NUVAXOVID

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
IB/0037/G	This was an application for a group of variations. B.II.f.1.e - Stability of FP - Change to an approved stability protocol B.II.f.1.e - Stability of FP - Change to an approved stability protocol	06/01/2023	n/a		

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

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IB/0041	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	04/01/2023	n/a		
IB/0040/G	This was an application for a group of variations. B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	22/12/2022	n/a		
IB/0036/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same	15/12/2022	n/a		

	pharmaceutical group as the currently approved manufacturer				
II/0034	B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method	15/12/2022	n/a		
IB/0033	B.II.f.1.b.2 - Stability of FP - Extension of the shelf life of the finished product - After first opening (supported by real time data)	15/12/2022	05/01/2023	SmPC, Labelling and PL	To extend the punctured vial shelf life from 6 hour at 2°C to 25°C to 12 hours at 2°C to 8°C or 6 hours at room temperature (maximum 25°C) from the time of first needle puncture to administration.
II/0027	B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS	08/12/2022	n/a		
IB/0038	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	02/12/2022	n/a		
II/0028	C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required	01/12/2022	n/a		

IB/0032	B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place	17/11/2022	n/a		
IB/0031	B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	20/10/2022	n/a		
II/0025/G	This was an application for a group of variations. B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.3.c - Change in batch size (including batch size	20/10/2022	n/a		

	ranges) of AS or intermediate - The change requires assessment of the comparability of a biological/immunological AS B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation				
IB/0029	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	14/10/2022	n/a		
II/0011/G	This was an application for a group of variations. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	13/10/2022	n/a		
R/0020	Renewal of the marketing authorisation.	15/09/2022	03/10/2022		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for NUVAXOVID, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion. Please refer to Scientific Discussion 'Nuvaxovid/H/C/005808/R/0020'.

II/0022	Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on pericarditis and myocarditis and to add pericarditis and myocarditis to the list of adverse drug reactions (ADRs) with frequency 'Not known' following the outcome of MEA 014.4 based on PRAC assessment on pericarditis and myocarditis. The Package Leaflet is updated accordingly. C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH	29/09/2022	05/01/2023	SmPC and PL	There is an increased risk of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) following vaccination with Nuvaxovid. These conditions can develop within just a few days after vaccination and have primarily occurred within 14 days. Available data suggest that the course of myocarditis and pericarditis following vaccination is not different from myocarditis or pericarditis in general. Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees (including parents or caregivers) should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination. Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition. For more information, please refer to the Summary of Product Characteristics.
IB/0023/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site	14/09/2022	n/a		
IA/0026	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	13/09/2022	n/a		

II/0014	Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include a third dose for Nuvaxovid, to boost individuals who have previously completed a primary vaccination series with Nuvaxovid (homologous booster dose) or with an mRNA or adenoviral vector vaccine (heterologous booster dose); based on interim data from study 2019nCoV-101 (Part 2), final data from study 2019nCoV-501, and data from the COV-BOOST study; the Package Leaflet is updated accordingly. The RMP version 2.0 has also been approved. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	01/09/2022	06/09/2022	SmPC and PL	The homologous third booster recommendation is supported by data from studies 2019nCoV-101 (Part 2) and 2019nCoV-501; both are randomised, placebo-controlled, observer-blinded clinical trials. The results from study 2019nCoV-101 (part 2) indicated an approx. 86.7-folder increase of neutralising antibody geometric mean titres (GMTs) post-boost compared to pre-boost, 28 days following booster vaccination. The observed titres were approx. 4.1-fold greater than titres reported following the primary vaccination series. A similar response was not observed in the placebo group. The results from study 2019nCoV-501 showed that 35 days after the booster dose the neutralising antibody GMT were 2-fold higher than those measured 7 days after the primary vaccination series as given to the placebo-arm. Also, titres at post-booster dose)were higher than at post-primary series in subjects initially randomised to the Nuvaxovid group. This is suggestive of an adequate boosting response. Moreover, the results from 2019nCoV-501 indicated a consistent response in people living with HIV, albeit of a lower magnitude. The reactogenicity with the third booster dose given 6 months following the second dose was acceptable. With the third dose an increase in the frequency and severity of local and systemic reactions was observed as compared to the second dose although they were transient (median duration of 1 to 3 days following vaccination). The most frequent solicited adverse reactions were injection site tenderness, fatigue, injection site pain, muscle pain, malaise and headache, joint pain, and fever. No new safety concerns were identified. The heterologous booster dose recommendation is supported by data from the COV-BOOST study*. This was a

					randomised, controlled clinical trial where participants who had received two doses of either an mRNA-vaccine or an adenoviral vector vaccine and had no history of laboratory confirmed SARS-CoV-2 infection were randomised to receive a booster with different a COVID-19 vaccine, including Nuvaxovid as a full dose (as approved in the SmPC) and half dose. In participants who received either a full or half dose, it was observed a 2.6-6.3 fold-increase of neutralising antibody titres 28 days after the booster vaccination compared to the control group (who received a single dose of an MenACWY vaccine). This is suggestive of an adequate boosting response. Overall the frequency and severity of local and systemic reactions were similar between the groups that received either full or half dose of Nuvaxovid and control vaccine. No new safety concerns were identified. * Munro et al, 2021 "Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicentre, randomised, controlled, phase 2 trial", Lancet 2021; 398: 2258–76, https://doi.org/10.1016/S0140-6736(21)02717-3.
IB/0021	C.I.3.z - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation	26/08/2022	06/09/2022	SmPC and PL	SmPC updated in section 4.4 and section 4.8. (Adverse Effects; frequency not known) and also relevant section of package leaflet regarding anaphylaxis, paraesthesia and hypoesthesia following PRAC outcome for MSSR MEA 14.3
IB/0015	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	05/07/2022	n/a		

IB/0013/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	04/07/2022	06/09/2022	Annex II	Addition of SK Bioscience Co. Ltd as a new manufacturing site for the active substance
II/0009	Extension of indication to include use in adolescents 12 to 17 years of age for Nuvaxovid, based on data from study 2019nCoV-301, a Phase 3, Randomized, 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-M Adjuvant in Adult Participants ≥ 18 Years with a Pediatric Expansion in Adolescents (12 to < 18 Years); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. The variation leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP). C.I.6.a - Change(s) to therapeutic indication(s) -	23/06/2022	01/07/2022	SmPC and PL	Please refer to Scientific Discussion ‘EMEA/H/C/005808/II/0009’

	Addition of a new therapeutic indication or modification of an approved one				
IB/0018	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	27/06/2022	n/a		
IB/0017/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	21/06/2022	n/a		

IB/0016	B.II.c.3.z - Change in source of an excipient or reagent with TSE risk - Other variation	15/06/2022	n/a		
IB/0012/G	This was an application for a group of variations. B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation B.II.c.3.z - Change in source of an excipient or reagent with TSE risk - Other variation B.II.c.4.z - Change in synthesis or recovery of a non-pharmacopoeial or novel excipient - Other variation	13/05/2022	n/a		
IB/0010	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	03/05/2022	n/a		
II/0007	B.II.b.3.e - Change in the manufacturing process of the finished or intermediate product - Introduction or increase in the overage that is used for the AS	22/04/2022	n/a		
IB/0008	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	06/04/2022	n/a		
IB/0006/G	This was an application for a group of variations. B.I.c.1.c - Change in immediate packaging of the AS - Liquid ASs (non sterile) B.I.c.1.c - Change in immediate packaging of the AS	06/04/2022	n/a		

	- Liquid ASs (non sterile)				
II/0004	B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method	24/03/2022	n/a		
IB/0005	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	18/03/2022	01/07/2022	SmPC, Labelling and PL	Sections 4.4, 4.8, 5.3 and 6.4 of the SmPC, section 3 of the Labelling and sections 2 and 6 of the PL have been updated to include minor corrections.
IB/0003	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	11/03/2022	n/a		
IB/0002/G	This was an application for a group of variations. B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place	02/03/2022	n/a		
IAIN/0001	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	27/01/2022	n/a		
