Risk Management Plan – Philippine-Specific Annex

Version number: 1
Related: EU- RMP version, succession 1
**EU RMP Version 1, succession 1 represents the Core position of AstraZeneca's Risk Management Plan for COVID-19 Vaccine AstraZeneca*

1. INTRODUCTION / PRODUCT OVERVIEW

The objective of this Philippine Specific Risk Management Plan (RMP) Annex is to describe how the EU RMP will be applied in the Philippines. Additional pharmacovigilance activities and additional risk minimization activities outlined in the EU RMP are intended for implementation in the EEA and will not be implemented in Philippines.

The COVID-19 Vaccine AstraZeneca EU RMP submitted with this Philippine Specific Annex includes a description of the risk management system based on all information AstraZeneca deems relevant to the safety profile of COVID-19 Vaccine AstraZeneca.

Inclusion of information relating to a potential new safety risk within this plan should not be taken to imply that causal association with the use of COVID-19 Vaccine AstraZeneca has been established.

1.1 Product information

Active ingredients	ChAdOx1-S [recombinant] (AZD1222) (formerly ChAdOx1 nCoV-19)
Product Name	COVID-19 Vaccine AstraZeneca
Indication	**Proposed** COVID-19 Vaccine AstraZeneca is indicated for active immunization of individuals ≥ 18 years old for the prevention of coronavirus disease 2019 (COVID-19).
Dosage	**Proposed** The vaccination course consists of two separate doses of 0.5 mL each. The second dose should be administered between 4 and 12 weeks after the first dose.
Pharmaceutical form(s) and strengths	**Proposed** Solution for injection. One dose (0.5 mL) contains COVID-19 Vaccine (ChAdOx1-S [recombinant]) 5×10^{10} vp.
FDA Registration No(s).	Not applicable

1.2. Indication(s) and Target Population(s)

COVID-19 Vaccine AstraZeneca is authorized for active immunization of individuals ≥ 18 years for the prevention of coronavirus disease 2019 (COVID-19). It contains ChAdOx1-S* (recombinant) 5×10^{10} vp (viral particles) as the active substance, and it is given by intramuscular injection only, preferably in the deltoid muscle.

**Recombinant, replication-deficient chimpanzee adenovirus encoding the SARS-CoV-2 Spike (S) glycoprotein (GP). Produced in genetically modified human embryonic kidney (HEK) 293 cells by recombinant DNA technology.*

2. SAFETY SPECIFICATION

Important risks of COVID-19 Vaccine AstraZeneca are risks that need special risk management activities to further investigate or minimize 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 COVID-19 Vaccine AstraZeneca. 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

Important identified risks	None
Important potential risks	• Immune-mediated neurological conditions • Vaccine-associated enhanced disease (VAED)
Missing Information	• Use of AZD1222 in pregnant and breastfeeding women • Use of AZD1222 in subjects with severe immunodeficiency • Use of AZD1222 in subjects with severe and/or uncontrolled underlying disease • Use of AZD1222 with other vaccines

2.1 Important Identified Risks

None.

2.2 Important Potential Risks

Table 2 Important potential risk: Immune-mediated neurological conditions

Evidence for linking the risk to the medicine	The association between vaccines and acute demyelinating events has been assessed in a range of studies and expert reviews, including a population-based analysis of nearly 64 million vaccine doses in the United States, which concluded that if there is an association between transverse myelitis and vaccines, it is < 2 per million doses of live-zoster and live-attenuated influenza vaccines, and < 1 per million doses for other vaccines. Moreover, demyelinating diseases occur more frequently with infections than with vaccination. Taken together, the evidence is inconclusive regarding a causal relation between contemporary vaccines and acute demyelinating events.
Risk factors and risk groups	There are no known risk factors for the development of immune-mediated neurological conditions following vaccination.
Risk minimization measures	**Routine risk communication:** • SmPC Section 4.4
Additional pharmacovigilance activities (For EEA only)	**Additional pharmacovigilance activities:** • Enhanced Active Surveillance (EAS) • Post-marketing Safety Study See section VI.2.3.2 of EU RMP summary (Part VI) for an overview of the post-authorization development plan.

Table 3 Important potential risk: Vaccine-associated enhanced disease (VAED)

Evidence for linking the risk to the medicine	There is a theoretical concern that vaccination against SARS-CoV-2 may be associated with enhanced severity of COVID-19 episodes which would manifest as VAED. Vaccine-associated enhanced disease was observed in children given formalin-inactivated whole-virus vaccines against respiratory syncytial virus and measles virus, and findings from experimental models of SARS-CoV and MERS-CoV infection suggest that VAED may be possible in certain conditions.
Risk factors and risk groups	There are no known risk factors identified for VAED.
Risk minimization measures	None.
Additional pharmacovigilance activities (For EEA only)	**Additional pharmacovigilance activities:** • EAS • Post-marketing safety study See section VI.2.3.2 of EU RMP summary (Part VI) for an overview of the post-authorization development plan.

2.3 Missing Information

Table 4 Missing information: Use of AZD1222 in subjects with severe immunodeficiency

Risk minimization measures	**Routine risk minimization measures** • SmPC Section 4.4 • PL Section 2

Additional pharmacovigilance activities (For EEA only)	**Additional pharmacovigilance activities**: • EAS • Post-marketing Safety Study See section VI.2.3.2 of EU RMP summary (Part VI) for an overview of the post-authorization development plan.

Table 5 Missing information: Use of AZD1222 in subjects with severe and/or uncontrolled underlying disease

Risk minimization measures	None.
Additional pharmacovigilance activities (For EEA only)	**Additional pharmacovigilance activities**: • EAS • Post-marketing Safety Study See section VI.2.3.2 of EU RMP summary (Part VI) for an overview of the post-authorization development plan.

Table 6 Missing information: Use of AZD1222 with other vaccines

Risk minimization measures	**Routine risk minimization measures** • SmPC Sections 4.4 and 4.5 • PL Section 2
Additional pharmacovigilance activities (For EEA only)	**Additional pharmacovigilance activities**: • EAS • Post-marketing Safety Study See section VI.2.3.2 of EU RMP summary (Part VI) for an overview of the post-authorization development plan.

3. PHARMACOVIGILANCE PLAN

3.1. Routine Pharmacovigilance Activities

Information about adverse reactions is collected continuously and regularly analyzed, including Periodic Safety Update Report (PSUR) assessment, so that immediate action can be taken as necessary.

Full details of the routine pharmacovigilance measures including signal detection and evaluation, Individual Case Safety report (ICSR) reporting and summary safety reports are describe in the part III (pharmacovigilance plan) of the EU RMP.

The QR code to the electronic package insert (prescribers information and patient information leaflet) contains information on reporting suspected adverse reactions including links to the COVID-19 Vaccine AstraZeneca website and AstraZeneca's portal for Adverse Event and

Product Quality Complaint Report and Medical Information Request.

Pharmacovigilance obligations and post-authorization commitments will be shared with the Health program implementor, see attachment for Proposed Pharmacovigilance Protocol for EUA holder and Health Program Implementors for the Philippines

3.1.1 Traceability

To facilitate pharmacovigilance and batch/lot analysis, every effort will be made to support the recording and accessibility of brand and batch/lot numbers for HCPs and patients in the Philippines.

The QR code and batch/lot number will be printed in the outer carton which will also serve as route for HCPs and patients to access the COVID-19 Vaccine AstraZeneca website.

The batch/lot number for AZD1222, if not already provided will be systematically followed-up for each post-authorization ICSR. When available, batch information will be included in the global safety database.

3.2. Additional Pharmacovigilance Activities

No additional pharmacovigilance activities are planned for the Philippines.

Table 7 Additional Pharmacovigilance Plan

Additional activity	**Objectives**	**Safety concerns addressed**	**Status**	**Planned submission date**
Additional activity (with complete title and protocol ID)	*Provide the objective of the such activity*	*Safety concerns being addressed by such activity*	*Status of the activity (ongoing, planned)*	*Proposed date of submission to FDA*
N/A	*N/A*	*N/A*	*N/A*	*N/A*

4. PLANS FOR POST-AUTHORIZATION EFFICACY STUDIES (PASS)

There is no planned local post-authorization efficacy studies to be conducted in the Philippines.

Table 8 Local PASS

Post-authorization efficacy study	**Status (planned, on-going)**	**Summary of Objectives**	**Planned submission date**

Study (with complete title and protocol ID)	*Status of the activity (ongoing, planned)*	*Provide the summary of objectives of the study*	*Proposed date of submission to FDA Philippines*
N/A	*N/A*	*N/A*	*N/A*

5. RISK MINIMIZATION MEASURES

5.1. Routine Risk Minimization Measures

Important risks of COVID-19 Vaccine AstraZeneca, together with measures to minimize such risks and the proposed studies for learning more about COVID-19 Vaccine AstraZeneca's risks, are outlined below. Measures to minimize the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package insert/leaflet for healthcare professionals and patients
- The authorized pack size - the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly

Together, these measures constitute routine risk minimization measures.

If important information that may affect the safe use of COVID-19 Vaccine AstraZeneca is not yet available, it is listed under missing information (see section 2.3).

5.2. Additional Risk Minimization Measures

No additional risk minimization measures are planned for the Philippines.

Safety Concerns or Missing Information	**Routine Risk Minimization Measures**	**Additional Risk Minimization Measures**
List of safety concerns being addressed	*Include details of exact wording for package insert proposed for this safety concern*	*Include details of additional measures for this safety concern to be undertaken in the Philippines*
See section 2 of this Annex	*See section 2 of this Annex*	*N/A*

6. REFERENCES

6.1. List of Reference(s)

[1] European Union Risk Management Plan (EU RMP) for Covid-19 Vaccine AstraZeneca, (ChAdOx1-S [RECOMBINANT]), version no. 1.0, Data Lock dated 04 November 2020, Final Sign-off dated 21 December 2020

[2] FDA Circular 2020-036

6.2. Attachment (s)

Proposed Pharmacovigilance Protocol for EUA holder and Health Program Implementors for the Philippines

7. VERSION HISTORY

This is the first version (v1.0) of the RMP- Philippine Specific Annex for COVID-19 Vaccine AstraZeneca.