PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

ABRYSVO (RESPIRATORY SYNCYTIAL VIRUS VACCINE [BIVALENT, RECOMBINANT])

Marketing Authorization Number 69691

Powder and solvent for solution for injection

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LIST OF ABBREVIATIONS

CMV	Cytomegalovirus
EMA	European Medicines Agency
EPAR	European Public Assessment Report
GBS	Guillain-Barré Syndrome
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan
RSV	Respiratory Syncytial Virus
RSVpreF	Respiratory Syncytial Virus stabilised prefusion F subunit vaccine
SmPC	Summary of Product Characteristics (European Union)

OVERVIEW

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them. The RMP summary for Abrysvo is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g., by mentioning risks occurring in populations or indications not included in the Swiss marketing authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of Abrysvo in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorised by Swissmedic. Pfizer is fully responsible for the accuracy and correctness of the content of the published RMP summary of Abrysvo.

SUMMARY OF RISK MANAGEMENT PLAN FOR ABRYSVO

This is a summary of the risk management plan (RMP) for Abrysvo. The RMP details important risks of Abrysvo, how these risks can be minimised, and how more information will be obtained about Abrysvo's risks and uncertainties (missing information).

Abrysvo's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and vaccine recipients on how Abrysvo should be used.

This summary of the RMP for Abrysvo should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Abrysvo's RMP.

I. The Medicine and What It Is Used For

Abrysvo is indicated for the maternal immunisation during pregnancy to provide protection in infants from birth through 6 months of age against lower respiratory tract disease caused by respiratory syncytial virus (RSV), and for active immunisation of individuals 60 years of age and older for the prevention of lower respiratory tract disease caused by RSV. It contains RSV subgroup A stabilised prefusion F protein (60 micrograms) and RSV subgroup B stabilised prefusion F protein (60 micrograms) as the active substances and it is given intramuscularly.

Further information about the evaluation of Abrysvo's benefits can be found in Abrysvo's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Abrysvo, together with measures to minimise such risks and the proposed studies for learning more about Abrysvo's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific Information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to vaccine recipients and healthcare professionals
- Important advice on the medicine's packaging;
- The authorised pack size - the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status - the way a medicine is supplied to the vaccine recipient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse events is collected continuously and regularly analysed, including PSUR assessment so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Abrysvo is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of Abrysvo are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Abrysvo. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

Table 1. List of important risks and missing information

Important identified risks	None
Important potential risks	Guillain-Barré syndrome
Missing information	Use in immunocompromised pregnant women and high-risk pregnancies
	Use in immunocompromised, or renally or hepatically impaired older adults ≥60 years old

II.B. Summary of Important Risks

There are no important identified risks for RSVpreF. *Guillain-Barré syndrome* has been reported in adults ≥60 years of age. Although GBS has not been reported in clinical trials in pregnant women, given the biological plausibility, GBS has been added as an important potential risk for both populations intended to be vaccinated with RSVpreF.

Table 2. Important potential risk - Guillain-Barré syndrome

Evidence for linking the risk to the medicine	Two cases of GBS and one case of Miller Fisher syndrome were reported in the older adult phase 3 study (C3671013) in participants vaccinated with RSV. Two cases were assessed as possibly related to the administered vaccine by the investigator (both had either confounding factors or an alternative aetiology), and one case, assessed as not related by the investigator, was reported eight months after RSV vaccination (unplausible temporal relationship). One additional case of GBS was reported in the placebo group. No cases of GBS were reported in the phase 3 study in maternal participants (C3671008).
Risk factors and risk groups	The annual incidence rate of GBS increase with age (0.6 per 100000 per year in children and 2.7 per 100000 per year in elderly people aged 80 years and over. Many different preceding infections have been identified in patients with the disorder, but only for a few microorganisms has an association been shown in case-control studies C *jejuni* is the predominant infection, found in 25–50% of the adult patients, with a higher frequency in Asian countries. Other infections associated with Guillain-Barré syndrome are cytomegalovirus (CMV), Epstein-Barr virus, influenza A virus, *Mycoplasma pneumoniae*, and *Haemophilus influenzae*. An association of Guillain-Barré syndrome with hepatitis E has been identified in patients from both the Netherlands and Bangladesh. An emerging relation between Guillain-Barré syndrome and acute arbovirus infection including Zika and chikungunya is being closely monitored and is the subject of major interest as the global epidemic spreads.

Table 2. Important potential risk - Guillain-Barré syndrome

Risk minimisation measures	Routine risk minimisation measures EU SmPC Section *4.8 Undesirable effects* Additional risk minimisation measures None
Additional pharmacovigilance activities	Additional pharmacovigilance activities Post-authorisation safety studies planned to be conducted in the EU include GBS as a safety outcome among immunocompromised, or renally or hepatically impaired older adults (C3671038) and among pregnant women and their offspring (C3671026). In addition, a post-marketing safety study focusing on GBS, other immune-mediated demyelinating conditions and polyneuropathies among older adults is planned to be conducted in US (C3671031). See section II.C of this summary for an overview of the post-authorisation development plan.

Table 3. Missing information - Use in immunocompromised pregnant women and high-risk pregnancies

Risk minimisation measures	Routine risk communication EU SmPC Section *4.4 Special warnings and precautions for use* Additional risk minimisation measures No risk minimisation measures
Additional pharmacovigilance activities	Additional pharmacovigilance activities Safety of respiratory syncytial virus stabilised prefusion F subunit vaccine (RSVpreF) in pregnant women and their offspring in a real world setting in Europe (C3671026). See Section II.C of this summary for an overview of the post-authorisation development plan.

Table 4. Missing information - Use in immunocompromised, or renally or hepatically impaired older adults ≥60 years old

Risk minimisation measures	Routine risk communication EU SmPC Section *4.4 Special warnings and precautions for use* Additional risk minimisation measures No risk minimisation measures
Additional pharmacovigilance activities	Additional pharmacovigilance activities Safety of respiratory syncytial virus stabilized prefusion F subunit vaccine (RSVpreF) in immunocompromised, or renally or hepatically impaired older adults aged 60 years and older in a real world setting in Europe (C3671038). See Section II.C of this summary for an overview of the post-authorisation development plan.

II.C. Post-Authorisation Development Plan

II.C.1 Studies which are Conditions of the Marketing Authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation for Abrysvo.

II.C.2 Other Studies in Post-Authorisation Development Plan

Study title: Safety of respiratory syncytial virus stabilised prefusion F subunit vaccine (RSVpreF) in pregnant women and their offspring in a real world setting in Europe (C3671026)

Purpose of the study: As immunocompromised pregnant women and high-risk pregnancies were not included in the clinical studies to date, Pfizer plans to address this missing information by conducting a PASS study with the following objectives:

To estimate the prevalence and rate ratios of adverse pregnancy and maternal outcomes at or after birth in all eligible pregnant, including immunocompromised pregnant women and women with high-risk pregnancies and their offspring a who receive RSVpreF, compared to a relevant matched comparator group of pregnant women and their offspring who do not receive RSVpreF.

Study title: Safety of respiratory syncytial virus stabilised prefusion F subunit vaccine (RSVpreF) in immunocompromised, or renally or hepatically impaired older adults aged 60 years and older in a real world setting in Europe (C3671038)

Purpose of the study: As immunocompromised, or renally or hepatically impaired older adults aged 60 years and older were not included in the clinical studies to date, Pfizer plans to address this missing information by conducting a PASS study with the following objectives:

To estimate the incidence and rate ratios of safety events of interest in immunocompromised, or renally or hepatically impaired older adults aged 60 years and older who receive RSVpreF compared to a relevant matched comparator group of persons who do not receive RSVpreF.

Study title: A post-marketing safety study of respiratory syncytial virus vaccine among older adults in the United States; version 4.0, 14 June 2023 (C3671031)

Purpose of the study: As the phase 3 study, RENOIR (C3671013), was not powered to evaluate the risk of rare adverse events, Pfizer plans to further evaluate the risk of GBS, other immune-mediated demyelinating conditions, and polyneuropathies following RSVpreF administration in older adults in the US.