swissmedic

Date: 20 November 2024
Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Abrysvo

International non-proprietary name: RSV subgroup A stabilised prefusion F antigen, RSV subgroup B stabilised prefusion F antigen

Pharmaceutical form: powder and solvent for solution for injection

Dosage strength(s): 60 µg/60 µg per dose

Route(s) of administration: intramuscular use

Marketing authorisation holder: Pfizer AG

Marketing authorisation no.: 69691

Decision and decision date: approved on 23 August 2024

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

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1 Terms, Definitions, Abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
API	Active pharmaceutical ingredient
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
CYP	Cytochrome P450
DDI	Drug-drug interaction
EMA	European Medicines Agency
ERA	Environmental risk assessment
FDA	Food and Drug Administration (USA)
GI	Gastrointestinal
GLP	Good Laboratory Practice
HPLC	High-performance liquid chromatography
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
INN	International non-proprietary name
ITT	Intention-to-treat
LoQ	List of Questions
LRTI	Lower respiratory tract infection
MAH	Marketing authorisation holder
Max	Maximum
Min	Minimum
MRHD	Maximum recommended human dose
N/A	Not applicable
NO(A)EL	No observed (adverse) effect level
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PIP	Paediatric investigation plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSP	Pediatric study plan (US FDA)
RMP	Risk management plan
RSV	Respiratory syncytial virus
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)

2 Background information on the procedure

2.1 Applicant's request(s)

New active substance status
The applicant requested new active substance status for RSV subgroup A stabilised prefusion F antigen, RSV subgroup B stabilised prefusion F antigen in the above-mentioned medicinal product.

Authorisation as human medicinal product in accordance with Article 13 TPA
The applicant requested a reduced assessment procedure in accordance with Article 13 TPA.

2.2 Indication and dosage

2.2.1 Requested indication

Abrysvo is indicated for:
- Passive protection against lower respiratory tract disease caused by respiratory syncytial virus (RSV) in infants from birth to 6 months of age following maternal immunisation during pregnancy. See dosage/administration and properties/effects sections.
- Active immunisation of individuals 60 years of age and older for the prevention of lower respiratory tract disease caused by RSV.

The use of this vaccine should be in accordance with official recommendations.

2.2.2 Approved indication

Abrysvo is indicated for:
- Passive protection against lower respiratory tract disease caused by respiratory syncytial virus (RSV) in infants from birth to 6 months of age following immunisation of pregnant individuals at 32 to 36 weeks gestational age (see "Warnings and precautions" and "Properties/Effects").
- Active immunisation of individuals 60 years of age and older for the prevention of lower respiratory tract disease caused by RSV.

The use of this vaccine should be in accordance with official recommendations.

2.2.3 Requested dosage

Summary of the requested standard dosage:
Pregnant individuals
A single dose of 0.5 mL should be administered between weeks 24 and 36 of gestation.
Individuals 60 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.
Method of administration
Abrysvo is for intramuscular injection into the deltoid region of the upper arm.

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	1 December 2023
Formal objection	18 December 2023
Preliminary decision	8 April 2024
Response to preliminary decision	15 May 2024
Labelling corrections	29 July 2024
Response to labelling corrections	5 August 2024
Final decision	23 August 2024
Decision	approval

Swissmedic has only assessed parts of the primary data submitted with this application. As regards the remaining data, Swissmedic relies for its decision on the assessment of the foreign reference authority, the European Medicines Agency (EMA). This SwissPAR relates to the publicly available EMA assessment report for Abrysvo, published 15 September 2023, Procedure No. EMEA/H/C/006027/0000.

3 Medical context

The human respiratory syncytial virus (RSV) causes acute respiratory tract disease in persons of all ages and is the most common cause of acute lower respiratory tract infection (LRTI) in young children. Almost all children are infected by 2 years of age, and reinfection is common. Young children, particularly infants below 6 months, and adults over 65 years of age are the most affected by RSV-associated severe disease. RSV bronchiolitis is the most common lower respiratory tract infection in infants and leads to the hospitalisation of 1-2% of the annual birth cohort as a result of respiratory insufficiency and/or inadequate fluid intake.
RSV infection is usually a self-limited process that results in no apparent long-term pulmonary sequelae. However, in infancy it has been associated with recurrent wheezing in some patients and with persistent decreased pulmonary function and chronic obstructive pulmonary disease in adulthood. Although mortality rates in healthy infants with RSV pneumonia are less than 0.5%, they can reach up to 60% in untreated immunocompromised children.[1]
Paediatric patients at risk for severe lower respiratory tract disease include infants younger than 6 months of age, infants and children with chronic lung disease or congenital heart disease, preterm infants born before 35 weeks gestation, and immunocompromised patients. RSV typically causes seasonal outbreaks throughout the world. In the Northern Hemisphere, these usually occur from October/November to April/May, with a peak in January or February. Disruption of the typical seasonal pattern of RSV may result in off-season outbreaks. During the coronavirus disease 2019 (COVID-19) pandemic, mitigation measures (e.g. mask wearing, physical distancing, school closures) were associated with marked reductions in non-COVID-19 respiratory infections in children, including RSV, during the winter season. Therapy for RSV LRTI is primarily supportive. Supportive care includes frequent monitoring of clinical status and provision of fluid and respiratory support, as necessary. Standard strategies to reduce the risk of a viral infection include hand hygiene, avoiding contact, and minimising passive smoking.

During the review process an adjuvanted recombinant vaccine (Arexvy) for the prevention of lower respiratory tract disease caused by RSV in adults 60 years and older was approved.

Two monoclonal antibodies (palivizumab and nirsevimab) are approved in Switzerland for the prevention of LRTI caused by RSV in infants.
Palivizumab (Synagis) needs to be administered monthly during the RSV season and has been available for decades for high-risk groups, such as preterm infants (born before 35 weeks gestation) before 6 months of age, infants/toddlers with bronchopulmonary dysplasia before their second birthday, and children with haemodynamically significant congenital heart disease.
Nirsevimab (Beyfortus) is a human recombinant monoclonal antibody targeting the RSV F protein. As it has as an extended half-life due to an YTE modification in its Fc region, a single dose is sufficient to cover the usual 6 month-long RSV season.
Beyfortus is indicated for the prevention of LRTI caused by RSV in (1) neonates and infants entering or during their first RSV season and (2) in toddlers up to 24 months of age who remain vulnerable to severe RSV disease in their second RSV season.

[1] Asner, Sandra MD; Stephens, Derek MSc; Pedulla, Paul BFc; Richardson, Susan E. MD, FRCPC; Robinson, Joan MD, FRCPC¶; Allen, Upton MBBS, MSc, FRCPC. Risk Factors and Outcomes for Respiratory Syncytial Virus–related Infections in Immunocompromised Children. The Pediatric Infectious Disease Journal 32(10):p 1073-1076, October 2013. | DOI: 10.1097/INF.0b013e31829dff4d

4 Quality aspects

Swissmedic has not assessed the primary data relating to quality aspects submitted with this application and relies on the assessment of the foreign reference authority, the European Medicines Agency (EMA). The SwissPAR relating to quality aspects refers to the publicly available EMA assessment report for Abrysvo, published 15 September 2023, Procedure No. EMEA/H/C/006027/0000.

5 Nonclinical aspects

Swissmedic has not assessed the primary data relating to nonclinical aspects submitted with this application and relies on the assessment of the foreign reference authority, the European Medicines Agency (EMA). The nonclinical aspects in this SwissPAR refer to the publicly available EMA assessment report for Abrysvo, published 15 September 2023, Procedure No. EMEA/H/C/006027/0000.

6 Clinical aspects

Concerning the indication of active immunisation of adults 60 years of age and older for the prevention of lower respiratory tract disease caused by respiratory syncytial virus (RSV) Swissmedic has not assessed the primary data relating to clinical aspects submitted with this application and relies on the results of the assessment of the foreign reference authority, the European Medicines Agency (EMA).
The clinical aspects in this SwissPAR refer to the EMA assessment report for Abrysvo, published 15 September 2023, Procedure No. EMEA/H/C/006027/0000.

Concerning the indication of passive protection against lower respiratory tract disease caused by RSV in infants from birth to 6 months of age following maternal immunisation during pregnancy, a more detailed assessment took place to understand the reasons for the different timing of the immunisation during pregnancy approved by the EMA and the FDA.
In addition to the assessment report and respective product information from the reference authority (EMA), the FDA BLA Clinical Review Memorandum (Abrysvo, application number 126768, approval date: 21 August 2023) and FDA-approved product information were also taken into account for the clinical and clinical pharmacology evaluation. The clinical evaluation focused on the safety results from the 2 controlled clinical studies (Study C3671008 and C3671003) evaluating the efficacy and safety of Abrysvo in infants born to women vaccinated during pregnancy.

The adverse reactions to Abrysvo in the vaccinated pregnant women were acceptable. The pregnancy outcomes (including days between vaccination and delivery, gestational age at delivery, live delivery, mode of delivery) were generally similar in the pooled vaccine and the placebo groups. Live birth outcomes, Apgar scores, development delay, and congenital abnormalities were reported at a similar frequency in the vaccine groups compared to the placebo group. None of the congenital anomalies were considered related to maternal vaccination with Abrysvo.

However, in the 2 clinical studies in pregnant women vaccinated between 24 and 36 weeks of gestation, a numerical imbalance was observed with respect to preterm birth in women who received Abrysvo compared to placebo.
Study C3671003 was a randomised, placebo-controlled, observer-blinded Phase 2 study that evaluated the safety of 2 dose levels (120 µg and 240 µg) of Abrysvo when administered to pregnant women. Abrysvo (120 µg) was administered to 115 participating mothers, and 114 infants were born to these participating mothers. In this study, preterm birth occurred in 5.3% (6 of 114) in the Abrysvo group and 2.6% (3 of 116) in the placebo group.
In the subsequent Phase 3 study C3671008, preterm birth occurred in 5.7% (95% CI: 4.9, 6.5; 202 of 3 568) in the Abrysvo group and 4.7% (95% CI: 4.1, 5.5; 169 of 3 558) in the placebo group.
Although the differences did not reach statistical significance and the causality could not be proven, based on the available data a causality could also not be excluded.
A smaller numerical imbalance in preterm birth was observed in the subgroup of infants vaccinated at 32 to 36 weeks of gestation: 4.2% (68/1,631) in the Abrysvo group and 3.7% (59/1,610) in the placebo group.
A post-hoc efficacy analysis for the subgroup of mothers vaccinated at 32-36 gestational weeks confirmed the efficacy for this subgroup, showing similar efficacy to that observed for the primary efficacy analyses (See Table 2 and 3 in the approved Information for healthcare professionals).
Thus, the benefit-risk assessment of the passive protection of infants born to mothers vaccinated during pregnancy was considered positive in case of vaccine administration at 32-36 gestational weeks.
This decision also took into account that other medicinal products for the prevention of lower respiratory tract infections caused by RSV were available from birth.
Post-marketing pharmacovigilance activities and safety studies will further monitor and provide information on premature births.

Concerning the safety of the maternal vaccination, the position of the FDA assessment was endorsed by Swissmedic. For further clinical aspects concerning the safety of maternal vaccination we refer to the FDA Assessment Report (BLA Clinical Review Memorandum).

7 Risk management plan summary

The RMP summaries contain information on the medicinal products' safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

8 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Abrysvo was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼ 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 new or serious adverse reactions. See the «Undesirable effects» section for advice on the reporting of adverse reactions.

Abrysvo®

Composition

Active substances

Antigenum F praefusionis stabilitum RSV subgrupi A[1,2], antigenum F praefusionis stabilitum RSV subgrupi B[1,2].

[1]glycoprotein F stabilised in the prefusion conformation.

[2]produced from genetically modified Chinese Hamster Ovary cells.

Excipients

Trometamolum, trometamoli hydrochloridum, saccharum, mannitolum, polysorbatum 80, natrii chloridum (corresp. 0.43 mg sodium per dose), acidum hydrochloridum (q.s. ad pH), aqua ad iniectabile.

Pharmaceutical form and active substance quantity per unit

Powder and solvent for solution for injection, intramuscularly.

After reconstitution 1 dose (0.5 ml) contains 60 µg of each RSV antigen: RSV subgroup A stabilised prefusion F antigen and RSV subgroup B stabilised prefusion F antigen. The powder is white. The solvent is a clear, colourless liquid.

Indications/Uses

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 immunization of pregnant individuals at 32 through 36 weeks gestational age (see «Warnings and precautions» and «Properties/Effects»).

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

The use of this vaccine should be in accordance with official recommendations.

Dosage/Administration

Pregnant individuals

A single dose of 0.5 ml should be administered between weeks 32 and 36 of gestation (see «Warnings and precautions» and «Properties/Effects»).

The need for revaccination with subsequent pregnancies has not been established.

Individuals 60 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. Very limited data are available in pregnant adolescents and their infants (see «Properties/Effects»).

Mode 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 «Instructions for handling».

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.

Contraindications

Hypersensitivity to the active substances or to any of the excipients (see «Composition»).

Warnings and precautions

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.

Potential risk of premature birth

A numerical imbalance in preterm births in Abrysvo recipients was observed compared to placebo recipients in the two clinical studies conducted in pregnant women. Available data are insufficient to establish or exclude a causal relationship between preterm birth and Abrysvo. To avoid the potential risk of preterm birth with use of Abrysvo before 32 weeks of gestation, administer Abrysvo as indicated in pregnant individuals at 32 through 36 weeks gestational age. Pregnant individuals who were at increased risk of preterm birth were generally excluded from clinical studies of Abrysvo (see «Pregnancy, lactation» and «Undesirable effects»).

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.

Limitations of vaccine effectiveness

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

Excipients of particular interest

This medicinal product contains less than 1 mmol sodium (23 mg) per 0.5 ml dose, i.e. it is almost «sodium-free».

Interactions

Use with other vaccines

In a randomised study in adults 65 years of age and older (N=1‘403, randomised 1:1) the concomitant administration of Abrysvo with a seasonal influenza vaccine (QIV, surface antigen, inactivated, adjuvanted) was investigated. 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.

The concomitant administration of Abrysvo with a tetanus-diphtheria-acellular pertussis vaccine (Tdap) was investigated. There were no safety concerns when Abrysvo was co-administered with Tdap in healthy non-pregnant women (N=141). 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; non-inferiority was not shown for any of the acellular pertussis antigens (pertussis toxoid [PT], filamentous hemagglutinin [FHA], and pertactin [PRN]) as the lower bound of the 95% CI for the GMC ratios of the co-administration group to the separate administration group did

not exceed 0.67. The lower limit of the 95% CI for the GMC ratio was 0.64 for PT, 0.50 for FHA, and 0.48 for PRN. 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).

The concomitant administration of Abrysvo with Tdap or influenza vaccines has not been studied in pregnant women.

Pregnancy, 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 «Preclinical data»).

In a phase 3 study (Study C3671008), maternal adverse events reported within 1 month after vaccination were similar in the Abrysvo group (13.8%) and the placebo group (13.1%). Serious adverse reactions observed in pregnant individuals in the Abrysvo group and the placebo group included pre-eclampsia (1.8% versus 1.4%), hypertension (0.4% versus 0.2%), gestational hypertension (1.1% versus 1.0%), premature rupture of membranes (0.4% versus 0.4%), preterm premature rupture of membranes (0.4% versus 0.3%), maternal death (<0.1% versus 0%) and foetal death (0.3% versus 0.3%).

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 (202/3568 (5.6%) and 169/3558 (4.7%), respectively), low birth weight (181 (5.1%) and 155 (4.3%), respectively) and congenital anomalies (174 (5.0%) and 203 (6.2%), respectively).

Available data are insufficient to establish or exclude a causal relationship between preterm birth and Abrysvo (see «Warnings and precautions» and «Undesirable effects»).

To minimize any potential risk of preterm birth Abrysvo should be given to pregnant individuals between 32-36 gestational weeks.

Lactation

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 «Preclinical data»).

Effects on ability to drive and use machines

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

Undesirable effects

Summary of the safety profile

The safety of administering a single dose of Abrysvo to pregnant women at 24-36 weeks of gestation (n=3‘682) and to individuals 60 years of age and older (n=18‘575) was evaluated in phase 3 clinical trials.

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 60 years of age and older

In individuals 60 years of age and older the most frequently reported adverse reaction was vaccination site pain (11%). The majority of reactions were mild to moderate in severity and resolved within 1-2 days of onset.

List of adverse reactions

The adverse reactions are arranged according to MedDRA system organ classes and the conventional frequencies as follows: «very common» (≥1/10), «common» (≥1/100, <1/10), «uncommon» (≥1/1’000, <1/100), «rare» (≥1/10’000, <1/1’000), «very rare» (<1/10’000), «not known» (frequency cannot be estimated from the available data).

Table 1 Adverse reactions following administration of Abrysvo

System Organ Class	*Adverse Drug Reactions Pregnant Individuals ≤49 years*	*Adverse Drug Reactions Individuals ≥60 years*
Immune system disorders		
Hypersensitivity		Very rare
Nervous system disorders		
Headache	Very common (31.0%)	
Guillain-Barré syndrome		Rare[a]
Musculoskeletal and connective tissue disorders		
Myalgia	Very common (26.5%)	
General disorders and administration site conditions		
Vaccination site pain	Very common (40.6%)	Very common (10.7%)
Vaccination site redness	Common	Common
Vaccination site swelling	Common	Common

[a] In a study in individuals 60 years of age and older, one case of Guillain-Barré syndrome and one case of Miller Fisher syndrome were reported with onset of 7 and 8 days, respectively, after receiving Abrysvo and assessed by the investigator as possibly related to the administered vaccine. Both cases had either confounding factors or an alternative aetiology. One additional case, with onset 8 months after receiving Abrysvo, was assessed as not related to the administered vaccine by the investigator. One case of Guillain-Barré syndrome was reported in the placebo group 14 months after administration.

Preterm births in clinical studies

A numerical imbalance in preterm births in Abrysvo recipients compared to placebo recipients was observed in two clinical studies conducted in pregnant women vaccinated between the 24-36 gestational weeks.

Study C3671003 was a phase 2, randomized, placebo-controlled, observer-blinded study that investigated the safety of two dose levels (120 µg and 240 µg) of Abrysvo administered to pregnant individuals. Abrysvo (120 µg) was administered to 115 maternal participants, and 114 infants were born to these maternal participants. In this study 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.

In the subsequent phase 3 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. In infants born preterm, 83 infants in the Abrysvo group and 80 infants in the placebo group remained hospitalized or were readmitted to the hospital in the neonatal period (up to 30 days after birth). Available data are insufficient to establish or exclude a causal relationship between preterm birth and Abrysvo. A numerical imbalance in preterm births was also observed in study C3671008 among the subgroup of infants born to participants who were vaccinated at 32 through 36 weeks

gestation, with 4.2% (68/1‘631) in the Abrysvo group and 3.7% (59/1‘610) in the placebo group (see «Warnings and precautions» and «Pregnancy, lactation»).

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

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.

Properties/Effects

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 during pregnancy, protection against RSV-associated lower respiratory tract disease is due to transplacental transfer of RSV neutralising antibodies. Adults 60 years of age and older are protected by active immunisation.

Pharmacodynamics

No information.

Clinical efficacy

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

Study C3671008 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.

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

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 (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.

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 (respiratory rate ≥60 bpm for <2 months of age [<60 days of age], ≥50 bpm for ≥2 months to <12 months of age, or ≥40 bpm for ≥12 months to 24 months of age), low oxygen saturation (SpO_2 <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 (respiratory rate ≥70 bpm for <2 months of age [<60 days of age], ≥60 bpm for ≥2 months to <12 months of age, or ≥50 bpm for ≥12 months to 24 months of age), low oxygen saturation (SpO_2 <93%), high-flow oxygen supplementation via nasal cannula or mechanical ventilation, ICU admission for >4 hours and/or failure to respond/unconscious.

In the population studied, the VE results met the statistical criterion for success (a CI lower bound >20%) for reducing severe medically attended lower respiratory tract illness illness due to RSV, at all timepoints to within 180 days. The VE results did not meet the statistical criterion for success for reducing medically attended lower respiratory tract illness illness due to RSV; however, clinically meaningful efficacy was observed after 90 days through 180 days after birth.

Vaccine efficacy in infants from birth to 180 days of age whose mothers were vaccinated between 32 and 36 weeks of gestation was based on a post-hoc analysis. 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 at 32 through 36 weeks gestational age – Study C3671008[a]

Time period	*Abrysvo Number of cases N=1'572*[b]	*Placebo Number of cases N=1'539*[b]	*VE % (CI)*[c]
90 days	1	11	91.1 (38.8, 99.8)
180 days	6	25	76.5 (41.3, 92.1)

CI = confidence interval; VE = vaccine efficacy
[a] This post-hoc descriptive subgroup analysis was not controlled for multiple comparisons; results from 90 days and 180 days are presented.
[b] Evaluable efficacy population.
[c] 95% CI

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 at 32 through 36 weeks gestational age – Study C3671008 [a]

Time period	*Abrysvo Number of cases N=1'572*[b]	*Placebo Number of cases N=1'539*[b]	*VE % (CI)*[c]
90 days	14	21	34.7 (-34.6, 69.3)
180 days	24	55	57.3 (29.8, 74.7)

CI = confidence interval; VE = vaccine efficacy
[a] This post-hoc descriptive subgroup analysis was not controlled for multiple comparisons; results from 90 days and 180 days are presented.
[b] Evaluable efficacy population.
[c] 95% CI

Active immunisation of individuals 60 years of age and older

Study C3671013 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 one 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 compared to placebo.

Vaccine efficacy information is presented in Table 4.

Table 4 Vaccine efficacy of Abrysvo against RSV lower respiratory tract disease - active immunisation of individuals 60 years of age and older – Study C3671013

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	15	43	65.1 (35.9, 82.0)
First episode of RSV-associated lower respiratory tract illness with ≥3 symptoms	2	18	88.9 (53.6, 98.7)

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

Pharmacokinetics

Absorption

Not applicable.

Distribution

Not applicable.

Metabolism

Not applicable.

Elimination

Not applicable.

Preclinical data

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

Other information

Incompatibilities

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

Shelf life

Do not use this medicine after the expiry date («EXP») stated on the pack.

The unopened vial is stable for 5 days when stored at temperatures from 8-30 °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.

Shelf life after opening

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

Chemical and physical in-use stability has been demonstrated for 4 hours between 15-30 °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.

Special precautions for storage

Store in a refrigerator (2-8ºC).

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

Keep out of the reach of children.

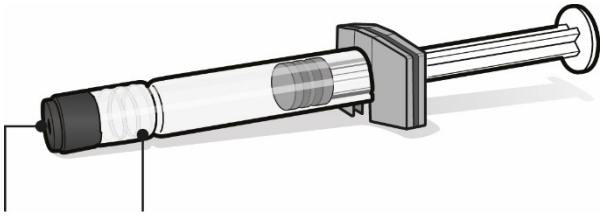
Instructions for handling

Abrysvo must be reconstituted prior to the 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.

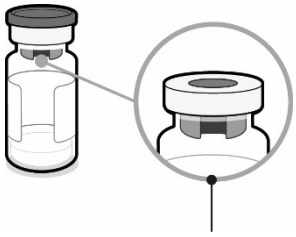
Preparation for administration

Pre-filled syringe containing solvent for Abrysvo



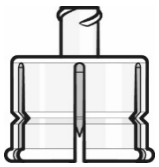
Syringe cap Luer lock adaptor

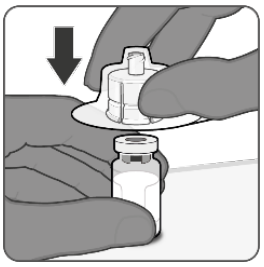
Vial containing antigens for Abrysvo (powder)



Vial stopper (with flip off cap removed)

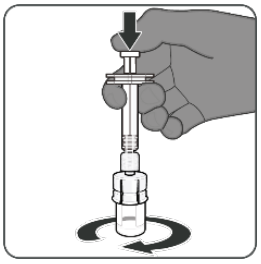
Vial adaptor





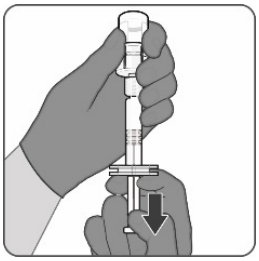
Step 1. Attach the vial adapter

- 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 lyophilised 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 (approximately 1-2 minutes). Do not shake.



Step 3. Withdraw the 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.

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.

Authorisation number

69691 (Swissmedic).

Packs

Pack containing 1 vial with powder, 1 pre-filled syringe with solvent, 1 vial adaptor and 1 needle. [B]

Pack containing 5 vials with powder, 5 pre-filled syringes with solvent, 5 vial adaptors and 5 needles. [B]

Pack containing 10 vials with powder, 10 pre-filled syringes with solvent, 10 vial adaptors and 10 needles. [B]

Marketing authorisation holder

Pfizer AG, Zürich.

Date of revision of the text

April 2024

LPD V003