Swiss Summary of the Risk Management Plan (RMP)

GARDASIL9

Human Papillomavirus 9-valent Vaccine, Recombinant

Intramuscular injection

Date of this document: 08-Sep-2023

Based on EU RMP version 5.1: 12-May-2023

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 Gardasil® 9 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 Gardasil® 9 in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic.

MSD Merck Sharp & Dohme AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Gardasil® 9.

PART VI SUMMARY OF THE RISK MANAGEMENT PLAN BY PRODUCT

SUMMARY OF RISK MANAGEMENT PLAN FOR GARDASIL 9 (HUMAN PAPILLOMAVIRUS 9-VALENT VACCINE, RECOMBINANT OR 9VHPV VACCINE)

This is a summary of the risk management plan (RMP) for 9vHPV vaccine. The RMP details important risks of 9vHPV vaccine, how these risks can be minimised, and how more information will be obtained about 9vHPV vaccine's risks and uncertainties (missing information).

9vHPV vaccine's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how 9vHPV vaccine should be used.

This summary of the RMP for 9vHPV vaccine 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 9vHPV vaccine's RMP.

I. The Medicine and What it is Used For

9vHPV vaccine is authorised for active immunisation of individuals from the age of 9 years against the following HPV diseases:

– Premalignant lesions and cancers affecting the cervix, vulva, vagina and anus caused by vaccine HPV types

– Genital warts (Condyloma acuminata) caused by specific HPV types (see SmPC for the full indication). It contains Human Papillomavirus 9-valent Vaccine, Recombinant as the active substance and it is given by intramuscular injection.

Further information about the evaluation of 9vHPV vaccine’s benefits can be found in Human Papillomavirus 9-valent Vaccine, Recombinant’s EPAR, including in its plain- language summary, available on the EMA website, under the medicine’s webpage:

https://www.ema.europa.eu/medicines/human/EPAR/gardasil-9

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

Important risks of 9vHPV vaccine, together with measures to minimise such risks and the proposed studies for learning more about 9vHPV vaccine'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.

In addition to these measures, information about adverse reactions 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 9vHPV vaccine is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of 9vHPV vaccine 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 9vHPV vaccine.
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).

Based on scientific information to date and the latest guidance on Risk Management Planning from the EMA, the Important Identified and Potential Risks have been removed:

- Analysis of the post-marketing data gathered on 9vHPV vaccine shows that there are no outstanding additional pharmacovigilance activities to address the previously identified and potential risks listed in the RMP.
- The risks are fully characterized and appropriately managed through labelling.
- There is no reasonable expectation that any pharmacovigilance activity can further characterize the previously listed Important identified and potential risks.

For Missing Information, the MAH is retaining the safety issues listed in the table below, given that there are ongoing pharmacovigilance activities that could further characterize the safety profile of the product with respect to the area of missing information.

Table II.A.1: List of Important Risks and Missing Information

List of Important Risks and Missing Information	
Important identified risks	None
Important potential risks	None
Missing information	Long term effectiveness and immunogenicity

II.B Summary of Important Risks

Table II.B.1: Missing Information: Long Term Effectiveness and Immunogenicity

Risk minimisation measures	**Routine risk minimisation measures** See section 5.1 of the SmPC
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** V503-021: Nordic Long-Term Follow-Up Study (10-year extension in subjects from V503-001)

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 of 9vHPV vaccine.

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

Study Short Name and Title: V503-021: Nordic Long-Term Follow-Up Study (10-year extension in subjects from V503-001)
A Registry-Based Extension of Protocol V503-001 in Countries with Centralized Cervical Cancer Screening Infrastructures to Evaluate the Long-Term Effectiveness, Immunogenicity, and Safety of Multivalent Human Papillomavirus (HPV) L1 Virus-Like Particle (VLP) Vaccine as Administered to 16- to 26- Year- Old Women.

Purpose of the Study:

Rationale and Study Objectives:

Protocol V503-021 is a long-term follow-up study extension of the V503-001 base study in the Scandinavian countries of Denmark, Norway and Sweden to evaluate the safety, immunogenicity, and long-term effectiveness of 9vHPV vaccine in preventing cervical, vulvar, and vaginal cancers and related precancers caused by the vaccine HPV types (6, 11, 16, 18, 31, 33, 45, 52, and 58). Safety and effectiveness are assessed using information from national health registries of the Scandinavian countries. The subjects entered the V503-021 study extension after they completed the V503-001 base study. Each subject will be followed for approximately 10 years in the V503-021 study extension. No vaccination will be administered during this study.

The objectives of the study address important missing information for long-term effectiveness/Immunogenicity.

Primary Objective: To assess the long-term effectiveness of the 9vHPV vaccine by monitoring the combined incidence of Cervical Intraepithelial Neoplasia (CIN) 2, CIN 3, Adenocarcinoma In Situ (AIS) and cervical cancer related to HPV 16, 18, 31, 33, 45, 52, and 58 in women from Protocol V503-001 in the Nordic region vaccinated with the 9vHPV vaccine.