EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Vaxzevria

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
II/0097	Submission of the final report from study D8110C00001 listed as a category 3 study in the RMP (SOB/020). This is a phase III, randomised, placebo-controlled study of AZD1222 (Vaxzevria) conducted in the US, Peru and Chile. The purpose of the final CSR addendum is to provide long-term	07/03/2024	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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	safety data through to study completion and include the second year of follow-up post-first dose and final day 730 visit. The RMP version 8 succession number 3 was submitted to consolidate the updates made in RMP as part of two parallel procedures (EMEA/H/C/005675/II/0096 and EMEA/H/C/005675/II/0097). In addition, the MAH took the opportunity to update in the EU-RMP the submission milestone date for study D8111R00010. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
II/0096	Update of sections 4.8 and 5.1 of the SmPC based on final results from study D7220C00001; this is a phase 2/3 partially double-blinded, randomised, multinational, active-controlled study in both previously vaccinated and unvaccinated adults to determine the safety and immunogenicity of AZD2816, a vaccine for the prevention of COVID-19 caused by variant strains of SARS-CoV-2. The RMP version 8 succession number 3 was submitted to consolidate the updates made in RMP as part of two parallel procedures (EMEA/H/C/005675/II/0096 and EMEA/H/C/005675/II/0097). In addition, the MAH took the opportunity to update in the EU-RMP the submission milestone date for study D8111R00010. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	07/03/2024		SmPC	Submission of the final study results of study D7220C00001. The interim analysis results for the Boost Cohort of Study D7220C00001 were submitted previously based on a data lock point of 11 October 2021. These data were assessed within the procedure EMEA/H/C/005675/II/0052, and consequently, the product information was updated including the possibility of administering Vaxzevria as a homologous or heterologous booster (in subjects who previously had received an mRNA vaccine). In this procedure, the final study results have been submitted. The results from the final analysis are consistent with those provided with the interim analysis. No new safety concern has been identified. Minor labelling updates, such as, for example, update of the percentages of adverse drug reactions, neutralising antibody titres and GMT ratio, have been implemented in Sections 4.8 and 5.1.

	data				For more information, please refer to the Summary of Product Characteristics.
IA/0098/G	This was an application for a group of variations. B.II.e.5.b - Change in pack size of the finished product - Deletion of a pack size(s) A.7 - Administrative change - Deletion of manufacturing sites	13/12/2023		SmPC, Annex II, Labelling and PL	
PSUSA/10912 /202212	Periodic Safety Update EU Single assessment - COVID-19 Vaccine (ChAdOx1-S [recombinant]) (Vaxzevria)	20/07/2023	15/09/2023	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10912/202212.
IB/0094	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	07/08/2023	n/a		
IB/0093	B.I.d.z - Stability of AS - Other variation	07/08/2023	n/a		
II/0090	Submission of the final report from study D8111R00007 (RAVEN) listed as a category 3 study in the RMP. This is an observational retrospective cohort study using secondary databases to establish effectiveness of Vaxzevria in England. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	20/07/2023	n/a		

II/0089	Update of sections 4.8 of the SmPC in order to update the frequencies of 'dizziness' and 'abdominal pain' in the list of adverse drug reactions (ADRs) to common and the frequency of 'fever' to very common based on final results and final pooled analysis for studies COV001, COV002, COV003 and COV005. Update of section 5.1 of the SmPC in order to update safety and efficacy information, based on final results and final pooled analysis for studies COV001, COV002, COV003 and COV005 as well as the final manuscript for COV004, listed as category 3 studies in the RMP. Study COV001 is phase I/II, single-blind, randomised, active-controlled, multicenter study in healthy adults aged 18-55 years; Study COV002 is a phase II/III, single-blind, randomised, active-controlled, multicenter study in adults ≥ 18 years of age and at high risk of exposure to COVID-19; Study COV003 is a phase III, single-blind, randomised, controlled, multicenter study in adults ≥ 18 years of age at high risk of exposure to SARS-CoV-2; Study COV005 is a phase I/II, double-blind, randomised, placebo-controlled, multicenter study in adults 18 to 65 years of age with or without HIV. Study COV004 a phase IB/II single-blind, randomized controlled trial of the (AZD1222) vaccine in adults in Kenya. The Package Leaflet is updated accordingly. The RMP version 7.0 has also been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	20/07/2023	15/09/2023	SmPC and PL	SmPC new text The MAH has submitted the final pooled analysis of the safety, durability of efficacy, and immunogenicity of primary vaccination with AZD1222, based on data collected for up to 12 months after the first dose in studies COV001, COV002, COV003 and COV005 with a data cut-off (DCO) of 31 December 2021. In addition, the MAH provided the individual clinical study reports (CSRs) for COV001, COV002, COV003 and COV005 that summarise durability of efficacy results and cumulative immunogenicity and safety results. Overall, the final pooled vaccine efficacy (VE) results demonstrate an estimated durability of VE consistent with the previously submitted primary pooled analysis estimates of VE against SARS-CoV-2 virologically confirmed symptomatic illness, severe disease and death. The final pooled immunogenicity analysis provided similar results to those obtained at the time of the initial conditional marketing authorisation, both in terms of GMTs and seroconversion rates reached after first and second dose regardless of the humoral immunological assay used. The safety evaluation based on the results presented from the updated pooled analysis does not differ substantially from those submitted at the time of the conditional marketing authorisation. A higher reactogenicity (both local and systemic events) was observed in participants in the in AZD1222 group compared to those in the control group. These events were reported less frequently and milder after the second dose than after the first dose. Similarly, unsolicited adverse events (AE) were reported more frequently in AZD1222 group than in control group. The majority were mild to moderate in severity and were

					reported less frequently after the second dose in both AZD1222 and the comparator. Overall frequencies of either solicited local and systemic AEs and unsolicited AEs remain barely unchanged to those initially provided, except for "dizziness" and "abdominal pain" which frequency has increased from uncommon to common and "fever" which frequency has increased from common to very common. For more information, please refer to the Summary of Product Characteristics.
II/0091	Submission of the final report from study D8111R00020 listed as a category 3 study in the RMP. This is a systematic literature review of observational studies evaluating safety after vaccination with Vaxzevria in patients taking immunosuppressant medications and/or with primary immunodeficiency. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	08/06/2023	n/a		
IA/0092/G	This was an application for a group of variations. A.6 - Administrative change - Change in ATC Code/ATC Vet Code A.7 - Administrative change - Deletion of manufacturing sites	12/05/2023	15/09/2023	SmPC and Annex II	
PSUSA/10912 /202206	Periodic Safety Update EU Single assessment - COVID-19 Vaccine (ChAdOx1-S [recombinant]) (Vaxzevria)	26/01/2023	09/03/2023	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for

					PSUSA/10912/202206.
II/0084/G	This was an application for a group of variations. Submission of an updated RMP version 6 succession 3 in order to request the discontinuation of the category 1 study D8111C00010 and remove it from the Annex II; this is an interventional safety study of AZD1222 vaccine in immunocompromised adults. In addition, the important potential risk of 'Nervous system disorders, including immune mediated neurological conditions' has been amended to 'Immune mediated neurological conditions', due dates of additional pharmacovigilance activities have been updated and other editorial wordings of the RMP have been implemented. 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 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	09/02/2023	15/09/2023	Annex II	For more information, please refer to the Summary of Product Characteristics.
IB/0086	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a	04/01/2023	n/a		

	re-test period/storage period supported by real time data				
IA/0087	B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol	21/12/2022	n/a		
IA/0085	A.7 - Administrative change - Deletion of manufacturing sites	06/12/2022	n/a		
R/0079	Renewal of the marketing authorisation.	13/10/2022	31/10/2022	SmPC, Annex II, Labelling and PL	Summary 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. Furthermore, the CHMP considered that, as all Specific Obligations have been fulfilled or reclassified as Recommendations or Category 3 studies in the RMP, there are no remaining grounds for the marketing authorisations to remain conditional and therefore recommends the granting of the MA no subject to Specific Obligations for Vaxzevria. Please refer to Scientific Discussion 'Vaxzevria/H//C/005675/R/0079'
IB/0081	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	07/10/2022	20/10/2022	SmPC	To extend the shelf life of the finished product from 6 months to 9 months.
II/0075	Update of section 5.1 of the SmPC in order to include updated efficacy information based on the 6 months	15/09/2022	20/10/2022	SmPC	SmPC new text Updated efficacy analysis were performed with additional

	follow-up analysis from study D8110C00001 listed as a specific obligation in the Annex II; this is a phase III randomised, double-blind, placebo-controlled, multicenter study in adults to determine the safety, efficacy and immunogenicity of Vaxzevria. In addition, the MAH took the opportunity to implement other administrative updates in the product information. The RMP version 5.2 has also been submitted. The MAH removed the important identified risk of anaphylaxis from the list of safety concerns, updated the routine and additional pharmacovigilance activities section and took the opportunity to implement other administrative updates. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				confirmed COVID-19 cases accrued during blinded placebo controlled follow up, representing up to 6 months follow-up data (data cut-off date: 30 July 2021). The analysis of the primary efficacy endpoint for the double-blind period included 325 adjudicated events occurring at least 15 days post second dose of study vaccine. There were 141 events in the AZD1222 group and 184 events in the placebo group, with a vaccine efficacy (VE) estimate of 66.98% and a lower bound of the 95% CI of 58.87%. In participants between 18 to and 65 years of age, a VE estimate of 64.76% and a lower bound of the 95% CI of 55.73%. In participants older than 65 years of age, a VE estimate of 86.35% and a lower bound of the 95% CI of 65.79%. The SmPC section 5.1 has been updated with a summary of these results. Four secondary endpoints were analysed for events at least 15 days post second dose of study intervention, and all 4 results were generally consistent with the primary analysis. In participants with or without evidence of prior infection, the VE was 66.96%. VE against severe or critical symptomatic COVID-19 was 95.69%. In relation to the incidence of COVID-19 related emergency departments visits, a VE of 94.17% was shown. The incidence of the first post treatment response for SARS-CoV-2 nucleocapsid antibodies occurring at least 15 days after the second dose of study intervention, regardless of symptoms, resulted in a VE estimate of 61.01%. The safety data reported from the 6-months follow-up did not reveal new safety concerns for AZD1222. The most common adverse drug reactions (ADR) were consistent with the adverse reactions commonly observed following

					vaccination which were already included in the SmPC. The benefit-risk balance of Vaxzevria, remains positive. For more information, please refer to the Summary of Product Characteristics.
II/0076/G	This was an application for a group of variations. 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 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	01/09/2022	n/a		
II/0038	Submission of the final report from study MS1222-0003 ''Assessment of anti-PF4 antibodies prior to, and following, vaccination with AZD1222" listed as a category 3 study in the RMP. This is a study where sera of vaccinated individuals in study D8110C00001 are tested to elucidate whether vaccination with Vaxzevria leads to increased levels of circulating anti-PF4 antibodies, a key component of the hypothesized mechanism underlying thrombosis with thrombocytopenia syndrome (TTS). C.I.13 - Other variations not specifically covered	01/09/2022	n/a		

	elsewhere in this Annex which involve the submission of studies to the competent authority				
IA/0080	A.7 - Administrative change - Deletion of manufacturing sites	26/08/2022	n/a		
PSUSA/10912 /202112	Periodic Safety Update EU Single assessment - COVID-19 Vaccine (ChAdOx1-S [recombinant]) (Vaxzevria)	21/07/2022	08/08/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10912/202112.
IB/0078/G	This was an application for a group of variations. B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	05/08/2022	20/10/2022	Annex II	Updated annex II with a new manufacturing site for the active substance mAbxience S.A.U, Calle Jose Zabala 1040, Garin, B1619JNA, Buenos Aires, Argentina
II/0071	B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS	21/07/2022	n/a		
II/0031	Submission of the final study report for MS1222-0002 "In Vitro Assay to Determine Release of Spike Protein From Transduced Cells" to fulfil the imposed study as reflected in Annex II of the product information and the RMP. As a result, Annex II of the	21/07/2022	08/08/2022	Annex II	SmPC new text Within this type II variation, the MAH submits the final study report for study MS1222-0002 which fulfils the Annex II obligation as well as the Post-Authorisation Measure (PAM) "In Vitro expression of Spike protein" as detailed

	product information is being updated to remove this study. The MAH is taking the opportunity to provide two additional studies linked to support the investigation on the platelet activation: the final study report for MS1222-0001 "Computational Prediction of Spike Protein Interaction with Platelet Factor 4 (PF4)" which is the first report requested within the required studies for "in vitro interaction of AZD1222 or spike protein with PF4 and/or platelets" as reflected in the RMP; and the study report for 520447 "Investigative Vaccine Study in the Mouse" to evaluate spike protein levels and haematology parameters. 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				under Additional Pharmacovigilance Activities in the EU Risk Management Plan (RMP) for Vaxzevria. This in vitro assay was conducted to determine the release of spike protein from transduced cells. The study results show that spike protein is produced by AZD1222-transduced cells, which is cleaved and released from the cell surface. The lack of full-length spike protein detection in the supernatant and the fact that lactate dehydrogenase (LDH) levels did not rise with multiplicities of infection (MOI) suggests that the presence of shed spike protein was not responsible of cell death. In view of the data submitted with the variation, the above mentioned obligation has been fulfilled, and therefore it is recommended that it is deleted from the Annex II. For more information, please refer to the Summary of Product Characteristics.
II/0074	Type II C.I.11.b, To update Annex IIE to remove the specific obligation relating to provision of process validation data for the active substance and finished product (SO1) which has been fulfilled, and to change the date of the specific obligation relating to the provision of additional information on stability of the active substance and finished product (and review the finished product specifications following further manufacturing experience) from June 2022 to	23/06/2022	08/08/2022	Annex II	To address specific obligations on quality, the MA Holder provided relevant data in line with the requirements and due dates set by CHMP. Protocols and reports were provided in monthly Post Authorisation Measures since initial authorisation (2021) until March 2022, and a number of variations were submitted. The information provided by the MA Holder in these submissions was evaluated and the specific obligation relating to provision of process validation data is now considered fulfilled. Stability studies are

	January 2023 (SO2). 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				ongoing and further data from these studies are expected to be submitted in due course. The Annex IIE has been updated as follows: • SO1 (relating to provision of process validation data for the active substance and finished product) is deleted from the list of specific obligations. • SO2 (relating to the provision of additional information on stability of the active substance and finished product (and review the finished product specifications following further manufacturing experience), due date is extended from June 2022 to January 2023.
IB/0077	B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits	17/06/2022	n/a		
II/0052	Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to introduce a booster dose of Vaxzevria (homologous or heterologous) based on interim immunogenicity and safety data from the pivotal study D7220C00001, a partially double-blinded, randomised, multinational, active-controlled phase II/III clinical study and supportive literature evidence from studies COV001, COV-BOOST and Com-COV studies. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes/corrections throughout the product information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	19/05/2022	20/05/2022	SmPC and PL	Please refer to Scientific Discussion 'EMEA/H/C/005675/II/0052' For more information, please refer to the Summary of Product Characteristics.

IB/0073	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	21/04/2022	n/a		
IB/0072	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	08/04/2022	n/a		
II/0064/G	This was an application for a group of variations. 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 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	07/04/2022	n/a		
II/0062	B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol	07/04/2022	n/a		

IB/0069	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	23/03/2022	31/03/2022	Annex II	To change the due date for the final clinical study reports for studies COV001, COV002, COV003 and COV005 and for the final analysis from the pooled pivotal studies listed as specific obligation in Annex IIE from 31 May 2022 to 31 December 2022.
IB/0063	B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation	04/03/2022	n/a		
IB/0065/G	This was an application for a group of variations. 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 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	25/02/2022	n/a		
IB/0068	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	17/02/2022	n/a		
IB/0066	B.II.e.1.z - Change in immediate packaging of the finished product - Other variation	11/02/2022	n/a		
IB/0060/G	This was an application for a group of variations. B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure	07/02/2022	n/a		

	(including replacement or addition) B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
IB/0067	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	01/02/2022	02/02/2022	SmPC and PL	Sections 4.4 and 4.8 of the SmPC and sections 2 & 4 of the PL have been updated to implement wording in relation to transverse myelitis
IB/0059	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	26/01/2022	02/02/2022	Annex II	Update of Annex IIE to extend the due date for a specific obligation (SO13) from December 2021 to March 2022
II/0061/G	This was an application for a group of variations. B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability	20/01/2022	n/a		
II/0055	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/01/2022	14/01/2022	SmPC and PL	Based on post-marketing data with data cut-off 30th September 2021, 1809 cases of thrombosis and thrombocytopenia syndrome (TTS) have been identified, of which 166 were reported after the second dose. Overall TTS reporting rate following dose 2 was estimated at 1.87 cases/million doses administered, which is lower than the

					estimated reporting rate after dose 1 (14.45/million doses) and also lower than preliminary estimates of the background rate (5.62-10.75/million person-years). No new unexpected safety findings regarding the events of thrombosis with TTS have been identified.
PSUSA/10912 /202106	Periodic Safety Update EU Single assessment - COVID-19 Vaccine (ChAdOx1-S [recombinant]) (Vaxzevria)	13/01/2022	n/a		PRAC Recommendation - maintenance
IB/0058	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	17/12/2021	n/a		
II/0047	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	16/12/2021	n/a		
IB/0054	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	06/12/2021	n/a		
II/0040	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	02/12/2021	n/a		
IB/0057	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	30/11/2021	n/a		

IB/0053	B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	24/11/2021	n/a		
IB/0056	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	22/11/2021	23/11/2021	SmPC and PL	Section 4.4 and 4.8 of the SmPC and sections 2 & 4 of the PL have been updated to implement wording agreed by PRAC in relation to the Events of cerebrovascular venous and sinus thrombosis without thrombocytopenia
II/0051/G	This was an application for a group of variations. 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 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	18/11/2021	n/a		
II/0050	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	18/11/2021	n/a		
R/0037	Renewal of the marketing authorisation.	14/10/2021	09/11/2021	SmPC,	The CHMP, having reviewed the available information on

				Labelling and PL	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 Vaxzevria, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
IB/0049/G	This was an application for a group of variations. 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 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	03/11/2021	n/a		
II/0035/G	This was an application for a group of variations. 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 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	03/11/2021	n/a		

	biological AS				
II/0030/G	This was an application for a group of variations. 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 B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	14/10/2021	n/a		
II/0026	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/10/2021	15/10/2021	SmPC, Annex II and PL	The MAH has provided the primary analysis of study D8110C00001. This is a randomised, double-blinded, placebo-controlled phase III study conducted in the United States, Peru and Chile aimed to assess the efficacy, safety and immunogenicity of Vaxzevria. The vaccine efficacy (VE) results against COVID-19 symptomatic disease was 74.0% (95%CI: 65.3 – 80.5). The VE estimate was also determined in participants ≥65 years of age [VE: 83.5% (95%CI: 54.2 – 94.1)]. Severe or critical symptomatic COVID-19 disease was also evaluated. No cases of severe or critical symptomatic COVID-19 were reported in the vaccine group compared with 8 cases reported in the placebo group. Overall, the observed safety profile is in line with the results included in the product information. The study results led to the addition of the following adverse drug reactions (with their respective frequencies) in the product information: facial paralysis (rare) and muscle spasms (uncommon).

IAIN/0048	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	13/10/2021	15/10/2021	SmPC and PL	Sections 4.4 and 4.8 of the SmPC and sections 2 and 4 of the PL have been updated to implement signal recommendations on Immune Thrombocytopenia
IA/0046	A.7 - Administrative change - Deletion of manufacturing sites	27/09/2021	15/10/2021	Annex II	Update of Annex II A of the product information to remove reference to the temporary testing exemption.
IB/0045	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	17/09/2021	n/a		
IB/0042	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	17/09/2021	n/a		
IB/0044	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	13/09/2021	14/09/2021	SmPC and PL	• To update section 4.8 of the SmPC and sections 2 & 4 of the PL to implement wording agreed by PRAC in relation to Guillain-Barre Syndrome. • To remove text from section 4.4 of the SmPC and section 2 of the PL in relation to TTS (Thrombosis with thrombocytopenia syndrome and coagulation disorders occurred mostly in women under 60 years of age).
IB/0041	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	06/09/2021	n/a		
II/0032/G	This was an application for a group of variations. 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	13/08/2021	n/a		

	method at the site is a biol/immunol method 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 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				
IB/0039	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	11/08/2021	n/a		
IB/0036	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	27/07/2021	n/a		
II/0033/G	This was an application for a group of variations. 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 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	27/07/2021	n/a		

	control/testing takes place and any of the test method at the site is a biol/immunol method 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				
II/0017/G	This was an application for a group of variations. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/07/2021	14/09/2021	SmPC and Annex II	To update information about pregnancy and breastfeeding information in section 4.6 of the SmPC as a result of the development and reproductive toxicity (DART) study to indicate that animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development animal studies, and that lactational transfer of anti-SARS-CoV-2 S antibodies from maternal female mice to pups was observed. It is unknown whether Vaxzevria is excreted in human milk. Based on the DART study, section 5.3 of the SmPC is also updated to indicate that vaccine elicited detectable anti-SARS-CoV-2 S-glycoprotein maternal antibodies were transferred to the foetuses and pups, indicating placental and lactational transfer, respectively. No Vaxzevria data are available on vaccine excretion in milk. Section 5.3 was also update to reflect in more detail the outcome from the repeat-dose toxicity study in mice, where intramuscular administration of Vaxzevria was well tolerated.
IB/0034	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	16/07/2021	19/07/2021	SmPC, Annex II and PL	To update section 4.4 of the SmPC and section 2 of the PL to implement wording agreed by PRAC in relation to

	assessment done under A 45/46 - Other variation				Guillain-Barré Syndrome.
IB/0024	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	15/07/2021	n/a		
II/0015	Submission of an updated RMP version 3 succession 3 in order to update the safety concerns to add 'Thrombosis in combination with thrombocytopenia' as an important identified risk and 'Thrombosis' as an important potential risk, with consequential changes in the RMP and to update the pharmacovigilance plan following the request by PRAC in the outcome of signal assessment procedure on embolic and thrombotic events with Vaxzevria EPITT no: 196833. The MAH has taken the opportunity to further update the RMP to reclassify "anaphylaxis" as an important identified risk, already reflected in the product information as an adverse reaction. 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	08/07/2021	n/a		
II/0019	Submission of the interim and primary reports clinical study reports from study D8111C00002, listed as a category 3 study in the RMP. This study is	01/07/2021	n/a		

	a Phase I/II randomised, double-blind, placebo-controlled, multicentre study in participants aged 18 years or older to determine the safety and immunogenicity of Vaxzevria. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
IAIN/0029	Sections 4.3, 4.4, 4.8 of the SmPC and sections 2 & 4 of the PL have been updated to add a contraindication in case of capillary leak syndrome and include capillary leask syndrome as a side effect. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	30/06/2021	01/07/2021	SmPC and PL	Sections 4.3, 4.4, 4.8 of the SmPC and sections 2 & 4 of the PL have been updated to add a contraindication in case of capillary leak syndrome and include capillary leask syndrome as a side effect.
IB/0028	Update on Annex II to include a temporary exemption from Article 51, 1(b) of 2001/83/EC until 31 July 2021. 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	28/06/2021	01/07/2021	Annex II	Update on Annex II to include a temporary exemption from Article 51, 1(b) of 2001/83/EC until 31 July 2021.
IB/0027	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	28/06/2021	n/a		
II/0002	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	24/06/2021	01/07/2021	SmPC, Labelling and	The MAH has provided the primary analysis (based on the 7th December data cut-off) for studies: COV001 (Phase

	data			PL	I/II), COV002 (Phase II/III), COV003 (Phase II/III) and COV005 (Phase I/II). These trials were the basis of granting the conditional marketing authorisation. At the time of analysis, participants that received 1 dose of Vaxzevria was extended from 12,021 to 12,282 and from 8,266 to 10,448 those who received 2 doses of Vaxzevria. With 7,158 participants completing >2 months follow-up post-dose 2. Due to the modest extend of both the size and long-term exposure of the safety database, the overall frequencies of adverse events remain barely unchanged to those initially approved. The updated safety data has resulted in the addition of the following adverse drug reactions (with their respective frequencies) in the product information: urticaria (uncommon), abdominal pain (uncommon), pain in extremity (common), influenza-like illness (common), asthenia (common) and lethargy (uncommon). The MAH also took the opportunity to add angioedema with frequency not known, as requested within procedure EMEA/H/C/005675/LEG/036.1. The vaccine efficacy estimates in the product information remained unchanged. The product information wording in relation to shelf-life for opened vials and genetically modified organisms has been updated for clarity purposes.
II/0020/G	This was an application for a group of variations. 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	22/06/2021	n/a		

	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.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				
IB/0025	Section 6.3 of the SmPC has been updated to introduce conditions for temperature excursions for the unopened vials from refrigerated storage (2°C – 8°C), for a single period of 12 hours up to 30°C or 72 hours down to -3°C. B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	18/06/2021	01/07/2021	SmPC	Section 6.3 of the SmPC has been updated to introduce conditions for temperature excursions for the unopened vials from refrigerated storage (2°C – 8°C), for a single period of 12 hours up to 30°C or 72 hours down to -3°C.
IB/0023/G	This was an application for a group of variations. B.II.g.4.b - Changes to an approved change management protocol - Minor changes that do not change the strategy defined in the protocol 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 B.II.g.5.c - Implementation of changes foreseen in	28/05/2021	n/a		

	an approved change management protocol - For a biological/immunological medicinal product				
IB/0022/G	This was an application for a group of variations. 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 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 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.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	27/05/2021	n/a		
II/0016	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	27/05/2021	n/a		
II/0014	C.I.4 - Change(s) in the SPC, Labelling or PL due to	20/05/2021	21/05/2021	SmPC and PL	Thrombocytopenia in combination with thrombo-embolic

	new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				events were assessed within the signal procedure on embolic and thrombotic events with Vaxzevria (EPITT 19683). The signal evaluation lead to the update of the sections 4.4 and 4.8 of the SmPC to reflect thrombocytopenia as an adverse reaction, with a frequency of common, based on data from clinical trials and to include thrombosis in combination with thrombocytopenia with frequency of very rare. Following an update to the Company Core Data Sheet (CCDS) in relation to thromboembolism with thrombocytopenia, the marketing authorisation holder (MAH) presented a dataset including thromboembolic events with thrombocytopenia, along with proposals to contraindicate the vaccine to patients who have experienced major venous and/or arterial thrombosis in combination with thrombocytopenia following vaccination with any COVID-19 vaccine, to update the warnings on thrombocytopenia and coagulation disorders and include the frequency thrombosis with thrombocytopenia of "less than 1/100,000". No new unexpected safety findings regarding the events of thrombosis with thrombocytopenia were identified based on the submitted data (cut-off date of 08 April 2021). Based on a thorough review of this latest information, the product information has been updated to introduce a contraindication to individuals who have experienced thrombosis with thrombocytopenia syndrome (TTS) following vaccination with Vaxzevria, and warnings for Healthcare professionals to check for signs of thrombosis in any person who has thrombocytopenia within 3 weeks of vaccination with Vaxzevria, and similarly, for signs of thrombocytopenia in any person who has thrombosis within

					3 weeks of vaccination. It was also highlighted that any symptoms suggestive of thrombosis and/or thrombocytopenia should trigger immediate medical attention. The package leaflet was updated accordingly. For more information, please refer to the Summary of Product Characteristics.
II/0018	B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability	12/05/2021	n/a		
IB/0012	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	28/04/2021	n/a		
IB/0013	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	23/04/2021	21/05/2021	Annex II	Update of Annex II of the product information to add an alternative site responsible for manufacture of the active substance.
IAIN/0011	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/04/2021	21/05/2021	SmPC and PL	To update section 4.4 & 4.8 of the SmPC and section 4 of the PL to implement the signal recommendations on hypersensitivity and anaphylaxis (EPITT no 19668) as recommended by PRAC.
IB/0009/G	This was an application for a group of variations. B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a	14/04/2021	21/05/2021	Annex II	Update of Annex II of the product information to add an alternative site responsible for manufacture of the active substance.

	biological/immunological medicinal product B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product				
IAIN/0010	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	08/04/2021	08/04/2021	SmPC, Annex II and PL	To update sections 4.4 and 4.8 of the SmPC, Annex II Part D and sections 2 and 4 of the PL to implement further signal recommendations on embolic and thrombotic events. In addition, minor editorial updates are included in section 2 of the PL to improve readability with regards to blood disorder.
IAIN/0008	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	06/04/2021	08/04/2021	SmPC, Annex II and PL	Update of Annex II of the product information to change the name of the site responsible for batch release of the finished product. In addition, minor editorial changes were introduced Annex I, French translation and Annex II, Italian translation.
IB/0005	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	26/03/2021	08/04/2021	Annex II	Update of Annex II of the product information to add an alternative site responsible for manufacture of the active substance.
IAIN/0007	A.2.a - Administrative change - Change in the (invented) name of the medicinal product for CAPs	25/03/2021	08/04/2021	SmPC, Annex II, Labelling and PL	To change the invented name of the medicinal product from COVID-19 Vaccine AstraZeneca to VAXZEVRIA
IB/0006	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	24/03/2021	n/a		
IB/0003/G	This was an application for a group of variations. B.II.b.2.a - Change to importer, batch release	23/03/2021	n/a		

	arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place 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				
IAIN/0004	To update section 4.4 of the SmPC and section 2 of the PL to implement the recommendations on embolic and thrombotic events. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/03/2021	19/03/2021	SmPC and PL	To update section 4.4 of the SmPC and section 2 of the PL to implement the recommendations on embolic and thrombotic events.
IB/0001	B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits	18/02/2021	n/a		