) in the placebo group. Severe adverse events were reported in 4.5% (n = 161) of the Abrysvo group and 3.8% (n = 134) of the placebo group.

Serious Adverse Events and Adverse Events of Special Interest

Maternal Participants

All maternal participants were monitored for serious adverse events and adverse events of special interest (e.g. premature delivery and positive SARS-CoV-2 tests) during the 6 months following delivery. Serious adverse events in maternal participants were reported by 16.2% (n=598) in the Abrysvo group and 15.2% (n=558) in the placebo group occurring any time during the study with 4.2% serious adverse events in the Abrysvo group and 3.7% in the placebo group occurring within 1 month after vaccination. The most frequently reported serious adverse events were preeclampsia (1.8% [n= 68] in the Abrysvo group and 1.4% [n = 53] in the placebo group) and fetal distress syndrome (1.8% [n = 66] in the Abrysvo group and 1.6% [n = 60] in the placebo group).

Adverse events of special interest were reported at a similar frequency (5.6% [n=206, 95% CI: 4.9, 6.4] versus 4.7% [n=174, 95% CI: 4.1, 5.5] and 3.9% [n=143, 95% CI: 3.3, 4.6] versus 3.0% [n=111, 95% CI: 2.5, 3.6], respectively for premature delivery and positive SARS-CoV-2 tests when recorded after vaccination to 6 months after delivery.

Infant Participants

All infant participants were monitored for serious adverse events (including congenital anomalies) and adverse events of special interest from birth through 24 months of age for those enrolled in the first year of study, and from birth through 12 months of age for those enrolled in the second year of study. Serious adverse events in infant participants were reported by 17.5% (n = 625) in the Abrysvo group and 17.5% (n=623) in the placebo group occurring any time during the study. The most frequently reported serious adverse events were neonatal jaundice (2.1% [n= 75] in the Abrysvo group and 1.9% [n = 66] in the placebo group). Pregnant individuals with prior pregnancy complications (e.g., history of preterm birth ≤34 weeks gestation, prior stillbirth, neonatal death, previous infant with a known genetic disorder or significant congenital anomaly) could be included, based on the investigators' judgment, but were generally not enrolled in the study.

At the time of the primary analysis, when 97% of mothers had delivered, a numerical imbalance in preterm births in all Abrysvo recipients compared with all placebo recipients was observed in study C3671008. Preterm birth events occurred in 5.7% [95% CI: 4.9, 6.5] (202 out of 3,568) in the Abrysvo group and 4.7% [95% CI: 4.1, 5.5] (169 out of 3,558) in the placebo group. No observed increase in mortality (1 in RSVpreF, 2 in placebo), was seen in preterm births.

The imbalance of preterm births in infant participants born to mothers immunized with Abrysvo was most pronounced in the 28 through 31 weeks' gestation subgroup. There was also an imbalance noted regarding low birth weight, but only in the earliest gestational age group for maternal immunization (**Table 6**). The majority of this imbalance came from investigational sites in South Africa and Argentina

with no imbalance seen in the aggregate incidence among participants from high income countries such as Canada, as per World Bank Group categories.

Table 6: Adverse Events of Premature Baby and Low Birth Weight Baby by Maternal Vaccination Window - Infant Participants - Safety Population (Study C3671008)

	ABRYSVO				PLACEBO			
Gestational Week When Vaccine Administered	**N[b]**	**Median Maternal Age (Range)**	**Premature Baby[a] n (%)**	**Low Birth Weight Baby[c] n (%)**	**N[b]**	**Median Maternal Age (Range)**	**Premature Baby[a] n (%)**	**Low Birth Weight Baby[c] n (%)**
All gestational weeks	3568	29.0 (16 – 45)	202 (5.7)	181 (5.1)	3558	29.0 (16 – 47)	169 (4.7)	155 (4.4)
24 to <28 weeks	897	28.0 (17 – 45)	63 (7.0)	65 (7.2)	872	28.0 (17 – 44)	59 (6.8)	51 (5.8)
28 to <32 weeks	1040	29.0 (17 – 44)	71 (6.8)	49 (4.7)	1076	28.0 (16 – 44)	51 (4.7)	49 (4.6)
32 to <37 weeks	1631	30.0 (16 – 45)	68 (4.2)	67 (4.1)	1610	30.0 (16 – 47)	59 (3.7)	55 (3.4)

a. infant AE of premature baby.
b. denominator for percentages = number of infants whose mothers were vaccinated in that vaccination range.
c. infant AE of low birth weight baby.

Additionally, no increase in overall infant mortality was observed (5 in RSVpreF, 12 in placebo), and no differences were observed in neonatal hospitalization / prolongation of hospitalization in infants overall (391[11%] in RSVpreF, 353 [9.9%] in placebo), or in those born premature (83 [2.3%] in RSVpreF, 80 [2.2%] in placebo). Available data are insufficient to establish or exclude a causal relationship between preterm birth and Abrysvo. As a precaution, the indication for Abrysvo is currently limited to 32 through 36 weeks gestation in maternal participants.

Deaths and Withdrawals from Study

Maternal Participants

All maternal participants were monitored for deaths and withdrawals from the study following administration of Abrysvo or placebo. Approximately 95% of the maternal participants had completed the study or were in ongoing follow-up at the time of the analysis. There was a single withdrawal due to an adverse event in the placebo group. There were no maternal deaths in the placebo group and one maternal death in the Abrysvo group due to postpartum hemorrhage that was determined to be not likely associated with vaccination.

Infant Participants

All infant participants were monitored for deaths and withdrawals from the study following administration of Abrysvo or placebo. Approximately 94% of the infant participants had completed the study or were in ongoing follow-up at the time of the analysis. There were no infants withdrawn due to adverse events. Among live born infants, there were 5 (0.1%) deaths in the Abrysvo group and 12 (0.3%) in the placebo group. No deaths in the study were considered related to vaccination.

Adverse Events from Other Studies

In Study C3671003, the safety and immunogenicity of two dose levels of active RSV vaccine (i.e., Abrysvo and a higher dose formulation) with or without an adjuvant (i.e., aluminum hydroxide) vs placebo was investigated in vaccinated maternal participants and their infant participants following delivery. AEs in maternal and infant participants within 1 month after vaccination or birth respectively were reported in a similar frequency across all groups, including placebo, with no clear association with dose level or formulation. In the infants who were born to maternal participants receiving the final selected dose, preterm births occurred in 5.3% (6 out of 114) in the Abrysvo group and 2.6% (3 out of 116) in the placebo group.

Individuals 60 years of age and older by active immunization

Of the study participants in the pivotal Study C3671013, 49% were female, 78% were White, 13% were Black or African American, 8% were Asian, and 37% were Hispanic/Latino. The median age of participants was 67 years (range 59-97 years).

The most frequently reported adverse reaction in Study C3671013 was vaccination site pain. The majority of reactions were mild to moderate in severity and resolved within 1-2 days of onset.

Solicited Adverse Reactions

In Study C3671013, a subset of study participants was monitored for solicited local and systemic adverse reactions using e-diary during the 7 days following administration of Abrysvo or placebo in 7,169 participants (3,630 Abrysvo participants and 3,539 placebo recipients) from a subset of sites. Solicited local and systemic reactions reported within 7 days after vaccination in Study C3671013 are presented in **Tables 7** and **8**. Solicited local and systemic reactions had a median duration of 1-2 days.

Table 7: Percentage of Adult Participants 60 Years of Age and Older with Solicited Local Adverse Reactions within 7 Days after Vaccination – Safety Population (Study C3671013)[a]

Local Reactions	ABRYSVO N=3,619-3,621[b] n (%)	PLACEBO N=3,532-3,539[b] n (%)
Injection site pain[c]		
Any[d]	382 (10.5)	212 (6.0)
Mild	340 (9.4)	188 (5.3)
Moderate	40 (1.1)	24 (0.7)
Severe	2 (<0.1)	(0)
Redness[d,e]		
Any[d]	97 (2.7)	23 (0.7)
Mild	55 (1.5)	16 (0.5)
Moderate	38 (1.1)	7 (0.2)
Severe	4 (0.1)	(0)
Swelling[d,e]		
Any[d]	88 (2.4)	16 (0.5)
Mild	53 (1.5)	8 (0.2)
Moderate	31(0.9)	6 (0.2)
Severe	4 (0.1)	2 (<0.1)

[a] NCT05035212 (C3671013)

[b] N = number of participants who provided e-diary data for a specific reaction after vaccination.

[c] Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily activity.

[d] Any includes all participants who reported a reaction as mild, moderate, or severe during Day 1 to Day 7 after vaccination.

[e] Mild: 2.5 cm to 5 cm; moderate: >5 cm to 10 cm; severe: >10 cm (for data reported from e-diaries).

Table 8: Percentage of Adult Participants 60 Years of Age and Older with Solicited Systemic Adverse Reactions within 7 Days after Vaccination – Safety Population (Study C3671013)[a]

Systemic Reactions	ABRYSVO N=3,619-3,621[b] n (%)	PLACEBO N=3,532-3,539[b] n (%)
Fever (≥38.0°C)		
≥38.0°C	51 (1.4)	51 (1.4)
≥38.0°C to 38.4°C	22 (0.6)	27 (0.8)
>38.4°C to 38.9°C	28 (0.8)	21 (0.6)
>38.9°C to 40.0°C	1 (<0.1)	2 (<0.1)
>40.0°C	0	1 (<0.1)
Fatigue[c]		
Any[d]	562 (15.5)	508 (14.4)
Mild	335 (9.3)	296 (8.4)
Moderate	215 (5.9)	207 (5.8)
Severe	12 (0.3)	5 (0.1)
Headache[c]		
Any[d]	465 (12.8)	415 (11.7)
Mild	326 (9.0)	299 (8.4)
Moderate	135 (3.7)	113 (3.2)
Severe	4 (0.1)	3 (<0.1)
Muscle pain[c]		
Any[d]	367 (10.1)	297 (8.4)
Mild	234 (6.5)	196 (5.5)
Moderate	125 (3.5)	98 (2.8)
Severe	8 (0.2)	3 (<0.1)
Joint pain[c]		
Any[d]	272 (7.5)	244 (6.9)
Mild	163 (4.5)	139 (3.9)
Moderate	106 (2.9)	103 (2.9)
Severe	3 (<0.1)	2 (<0.1)
Nausea[c]		

Systemic Reactions	ABRYSVO N=3,619-3,621[b] n (%)	PLACEBO N=3,532-3,539[b] n (%)
Any[d]	124 (3.4)	132 (3.7)
Mild	92 (2.5)	108 (3.1)
Moderate	32 (0.9)	21 (0.6)
Severe	0	3 (<0.1)
Vomiting[e]		
Any[d]	32 (0.9)	30 (0.8)
Mild	26 (0.7)	24 (0.7)
Moderate	6 (0.2)	4 (0.1)
Severe	0	2 (<0.1)
Diarrhea[f]		
Any[d]	213 (5.9)	183 (5.2)
Mild	161 (4.4)	148 (4.2)
Moderate	48 (1.3)	31 (0.9)
Severe	4 (0.1)	4 (0.1)

[a] NCT05035212 (C3671013)

[b] N = number of participants who provided e-diary data for a specific reaction after vaccination.

[c] Mild: does not interfere with activity; moderate: some interference with activity; severe: prevents daily routine activity.

[d] Any includes all participants who reported a reaction as mild, moderate, or severe during Day 1 to Day 7 after vaccination.

[e] Mild: 1 to 2 times in 24 hours; moderate: >2 times in 24 hours; severe: requires intravenous hydration.

[f] Mild: 2 to 3 loose stools in 24 hours; moderate: 4 to 5 loose stools in 24 hours; severe: 6 or more loose stools in 24 hours.

Unsolicited Adverse Events

Unsolicited adverse events occurring within 1 month after vaccination were similar between groups, reported in 8.9% and 8.5% of participants who received Abrysvo and placebo, respectively.

Within 30 days after vaccination, atrial fibrillation was reported in 10 vaccine recipients and 4 placebo recipients (of which 4 in the Abrysvo group and 3 in the placebo group were serious adverse events); the onset of symptoms was 18 to 30 days post vaccination. The currently available information on atrial fibrillation is insufficient to determine a causal relationship to the vaccine. There were no other notable patterns or numerical imbalances between groups for specific categories of unsolicited adverse events.

Serious Adverse Events and Adverse Events of Special Interest

In Study C3671013, SAEs were reported by 2.3% of participants in both the Abrysvo and placebo groups. Three participants in the Abrysvo group had SAEs which were assessed as possibly related to study

vaccination: Guillain-Barré Syndrome reported 7 days after vaccination, Miller-Fisher Syndrome reported 8 days after vaccination, and hypersensitivity reported 8 hours after vaccination.

Deaths and Withdrawals from Study

AEs leading to death were reported in 52 (0.3%) RSVpreF recipients and 49 (0.3%) placebo recipients. None of these deaths were assessed as related to study intervention.

AEs leading to withdrawal from the study were similar in the RSVpreF and placebo groups: 10 (<0.1%) and 6 (<0.1%) participants, respectively. None of the events were assessed as related.

9 DRUG INTERACTIONS

9.4 Drug-Drug Interactions

Use with other vaccines

Immunogenicity data in healthy non-pregnant women who received concomitant administration of Abrysvo and a tetanus, diphtheria and acellular pertussis vaccine (Tdap) indicated the immune response induced by Abrysvo when administered concomitantly with Tdap was non-inferior to the immune response induced by Abrysvo alone. In addition, immunogenicity data indicated non-inferiority in immune response to the diphtheria and tetanus components. Immune response to the pertussis component of Tdap was lower when Abrysvo and Tdap were administered concomitantly as compared to Tdap administered alone. The clinical relevance of this observation is unknown.

Data on concomitant administration of Abrysvo and vaccines other than those listed above, including influenza vaccine, are not available.

Concomitant administration of Abrysvo with Tdap or seasonal influenza vaccines in pregnant subjects has not been studied.

Different injectable vaccines should always be given at different vaccination sites.

Do not mix Abrysvo with other vaccines or medicinal products in the same syringe (see **4.4 Administration**).

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Abrysvo is a bivalent formulation containing two recombinant stabilized RSV prefusion F antigens, each representing the two major virus subgroups, RSV A and RSV B. RSV F can exist in two antigenically distinct forms – prefusion and postfusion. Unlike postfusion F, prefusion F is the active form of the protein and is capable of mediating fusion of virus and host cell membranes during cell entry. Therefore, prefusion F is the primary target of the most potent neutralising antibodies that block RSV infection. Following intramuscular administration, the prefusion F antigens elicit an immune response, which protects against RSV associated lower respiratory tract disease.

In pregnant individuals, the action of neutralising antibodies conferring protection is mediated through passive transfer of these antibodies from mother to infant. Adults 60 years of age and older are protected by active immunization.

10.2 Pharmacodynamics

Not applicable.

10.3 Pharmacokinetics

Not applicable.

11 STORAGE, STABILITY AND DISPOSAL

Store in a refrigerator between 2°C and 8°C in the original carton to protect from light.

Do not freeze. Discard if the vaccine has been frozen.

After reconstitution: Abrysvo should be administered immediately (within 4 hours) after reconstitution. Store the reconstituted vaccine between 15°C and 30°C. Do not freeze reconstituted vaccine.

12 SPECIAL HANDLING INSTRUCTIONS

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

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

ABRYSVO™

(Respiratory Syncytial Virus Stabilized Prefusion F Subunit Vaccine)

Lyophilized powder for solution for Intramuscular Injection

Read this carefully before you receive **Abrysvo**. This leaflet is a summary and will not tell you everything about this vaccine. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Abrysvo**.

What is Abrysvo used for?

Abrysvo is a vaccine to prevent disease of the respiratory tract (lung) caused by a virus called respiratory syncytial virus (RSV). Abrysvo is given to:

- pregnant individuals (32– 36 week gestation) to protect their infants from birth through 6 months of age;
- individuals 60 years of age and older.

How does Abrysvo work?

The vaccine works by helping the body to make antibodies (substances your body uses to fight an infection) which protect against this disease. In pregnant individuals, these antibodies are passed to the infant through the placenta before birth which protects infants after birth when they are at most risk from RSV.

What are the ingredients in Abrysvo?

Medicinal ingredients: One dose (0.5 mL) contains the following active substances:

- RSV subgroup A stabilized prefusion F protein: 60 micrograms
- RSV subgroup B stabilized prefusion F protein: 60 micrograms

Non-medicinal ingredients: Mannitol, polysorbate 80, sodium chloride, sucrose, tromethamine, trometamol hydrochloride, sterile water for injection.

Abrysvo comes in the following dosage forms:

White powder for solution.

Do not use Abrysvo if:

- you are allergic (hypersensitive) to the active substances or to any of the other ingredients in this vaccine.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you receive Abrysvo. Talk about any health conditions or problems you may have, including if you:

- have ever had a severe allergic reaction or breathing problems after any other vaccine injection or after you were given Abrysvo in the past.
- have a bleeding problem or bruise easily.
- have an infection with a high fever. If this is the case, then vaccination will be postponed. There is no need to delay vaccination for a minor infection, such as a cold, but talk to your doctor first.

- are feeling nervous about the vaccination process or have ever fainted following any needle injection.
- have a weakened immune system which may prevent you from getting the full benefit from Abrysvo.
- are less than 32 weeks pregnant. Pregnant individuals can be given this vaccine in the third trimester (from 32 through 36 weeks gestation). Abrysvo is not recommended in children and adolescents below 18 years, except in pregnancy.

Other warnings you should know about:

As with any vaccine, Abrysvo will not protect all persons who are vaccinated.

Abrysvo is unlikely to affect your ability to drive or use machines.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Tell your healthcare professional if you have recently received any other vaccine.

How Abrysvo is given:

A healthcare professional will inject the recommended dose (0.5 mL) of the vaccine into your arm.

If you have any further questions on the use of Abrysvo, ask your healthcare professional.

Usual dose:

Individuals 60 years of age and older:

You should receive one injection (0.5 mL dose) of the vaccine.

Pregnant individuals:

You should receive one injection (0.5 mL dose) of the vaccine in the third trimester of pregnancy (from 32 through 36 weeks gestation).

Overdose:

Overdose with Abrysvo is unlikely as it is administered as a single-dose pre-filled syringe.

If you think you, or a person you are caring for, have received too much Abrysvo, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using Abrysvo?

Fainting, feeling faint, or other stress-related reactions can occur as a response to any needle injection.

Like all vaccines, Abrysvo can cause side effects, although not everybody gets them.

The following side effects include those reported for Abrysvo in pregnant individuals:

Very common: may affect more than 1 in 10 people

- pain where the injection is given
- headache
- muscle pain (myalgia).

Common: may affect up to 1 in 10 people

- redness where the injection is given

- swelling where the injection is given.

No side effects were reported in infants born to vaccinated mothers.

The following side effects were reported in individuals 60 years of age and older:

Very common: may affect more than 1 in 10 people

- pain where the injection is given

Common: may affect up to 1 in 10 people

- redness where the injection is given
- swelling where the injection is given.

These are not all the possible side effects you may have when receiving Abrysvo. If you experience any side effects not listed here, tell your healthcare professional.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY RARE			
Allergic reactions: swelling of the face, lips, tongue or throat, hives, difficulty breathing or swallowing, dizziness which are signs and symptoms of hypersensitivity reactions.		X	

Reporting Suspected Side Effects for Vaccines

For the general public: Should you experience a side effect following immunization, please report it to your healthcare professional.

Should you require information related to the management of the side effect, please contact your healthcare professional. The Public Health Agency of Canada, Health Canada and Pfizer Canada ULC cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (http://www.phac-aspc.gc.ca/im/aefi-essi-form-eng.php) and send it to your local Health Unit.

Storage:

Store the unreconstituted vaccine in a refrigerator (2°C to 8°C). Abrysvo should be used as soon as possible after being removed from refrigeration.

After reconstitution:

Abrysvo should be administered immediately (within 4 hours) after reconstitution. Store the reconstituted vaccine between 15°C and 30°C.

Do not freeze. Discard if vaccine has been frozen.

Keep out of reach and sight of children.

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

If you want more information about Abrysvo:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website www.pfizer.ca, or by calling 1-800-463-6001.

This leaflet was prepared by Pfizer Canada ULC.

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