Summary of the risk management plan for Nuvaxovid (NVX-CoV2373)

Introduction

This document is a summary of the risk management plan (RMP) for Nuvaxovid, previously known as the Novavax COVID-19 vaccine. The RMP was created by the vaccine manufacturer and is submitted to medicine regulators as part of the vaccine approval and safety monitoring processes.

The RMP details the important potential risks of Nuvaxovid and how they can be minimised. It also describes how more information will be obtained about these risks and any uncertainties (missing information). The RMP will be updated as more information becomes available, including any new risks or changes to current ones.

The Nuvaxovid data sheet, consumer medicine information and the package leaflet give essential information for healthcare professionals and patients on how to use the vaccine.

See also the European Public Assessment Report (EPAR), including the risk management plan, available on the European Medicines Agency website.

RMP definitions

Important risks

Important risks need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered.

Important risks are classified as identified or potential.

- Identified risks are concerns for which there is sufficient proof of a link with the use of the medicine
- 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

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).

Activities to minimise or further characterise identified risks

Measures to minimise the identified risks for medicinal products may include:

- specific information for healthcare professionals and patients, such as warnings, precautions and advice on correct use, in the data sheet, consumer medicine information and package leaflet
- 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 (eg, 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 by the company and regularly analysed, so that immediate action can be taken by the company as necessary. These measures constitute *routine pharmacovigilance activities*.

Other non-routine measures to further characterise the risks include safety and efficacy studies. The studies may be in particular risk groups or for particular safety concerns. They may also be a condition of the medicine's approval. These measures constitute *additional pharmacovigilance activities*.

Nuvaxovid RMP

The medicine and what it is used for

Nuvaxovid (NVX-CoV2373) is authorised for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older. It contains SARS-CoV-2 recombinant spike protein (SARS-CoV-2 rS) as the active substance. It is given by intramuscular injection only, preferably in the deltoid muscle.

Further information about the evaluation of Nuvaxovid's benefits can be found in Nuvaxovid's EPAR, including in its plain-language summary, available on the European Medicines Agency website.

Important risks, missing information and additional pharmacovigilance activities

The tables below summarise the risks for Nuvaxovid, as described in the RMP.

- Table 1 is a list of the important risks (identified and potential) and missing information.
- Tables 2–10 provide the evidence for linking the risk to the medicine, risk factors and risk groups, risk minimisation measures and a list of additional pharmacovigilance activities.
- Table 11 summarises the additional pharmacovigilance activities (studies) and Table 12 summarises a list of other studies.

Table 1: List of important risks and missing information

Important identified risks	None
Important potential risks	Vaccine associated enhanced disease including vaccine associated enhanced respiratory disease Anaphylaxis Myocarditis and pericarditis
Missing information	Use in pregnancy and breastfeeding Use in immunocompromised patients Use in frail patients with co-morbidities (eg COPD, diabetes, chronic neurological disease, cardiovascular disorders) Use in patients with autoimmune or inflammatory disorders Interactions with other vaccines Long-term safety

Table 2: Important potential risk: Vaccine associated enhanced disease including vaccine associated enhanced respiratory disease (VAED/VAERD)

Evidence for linking the risk to the medicine	Vaccine-associated enhanced disease (VAED) has been observed rarely with existing vaccines and viral infections. It was observed in children given formalin inactivated whole-virus vaccines against respiratory syncytial virus (RSV) and measles virus. No events of VAED/VAERD have been reported in the current Nuvaxovid clinical development programme. 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/VAERD.
Risk factors and risk groups	None known.
Risk minimisation measures	None.
Additional pharmacovigilance activities*	Study 2019nCoV-101 Study 2019nCoV-501 Study 2019nCoV-301 Study 2019nCoV-302 Post-marketing observational studies using existing secondary health data sources (2019nCoV-402 [UK] and 2019nCoV-404 [US])

* See Table 11 for a summary of the studies.

Table 3: Important potential risk: Anaphylaxis

Evidence for linking the risk to the medicine	The risk of anaphylaxis is idiosyncratic in nature, with anaphylaxis risk after all vaccines estimated to be 1.31 (95% confidence interval: 0.90-1.84) per million vaccine doses. No serious or acute events of anaphylaxis were reported in Nuvaxovid clinical trials, and therefore the risk of anaphylaxis is a theoretical concern based on data from other vaccines.
Risk factors and risk groups	Known hypersensitivity to any component of Nuvaxovid and/or a history of allergic reactions.
Risk minimisation measures	Data sheet section 4.4 Consumer medicine information leaflet
Additional pharmacovigilance activities*	Study 2019nCoV-101 Study 2019nCoV-501 Study 2019nCoV-301 Study 2019nCoV-302 Post-marketing observational studies using existing secondary health data sources (2019nCoV-402 [UK] and 2019nCoV-404 [US])

* See Table 11 for a summary of the studies.

Table 4: Important potential risk: Myocarditis and pericarditis

Evidence for linking the risk to the medicine	Myocarditis/pericarditis has been recognised as a rare complication of mRNA COVID-19 vaccines. Although myocarditis has also been reported after administration of a number of vaccines for viral infections, reported rates are lower than the rates after mRNA vaccines and the reported rates are considered to be similar to expected background rates. Following exposure to mRNA vaccines, acute clinical courses were generally mild and the majority of patients experienced resolution of symptoms with conservative treatment, such as receipt of nonsteroidal anti-inflammatory drugs.
Risk factors and risk groups	Adolescent and young adult males following the second dose of vaccine may be at higher risk. Immunocompromised patients may be at a higher risk.
Risk minimisation measures	None.
Additional pharmacovigilance activities*	Study 2019nCoV-101 Study 2019nCoV-501 Study 2019nCoV-301 Study 2019nCoV-302 Post-marketing observational study using existing secondary health data sources (2019nCoV-402 [UK] and 2019nCoV-404 [US]).

* See Table 11 for a summary of the studies.

Table 5: Missing information: Use during pregnancy and while breastfeeding

Risk minimisation measures	Data sheet sections 4.6 and 5.3 Consumer medicine information leaflet
Additional pharmacovigilance activities*	Pregnancy exposure registry (2019nCoV-405)

* See Table 11 for a summary of the studies.

Table 6: Missing information: Use in immunocompromised patients

Risk minimisation measures	Data sheet section 4.4 Consumer medicine information leaflet
Additional pharmacovigilance activities*	Study 2019nCoV-302 Study 2019nCoV-301 Study 2019nCoV-501 Post-marketing observational studies using existing secondary health data sources (2019nCoV-402 [UK] and 2019nCoV-404 [US])

* See Table 11 for a summary of the studies.

Table 7: Missing Information: Use in frail patients with co-morbidities (eg COPD, diabetes, chronic neurological disease, cardiovascular disorders)

Risk minimisation measures	None
Additional pharmacovigilance activities*	Post-marketing observational studies using existing secondary health data sources (2019nCoV-402 [UK] and 2019nCoV-404 [US])

* See Table 11 for a summary of the studies.

Table 8: Missing Information: Use in patients with autoimmune or inflammatory disorders

Risk minimisation measures	Consumer medicine information leaflet
Additional pharmacovigilance activities*	Post-marketing observational studies using existing secondary health data sources (2019nCoV-402 [UK] and 2019nCoV-404 [US])

* See Table 11 for a summary of the studies.

Table 9: Missing Information: Interaction with other vaccines

Risk minimisation measures	Data sheet section 4.5 and 5.1 Consumer medicine information leaflet
Additional pharmacovigilance activities*	Study 2019nCoV-302 Post-marketing observational studies using existing secondary health data sources (2019nCoV-402 [UK] and 2019nCoV-404 [US])

* See Table 11 for a summary of the studies.

Table 10: Missing Information: Long-term safety data

Risk minimisation measures	None
Additional pharmacovigilance activities*	Study 2019nCoV-101 Study 2019nCoV-501 Study 2019nCoV-301 Study 2019nCoV-302 Post-marketing observational studies using existing secondary health data sources (2019nCoV-402 [UK] and 2019nCoV-404 [US])

* See Table 11 for a summary of the studies.

Studies

Table 11: Summaries of the Nuvaxovid (NVX-CoV2373) studies listed in Tables 2–10

2019nCoV-101; A 2-part, Phase 1/2, Randomised, Observer-Blinded Study to Evaluate the Safety and Immunogenicity of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-CoV-2 rS) With or Without Matrix-M™ Adjuvant in Healthy Subjects The objectives of this study are to evaluate the safety and immunogenicity of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine (SARS-CoV-2 rS) with or without Matrix-M adjuvant in healthy subjects.
2019nCoV-501; A Phase 2a/b, Randomised, Observer-Blinded, Placebo-Controlled Study to Evaluate the Efficacy, Immunogenicity, and Safety of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-CoV-2 rS) With Matrix-M1™ Adjuvant in South African Adult Subjects Living Without HIV; and Safety and Immunogenicity in Adults Living With HIV The objectives of the study are to evaluate the efficacy, immunogenicity, and safety of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine (SARS-CoV-2 rS) with Matrix-M adjuvant in South African adult subjects living without HIV; and safety and immunogenicity in adults living with HIV.
2019nCoV-302; A Phase3, Randomised, Observer-Blinded, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-CoV-2 rS) with Matrix-M1TM adjuvant in Adult Participants 18-84 Years of Age in the United Kingdom The objectives of the study are to evaluate the efficacy and safety of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine (SARS-CoV-2 rS) with Matrix-M adjuvant in adult participants 18-84 years of age in the UK.
2019nCoV-301; A phase 3, Randomised, Observer-Blinded, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of a SARS-COV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-COV-2 rS) with Matrix-M1™ Adjuvant in Adult Participants ≥ 18 years with a Pediatric Expansion in Adolescents (12 to < 18 years) The objectives of the study are to evaluate the efficacy, safety, and immunogenicity of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine (SARS-CoV-2 rS) with Matrix-M adjuvant in adult participants ≥ 18 years with a paediatric expansion in adolescents (12 to <18 years).

2019nCoV-402 UK Post-Authorisation Safety Study Using the Clinical Practice Research Datalink (CPRD)

The objectives of this study are to:

1. Evaluate any increased risk of select safety outcomes of interest following vaccination
2. Describe and characterise the safety profile of the Nuvaxovid vaccine
3. Evaluate any differences in the risk of safety outcomes by characteristics such as age, sex, race/ethnicity, comorbidities/coinfections, prior COVID-19 infection, concomitant vaccinations, concomitant medications, and/or other characteristics.

2019nCoV-405 Global Pregnancy and infant outcomes study using the COVID-19 Vaccines International Pregnancy Exposure Registry (C-VIPER)

The objectives of this study are to:

1. Describe and characterise the population of pregnant women who are vaccinated with the Nuvaxovid vaccine.
2. Estimate the frequency of select adverse pregnancy outcomes
3. Estimate the frequency of select adverse fetal/neonatal/infant outcomes at birth and up to the first 12 months of life
4. Compare the frequency of each safety event of interest between pregnant women (or infants born to these pregnancies) who were exposed to the Nuvaxovid vaccine and those who were not exposed.
5. Assess whether the frequency of pregnancy and infant outcomes following vaccination with Nuvaxovid differs by age, sex, race/ethnicity, comorbidities/coinfections, prior COVID-19 infection, concomitant vaccinations, concomitant medications, and/or other characteristics.

2019nCoV-404 US Post-authorisation safety study using a claims and/or EHR (Electronic Health Record) database

The objectives of this study are to evaluate the pooled risk of select AESIs within specified time periods after vaccination with the Novavax COVID-19 vaccine, compared to risk during all other times after COVID-19 vaccination within the same individual using a self-controlled design; or where relevant, compared to unvaccinated individuals or those who received an alternative COVID-19 vaccine using a comparative cohort study design.

Table 12: Other studies

2019nCoV-403 US Post-authorisation effectiveness study using a claims and/or EHR database

The objectives of this study are to estimate Nuvaxovid effectiveness in reducing clinically defined SARS-CoV-2 infection.

2019nCoV-401 EU/EEA Post-authorisation effectiveness study based on a test-negative design using the COVIDRIVE platform

The objectives of the study are to estimate Nuvaxovid effectiveness against COVID-19 hospitalisations confirmed by reverse transcription polymerase chain reaction (RT-PCR), after adjusting for potential confounders.