PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for IMVANEX (Smallpox Vaccine Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN®) (live attenuated, non-replicating))

This is a summary of the risk management plan (RMP) for IMVANEX. The RMP details important risks of IMVANEX, and how more information will be obtained about IMVANEX's risks and uncertainties (missing information).
IMVANEX's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how IMVANEX should be used.

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

I. The medicine and what it is used for

IMVANEX is authorised for active immunisation against smallpox in adults (see SmPC for the full indications). It contains smallpox vaccine live Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN®) (live attenuated, non-replicating) as the active substance and it is given by subcutaneous (SC) injection.

Further information about the evaluation of IMVANEX's benefits can be found in IMVANEX'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/imvanex.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of IMVANEX, together with measures to minimise such risks and the proposed studies for learning more about IMVANEX'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 (e.g. with or without prescription) can help to minimise its risks.

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

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

II.A List of important risks and missing information

Important risks of IMVANEX 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 IMVANEX. 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).

As of the date of this report, BN oversees 8992 subjects exposed with IMVANEX, including at-risk populations for which replicating smallpox vaccines such as Dryvax and ACAM2000 are contraindicated, e.g. individuals with AD or HIV infected subjects.

No trends for unexpected and/or serious adverse reactions were detected and no difference in the safety profile has been observed between vaccinia-naïve and vaccinia-experienced subjects receiving IMVANEX.

Important identified risks	None
Important potential risks	• Myo-/pericarditis • Postvaccinal encephalitis
Important missing information	• Children and adolescents (<18 years) • Pregnant and lactating women • Elderly subjects • Individuals with organ impairment • Clinically immunocompromised individuals • Safety experience in mass vaccination due to smallpox outbreak • Interactions with other vaccines and concomitantly administered immunoglobulins

II.B Summary of important risks

Important potential risk: Myo-/pericarditis	
Evidence for linking the risk to the medicine	Pharmacological class effect, US Department of Defense Smallpox Vaccination Program (US DoD 2007); ACAM2000 package information leaflet
Risk factors and risk groups	No risk factors identified; use is currently limited primarily to military personnel
Risk minimisation measures	Routine risk minimisation measures

	• All cases of suspected/possible myo-/pericarditis will be followed-up according to the case definitions as published by the Centers of Disease Control and Prevention • As no confirmed cases of myo-/pericarditis have been reported for IMVAMUNE, no additional risk minimisation activities are considered necessary. Additional risk minimisation measures None proposed
Additional pharmacovigilance activities	Additional pharmacovigilance activities: POX-MVA-039 See section II.C of this summary for an overview of the post-authorisation development plan.
Important potential risk: Postvaccinal encephalitis	
Evidence for linking the risk to the medicine	Pharmacological class effect, US Department of Defense Smallpox Vaccination Program (US DoD 2007); ACAM2000 package information leaflet
Risk factors and risk groups	Unknown
Risk minimisation measures	Routine risk minimisation measures • All cases of suspected/possible postvaccinal encephalitis will be followed-up • As postvaccinal encephalitis has not been reported for IMVAMUNE, no additional risk minimisation activities are considered necessary. Additional risk minimisation measures None proposed
Additional pharmacovigilance activities	Additional pharmacovigilance activities: POX-MVA-039 See section II.C of this summary for an overview of the post-authorisation development plan.
Missing information: Children and adolescents (<18 years)	
Risk minimisation measures	Routine risk minimisation measures SmPC section INDICATIONS AND CLINICAL USE 4.1 'Therapeutic indications' clearly indicates correct age group (persons 18 years of age and older). Additional risk minimisation measures None proposed
Missing information: Pregnant and lactating women	
Risk minimisation measures	Routine risk minimisation measures

	SmPC Section 4.6 'WARNINGS AND PRECAUTIONS Pregnancy and lactation' clearly points out that vaccinating of pregnant or lactating women is not recommended. Additional risk minimisation measures None proposed
Missing information: Interactions with other vaccines and concomitantly administered immunoglobulins	
Risk minimisation measures	Routine risk minimisation measures SmPC section DRUG INTERACTIONS states: 'No interaction studies with other vaccines or medicinal products have been performed. Therefore, concomitant administration of IMVANEX with other vaccines should be avoided'. 'The concomitant administration of the vaccine with any immunoglobulin including Vaccinia Immune Globulin (VIG) has not been studied and should be avoided Additional risk minimisation measures None proposed

No table is applicable for important missing information on elderly subjects, on individuals with organ impairment, on clinically immunocompromised individuals and on safety experience in mass vaccination due to smallpox outbreak, as no risk minimization measures are proposed.

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorization

Study short name: PASS/PAES POX-MVA-039: An observational post-authorization safety and efficacy study for the prophylactic vaccination with IMVAMUNE following re-emergence of circulating smallpox infections

Purpose of the study: The primary objective of the study will be to monitor and characterise incidence of serious adverse events and/or medically attended adverse events in patients exposed to IMVAMUNE in accordance with a national public health vaccination program and/or other real-life use.

Effectiveness endpoints will also be included in the PASS/PAES.

II.C.2 Other studies in post-authorisation development plan

POX-MVA-035: Open-label, non-controlled, multicenter immunogenicity and safety study of MVA-BN smallpox vaccine in children from birth to less than 12 years of age

Purpose of the study: Assessing immunogenicity and safety of MVA-BN smallpox vaccine in children from birth to less than 12 years of age.