เอกสารกำกับยา

ABRYSVO™

1. NAME OF THE MEDICINAL PRODUCT

1.1 Product Name

Abrysvo

1.2 Strength

120 micrograms/0.5 mL

1.3 Pharmaceutical Dosage Form

Powder and solvent for solution for injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 Qualitative Declaration

Active ingredient: Respiratory syncytial virus vaccine (bivalent, recombinant)

2.2 Quantitative Declaration

After reconstitution, one dose (0.5 mL) contains:

RSV subgroup A stabilised prefusion F antigen[1,2]	60 micrograms
RSV subgroup B stabilised prefusion F antigen[1,2]	60 micrograms

(RSV antigens)

[1]glycoprotein F stabilised in the prefusion conformation

[2]produced in Chinese Hamster Ovary cells by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

The powder is white.

The solvent is a clear, colourless liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Abrysvo is indicated for:

- Passive protection against lower respiratory tract disease caused by respiratory syncytial virus (RSV) in infants from birth through 6 months of age following maternal immunisation during pregnancy. See sections 4.2 and 5.1.
- Active immunisation of individuals 18 years of age and older for the prevention of lower respiratory tract disease caused by RSV.

4.2. Posology and Method of Administration

Posology

Pregnant individuals

A single dose of 0.5 mL should be administered between weeks 24 and 36 of gestation (see sections 4.4 and 5.1).

Individuals 18 years of age and older

A single dose of 0.5 mL should be administered.

Paediatric population

The safety and efficacy of Abrysvo in children (from birth to less than 18 years of age) have not yet been established. Limited data are available in pregnant adolescents and their infants (see section 5.1).

Method of administration

Abrysvo is for intramuscular injection into the deltoid region of the upper arm.

The vaccine should not be mixed with any other vaccines or medicinal products.

For instructions on reconstitution and handling of the medicinal product before administration, see section 6.6.

4.3. Contraindications

Hypersensitivity to the active substances 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 and anaphylaxis

Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.

Anxiety-related reactions

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from fainting.

Concurrent illness

Vaccination 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.

Thrombocytopenia and coagulation disorders

Abrysvo should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding or bruising may occur following an intramuscular administration to these individuals.

Immunocompromised individuals

The efficacy and safety of the vaccine have not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of Abrysvo may be lower in immunosuppressed individuals.

Individuals less than 24 weeks of gestation

Abrysvo has not been studied in pregnant individuals less than 24 weeks of gestation. Since protection of the infant against RSV depends on transfer of maternal antibodies across the placenta, Abrysvo should be administered between weeks 24 and 36 of gestation (see sections 4.2 and 5.1).

Limitations of vaccine effectiveness

As with any vaccine, a protective immune response may not be elicited after vaccination.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

Abrysvo contains polysorbate 80. Polysorbate 80 may cause hypersensitivity reactions.

4.5. Interaction with Other Medicinal Products and Other Forms of Interaction

Abrysvo can be administered concomitantly with seasonal quadrivalent influenza vaccine (QIV, surface antigen, inactivated, adjuvanted). In a randomised study in adults 65 years of age and older, the criteria for non-inferiority of the immune responses in the co-administration versus the separate administration group were met. However, numerically lower RSV A and B neutralising titres and numerically lower influenza A and B haemagglutination inhibition titres were observed when Abrysvo and inactivated adjuvanted seasonal influenza vaccine were co-administered than when they were administered separately. The clinical relevance of this finding is unknown.

A minimum interval of two weeks is recommended between administration of Abrysvo and administration of a tetanus, diphtheria and acellular pertussis vaccine (Tdap). There were no safety concerns when Abrysvo was co-administered with Tdap in healthy non-pregnant women. Immune responses to RSV A, RSV B, diphtheria and tetanus on co-administration were non-inferior to those after separate administration. However, the immune responses to the pertussis components were lower on co-administration compared to separate administration and did not meet the criteria for non-inferiority. The clinical relevance of this finding is unknown.

4.6. Fertility, Pregnancy and Lactation

Pregnancy

Data on pregnant women (more than 4,000 exposed outcomes) indicate no malformative nor feto/neonatal toxicity.

Results from animal studies with Abrysvo do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

In a phase 3 study (Study 1), maternal adverse events reported within 1 month after vaccination were similar in the Abrysvo group (14%) and the placebo group (13%).

No safety signals were detected in infants up to 24 months of age. The incidences of adverse events reported within 1 month after birth in infants were similar in the Abrysvo group (37%) and the placebo group (35%). Major birth outcomes assessed in the Abrysvo group compared to

placebo included premature birth (201 (6%) and 169 (5%), respectively), low birth weight (181 (5%) and 155 (4%), respectively) and congenital anomalies (174 (5%) and 203 (6%), respectively).

Breast-feeding

It is unknown whether Abrysvo is excreted in human milk. No adverse effects of Abrysvo have been shown in breastfed newborns of vaccinated mothers.

Fertility

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 section 5.3).

4.7. Effects on Ability to Drive and Use Machines

Abrysvo has no or negligible influence on the ability to drive and use machines.

4.8. Undesirable Effects

Summary of the safety profile

Pregnant individuals

In pregnant women at 24-36 weeks of gestation the most frequently reported adverse reactions were vaccination site pain (41%), headache (31%) and myalgia (27%). The majority of local and systemic reactions in maternal participants were mild to moderate in severity and resolved within 2-3 days of onset.

Individuals 18 years of age and older

In individuals 18 years of age and older the most frequently reported adverse reactions were fatigue (23%), headache (20%), vaccination site pain (19%) and myalgia (16%). The majority of reactions were mild to moderate in severity and resolved within 1-2 days of onset.

Tabulated list of adverse reactions

The safety of administering a single dose of Abrysvo to pregnant women at 24-36 weeks of gestation (n=3,682) and to individuals 18 years of age and older (n=20,275) was evaluated in clinical trials.

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);
Not known (cannot be estimated from the available data).

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

Table 1 Adverse reactions following administration of Abrysvo

System organ class	**Adverse drug reactions pregnant individuals ≤49 years**	**Adverse drug reactions individuals ≥18 years**
Blood and lymphatic system disorders		
Lymphadenopathy	Rare	Rare
Immune system disorders		
Anaphylaxis		Very rare
Hypersensitivity reactions (includes rash, urticaria)	Rare	Rare
Nervous system disorders		
Headache	Very common	Very common
Guillain-Barré syndrome		Very rare
Musculoskeletal and connective tissue disorders		
Myalgia	Very common	Very common
Arthralgia		Common
General disorders and administration site conditions		
Fatigue		Very common

System organ class	Adverse drug reactions pregnant individuals ≤49 years	Adverse drug reactions individuals ≥18 years
Vaccination site pain	Very common	Very common
Vaccination site redness	Common	Common
Vaccination site swelling	Common	Common
Pyrexia		Uncommon
Vaccination site pruritus		Rare
Vaccination site bruising		Rare
Vaccination site haematoma		Rare

4.9. Overdose

Overdose with Abrysvo is unlikely due to its single dose presentation.

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

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: Vaccines, other viral vaccines; ATC code: J07BX05

Mechanism of action

Abrysvo contains two recombinant stabilised RSV prefusion F antigens representing subgroups RSV-A and RSV-B. Prefusion F is the primary target of 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 infants born to mothers who were vaccinated with Abrysvo between weeks 24 and 36 of gestation, protection against RSV-associated lower respiratory tract disease is due to transplacental transfer of RSV neutralising antibodies. Adults 18 years of age and older are

protected by active immunisation.

Clinical efficacy

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

Study 1 is a phase 3, multicentre, randomised (1:1), double-blind, placebo-controlled study to assess the efficacy of a single dose of Abrysvo in the prevention of RSV-associated lower respiratory tract disease in infants born to pregnant individuals vaccinated between weeks 24 and 36 of gestation. The need for revaccination with subsequent pregnancies has not been established.

RSV-associated lower respiratory tract illness was defined as a medically attended visit with a reverse transcription-polymerase chain reaction (RT-PCR) confirmed RSV illness with one or more of the following respiratory symptoms: fast breathing, low oxygen saturation (SpO2 <95%) and chest wall indrawing. RSV-associated severe lower respiratory tract illness was defined as an illness that met the lower respiratory tract illness-RSV criteria plus at least one of the following: very fast breathing, low oxygen saturation (SpO2 <93%), high-flow oxygen supplementation via nasal cannula or mechanical ventilation, ICU admission for >4 hours and/or failure to respond/unconscious.

In this study, 3,695 pregnant individuals with uncomplicated, singleton pregnancies were randomised to the Abrysvo group and 3,697 to placebo.

Vaccine efficacy (VE) was defined as the relative risk reduction of the endpoint in the Abrysvo group compared to the placebo group for infants born to pregnant individuals who received the assigned intervention. There were two primary efficacy endpoints, assessed in parallel, severe RSV-positive medically attended lower respiratory tract illness and RSV-positive medically attended lower respiratory tract illness, occurring within 90, 120, 150 or 180 days after birth.

Of the pregnant women who received Abrysvo, 65% were White, 20% were Black or African American and 29% were Hispanic/Latino. The median age was 29 years (range 16-45 years); 0.2% of participants were under 18 years of age and 4.3% were under 20 years of age. The median gestational age at vaccination was 31 weeks and 2 days (range 24 weeks and 0 days to 36 weeks and 4 days). The median infant gestational age at birth was 39 weeks and 1 day (range 27 weeks and 3 days to 43 weeks and 6 days).

Vaccine efficacy is presented in Tables 2 and 3.

Table 2 Vaccine efficacy of Abrysvo against severe medically attended lower respiratory tract illness caused by RSV in infants from birth through 6 months of age by active immunisation of pregnant individuals – Study 1

Time period	Abrysvo Number of cases N=3,495	Placebo Number of cases N=3,480	VE % (CI)[a]
90 days	6	33	81.8 (40.6, 96.3)
120 days	12	46	73.9 (45.6, 88.8)
150 days	16	55	70.9 (44.5, 85.9)
180 days	19	62	69.4 (44.3, 84.1)

CI = confidence interval; VE = vaccine efficacy

[a] 99.5% CI at 90 days; 97.58% CI at later intervals

Table 3 Vaccine efficacy of Abrysvo against medically attended lower respiratory tract illness caused by RSV in infants from birth through 6 months of age by active immunisation of pregnant individuals - Study 1

Time period	Abrysvo Number of cases N=3,495	Placebo Number of cases N=3,480	VE % (CI)[a]
90 days	24	56	57.1 (14.7, 79.8)
120 days	35	81	56.8 (31.2, 73.5)
150 days	47	99	52.5 (28.7, 68.9)
180 days	57	117	51.3 (29.4, 66.8)

CI = confidence interval; VE = vaccine efficacy

[a] 99.5% CI at 90 days; 97.58% CI at later intervals

A post-hoc analysis of VE by maternal gestational age was conducted. For severe medically attended lower respiratory tract illness occurring within 180 days, VE was 57.2% (95% CI 10.4, 80.9) for women vaccinated early in pregnancy (24 to <30 weeks) and 78.1% (95% CI 52.1, 91.2) for women vaccinated later in the pregnancy eligible window (30 to 36 weeks). For medically attended lower respiratory tract illness occurring within 180 days, VE was 30.9% (95% CI -14.4,

58.9) for women vaccinated early in pregnancy (24 to <30 weeks) and 62.4% (95% CI 41.6, 76.4) for women vaccinated later in the pregnancy eligible window (30 to 36 weeks).

Active immunisation of individuals 60 years of age and older

Study 2 is a phase 3, multicentre, randomised, double-blind, placebo-controlled study to assess the efficacy of Abrysvo in the prevention of RSV-associated lower respiratory tract illness in individuals 60 years of age and older.

RSV-associated lower respiratory tract illness was defined as RT-PCR confirmed RSV illness with two or more or three or more of the following respiratory symptoms within 7 days of symptom onset and lasting more than 1 day during the same illness: new or increased cough, wheezing, sputum production, shortness of breath or tachypnoea (≥25 breaths/min or 15% increase from resting baseline).

Participants were randomised (1:1) to receive Abrysvo (n=18,488) or placebo (n=18,479). Enrollment was stratified by age 60-69 years (63%), 70-79 years (32%) and ≥80 years (5%). Subjects with stable chronic underlying conditions were eligible for this study and 52% of participants had at least 1 prespecified condition; 16% of participants were enrolled with stable chronic cardiopulmonary conditions such as asthma (9%), chronic obstructive pulmonary disease (7%) or congestive heart failure (2%). Immunocompromised individuals were ineligible.

The primary objective was assessment of vaccine efficacy (VE), defined as the relative risk reduction of first episode of RSV-associated lower respiratory tract illness in the Abrysvo group compared to the placebo group in the first RSV season.

Of the participants who received Abrysvo, 51% were male and 80% were White, 12% were Black or African American and 41% were Hispanic/Latino. The median age of participants was 67 years (range 59-95 years).

At the end of the first RSV season the analysis demonstrated statistically significant efficacy for Abrysvo for reduction of RSV-associated lower respiratory tract illness with ≥2 symptoms and with ≥3 symptoms.

Vaccine efficacy information is presented in Table 4.

Table 4 Vaccine efficacy of Abrysvo against RSV disease - active immunisation of individuals 60 years of age and older – Study 2

Efficacy endpoint	Abrysvo Number of cases N=18,058	Placebo Number of cases N=18,076	VE (%) (95% CI)
First episode of RSV-associated lower respiratory tract illness with ≥2 symptoms[a]	15	43	65.1 (35.9, 82.0)
First episode of RSV-associated lower respiratory tract illness with ≥3 symptoms[b]	2	18	88.9 (53.6, 98.7)

CI = confidence interval; RSV = respiratory syncytial virus; VE = vaccine efficacy

[a] In an exploratory analysis in RSV subgroup A (Abrysvo n=3, placebo n=16) VE was 81.3% (CI 34.5, 96.5); and in RSV subgroup B (Abrysvo n=12, placebo n=26) VE was 53.8% (CI 5.2, 78.8).

[b] In an exploratory analysis in RSV subgroup A (Abrysvo n=1, placebo n=5) VE was 80.0% (CI -78.7, 99.6); and in RSV subgroup B (Abrysvo n=1, placebo n=12) VE was 91.7% (CI 43.7, 99.8).

Immunogenicity in individuals 18 through 59 years of age

Study 3 was a Phase 3, multicentre, randomised, double-blind, placebo-controlled study to assess the safety and immunogenicity of Abrysvo in individuals 18 through 59 years of age considered to be at high risk of developing severe lower respiratory tract disease caused by RSV. Study 3 enrolled individuals who had chronic pulmonary (including asthma), cardiovascular (excluding isolated hypertension), renal, hepatic, neurologic, haematologic or metabolic disorders (including diabetes mellitus and hyper/hypothyroidism). Participants were randomised (2:1) to receive a single dose of Abrysvo (n=437) or placebo (n=217).

Demographic characteristics in study 3 were generally similar with regard to age, race and ethnicity among participants who received Abrysvo and those who received placebo. Fifty-three percent (53%) were 18 to 49 years and 47% were 50 to 59 years. The vaccine and placebo groups were similar with regards to having at least one prespecified medical condition, which included 53% with ≥1 chronic pulmonary condition, 8% with ≥1 cardiovascular condition, 42% with diabetes and 31% ≥1 other disease (liver, renal, neurologic, haematologic or other metabolic disease).

Vaccine efficacy in individuals 18 through 59 years of age is inferred by immunobridging to study 2 where vaccine efficacy was demonstrated in individuals 60 years of age and older. The non-inferiority criteria were met for high risk individuals 18 through 59 years of age compared to a randomly selected immunogenicity subset (external control group) of individuals ≥60 years of age from study 2 for the ratio of RSV neutralising geometric mean titres (GMTs) by the lower bounds of the 2-sided 95% CIs >0.667 (1.5-fold non-inferiority margin), and for the difference in seroresponse rates by the lower bounds of the 2-sided 95% CIs > -10% for both RSV A and RSV B.

Table 5 Comparison of model adjusted RSV neutralising titre GMTs at 1 month after vaccination with Abrysvo, 18 through 59 years at high risk (Study 3) versus 60 years and older (Study 2)

	Study 3 18-59 years of age at high risk		Study 2 ≥60 years		ANCOVA comparison
RSV subgroups	**n**	**Adjusted GMT (95% CI)**	**n**	**Adjusted GMT (95% CI)**	**Adjusted GMR (95% CI)**
A	435	41097 (37986, 44463)	408	26225 (24143, 28486)	1.57 (1.396, 1.759)
B	437	37416 (34278, 40842)	408	24680 (22504, 27065)	1.52 (1.333, 1.725)

CI - confidence interval; GMR - geometric mean ratio; GMT - geometric mean titre

Table 6 Comparison of RSV neutralising titre seroresponse rates 1 month after vaccination with Abrysvo, 18 through 59 years at high risk (Study 3) versus 60 years and older (Study 2)

	Study 3 18-59 years of age at high risk		Study 2 ≥60 years		Comparison
RSV subgroups	**n/N (%)**	**95% CI**	**n/N (%)**	**95% CI**	**Difference (95% CI)**
A	405/435 (93)	90.3, 95.3	359/408 (88)	84.4, 91.0	5.1 (1.2, 9.2)
B	408/437 (93)	90.6, 95.5	347/408 (85)	81.2, 88.4	8.3 (4.2, 12.6)

CI - confidence interval

5.2. Pharmacokinetic Properties

Not applicable.

5.3. Preclinical Safety Data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity and toxicity to reproduction and development.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Powder

Trometamol
Trometamol hydrochloride
Sucrose
Mannitol (E421)
Polysorbate 80 (E433)
Sodium chloride
Hydrochloric acid (for pH adjustment)

Solvent

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

See detail on carton.

The unopened vial is stable for 5 days when stored at temperatures from 8°C to 30°C. At the end of this period Abrysvo should be used or discarded. This information is used to guide healthcare professionals in case of temporary temperature excursions only.

After reconstitution

Abrysvo should be administered immediately after reconstitution or within 4 hours if stored between 15°C and 30°C. Do not freeze.

Chemical and physical in-use stability has been demonstrated for 4 hours between 15°C and 30°C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.4. Special Precautions for Storage

Store in a refrigerator (2ºC - 8ºC).

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

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

6.5. Nature and Contents of Container

Powder

Powder for 1 dose in a vial (type 1 glass or equivalent) with a stopper (synthetic chlorobutyl rubber) and a flip off cap

Solvent

Solvent for 1 dose in a pre-filled syringe (type 1 glass) with a stopper (synthetic chlorobutyl rubber) and a tip cap (synthetic isoprene/bromobutyl blend rubber)

Vial adaptor

Sterile vial adaptor

Pack size

Pack containing 1 vial of powder (antigens), 1 pre-filled syringe of solvent, 1 vial adaptor with 1 needle or without needles (1 dose pack).
Pack containing 5 vials of powder (antigens), 5 pre-filled syringes of solvent, 5 vial adaptors with 5 needles or without needles (5 dose pack).
Pack containing 10 vials of powder (antigens), 10 pre-filled syringes of solvent, 10 vial adaptors with 10 needles or without needles (10 dose pack).

Not all pack sizes may be marketed.

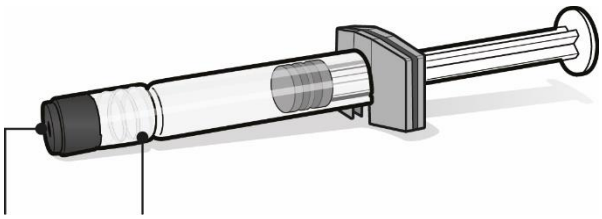
6.6. Special precautions for disposal and other handling

Abrysvo must be reconstituted prior to administration by adding the entire contents of the pre-filled syringe of solvent to the vial containing the powder using the vial adaptor.

The vaccine must be reconstituted only with the solvent provided.

Preparation for administration

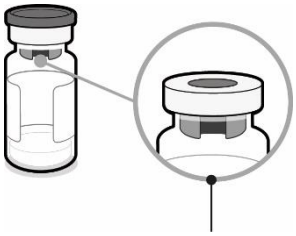
Pre-filled syringe containing solvent for Abrysvo



Syringe cap

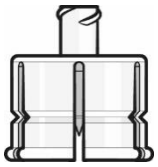
Luer lock adaptor

Vial containing antigens for Abrysvo (powder)



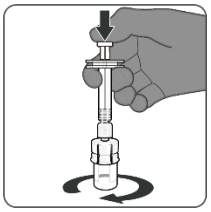
Vial stopper (with flip off cap removed)

Vial adaptor



Step 1. Attach vial adaptor

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



Step 2. Reconstitute the powder component (antigens) to form Abrysvo

- For all syringe assembly steps, hold the syringe only by the Luer lock adaptor. This will prevent the Luer lock adaptor from detaching during use.
- Twist to remove the syringe cap, then twist to connect the syringe to the vial adaptor. 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. 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 adaptor.
- Attach a sterile needle suitable for intramuscular injection.

The prepared vaccine is a clear and colourless solution. Visually inspect the vaccine for large particulate matter and discolouration prior to administration. Do not use if large particulate matter or discolouration is found.

7. MARKETING AUTHORIZATION HOLDER

Pfizer (Thailand) Limited

8. MARKETING AUTHORIZATION NUMBERS

2C 6/67 (NBC)

9. DATE OF AUTHORIZATION

31 July 2024

10. DATE OF REVISION OF THE TEXT

10 March 2025

LPD Revision No.: 4.0

LPD Date: March 10, 2025

Country: Thailand