JCOVDEN

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/0076	Update of section 4.5 of the SmPC in order to update information regarding the co-administration of JCOVDEN with influenza vaccine based on the final report from study VAC31518COV3005 listed as a category 3 study in the RMP; this is a randomized, double-blind, Phase 3 study to evaluate safety,	11/07/2024		SmPC and PL	SmPC new text The MAH has submitted the final Clinical Study Report (CSR) for the study COV3005. Study COV3005 is a randomized, double-blind, Phase 3 study to evaluate safety, reactogenicity, and immunogenicity of co-administration of Ad26.COV2.S and influenza vaccines in

[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).

	reactogenicity, and immunogenicity of co-administration of Ad26.COV2.S and influenza vaccines in healthy adults 18 years of age and older. The Package Leaflet is updated accordingly. Version 8.1 of the RMP has also been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				healthy adults 18 years of age and older. The humoral immunogenicity (HI) titres induced after co-administration of Ad26.COV2.S and a standard-dose influenza vaccine were demonstrated to be non-inferior to the HI titres induced after administration of a standard-dose influenza vaccine for 3 out of the 4 influenza strains composing the standard-dose vaccine (A/Cambodia [H3N2], B/Victoria, B/Phuket). The non-inferiority criteria was not met for A/Victoria (H1N1). The SARS-CoV-2 S-binding antibody titres induced 28 days after the co-administration of Ad26.COV2.S and a standard-dose influenza vaccine were demonstrated to be non-inferior to those elicited after administration of Ad26.COV2.S alone. Descriptive analyses suggest that concomitant administration of Ad26.COV2.S and a high-dose influenza vaccine induced lower HI titres for the A strains when compared to sequential administration. Similar titres for the B strains are observed at Day 28 in both groups. Regarding the SARS-CoV-2 immune responses, a difference in fold increase from baseline to Day 29 was observed between groups. However, Day 29-GMTs are not deemed to be different. Overall, the safety and reactogenicity profile of the Ad26.COV2.S vaccine administered concomitantly with the influenza vaccine is in line with the profile of the Ad26.COV2.S vaccine observed in previous studies. The safety and reactogenicity profile of concomitant administration of the Ad26.COV2.S vaccine and the standard-dose or high-dose influenza vaccine is considered acceptable.

					For more information, please refer to the Summary of Product Characteristics.
II/0075/G	This was an application for a group of variations. A grouped application consisting of five Type II variations, as follows: C.I.4: Update of section 5.1 of the SmPC in order to update efficacy information based on results on updated genomic sequencing data from study VAC31518COV3001 listed as a category 3 study in the RMP. This is a randomized, double-blind, placebo-controlled Phase 3 study to assess the efficacy and safety of Ad26.COV2.S for the prevention of SARS-CoV-2-mediated COVID-19 in adults aged 18 years and older. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes to section 6.1 of the SmPC and to the Package Leaflet. C.I.4: Update of section 5.1 of the SmPC in order to update efficacy information based on results on updated genomic sequencing data from study VAC31518COV3009 listed as a category 3 study in the RMP. This is a Phase 3 randomized, double-blind, placebo-controlled study to evaluate the efficacy, safety, reactogenicity, and immunogenicity of 2 doses of Ad26.COV2.S for the prevention of SARS-CoV-2-mediated COVID-19 in adults aged 18 years and older. C.I.13: Submission of the final report from	21/03/2024		SmPC and PL	SmPC new text The MAH has submitted the final study results of studies COV3001, COV3009 and COV4002. For both studies COV3001 and COV3009, efficacy against confirmed moderate to severe/critical COVID-19 cases and against confirmed severe/critical COVID-19 cases, with onset at least 14 days and/or 28 days after single or 2-dose vaccination by virus variant, for which there are sufficient cases available for meaningful interpretations are included in the SmPC. Final efficacy analysis by variant has been updated in section 5.1 of the SmPC based on complete genome sequencing data. Final safety results from the above studies are aligned with safety data from the primary analysis. No new safety concern is identified. Final results of the COV4002 collectively indicate that, in the US population, as compared to no vaccination and for the period covered by this study, administration of a single dose of JCOVDEN results in a lower risk for developing COVID-19, for being hospitalized for COVID-19, and for all-cause mortality temporally associated with COVID-19 for at least 12 months. Vaccine effectiveness increased as the outcome severity increased, and relatively lower vaccine effectiveness were estimated in groups at higher risk of COVID-19. For more information, please refer to the Summary of Product Characteristics.

	VAC31518COV2008 listed as a category 3 study in the RMP. This is a randomized, double- blind, Phase 2 study to evaluate the immunogenicity, reactogenicity and safety of Ad26.COV2.S administered as booster vaccination in adults 18 years of age and older who have previously received primary vaccination with Ad26.COV2.S or BNT162b2. C.I.13: Submission of the final report from the open label phase of study VAC31518COV3001 listed as a category 3 study in the RMP. C.I.13: Submission of the final report from VAC31518COV4002 listed as a category 3 study in the RMP. This is an observational post-authorization study to assess the effectiveness of Ad26.COV2.S for prevention of COVID-19 using real-world data. 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 C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission				

	of studies to the competent authority				
II/0074/G	This was an application for a group of variations. Grouped application comprising two type II variations (C.I.13) as follows: - Submission of the final report from study TOX15258 - Ad26.COV2.S (Prophylactic COVID-19 Vaccine): A Transcriptomics Exploratory Study in Cambodian Cynomolgus Monkey. - Submission of the report from study TV-TEC-236300 - Biophysical studies on interactions between human platelet 4 and Ad26.COV2.S. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	12/10/2023	n/a		
PSUSA/10916 /202302	Periodic Safety Update EU Single assessment - COVID-19 vaccine (Ad26.COV2-S [recombinant]) (JCOVDEN)	28/09/2023	n/a		PRAC Recommendation - maintenance
II/0072/G	This was an application for a group of variations. Update of section 4.4 of the SmPC in order to add a new warning on myocarditis and pericarditis and update of section 4.8 of the SmPC to add myocarditis and pericarditis to the list of adverse drug reactions (ADRs) with frequency not known based on post-	25/05/2023	29/06/2023	SmPC and PL	The overall current safety profile of the JCOVDEN is established based on available data from all sources, including spontaneous reports from the MAH's global safety database, available clinical study data and Real World Evidence (RWE) analyses. Myocarditis and pericarditis are adverse events of special interest (AESI) which have been reviewed in previous

	marketing data and three observational claims databases in US. The Package Leaflet is updated accordingly. A revised RMP version 6.4 has been approved. In addition, the MAH took the opportunity to update the ATC Code as amended by the WHO. 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 A.6 - Administrative change - Change in ATC Code/ATC Vet Code				procedures for JCOVDEN, including summary safety reports (SSR) and periodic safety update reports (PSUR). Following a regulatory authority request, the MAH performed a detailed analysis of all available safety data on myocarditis/pericarditis up to 24th February 2023 as summarised next: Most of the spontaneous reports of myocarditis from the post-marketing were assessed as Brighton Collaboration (BC) Level 4 and Level 5, indicating cases providing insufficient information to meet the diagnostic certainty (Level 1, 2, or 3), or there were clear alternative explanations for the event onset. However, some BC Level 1 to 3 cases were reported in close temporal association to the vaccine for which causality could not be excluded, and in particular, several BC Level 2 cases were reported among males under 40 years of age. Pericarditis followed a similar pattern. In the pooled analysis of clinical study data, 0 cases of "non-infectious myocarditis" and 2 cases of MedDRA High level terms (HLTs) of "non-infectious pericarditis" were reported in the JCOVDEN group within 28 days post-dose 1; no cases were reported in males below 40 years of age. No events were reported in the placebo group within the same timeframe. The MAH has also performed an analysis of the available safety data for myocarditis and pericarditis using RWE Rapid Cycle Analysis (RWE RCA) methods. The MAH used a Self-Controlled Case Series analysis design to estimate the risk of occurrence of the AESI following the first JCOVDEN administration relative to unexposed time (control period) within the same individual, and a Comparative Cohort design to estimate risk of occurrence of the predefined

					AESI following the administration of the first JCOVDEN dose compared to the first mRNA COVID-19 vaccine exposure. The analyses were performed overall and stratified by sex and age. Overall, the results indicated a high level of certainty of an increased risk of myocarditis-pericarditis for males aged 18-39 years following the first JCOVDEN dose in the 1-14 day risk period (meta-analysis relative risk estimates = 2.3-5.4) and the 1-28 days risk period (meta-analysis relative risk estimates = 1.1-3.3). Based on the above, it is agreed with the MAH that there is at least a reasonable possibility for a causal relationship between occurrence of myocarditis or pericarditis after vaccination with JCOVDEN. Available data suggest that these conditions can develop within just a few days after vaccination, occurred primarily within 14 days and have been observed more often in males younger than 40 years of age. The available data does not allow to estimate the size of the risk with any precision, thus a proposed frequency of not known is agreed. The PI and RMP have been updated accordingly. The benefit risk of JCOVDEN remains unchanged.
II/0071/G	This was an application for a group of variations. Grouped application consisting of: 1) Submission of the final study report of a clinical TTS characterization study listed as a category 3 study in the RMP. This is a Test Pre- and Post-Vaccination Serum Across All Populations Using Clinical Samples From Ad26-based Company Vaccine Studies Other Than Ad26.COV2.S; 2) Submission of the Addendum to final CSR of the study VAC31518COV2001 listed	08/06/2023	n/a		

	as a category 3 study in the RMP. This is a randomized, double-blind, placebo-controlled Phase 2a study to evaluate a range of dose levels and vaccination intervals of Ad26.COV2.S in healthy adults aged 18 to 55 years, and adults aged 65 years and older. The RMP version 7.1 is submitted and updated accordingly. In addition, the MAH updated the milestones of several studies. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
PSUSA/10916 /202208	Periodic Safety Update EU Single assessment - COVID-19 vaccine (Ad26.COV2-S [recombinant]) (JCOVDEN)	14/04/2023	n/a		PRAC Recommendation - maintenance
II/0065	Submission of an updated RMP version 5.3 in order to update the clinical exposure and risk sections. In addition, the study VAC31518COV3018 is removed from the RMP. This is an interventional clinical trial to evaluate the immunogenicity and safety of JCOVDEN in immunocompromised patients. 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	09/02/2023	n/a		For more information, please refer to the Summary of Product Characteristics.

	where significant assessment is required				
R/0063	Renewal of the marketing authorisation.	15/12/2022	09/01/2023	Annex II	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 either been fulfilled or reclassified as Category 3 study in the RMP, there are no remaining grounds for the marketing authorisations to remain conditional and therefore recommends the granting of the MA no longer subject to Specific Obligations for JCOVDEN. Please refer to Scientific Discussion 'JCOVDEN/H/C/005737/R/0063'
IB/0070/G	This was an application for a group of variations. B.II.z - Quality change - Finished product - 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	22/12/2022	n/a		
II/0067	B.I.z - Quality change - Active substance - Other variation	08/12/2022	05/01/2023	Annex II	Annex II.E has been updated to remove the specific obligation related to the request for additional active substance comparability and validation data.
II/0064	B.II.b.z - Change in manufacture of the Finished Product - Other variation	08/12/2022	05/01/2023	Annex II	Annex II.E has been updated to remove the specific obligation related to the request for additional finished product comparability and validation data.

II/0053/G	This was an application for a group of variations. Update of section 4.2 of the SmpC to introduce an heterologous booster dose of JCOVDEN following priming with another adenoviral vector-based vaccine based on literature evidence from COV-BOOST study. Update of sections 4.8 and 5.1 of the SmPC to include safety and immunogenicity data of JCOVDEN as heterologous booster dose based on data from studies COV-BOOST study. Update of sections 4.8 of the SmPC to include safety and immunogenicity data of JCOVDEN as homologous and heterologous booster dose based on data from COV2008 study, a randomised, double-blind Phase 2 Study Update of sections 4.8 and 5.1 of the SmPC to include safety and immunogenicity data of JCOVDEN as heterologous booster dose based on data from DMID 21-0012 study. In addition, updated vaccine efficacy by variant has been updated based on updated genomic sequencing data from study COV3009 and some minor corrections have been implemented in in section 5.1 of the SmPC. The Package Leaflet is updated accordingly. 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	10/11/2022	11/11/2022	SmPC and PL	SmPC new text This variation has been submitted to introduce an heterologous booster with Ad26.COV2.S following primary vaccination with another adenoviral vector-based vaccine and to provide updated follow-up data from studies which were included in variation EMEA/H/C/005737/II/0033. As a consequence, section 4.2, 4.8 and 5.1 of the SmpC have been updated. The PL has been updated accordingly. Data of the COV-BOOST study were submitted to support the heterologous booster with Ad26.COV2.S following another adenoviral vector-based primary vaccination. This study evaluates safety and immunogenicity of different COVID-19 vaccines given as third dose (booster) after primary vaccination with adenoviral-vector based or mRNA COVID-19 vaccines. The data showed that a booster dose of Ad26.COV2.S induces anamnestic humoral responses in individuals who completed their primary vaccination schedule with 2 doses of ChAdOx1 approximately 77 days before the booster vaccination. Data from study DMID 21-0012, and independent Phase 1/2 open-label clinical trial study (NCT04889209) that evaluated immunogenicity and safety of a booster injection of Ad26.COV2.S or an mRNA vaccine 12 weeks after primary vaccination with a COVID-19 vaccine were further complemented with long-term nAb data for the reference strain D614G, nAb data against the Delta and Beta variants, as well as CMI data. Ad26.COV2.S induced a booster response 15 days post boost against the reference strain as well as the Beta and the Delta variants in individuals primed with a mRNA vaccine who received the booster at least 12 weeks after primary vaccination. Immunogenicity data against the Omicron BA.1 variant

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				were available from studies DMID 21-0012 and COV2008. COV2008 is a Phase 2 study to evaluate immunogenicity, safety and reactogenicity of Ad26.COV2.S when administered as a homologous or heterologous booster following primary vaccination with an mRNA vaccine. In both studies, GMTs against the Omicron BA.1 variant are lower compared to the D614G strain, the Delta and the Beta variants. A booster dose with Ad26.COV2.S induces a humoral immune response in individuals primary vaccinated with an mRNA vaccine or with Ad26.COV2.S. Highest titers are observed in the groups primary vaccinated with an mRNA vaccine. A heterologous boost with Ad26.COV2.S results in similar or slightly lower titers compared to a homologous mRNA boost. Very low titers are obtained after a homologous Ad26.COV2.S boost. Data from study DMID 21-0012 also indicates that higher titers are obtained after a heterologous mRNA boost in Ad26.COV2.S primed individuals. In contrast to nAb against the D614G strain, a decrease in nAb against the Omicron BA.1 variant is observed by Day 91 after a boost with Ad26.COV2.S in all groups boosted. Finally, the SmPC has been updated with additional information on the safety profile of a homologous and heterologous booster dose. Heterologous boosting after primary vaccination with an adenoviral-vector based had an acceptable safety profile. No new safety concern was identified after both, homologous and heterologous booster. For more information, please refer to the Summary of Product Characteristics.
N/0066	Minor change in labelling or package leaflet not	08/11/2022	11/11/2022	PL	

	connected with the SPC (Art. 61.3 Notification)				
IA/0069/G	This was an application for a group of variations. A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)	01/11/2022	n/a		
PSUSA/10916 /202202	Periodic Safety Update EU Single assessment - COVID-19 vaccine (Ad26.COV2-S [recombinant]) (JCOVDEN)	13/10/2022	31/10/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10916/202202.
II/0047/G	This was an application for a group of variations. Submission of the final reports from the non-clinical studies TV-TEC-207316, TV-TEC-207437, TOX15155, TV-TEC-215524 and TOX15252, listed as category 3 in the RMP. These are non-clinical studies conducted to further characterise the potential mechanisms underlying the important identified risks of thrombosis with thrombocytopenia syndrome (TTS) and thrombocytopenia, including immune thrombocytopenia (ITP). 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		

	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
II/0060	Update of section 4.8 of the SmPC in order to update the list of adverse drug reactions (ADRs) based on pooled analyses of clinical safety data from the following Phase III interventional studies: VAC31518COV3001 and VAC31518COV3009; and from the Phase I/II interventional studies: VAC31518COV1001, VAC31518COV1002, VAC31518COV1003 and VAC31518COV2001. The Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	15/09/2022	31/10/2022	SmPC and PL	SmPC new text The safety profile of the primary vaccination with Ad26.COV2.S in adults aged 18 years of age and older described in the current SmPC is based on the safety results from the primary analysis from the double-blind phase of the Phase 3 Study VAC31518COV3001 (data cut-off: 22 January 2021) and on post-marketing data which became available following the initial authorization of the vaccine. With the availability of data from final analyses of the double-blind phases of Study VAC31518COV3001 and the second large double-blind Phase 3 Study VAC31518COV3009, available safety data on vaccination with Ad26.COV2.S in a randomized, placebo-controlled clinical setting data increased substantially compared with the amount of safety data available at the time of the initial filing. The Marketing Authorisation Holder (MAH) has performed a primary pooled analysis of clinical safety data from the

					double-blind phases of Phase 3 studies (VAC31518COV3001 and VAC31518COV3009), and from Phase 1 and Phase 2 clinical studies (VAC31518COV1001, VAC31518COV1002, VAC31518COV2001) with Ad26.COV2.S 5×1010 vp (18 November 2021) to assess the reactogenicity profile and the frequency of adverse events after primary vaccination with Ad26.COV2.S in adults aged 18 years and older. Current identified adverse drug reactions (ADRs) in the approved SmPC were retained as ADRs in the proposed SmPC, but their frequency categories were revised. No new ADRs following vaccination with Ad26.COV2.S were identified based on the results of the primary pooled analysis compared to the current approved safety profile. The package leaflet is updated accordingly. The benefit-risk balance of JCOVDEN remains positive. For more information, please refer to the Summary of Product Characteristics.
IB/0062	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	08/09/2022	n/a		
II/0058/G	This was an application for a group of variations. B.II.d.z - Change in control of the Finished Product - Other variation B.II.b.z - Change in manufacture of the Finished Product - Other variation	01/09/2022	n/a		
II/0057	B.II.b.z - Change in manufacture of the Finished Product - Other variation	01/09/2022	n/a		

IB/0061	B.I.a.4.f - Change to in-process tests or limits applied during the manufacture of the AS - Addition or replacement of an in-process test as a result of a safety or quality issue	09/08/2022	n/a		
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	14/07/2022	31/10/2022	Annex II	To extend the due date of SOB "Ïn order to confirm the consistency of the finished product manufacturing process, the MAH should provide additional comparability and validation data." from 31st of October 2022to 30th of September 2022.
II/0048/G	This was an application for a group of variations. Submission of the final reports from four exploratory studies conducted to further characterise the potential mechanisms underlying the important identified risk of thrombosis with thrombocytopenia syndrome (TTS). These studies evaluated the levels of anti-PF4 antibodies using clinical samples, both from Ad26.COV2.S and other non-COVID-19 Ad26-based vaccine clinical studies. Interim results from an additional exploratory study are provided and the submission milestone for the final results has been updated. The RMP version 4.2 has been updated accordingly. In addition, the MAH removed the important identified risk of anaphylaxis from the list of safety concerns (PSUSA/00010916/202108), updated the routine pharmacovigilance activities section and took the opportunity to implement other administrative updates in the RMP in alignment with procedure EMEA/H/C/005737/II/033.	07/07/2022	n/a		

	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
II/0050	B.II.b.z - Change in manufacture of the Finished Product - Other variation	10/06/2022	n/a		
IB/0056	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	09/06/2022	n/a		
IB/0055/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	31/05/2022	31/10/2022	Annex II	This variation resulted in an update of annex II to include a new specific obligation to confirm the consistency of the active substance manufacturing process.

IB/0052/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 (including replacement or addition) B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	24/05/2022	31/10/2022	Annex II	This variation resulted in an update of annex II to amend due date of the specific obligation to confirm the consistency of the finished product manufacturing process.
IB/0051	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	18/05/2022	25/05/2022	SmPC, Annex II and PL	To update section 4.8 of the SmPC and section 4 of the PL to add Cutaneous small vessel vasculitis as adverse reaction with frequency 'Not known'
IB/0046	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	05/05/2022	n/a		
IAIN/0049	A.2.a - Administrative change - Change in the (invented) name of the medicinal product for CAPs	28/04/2022	17/05/2022	SmPC, Labelling and PL	To change the (invented) name of the medicinal product from COVID-19 Vaccine Janssen to JCOVDEN.
II/0041/G	This was an application for a group of variations. B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.a.4.e - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of an in-process test which may have a significant effect on the overall quality of the AS B.I.a.4.d - Change to in-process tests or limits applied during the manufacture of the AS - Widening	31/03/2022	n/a		

	of the approved in-process test limits, which may have a significant effect on the overall quality of the AS 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 B.I.e.4.a - Changes to an approved change management protocol - Major changes				
II/0040	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	17/03/2022	n/a		
PSUSA/10916 /202108	Periodic Safety Update EU Single assessment - COVID-19 vaccine (Ad26.COV2-S [recombinant]) (JCOVDEN)	10/03/2022	n/a		PRAC Recommendation - maintenance
IB/0045/G	This was an application for a group of variations. B.II.d.1.b - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits for medicinal products subject to OCABR 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.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.1.b - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits for medicinal products subject to	08/03/2022	n/a		

	OCABR				
IB/0044/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.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	01/03/2022	n/a		
IB/0043/G	This was an application for a group of variations. B.II.d.1.b - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits for medicinal products subject to OCABR B.I.b.1.a - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits for medicinal products subject to OCABR B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol	24/02/2022	02/03/2022	SmPC, Labelling and PL	Update of the PI to extend the shelf life from 4.5 months to 11 months when stored at 2°C to 8°C.
IB/0042	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	14/02/2022	n/a		

II/0037	B.I.z - Quality change - Active substance - Other variation	10/02/2022	02/03/2022	Annex II	Annex II has been updated to delete the following obligation: "In order to confirm the consistency of the active substance manufacturing process, the MAH should provide additional comparability and validation data."
II/0035	Update of section 4.4 and 4.8 of the SmPC in order to add transverse myelitis to the list of warnings and precautions and to the list of adverse drug reactions (ADRs) with frequency 'not known' based on the PRAC request from the post-authorisation measures MEA 14.5 and MEA 14.6 (6th and 7th Monthly Summary Safety Report covering the months of August 2021 and September 2021, respectively). The Package Leaflet is updated accordingly. Update of section 4.4 of the SmPC in order to amend the wording on Thrombosis and thrombocytopenia syndrome (TTS) following the PRAC request from the post-authorisation measure MEA 14.5. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement an editorial Quality review document (QRD) comment in the labelling following procedure EMEA/H/C/005737/II/014. 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, Labelling and PL	As an outcome of the post-authorisation measure MEA 14.5 and 14.6 (6th and 7th Monthly Summary Safety Report covering the months of August and September 2021), the MAH was requested to update of sections 4.4 and 4.8 of the SmPC in order to add transverse myelitis to the list of warnings and precautions and to the list of adverse drug reactions (ADR) with frequency not known. Based on a cumulative review of post-marketing data and literature on transverse myelitis up to 31st September 2021, it was concluded that there was a reasonable possibility to consider transverse myelitis as causally related to the COVID-19 vaccine Janssen and therefore, it was added to section 4.8 of the SmPC. The frequency of this event was calculated as 'not known'. In addition, considering transverse myelitis is a serious condition, albeit occurring very rarely, it is considered warranted to add information in section 4.4 to raise awareness among prescribers as well as vaccinees in case of experiences signs and symptoms which may suggest transverse myelitis. In addition, section 4.4 of the SmPC has been updated in order to amend the wording on Thrombosis and thrombocytopenia syndrome (TTS) and reflect the observed balanced gender in the TTS cases reported through the post-marketing data. The package leaflet is updated accordingly.

					For more information, please refer to the Summary of Product Characteristics.
II/0029	Submission of an updated RMP version 3.1 in order to upgrade the important potential risk of venous thromboembolism (VTE) to an important identified risk as an outcome of the procedure MEA-32, addition of the clinical trial VAC31518COV3003 and update of study VAC18193RSV2008 as additional pharmacovigilance activities to further characterize the important identified risks of Thrombosis with thrombocytopenia syndrome (TTS), thrombocytopenia (including immune thrombocytopenia) and VTE as an outcome of MEA 14.4. The MAH took the opportunity to include other minor updates in the RMP. In addition, the MAH consolidated in RMP version 3.1 the updates made in the RMP as part of the approved procedure EMEA/H/C/005737/II/0018 and procedure EMEA/H/C/005737/II/0029. 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	13/01/2022	n/a		
IB/0039/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	04/01/2022	n/a		

	biological/immunological medicinal product B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a 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				
R/0023	Renewal of the marketing authorisation.	16/12/2021	03/01/2022		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 COVID-19 Vaccine Janssen, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
II/0033	Update of sections 4.2, 4.3, 4.4, 4.8 and 5.1 of the SmPC in order to introduce an homologous booster dose (second dose) of COVID-19 vaccine Janssen based on interim efficacy, immunogenicity and safety results from different clinical studies including the two randomised, double blind, placebo-controlled Phase 3 studies COV3001 and COV3009. A contraindication in individuals with a history thrombosis with thrombocytopenia syndrome following vaccination with any COVID-19 vaccine is also included. In addition, an update to introduce an heterologous booster dose of COVID-19 vaccine Janssen following completion of a primary vaccination with an approved mRNA COVID-19	14/12/2021	16/12/2021	SmPC and PL	A booster dose (second dose) of 0.5 mL of COVID-19 Vaccine Janssen may be administered intramuscularly at least 2 months after the primary vaccination in individuals 18 years of age and older. A booster dose of the COVID-19 Vaccine Janssen (0.5 mL) may be administered as a heterologous booster dose following completion of primary vaccination with another approved COVID-19 vaccine. The dosing interval for the heterologous booster dose is the same as that authorised for a booster dose of the vaccine used for primary vaccination. Individuals who have experienced thrombosis with thrombocytopenia syndrome (TTS) following vaccination with any COVID-19 vaccine should not receive COVID-19

	vaccine is introduced based on immunogenicity and safety interim results from the phase 1/2 study DMID 21-0012. In addition, the MAH took the opportunity to update the efficacy data for the primary vaccination schedule based on final analysis from study COV3001. The Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				Vaccine Janssen The risk of very rare events (such as coagulation disorders including thrombosis with thrombocytopenia syndrome, CLS and GBS) after a booster dose of COVID-19 Vaccine Janssen has not yet been characterised. Efficacy of two-doses of COVID-19 Vaccine Janssen administered 2 months apart A final analysis (cut-off date 25 June 2021) of a multicentre, randomised, double-blind, placebo-controlled Phase 3 study (COV3009) was conducted to assess the efficacy, safety, and immunogenicity of 2 doses of COVID-19 Vaccine Janssen administered with a 56-day interval. In total, 14492 individuals were included in the per-protocol efficacy population (7484 individuals received COVID-19 Vaccine Janssen and 7008 individuals received placebo). Vaccine efficacy against symptomatic infections at least 14 days after second vaccination was 75.2% (95% CI: 54.6; 87.3). Immunogenicity of a booster dose (second dose) following primary vaccination with COVID-19 Vaccine Janssen In a Phase 2 Study (COV2001), individuals 18 through 55 years of age and 65 years and older received a booster dose of the COVID-19 Vaccine Janssen approximately 2 months after the primary vaccination. Immunogenicity data are available from 39 individuals, of whom 15 were 65 years of age and older. Neutralising antibody and binding antibody increases against the reference SARS-CoV-2 strain were also observed in studies COV1001, COV1002 and COV2001 in a limited number of study participants after a boost given at 2, 3 and 6 months, when compared to pre-boost values. Overall, the increases of GMTs pre-boost to

					1-month post-boost ranged from 1.5 to 4.4 fold for neutralising antibodies, and from 2.5 to 5.8 fold for binding antibodies. A 2-fold decrease in antibody levels was observed 4 months following 2-month booster dose, compared to 1 month following 2-month booster dose. Antibody levels were still higher than antibody levels following a single-dose at a similar timepoint. These data support the administration of a booster dose when administered at an interval of 2 months or longer after primary vaccination. Immunogenicity of a booster dose following primary vaccination with an approved mRNA COVID-19 vaccine An independent Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States evaluated a heterologous booster dose of the COVID-19 Vaccine Janssen. Due to the limited sample size, differences observed are only descriptive. In this study, adults who had completed primary vaccination with a Spikevax 2-dose series (N=151), a COVID-19 Vaccine Janssen single-dose (N=156), or a Comirnaty 2-dose series (N=151) at least 12 weeks prior to enrollment and who reported no history of SARS-CoV-2 infection were randomised 1:1:1 to receive a booster dose of one of three vaccines: Spikevax, COVID-19 Vaccine Janssen or Comirnaty. Neutralising antibody titres were assessed on Day 1 prior to administration of the booster dose and on Day 15 and Day 29 after the booster dose. A booster response to the COVID-19 Vaccine Janssen was demonstrated regardless of primary vaccination. The antibody level 14 days after a heterologous boost by COVID-19 Vaccine Janssen is lower than after a homologous boost by a licensed mRNA vaccine while after 1 month, neutralising antibody titers are roughly similar

					between both regimens. Data indicate the homologous regimen with COVID-19 Vaccine Janssen induces lower antibody responses compared to heterologous boosting with a licensed mRNA vaccine. The clinical relevance of this is unknown. Only short-term immunogenicity data are available, long-term protection and immunological memory are currently unknown. For more information, please refer to the Summary of Product Characteristics.
II/0026/G	This was an application for a group of variations. A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) B.II.b.z - Change in manufacture of the Finished Product - Other variation	16/12/2021	n/a		
IB/0036	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	13/12/2021	16/12/2021	Annex II	Update on the dates for a Specific Obligation listed in Annex II.
IB/0032	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	10/12/2021	n/a		
IA/0038	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	03/12/2021	n/a		
II/0018	Submission of an updated RMP version 2.5 in order	02/12/2021	n/a		

	to include the following: • To include thrombocytopenia (including immune thrombocytopenia) as an important identified risk following the outcome of the signal of Embolic and Thrombotic events (SDA 018.1, EPITT number 19689) and the opinion of procedure EMEA/H/C/005737/II/0006/G • To propose studies aimed at further characterization of Thrombosis with Thrombocytopenia syndrome (TTS) and thrombocytopenia, following the outcome of the signal of Embolic and Thrombotic events (SDA 018.1, EPITT number 19689) • To include Guillain-Barré syndrome as an important identified risk and update the RMP accordingly (EMEA/H/C/005737/II/0012) In addition, the MAH took the opportunity to update in the EU-RMP the submission milestone dates for VAC31518COV4001 and VAC31518COV4002 studies. 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				
IA/0034	A.7 - Administrative change - Deletion of manufacturing sites	29/11/2021	16/12/2021	Annex II	Annex II is updated to remove a site responsible for manufacture of the active substance

IB/0030	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	23/11/2021	n/a		
II/0017	B.II.b.z - Change in manufacture of the Finished Product - Other variation	21/10/2021	n/a		
IB/0028/G	This was an application for a group of variations. B.II.b.2.z - Change to importer, batch release arrangements and quality control testing of the FP - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	11/10/2021	n/a		
IB/0027	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	08/10/2021	11/10/2021	SmPC and PL	To include Venous Thromboembolism (VTE) as Adverse Drug Reaction.
IB/0025/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	01/10/2021	11/10/2021	Annex II	This variation resulted in an update of annex II to include an update of the specific obligation to confirm the consistency of the finished product manufacturing process, with the addition of interim reports
II/0020	Update of sections 4.4 and 4.8 of the SmPC to add a new warning on immune thrombocytopenia (ITP), and to add dizziness and ITP to the list of adverse drug reactions with frequencies uncommon and not	30/09/2021	01/10/2021	SmPC and PL	As an outcome of the post-authorisation measure MEA 14.3 (4th Monthly Summary Safety Report covering June 2021), the MAH was requested to update of sections 4.4 and 4.8 of the SmPC to add a new warning on immune

	known, respectively; based on the PRAC request from the post-authorisation measure MEA/014.3 (4th Monthly Summary Safety Report covering the month of June 2021). The package leaflet is updated accordingly. A DHPC and communication plan was adopted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				thrombocytopenia (ITP), and to add dizziness and ITP to the list of adverse drug reactions with frequencies uncommon and not known, respectively. Based on a cumulative review of post-marketing data on anxiety related reactions, including dizziness, it was concluded there was a reasonable possibility to consider dizziness as causally related to the COVID-19 vaccine Janssen, and therefore, it was added to section 4.8 of the SmPC. The frequency of this event was calculated as 'uncommon' based on clinical data from study VAC31518COV3001. ITP was added to section 4.8 following a review of the available post-marketing and clinical trial data. In addition, taking case reviews into account, and particularly due to the severity of some cases reported, as well as limited post-marketing and literature data showing significant decrease in platelet values in patients with a prior medical history of ITP following vaccination with the Janssen COVID-19 vaccine, a warning in section 4.4 of the SmPC is added. A Direct Healthcare Professional Communication (DHPC) is considered necessary in order to communicate on the new recommendations in relation to ITP; namely that Healthcare professionals (HCPs) 1. should assess an individual's relevant medical history prior to administering COVID-19 Vaccine Janssen and discuss the risks and benefits of developing low platelet levels before administering the vaccine, 2.should be alert to signs and symptoms of ITP, such as spontaneous bleeding, bruising or petechiae and 3. are recommended to monitor platelet levels in individuals with a history of ITP following vaccination with COVID-19 Vaccine Janssen.

					For more information, please refer to the Summary of Product Characteristics.
IB/0024/G	This was an application for a group of variations. B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	21/09/2021	29/09/2021	SmPC, Labelling and PL	To extend the shelf life of the Covid-19 vaccine Janssen drug product in accordance with the approved stability protocol from the current shelf-life of 3 months to 4.5 months when stored at 2 to 8°C. To clarify in Annex 1 - Summary of Product Characteristics, 6.3 Shelf life and 6.4 Special precautions for storage and the corresponding section in the Package leaflet that transportation is also part of the chemical and physical in-use stability of the opened vial (after first puncture).
IB/0022/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 biological/immunological medicinal product B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	07/09/2021	n/a		
IB/0021/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 biological/immunological medicinal product B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a	06/09/2021	n/a		

	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 B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a 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				
II/0014	Update of section 4.8 of the SmPC in order to include diarrhoea and paraesthesia as adverse drug reactions (ADRs) with frequency uncommon; and hypoesthesia, lymphadenopathy, vomiting and tinnitus as ADRs with frequency rare, as requested by PRAC from post-authorisation measures MEA 014.2 and MEA 014.3 (3rd and 4th Monthly Summary Safety Report covering May 2021 and June 2021, respectively). In addition, the MAH took the opportunity to add editorial changes on sections 6.4 and 6.6 of the SmPC in line with the WHO recommendations. Also, the labelling has been updated to improve readability. The labelling and package leaflet are updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	02/09/2021	03/09/2021	SmPC, Labelling and PL	Update of section 4.8 of the SmPC in order to include diarrhoea and paraesthesia as adverse drug reactions (ADRs) with frequency uncommon; and hypoesthesia, lymphadenopathy, vomiting and tinnitus as ADRs with frequency rare as requested by PRAC from post authorisation measures MEA 014.2 and MEA 014.3 (3rd and 4th Monthly Summary Safety Report covering May 2021 and June 2021, respectively). The frequencies of these ADRs derive from the clinical trial reporting of study VAC31518COV3001.

IB/0019	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	02/09/2021	n/a		
IB/0016	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	26/08/2021	n/a		
IA/0015	A.7 - Administrative change - Deletion of manufacturing sites	30/07/2021	03/09/2021	Annex II	
II/0012	Update of sections 4.4 and 4.8 of the SmPC in order to add a warning related to the possibility of developing a Guillain-Barré syndrome (GBS) following the administration of Ad26.COV2.S and to add GBS as an adverse drug reaction (ADR). This is based on the information accumulated on cases of GBS reported to the vaccine adverse event reporting system (VAERS) in recipients of the Janssen COVID-19 Vaccine and subsequently, on the analysis performed by the company on cases of GBS based on the available cumulative data from launch. In addition, the company took the oportunity to make some editorial changes. The Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/07/2021	23/07/2021	SmPC and PL	SmPC new text A warning is added in 4.4 of the SmPC regarding the possibility of presenting a Guillain -Barré Syndrome (GBS) after the administration of Janssen COVID-19 Vaccine. This adverse event is also added in 4.8 of the SmPC with a frequency of very rare. Healthcare professionals should be alert of GBS signs and symptoms to ensure correct diagnosis, in order to initiate adequate supportive care and treatment and to rule out other causes.

IB/0013	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	21/07/2021	23/07/2021	Annex II	To extend the due date of the specific obligation and update Annex II of the product information accordingly.
II/0010	Update of section 4.3, 4.4 and 4.8 of the SmPC in order to add a contraindication related to the administration of Ad26.COV2.S to individuals with a history of Capillary Leak Syndrome (CLS) based on the cases reported following administration of this vaccine in the Global Medical Safety (GMS) up to the data lock point (DLP) of 21 June 2021. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to add some minor editorial changes throughout the product information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	07/07/2021	09/07/2021	SmPC and PL	SmPC new text The administration of this vaccine (Ad26.COV2.S) is contraindicated in individuals with a history of Capillary Leak Syndrome (CLS). A joint DHPC is issued to alert health care professionals to the signs and symptoms of thromboembolism and/or thrombocytopenia in follow up to the adopted signal procedure at PRAC for TTS (Thrombosis with Thrombopenia Syndrome).This letter also communicate the new contraindication of this vaccine in individuals who have previously experienced episodes of Capillary Leak Syndrome (CLS). For more information, please refer to the Summary of Product Characteristics.
II/0006/G	This was an application for a group of variations. To update the EU-RMP for COVID-19 Vaccine Janssen to include thrombosis with thrombocytopenia syndrome (TTS) in the list of the safety concerns as an important identified risk following the PRAC recommendation, dated 6 May 2021 in the outcome of the related signal of Embolic and Thrombotic events (procedure number SDA 018.1) with COVID-19 Vaccine Janssen (Ad26.COV2-S [recombinant]) . In addition, the MAH sought agreement on a DHPC to alert health care professionals to the signs and symptoms of thromboembolism and/or	07/07/2021	n/a		Thrombosis with thrombocytopenia syndrome (TTS) is included in the list of the safety concerns as an important identified risk in the outcome of the related signal of Embolic and Thrombotic events (procedure number SDA 018.1) with COVID-19 Vaccine Janssen (Ad26.COV2-S [recombinant]). In addition, Thrombocytopenia is also agreed to be included as an important potential risk in the summary of safety concerns in the RMP. The RMP will be updated within the next expected variation to update the RMP. Finally, a joint DHPC is issued to alert health care professionals to the signs and symptoms of thromboembolism and/or thrombocytopenia in follow up to

	thrombocytopenia in follow up to the adopted signal procedure at PRAC for TTS (Thrombosis with Thrombopenia Syndrome). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data 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				the adopted signal procedure at PRAC for TTS (Thrombosis with Thrombopenia Syndrome). This letter also communicates the new contraindication of this vaccine in individuals who have previously experienced episodes of Capillary Leak Syndrome (CLS). SmPC new text No changes are introduced in the SmPC or in the Product Leaflet.
IB/0011	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	30/06/2021	09/07/2021	Annex II	This variation resulted in an update of annex II to add a specific obligation to confirm the consistency of the active substance manufacturing process by submitting additional comparability and validation data.
IA/0009	A.7 - Administrative change - Deletion of manufacturing sites	25/06/2021	n/a		
II/0005	B.II.b.z - Change in manufacture of the Finished Product - Other variation	24/06/2021	n/a		
IB/0008	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	21/06/2021	09/07/2021	Annex II	This variation resulted in an update of annex II to amend the specific obligation to confirm the consistency of the finished product manufacturing process, with the addition of interim reports.
IB/0007	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	01/06/2021	n/a		

IA/0004	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	07/05/2021	07/05/2021	SmPC and PL	This variation is to update section 4.4 of the SmPC and sections 2, 4 and 6 of the package leaflet (PL) to implement the updated signal recommendations on embolic and thrombotic events (EPITT no 19689), following receipt of an updated PRAC signal assessment report on additional data and adoption at PRAC plenary on 05th of April 2021. Leg pain, seizures and mental status changes have been added as symptoms for thrombosis with thrombocytopenia syndrome, as well as the need to actively investigate for sign of thrombosis individuals diagnosed with thrombocytopenia within 3 weeks after vaccination with COVID-19 Vaccine Janssen. Similarly, individuals who present with thrombosis within 3 weeks of vaccination should be evaluated for thrombocytopenia.
IA/0003	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	21/04/2021	22/04/2021	SmPC and PL	This variation is to update sections 4.4 and 4.8 of the SmPC and sections 2, 4 and 6 of the package leaflet (PL) to implement the signal recommendations on embolic and thrombotic events (EPITT no 19689), following receipt of an updated PRAC signal assessment report on additional data and adoption at PRAC plenary on 20th of April 2021. A new warning on thrombocytopenia and coagulation disorder is added and the adverse reaction: thrombosis in combination with thrombocytopenia is introduced with a frequency: very rare (<1/10 000).
IB/0002/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 biological/immunological medicinal product B.II.f.z - Stability of FP - Other variation	15/04/2021	22/04/2021	SmPC, Annex II, Labelling and PL	This variation resulted in an update of sections 6.1, 6.4, 6.5 and 8 of the SmPC, annex II, labelling and Package Leaflet to include: - the addition of a new pack size of 20 vials with a slightly different composition (removal of Trisodium citrate dihydrate)

	B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier B.II.a.3.b.6 - Changes in the composition (excipients) of the finished product - Other excipients - Replacement of a single excipient with a comparable excipient with the same functional characteristics and at a similar level B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product				- a change from 12 to 13 hours to the thawing time - an update of the specific obligation to confirm the consistency of the finished product manufacturing process, with the addition of interim reports
IB/0001/G	This was an application for a group of variations. A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	06/04/2021	22/04/2021	Annex II	This variation resulted in an update of annex II to amend the specific obligation to confirm the consistency of the finished product manufacturing process, with the addition of interim reports.