Summary of risk management plan for GARDASIL (Quadrivalent Human Papillomavirus 4-valent Vaccine, Recombinant or qHPV vaccine)

This is a summary of the risk management plan (RMP) for GARDASIL (Quadrivalent Human Papillomavirus 4-valent Vaccine, Recombinant or qHPV vaccine). The RMP details important risks of GARDASIL, how these risks can be minimised, and how more information will be obtained about GARDASIL'S risks and uncertainties (missing information).

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

This summary of the RMP for GARDASIL 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 GARDASIL'S RMP.

I. The Medicine and What It Is Used For

GARDASIL is authorised for use from the age of 9 years for the prevention of: premalignant genital lesions (cervical, vulvar and vaginal), premalignant anal lesions, cervical cancers and anal cancers causally related to certain oncogenic Human Papillomavirus (HPV) types, and genital warts (condyloma acuminate) causally related to specific HPV types (see SmPC for the full indication). It contains human papillomavirus (HPV) vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) as the active substance and it is given by intramuscular injection. The preferred site is the deltoid area of the upper arm or in the higher anterolateral area of the thigh.

Further information about the evaluation of GARDASIL'S benefits can be found in GARDASIL'S EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage [Ref. 5.4: 053BQD].

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

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

II.A List of Important Risks and Missing Information

Important risks of GARDASIL 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 GARDASIL. 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 Potential Risks of conditions of special interest have been removed.

- Analysis of the post-marketing data gathered on GARDASIL over the past 14 years shows that there are no outstanding additional pharmacovigilance activities to address the previous potential risks listed above.
- There is no reasonable expectation that any pharmacovigilance activity can further characterize the previously listed Important potential risks listed above.

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 for 2-dose regimen in adolescent girls

II.B Summary of Important Risks

Table II.B.1: Missing Information: Long-Term Effectiveness for 2-Dose Regimen in Adolescent Girls

Risk minimisation measures	**Routine risk minimisation measures**
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** Effectiveness study of 2-dose regimen in adolescent girls

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 qHPV vaccine.

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

Table II.C.2.1: Studies in Post Authorisation Development Plan

Study Status	Summary of Objectives	Safety Concern Addressed	Milestones	Due Dates
Category 1 - Imposed mandatory additional pharmacovigilance activities which are conditions of the marketing authorisation				
None				
Category 2 – Imposed mandatory additional pharmacovigilance activities which are Specific Obligations in the context of a conditional marketing authorisation or a marketing authorisation under exceptional circumstances				
None				
Category 3 - Required additional pharmacovigilance activities				
Effectiveness study of 2-dose regimen in adolescent girls titled GARDASIL 2-dose vaccine effectiveness study: a population-based study in Sweden/planned	To assess if a 2-dose schedule with GARDASIL is noninferior when compared to a 3-dose vaccination schedule in the prevention of CIN2+.	Effectiveness of a 2-dose schedule in adolescents aged 9 to 13 years	Start of data collection Study report	Planned 2027-2028 Planned 2030