Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Nuvaxovid XBB.1.5 dispersion for injection COVID-19 Vaccine (recombinant, adjuvanted)

SARS-CoV-2 (Omicron XBB.1.5) spike protein, adjuvanted with Matrix-M

PLGB 54180/0003

Novavax CZ a.s.

LAY SUMMARY

Nuvaxovid XBB.1.5 dispersion for injection
COVID-19 Vaccine (recombinant, adjuvanted)
SARS-CoV-2 (Omicron XBB.1.5) spike protein, adjuvanted with Matrix-M

This is a summary of the Public Assessment Report (PAR) for Nuvaxovid XBB.1.5 dispersion for injection. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Nuvaxovid XBB.1.5 in this lay summary for ease of reading.

This product has been authorised by the Medicines and Healthcare products Regulatory Agency (MHRA) for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 31/10/2023 (EMEA/H/C/005808/II/0058/G), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

This application was approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended).

For practical information about using Nuvaxovid XBB.1.5, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Nuvaxovid XBB.1.5 and what is it used for?
Nuvaxovid XBB.1.5 is a vaccine used to prevent COVID-19 caused by the SARS-CoV-2 virus.

Nuvaxovid XBB.1.5 is given to individuals 12 years of age and older.

How does Nuvaxovid XBB.1.5 work?
The vaccine causes the immune system (the body's natural defences) to produce antibodies and specialised white blood cells that work against the virus, to give protection against COVID-19. None of the ingredients in this vaccine can cause COVID-19.

How is Nuvaxovid XBB.1.5 used?
The pharmaceutical form of this medicine is a dispersion for injection and the route of administration is by injection into a muscle (intramuscular) in upper arm, administered by a health practitioner.

Nuvaxovid XBB.1.5 will be given to the patient as a single dose 0.5 mL injection.

If the patient was previously vaccinated with a COVID-19 vaccine, Nuvaxovid XBB.1.5 should be administered at least 3 months after the most recent dose of a COVID-19 vaccine.

During and after each injection of the vaccine, the patient's doctor, pharmacist, or nurse will watch over them for around 15 minutes to monitor for signs of an allergic reaction.

Additional doses (0.5 mL) of Nuvaxovid XBB.1.5 may be administered at the discretion of the patient's physician, taking into consideration their clinical conditions in line with national recommendations.

Immunocompromised individuals
If the patient's immune system does not work properly additional doses may be administered in line with national recommendations.

For further information on how Nuvaxovid XBB.1.5 is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should ask the administering healthcare practitioner if they have any questions concerning their medicine.

What benefits of Nuvaxovid XBB.1.5 have been shown in studies?
Results from two main clinical trials found that Nuvaxovid was effective at preventing COVID-19 in people from 12 years of age when given as primary vaccination. In these studies, over 47,000 people were given two doses of Nuvaxovid or placebo (a dummy injection).

In the first study, conducted in adolescents and adults, around two thirds of participants received the vaccine and the others were given placebo.

The study found a 90.4% reduction in the number of symptomatic COVID-19 cases from 7 days after the second dose in adults who received Nuvaxovid (14 cases out of 17,312 people) compared with adults given placebo (63 out of 8,140 people). This means that the vaccine had a 90.4% efficacy in this study.

The trial also showed that the immune response to Nuvaxovid, which was measured as the level of antibodies against SARS-CoV-2, was comparable between adolescents and young adults aged 18 to 25 years. Compared with placebo, the vaccine led to an 80% reduction in the number of symptomatic COVID-19 cases seen from 7 days after the second dose onward in adolescents; six out of 1,205 adolescents who received the vaccine and 14 out of 594 who received placebo developed COVID-19.

The second study included only adults. The study showed a similar reduction in the number of symptomatic COVID-19 cases in people who received Nuvaxovid (10 cases in 7,020 people) compared with people given placebo (96 in 7,019 people); in this study, the vaccine efficacy was 89.7%.

Taken together, the results of the two studies show that Nuvaxovid was effective at preventing COVID-19 in both adults and adolescents. The original strain of SARS-CoV-2 and variants of concern such as Alpha, Beta and Delta were the most common viral strains circulating when the studies were ongoing. There is currently limited clinical data on the efficacy of Nuvaxovid against other variants of concern, including Omicron.

Data from two studies showed a rise in antibody levels when a booster dose of Nuvaxovid was given in adults after primary vaccination with the vaccine. The vaccine is expected to produce a similar booster response in adolescents. Data from an additional study also showed a rise in

antibody levels when a booster dose of Nuvaxovid was given in adults after primary vaccination with an mRNA vaccine or adenoviral vector vaccine.

For the adapted vaccine Nuvaxovid XBB.1.5, to which this report relates, laboratory data showed that it is able to trigger an adequate immune response against Omicron XBB.1.5. In addition, data from a study in previously vaccinated adults showed that when Nuvaxovid was adapted to target another related strain, Omicron BA.5, it was able to trigger a strong immune response against this strain. Based on these data, Nuvaxovid XBB.1.5 is expected to trigger an adequate immune response against XBB.1.5.

What are the possible side effects of Nuvaxovid XBB.1.5?
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

The most common side effects with Nuvaxovid XBB.1.5 (which may affect more than 1 in 10 people) are-

- headache
- feeling sick (nausea) or getting sick (vomiting)
- muscle ache
- joint pain
- tenderness or pain where the injection is given
- feeling very tired (fatigue)
- generally feeling unwell

Why was Nuvaxovid XBB.1.5 approved?
It was concluded that Nuvaxovid XBB.1.5 dispersion for injection to be effective in the prevention of COVID-19 caused by the SARS-CoV-2 virus in individuals 12 years of age and older. Furthermore, the side effects observed with use of this product products are considered to be typical for this type of treatment. Therefore, the MHRA decided that the benefits are greater than the risks and recommended that this medicine can be approved for use.

What measures are being taken to ensure the safe and effective use of Nuvaxovid XBB.1.5?
As for all newly-authorised medicines, an Risk Management Plan (RMP) has been developed for Nuvaxovid XBB.1.5. The last approved RMP details the important risks of Nuvaxovid XBB.1.5, how these risks can be minimised, any uncertainties about Nuvaxovid XBB.1.5 (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Nuvaxovid XBB.1.5:

Summary of Safety Concerns	
Important identified risks	Myocarditis and/or pericarditis
Important potential risks	Vaccine-associated enhanced disease (VAED), including vaccine-associated enhanced respiratory disease (VAERD)
Missing information	Use in pregnancy and while breastfeeding Use in immunocompromised patients Use in frail patients with comorbidities (e.g., chronic obstructive pulmonary disease (COPD), diabetes, chronic neurological disease, cardiovascular disorders) Use in patients with autoimmune or inflammatory disorders Interaction with other vaccines Long-term safety

Continuation of safety surveillance from ongoing clinical trials is a priority and included as an additional pharmacovigilance activity

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Nuvaxovid XBB.1.5 are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Other information about Nuvaxovid XBB.1.5
A marketing authorisation was granted in Great Britain on 24 January 2024.

The full PAR for Nuvaxovid XBB.1.5 follows this summary.

This summary was last updated in March 2024.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Nuvaxovid XBB.1.5 dispersion for injection (PLGB 54180/0003) could be approved.

The product is approved for the following indications:

- for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older.

The use of this vaccine should be in accordance with official recommendations.

Nuvaxovid XBB.1.5 is composed of purified full-length SARS-CoV-2 Omicron XBB.1.5 recombinant spike (S) protein that is stabilised in its prefusion conformation. The addition of the saponin-based Matrix-M adjuvant facilitates activation of the cells of the innate immune system, which enhances the magnitude of the S protein-specific immune response. The two vaccine components elicit B- and T-cell immune responses to the S protein, including neutralising antibodies, which may contribute to protection against COVID-19.

This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 31/10/2023 (EMEA/H/C/005808/II/0058/G), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP).

For the scientific discussion of the quality, non-clinical and clinical assessment conducted by the European Medicines Agency (EMA), please refer to the European Public Assessment Report, available on the EMA website.

This application was approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended). In the EU this application was processed as a grouped II variation by the EMA and has been granted as a line extension in Great Britain. This product includes Omicron XBB.1.5 spike protein, a different sub-variant of SARS-CoV2 to that included in earlier authorised Nuvaxovid COVID-19 vaccine (PLGB 54180/0002).

In line with the legal requirements for children's medicines, the application included a licensing authority decision on the agreement of a paediatric investigation plan (PIP) MHRA-100149-PIP01-21-M02.

At the time of the submission of the application the PIP was not yet completed as some measures were deferred.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A marketing authorisation was granted on 24 January 2024.

II. PRODUCT INFORMATION

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

The SmPC is in line with current guidelines and was satisfactory.

PATIENT INFORMATION LEAFLET (PIL)

The PIL is in line with current guidelines and is satisfactory.

LABEL

The labelling is in line with current guidelines and is satisfactory.

III. QUALITY ASPECTS

MHRA considered that the quality data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

IV. NON-CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

V. CLINICAL ASPECTS

MHRA considered that the clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

VI. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. In addition to routine pharmacovigilance and risk minimisation measures, the following additional pharmacovigilance measures have been proposed:

Important Identified Risk: Myocarditis and/or Pericarditis	
Evidence for linking the risk to the medicine	Literature on COVID-19 vaccines, post-market safety data, and clinical trial data.
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	Routine risk minimisation measures: SmPC section 4.4 and 4.8. PL section 2 and 4. Additional risk minimisation measures: None
Additional pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: *Specific adverse reaction follow-up questionnaire* Additional pharmacovigilance activities: **Ongoing clinical trials** 2019nCoV-101 (Part 2); final CSR estimated date 31 December 2023 2019nCoV-501; final CSR estimated date 31 March 2023 2019nCoV-302; final CSR estimated date 31 March 2023 2019nCoV-505; final CSR estimated date 30 November 2023 2019nCoV-311; final CSR estimated date 31 March 2024 2019nCoV-301; final CSR estimated date 31 Dec 2023 **Post-authorisation studies** 2019nCoV-402 (Safety study using the CPRD Aurum database); final study report estimated date 30 June 2025 2019nCoV-404 (Safety study using a US-based claims and/or electronic health records (EHR) database); final study report estimated date 30 September 2025

Important potential risk: Vaccine-associated enhanced disease (VAED), including vaccine-associated enhanced respiratory disease (VAERD)	
Evidence for linking the risk to the medicine	Literature on viral vaccines, safety information of other COVID-19 vaccines, clinical trials. Vaccine-associated enhanced disease (VAED) has been rarely encountered with existing vaccines or viral infections. It was observed in children given formalin-inactivated whole-virus vaccines against 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	There are no known risk factors or specific risk populations identified for VAED/VAERD. The demonstration of some disease enhancement with any candidate vaccine after viral challenge in animal models should not necessarily represent a no-go signal for deciding whether to progress into early trials in clinical development of a COVID-19 vaccine (Lambert 2020). Population-based surveillance might give more insight in this, should any VAED occur.
Risk minimisation measures	Routine risk minimisation measures: None Additional risk minimisation measures: None
Additional pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: *Specific adverse reaction follow-up questionnaire* Additional pharmacovigilance activities: **Ongoing clinical trials** 2019nCoV-101 (Part 2); final CSR estimated date 31 December 2023 2019nCoV-501; final CSR estimated date 31 March 2023 2019nCoV-302; final CSR estimated date 31 March 2023 2019nCoV-505; final CSR estimated date 30 November 2023 2019nCoV-311; final CSR estimated date 31 March 2024 2019nCoV-301; final CSR estimated date 31 December 2023 **Post-authorisation studies** 2019nCoV-402 (Safety study using the CPRD Aurum database); final study report estimated date 30 June 2025 2019nCoV-404 (Safety study using a US-based claims and/or electronic health records (EHR) database); final study report estimated date 30 September 2025

Important missing information: Use in pregnancy and while breastfeeding	
Evidence for linking the risk to the medicine	There is limited experience with use of Nuvaxovid in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition, or post-natal development. Administration of Nuvaxovid in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus. Breastfeeding It is unknown whether Nuvaxovid is excreted in human milk. Fertility Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.
Risk factors and risk groups	Pregnant and breastfeeding women
Risk minimisation measures	Routine risk communication: SmPC Sections 4.6 and 5.3 PL Section 2 Additional risk minimisation: None
Additional pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None Additional pharmacovigilance activities: 2019nCoV-405 (Pregnancy and infant outcomes safety study using the "COVID-19 Vaccines International Pregnancy Exposure Registry" (C-VIPER)); final study report estimated date 30 June 2027

Important missing information: Use in immunocompromised patients	
Evidence for linking the risk to the medicine	The vaccine has not been studied in individuals with immunocompromised conditions, except for subjects with HIV. Subjects with HIV were not excluded from the clinical programme, and 244 were enrolled in the 2019nCoV-501 study. The safety profile of Nuvaxovid in HIV-positive participants in this study was similar to that seen in HIV-negative participants. There is no evidence that the safety profile of this population receiving Nuvaxovid will be different to that of the general population, but given the paucity of data, the possibility cannot be excluded.
Risk factors and risk groups	Individuals with compromised immune function due to acquired or genetic conditions or conditions requiring the use of immunosuppressants
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.4 PL section 2 Additional risk minimisation measures: None
Additional pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None Additional pharmacovigilance activities: **Ongoing clinical trials** 2019nCoV-501; final CSR estimated date 31 March 2023 2019nCoV-302; final CSR estimated date 31 March 2023 2019nCoV-505; final CSR estimated date 30 November 2023 2019nCoV-301; final CSR estimated date 31 December 2023 **Post-authorisation studies** 2019nCoV-402 (Safety study using the CPRD Aurum database); final study report estimated date 30 June 2025 2019nCoV-404 (Safety study using a US-based claims and/or electronic health records (EHR) database); final study report estimated date 30 September 2025

Important missing information: Use in frail patients with comorbidities (e.g., chronic obstructive pulmonary disease (COPD), diabetes, chronic neurological disease, cardiovascular disorders)	
Evidence for linking the risk to the medicine	The vaccine has not been studied in frail individuals with comorbidities that may compromise immune function due to the condition or treatment of the condition. Frail patients with comorbidities (e.g., chronic obstructive pulmonary disease, diabetes, chronic neurological disease, cardiovascular disorders) are potentially at risk of developing a more severe manifestation of COVID-19. There is no evidence that the safety profile of this population receiving Nuvaxovid will be different to that of the general population, but given the paucity of data, the possibility cannot be excluded
Risk factors and risk groups	Frail individuals with comorbidities (e.g., chronic obstructive pulmonary disease (COPD), obesity defined as BMI $\geq$ 30 kg/m^2, DM2, cardiovascular disease, chronic kidney disease or HIV).
Risk minimisation measures	Routine risk minimisation measures: None Additional risk minimisation measures: None
Additional pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None Additional pharmacovigilance activities: **Post-authorisation studies** 2019nCoV-402 (Safety study using the CPRD Aurum database); final study report estimated date 30 June 2025 2019nCoV-404 (Safety study using a US-based claims and/or electronic health records (EHR) database); final study report estimated date 30 September 2025

Important missing information: Use in patients with autoimmune or inflammatory disorders	
Evidence for linking the risk to the medicine	There is limited information on the safety of the vaccine in patients with autoimmune or inflammatory disorders. There is no evidence from Nuvaxovid clinical studies to date that the safety profile of this population differs with that of the general population. However, given the paucity of data, the possibility cannot be excluded.
Risk factors and risk groups	Patients with autoimmune or inflammatory disorders
Risk minimisation measures	Routine risk minimisation measures: PL section 2 Additional risk minimisation measures: None
Additional pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None Additional pharmacovigilance activities: **Post-authorisation studies** 2019nCoV-402 (Safety study using the CPRD Aurum database); final study report estimated date 30 June 2025 2019nCoV-404 (Safety study using a US-based claims and/or electronic health records (EHR) database); final study report estimated date 30 Sep 2025

Important missing information: Interaction with other vaccines	
Evidence for linking the risk to the medicine	There is limited information on the safety of the vaccine when administered other vaccines within 28 days prior to the first dose or any dose of Nuvaxovid, except for seasonal influenza vaccine, <14 days. Approximately 400 participants were concomitantly administered a seasonal influenza vaccine with Nuvaxovid or placebo. The binding antibody response to SARS-CoV-2 was lower when Nuvaxovid was given concomitantly with inactivated influenza vaccine. The clinical significance of this is unknown.
Risk factors and risk groups	Individuals who will receive other vaccines within 28 prior to 14 days after immunisation with Nuvaxovid.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section 4.5 and 5.1 PL section 2 Additional risk minimisation measures: None
Additional pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None Additional pharmacovigilance activities: **Ongoing clinical trials** 2019nCoV-302; final CSR estimated date 31 March 2023 **Post-authorisation studies** 2019nCoV-402 (Safety study using the CPRD Aurum database); final study report estimated date 30 June 2025 2019nCoV-404 (Safety study using a US-based claims and/or electronic health records (EHR) database); final study report estimated date 30 September 2025

Important missing information: Long-term safety	
Evidence for linking the risk to the medicine	Understanding of the long-term safety profile of Nuvaxovid is currently limited. The median duration of safety follow-up in each of the 2 Phase 3 studies was at least 60 days. Follow-up was conducted for one year post-vaccination (Studies 101 Part 1 and 2, 501, and 302) or 2 years post-vaccination (Study 301).
Risk factors and risk groups	There are no known risks with a potentially delayed onset, with the exception of the theoretical concern of VAED/VAERD. Whilst there is currently no evidence to suspect an adverse long-term safety profile, given the paucity of data, the possibility cannot be excluded
Risk minimisation measures	Routine risk minimisation measures: None Additional risk minimisation measures: None
Additional pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: None Additional pharmacovigilance activities: **Ongoing clinical trials** 2019nCoV-101 (Part 2); final CSR estimated date 31 December 2023 2019nCoV-501; final CSR estimated date 31 March 2023 2019nCoV-302; final CSR estimated date 31 March 2023 2019nCoV-311; final CSR estimated date 31 March 2024 2019nCoV-301; final CSR estimated date 31 December 2023 **Post-authorisation studies** 2019nCoV-402 (Safety study using the CPRD Aurum database); final study report estimated date 30 June 2025 2019nCoV-404 (Safety study using a US-based claims and/or electronic health records (EHR) database); final study report estimated date 30 September 2025

This is acceptable.

VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application, in accordance with legal requirements.

The PIL for Nuvaxovid dispersion for injection (PLGB 54180/0002) has been evaluated via a user consultation study in accordance with legal requirements. The results show that the PIL meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

A readability test has not been requested by the EMA for the current application in the EC Decision Reliance Procedure submission. The proposed changes to the PIL with this application are not expected to affect readability and this is acceptable.

VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the product is acceptable, and no non-clinical or clinical safety concerns have been identified. Clinical experience with NVX-CoV2373 is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

The following post-authorisation measures are recorded. Note, where a reference regulator is being utilised for the product lifecycle, the MAH must submit to that reference regulator by the dates shown below.

Description	Due date
The particle equilibration phenome should be further investigated by TEM and DLS	Q1 2024
Microflow analysis and TEM in order to support comparability should be provided	November 2023
A complete analysis of the interim stability data should be provided in an updated comparability report	November 2023
QAG_25069 with results for the thermal stress studies should be submitted	November 2023
A variation should be submitted to implement the HCP assay as a release assay	Q1 2024
DS stability should be submitted when the 12 months data are available	as soon as these are available
The report on the in-use stability study (punctured vials) of the XBB.1.5 vaccine should be submitted	November 2023
A release and stability specification should be established for Drug Substance for particle size	Q3 2024
For the equilibration phenomenon the presence of lipases as possible root cause for the PS80 hydrolysis should be investigated. In addition, it should be investigated if PS80 hydrolysis is absent in Wuhan batches in which the equilibration phenomenon is not observed. It should be shown that the initial decrease in potency is not accompanied by a loss in protein content	May 2024
A Drug Product specification for Total Protein should be re-introduced and, therefore, an assay for Total Protein should be developed and implemented (prior to the 2024-25 manufacturing campaign.	April 2024
A purity test for finished product using SDS-PAGE and to establishment of a release and shelf life purity specification should be performed.	Q4 2023
The DP stability study should be continued as planned and updates for the time intervals 6, 9 and 12 months should be provided.	as soon as these are available

The Summaries of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory.

In accordance with legal requirements, the current approved UK versions of the SmPC and PIL for this product are available on the MHRA website.

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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPCs and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**