PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

For

mRESVIA dispersion for injection in pre-filled syringe

Respiratory Syncytial Virus mRNA Vaccine

(single-stranded 5'capped mRNA encoding the RSV-A glycoprotein F stabilised in the prefusion conformation)

Marketing Authorization Number 69995

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Moderna Switzerland GmbH, Basel

Table of Contents

List of Tables

List of Abbreviations

Acronym	Definition
CEAC	Cardiac Event Adjudication Committee
EMA	European Medicine Agency
EPAR	European Public Assessment Report
EU	European Union
LRTD	Lower respiratory tract disease
mRNA	Messenger ribonucleic acid
PL	Package leaflet
RMP	Risk management plan
RSV	Respiratory syncytial virus
SARS	Severe acute respiratory syndrome
SmPC	Summary of Product Characteristics

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 of mRESVIA 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 authorization.

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

Summary of risk management plan for mRESVIA (single-stranded 5' capped mRNA encoding the RSV-A glycoprotein F stabilised in the prefusion conformation)

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

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

This summary of the RMP for mRESVIA 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 mRESVIA's RMP.

I The Medicine and What it is Used for

mRESVIA is authorised for active immunisation for the prevention of lower respiratory tract disease (LRTD) caused by RSV in adults 60 years of age and older (see SmPC for the full indication). The active substance in mRESVIA is a single-stranded 5' capped mRNA encoding the RSV-A glycoprotein F stabilised in the prefusion conformation and it is given by intramuscular route.

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

www.ema.europa.eu/en/medicines/human/EPAR/mresvia

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

Important risks of mRESVIA, together with measures to minimise such risks and the proposed studies for learning more about mRESVIA'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 patients 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 patient (eg, 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 reactions is collected continuously and regularly analysed, including Periodic Safety Update Report (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 mRESVIA is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of mRESVIA 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 mRESVIA. 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 (eg, on the long-term use of the medicine).

Table 1: List of Important Risks and Missing Information

List of Important Risks and Missing Information	
Important identified risks	None
Important potential risks	Myocarditis/pericarditis
Missing information	Co-administration with other vaccines Use in immunocompromised individuals Use in individuals with autoimmune or inflammatory disorders Long-term safety

II.B Summary of Important Risks

Table 2: Important Potential Risk: Myocarditis/pericarditis

Important Potential Risk: Myocarditis/pericarditis	
Evidence for linking the risk to the medicine	Myocarditis/pericarditis can be caused by a variety of factors; the most common aetiology is viral infection. In study mRNA-1345-P301, there were no CEAC adjudicated cases of acute myocarditis up to the data cutoff (30 April 2023) and no CEAC adjudicated cases of acute pericarditis up to 42 days after study injection in either the mRESVIA or placebo groups. While two participants in the mRESVIA group had CEAC adjudicated events of acute pericarditis with onset >42 days, they were assessed by the investigator as unrelated to study vaccine as other confounding factors provide an alternative causal association. No cases of acute pericarditis were reported in the placebo group up to data cutoff. Clinical trials can provide an estimation of the frequency and nature of an adverse reaction that is expected to occur post-authorisation.
Risk factors and risk groups	Acute myocarditis is overall more common in men than in women overall (Kytö et al 2013). The incidence rate occurs with two peaks: the highest in those under one year old with both genders combined (Vasudeva et al 2021) and young males aged 16 to <40 years old (Vasudeva et al 2021; Kytö et al 2013). Similarly, acute pericarditis is more common in men than in women overall. However, the gender difference is reduced with advancing age and became nominal in persons aged >65 years (Kytö et al 2014). In males, the incidence rate of acute pericarditis declines between 16 to 45 years followed by an increase in older individuals aged >50 years (Kytö et al 2014). In females, the incidence rate of acute pericarditis gradually increases with age, with a peak in the population aged 65 to 74 years (Kytö et al 2014; Kumar et al 2016).
Risk minimisation measures	Routine risk minimisation measures: None Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: mRNA-1345-P101 mRNA-1345-P301 mRNA-1345-P302 mRNA-1345-P303 mRNA-1345-P902 mRNA-1345-P903 See section II.C of this summary for an overview of the post-authorisation development plan.

Table 3: Missing Information: Co-Administration with Other Vaccines

Missing Information: Co-administration with other vaccines	
Risk minimisation measures	Routine risk minimisation measures: Information that no interaction studies have been performed and that concomitant administration of mRESVIA with other vaccines has not been studied in SmPC Section 4.5 Guidance for the individual to tell their doctor, pharmacist or nurse if they are taking, have recently taken or might take any other medicines in PL Section 2

Missing Information: Co-administration with other vaccines	
	Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: mRNA-1345-P302 mRNA-1345-P902 mRNA-1345-P903 See section II.C of this summary for an overview of the post-authorisation development plan.

Table 4: Missing Information: Use in Immunocompromised Individuals

Missing Information: Use in immunocompromised individuals	
Risk minimisation measures	Routine risk minimisation measures: Information that safety and immunogenicity data on mRESVIA are not available for immunocompromised individuals, and that individuals receiving immunosuppressant therapy or patients with immunodeficiency may have a diminished immune response to this vaccine in SmPC Section 4.4 Warning for the individual to talk to their doctor, pharmacist or nurse before they are given mRESVIA if they have a weakened immune system which may prevent them from getting the full benefit from mRESVIA in PL Section 2 Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: mRNA-1345-P303 mRNA-1345-P902 mRNA-1345-P903 See section II.C of this summary for an overview of the post-authorisation development plan.

Table 5 Missing information: Use in Individuals with Autoimmune or Inflammatory Disorders

Missing Information: Use in individuals with autoimmune or inflammatory disorders	
Risk minimisation measures	Routine risk minimisation measures: None Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: mRNA-1345-P902 mRNA-1345-P903 See section II.C of this summary for an overview of the post-authorisation development plan.

Table 6 Missing information: Long-Term Safety

Risk minimisation measures	Routine risk minimisation measures: None Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: mRNA-1345-P101 mRNA-1345-P301 mRNA-1345-P302 mRNA-1345-P303 mRNA-1345-P902 mRNA-1345-P903 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 obligations of mRESVIA.

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

The following studies are considered ongoing and/or planned additional pharmacovigilance activities:

Table 7 Other Studies in the Post-Authorisation Development Plan

Study Title and Number	Purpose of the Study
A Phase 1, Randomized, Observer-Blind, Placebo-Controlled, Dose Escalation Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of mRNA-1345, an mRNA Vaccine Targeting Respiratory Syncytial Virus (RSV), in Healthy Younger Adults Aged 18 to 49 Years, Women of Child-Bearing Potential Aged 18 to 40 Years, Healthy Older Adults Aged 65 to 79 Years, Japanese Older Adults Aged ≥60 Years, and RSV-Seropositive Children Aged 12 to 59 Months (mRNA-1345-P101)	Primary Objectives: • To evaluate the tolerability and reactogenicity of a single injection of up to 5 dose levels of mRNA-1345 in younger adults, women of child-bearing potential, and older adults, including Japanese older adults. • To evaluate the tolerability and reactogenicity of 3 injections of the middle dose level of mRNA-1345 given 56 days apart in younger adults. • To evaluate the tolerability and reactogenicity of a booster injection of mRNA-1345 given approximately 12 months after the primary injection in older adults. • To evaluate the tolerability and reactogenicity of 3 injections of 2 dose levels of mRNA-1345 given 56 days apart in RSV-seropositive children.
A Phase 2/3, Randomized, Observer-Blind, Placebo-Controlled Study to Evaluate the Safety and Efficacy of mRNA-1345, an mRNA Vaccine Targeting Respiratory Syncytial Virus (RSV), in Adults ≥60 Years of Age (mRNA-1345-P301)	**Primary Objectives:** • To evaluate the safety and tolerability of the mRNA-1345 vaccine. • To evaluate the efficacy of a single dose of mRNA-1345 vaccine in the prevention of a first episode of RSV-LRTD as compared with placebo within the period of 14 days post-injection up to 12 months post-injection.
A Phase 3 Randomized, Observer-Blind, Study to Evaluate Safety, Tolerability, and Immunogenicity of mRNA-1345, an mRNA Vaccine Targeting Respiratory Syncytial Virus (RSV), When Given Alone or Coadministered with a Seasonal Influenza Vaccine or SARS-CoV-2 Vaccine in Adults ≥50 Years of Age (mRNA-1345-P302)	**Primary Objectives Part A:** • To evaluate the safety and tolerability of mRNA-1345 coadministered with a seasonal influenza vaccine (Afluria® Quadrivalent). • To evaluate the impact of coadministered influenza vaccine on the immune response to RSV-A. • To evaluate the impact of coadministered RSV vaccine on the immune response to influenza. **Primary Objectives Part B:**

Study Title and Number	Purpose of the Study
	• To evaluate the safety and tolerability of mRNA-1345 coadministered with mRNA-1273.214. • To evaluate the effect of coadministered mRNA-1273.214 on the immune response to RSV-A. • To evaluate the effect of coadministered RSV vaccine on the immune response to SARS-CoV-2. **Primary Objectives Part C:** • To evaluate the safety and tolerability of a booster dose of mRNA-1345 administered at Year 1 following a primary dose. • To evaluate immune response to RSV-A of a booster dose of mRNA-1345 administered at Year 1 following a primary dose. • To evaluate the safety and tolerability of booster dose of mRNA-1345 administered at Year 2 following a primary dose. • To evaluate immune response to RSV-A of a booster dose of mRNA-1345 administered at Year 2 following a primary dose.
A Phase 3 Study to Evaluate the Immunogenicity and Safety of mRNA-1345, an mRNA Vaccine Targeting Respiratory Syncytial Virus, in High-risk Adults (mRNA-1345-P303)	**Primary Objectives Part A:** • To evaluate the safety and tolerability of mRNA-1345. • To evaluate the RSV-A nAb response to a single dose of 50 µg mRNA-1345 injection in high-risk adults (≥18 to <60 years) compared with that in high-risk older adults (≥60 years). **Primary Objectives Part B:** • To evaluate the safety and tolerability of mRNA-1345. • To evaluate the RSV-A and RSV B nAb responses to 2 doses of 50 µg mRNA-1345 injection administered 57 days apart in immunocompromised participants ≥18 years of age.
Post-Authorization Active Surveillance Safety Study Using Secondary Data to Monitor Real-World Safety of the mRNA-1345 Vaccine for respiratory syncytial virus (RSV) in the United States (mRNA-1345-P902)	**Primary Objectives:** 1) Describe the uptake of the mRNA-1345 vaccine and characterize mRNA-1345 vaccine recipients 2) Estimate incidence of pre-defined Safety Topics of Interest among mRNA-1345 vaccine recipients 3) For signal detection, compare the observed incidence rates of pre-defined Safety Topics of Interest among mRNA-1345 vaccine recipients with expected incidence rates of pre-defined Safety Topics of Interest from a similar comparator cohort(s) 4) When a safety signal is detected based on pre-defined statistical threshold, • Compare incidence rates of pre-defined Safety Topics of Interest in the risk interval with incidence rates in the post-vaccination control interval in a self-controlled risk interval analysis. Or

Study Title and Number	Purpose of the Study
	• Compare the observed incidence rates of pre-defined Safety Topics of Interest among mRNA-1345 vaccine recipients with incidence rates of pre-defined Safety Topics of Interest in a similar matched cohort who did not receive the mRNA-1345 vaccine **Secondary Objectives:** Secondary objectives are identical to the primary, but focused on specific populations considered to have missing information, including but not limited to • Immunocompromised patients • Stratification by age group and sex • Patients who, at cohort entry, had recently received other selected vaccines to prevent diseases other than the mRNA-1345 vaccine Patients with autoimmune or inflammatory disorders
Post-Authorization Active Surveillance Safety Study Using Secondary Data to Monitor Real-World Safety of the mRNA-1345 Vaccine for respiratory syncytial virus (RSV) in Europe (mRNA-1345-P903)	**Primary Objectives:** 1) Describe the uptake of the mRNA-1345 vaccine and characterize mRNA-1345 vaccine recipients 2) Estimate incidence of pre-defined Safety Topics of Interest among mRNA-1345 vaccine recipients 3) For signal detection, compare the observed incidence rates of pre-defined Safety Topics of Interest among mRNA-1345 vaccine recipients with expected incidence rates of pre-defined Safety Topics of Interest from a similar comparator cohort(s) 4) When a safety signal is detected based on pre-defined statistical threshold, • Compare incidence rates of pre-defined Safety Topics of Interest in the risk interval with incidence rates in the post-vaccination control interval in a self-controlled risk interval analysis. Or • Compare the observed incidence rates of pre-defined Safety Topics of Interest among mRNA-1345 vaccine recipients with incidence rates of pre-defined Safety Topics of Interest in a similar matched cohort who did not receive the mRNA-1345 vaccine **Secondary Objectives:** Secondary objectives are identical to the primary but focused on specific populations considered to have missing information, including but not limited to • Immunocompromised patients • Stratification by age group and sex • Patients who, at cohort entry, had recently received other selected vaccines to prevent diseases other than the mRNA-1345 vaccine • Patients with autoimmune or inflammatory disorders Stratification by country where appropriate

References in the Summary of the RMP

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