Summary of risk management plan for Trumenba (bivalent rLP2086)

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

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

This summary of the RMP for Trumenba should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all of 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 Trumenba's RMP.

I. The Medicine and What It Is Used For

Trumenba is a vaccine to prevent invasive meningococcal disease, caused by *Neisseria meningitidis* serogroup B, for use in people 10 years and older (See SmPC for the full indication). It contains *Neisseria meningitidis* serogroup B fHbp subfamily A (60 micrograms) and *Neisseria meningitidis* serogroup B fHbp subfamily B (60 micrograms) as active substances and it is a white suspension for injection, provided in a pre-filled syringe.

Further information about the evaluation of Trumenba's benefits can be found in Trumenba's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage: https://www.ema.europa.eu/en/medicines/human/EPAR/trumenba

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

Important risks of Trumenba, together with measures to minimise such risks and the proposed studies for learning more about Trumenba' 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 public (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 Trumenba is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of Trumenba 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 Trumenba. 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	None
Missing information	Use in co-administration with MMR and pneumococcal vaccines
	Use in immunocompromised individuals (eg, individuals with terminal complement deficiency or asplenia)
	Vaccine effectiveness

MMR = measles, mumps, and rubella.

II.B. Summary of Important Risks and Missing Information

There are no identified or potential risks that are considered important for Trumenba.

Table 2. Missing Information: Use in Co-Administration with MMR and Pneumococcal Vaccines

Risk minimisation measures	Routine risk minimisation measures: The risk is communicated through the label (SmPC Section 4.5) Additional risk minimisation measures: None.
Additional pharmacovigilance activities	A PASS protocol (C3511006) to assess the safety, tolerability and immunogenicity of MenABCWY in healthy participants ≥ 12 to <24 months of age, and when administered concomitantly with MMR and Pneumococcal vaccines in healthy participants ≥12 to< 16 months of age. See section II.C of this summary for an overview of the post-authorisation development plan.

MMR = Measles-Mumps-Rubella Vaccine; rLP2086 = Recombinant Lipoprotein 2086; SmPC = Summary of Product Charateristics

Table 3. Missing Information: Use in Immunocompromised Individuals (eg, Individuals with Terminal Complement Deficiency or Asplenia)

Risk minimisation measures	Routine risk minimisation measures: The risk is communicated through the label (SmPC Section 4.4) Additional risk minimisation measures: None.
Additional pharmacovigilance activities	A PASS protocol (B1971060) to investigate the safety, tolerability and immunogenicity of 2 doses of bivalent rLP2086 in immunocompromised individuals (including individuals with complement deficiency or asplenia) ≥10 years of age. See section II. C of this summary for an overview of the post-authorisation development plan.

rLP2086 = Recombinant Lipoprotein 2086 ; PASS = Post Authorization Safety Study.

Table 4. Missing Information: Vaccine Effectiveness

Risk minimisation measures	Routine risk minimisation measures: The risk is communicated through the label (SmPC Sections 4.4 and 5.1) Additional risk minimisation measures: None.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Investigation of bivalent rLP2086 effectiveness • Provide detailed meningococcal epidemiological reports in the PSURs. • Feasibility assessments of the ability to determine the effectiveness of bivalent rLP2086 in the US and Italy, plus any country that introduces bivalent rLP2086 into a national or regional immunization program (to be provided in the PSURs). For a Country that may be planning to introduce bivalent rLP2086 in the future the MAH proposed the following, if deemed feasible: A phase 4 observational study based on the active laboratory surveillance for IMD in all ages in a specific region or country where bivalent rLP2086 vaccine is part of the routine immunization program. The study will aim to evaluate the impact and effectiveness of bivalent rLP2086 on confirmed MenB cases. This will be dependent upon the availability of the necessary data on MenB cases and vaccine coverage through the existing surveillance systems See section II.C of this summary for an overview of the post-authorisation development plan.

IMD = invasive meningococcal disease; rLP2086= Recombinant Lipoprotein 2086; SmPC = Summary of Product Charateristics;

II.C. Post-Authorisation Development Plan

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

There are no planned or ongoing post-authorisation efficacy studies which are specific obligations and/or conditions of the MAA.

Other efficacy/effectiveness studies

B1971057:

Study title: A Phase 3, randomised, active-controlled, observer-blinded study to assess the immunogenicity, safety, and tolerability of bivalent rLP2086 when administered as a 2-dose regimen and a first-in-human study to describe the immunogenicity, safety, and tolerability of a bivalent rLP2086-containing pentavalent vaccine (MenABCWY) in healthy subjects ≥10 to <26 years of age.

Purpose of the study: To assess the immune response induced by bivalent rLP2086 measured 1 month after the second vaccination in the bivalent rLP2086 arms combined. To describe the safety profile of bivalent rLP2086 following Vaccinations 1 and 2 in the bivalent rLP2086 arms combined (Stage 1) and to assess persistence of immunity through 4 years after completing the primary series of MenABCWY and bivalent rLP2086+MenACWY-CRM group subjects (Stage 2).

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

The category 3 studies listed below are additional planned, or ongoing pharmacovigilance activities.

C3511006: A Phase 3, randomized, controlled, open-label trial to assess the safety, tolerability and immunogenicity of MenABCWY in healthy participants ≥ 12 to <24 months of age, and when administered concomitantly with MMR and Pneumococcal vaccines in healthy participants ≥12 to< 16 months of age. (Planned)

The study is designed to:

Assess the safety, tolerability, and immunogenicity of MenABCWY when administered concomitantly with MMR and 13vPnC pneumococcal vaccine in participants ≥12 to <16 months of age. The study is designed to demonstrate in this population responses to MenABCWY MMR and 13vPnC pneumococcal vaccine when administered concomitantly to be non-inferior to responses to MenABCWY, MMR and 13vPnC pneumococcal vaccine when MenABCWY is administered a month apart from MMR + pneumococcal vaccine13vPnC.

To demonstrate that the ACWY immune response following MenABCWY is noninferior to that following EU licensed quadrivalent meningococcal vaccine Nimenrix (MenACYW-TT) in participants ≥12 to <24 months of age.

B1971060: Phase 4, open-label, single-arm trial to describe the safety, tolerability, and immunogenicity of bivalent rLP2086 when administered to immunocompromised participants ≥10 years of age. (Ongoing)

Purpose of the study: to describe the safety and immunogenicity of 2 doses of bivalent rLP2086 administered on a 0- and 6-month schedule in immunocompromised participants ≥10 years of age.

Investigation of bivalent rLP2086 effectiveness. (Planned)

Purpose of the PV activity: to incorporate in the Periodic Safety Update Reports, in order to provide an update of progress towards executing a study to evaluate effectiveness of bivalent rLP2086:

- Detailed meningococcal epidemiological reports;
- Feasibility assessments of the ability to determine the effectiveness of bivalent rLP2086 in the US and Italy, plus any country that introduces bivalent rLP2086 into a national or regional immunization program.

For a Country that may be planning to introduce bivalent rLP2086 in the future the MAH proposed the following, if deemed feasible:

- A phase 4 observational study will be conducted based on the active laboratory surveillance for IMD in all ages in a specific region or country where bivalent rLP2086 vaccine is part of the routine immunization program. The study will aim to evaluate the impact and effectiveness of bivalent rLP2086 on confirmed MenB cases. This will be dependent upon the availability of the necessary data on MenB cases and vaccine coverage through the existing surveillance systems.