IMVANEX

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
S/0107	11th annual re-assessment	14/11/2024	13/01/2025	Annex II	The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of IMVANEX should be maintained. Annex II of the PI is ammended to remove the following

[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).

					SOB, since the final study report has been submitted To ensure adequate monitoring of safety and effectiveness, the MAH shall perform the following study to collect data where IMVANEX is used as a prophylactic vaccine and/or use in case of (re) emergence of circulating monkeypox. Non-interventional post-authorisation efficacy study (PAES): An observational, non-interventional post-authorisation safety and efficacy study for the prophylactic vaccination with IMVANEX following (re)-emergence of circulating monkeypox infections. The study should start as soon as possible after the start of the outbreak The following obligation is added to the Annex II in alignment with other products authorised via exceptional circumstances. In order to ensure adequate monitoring of safety and efficacy of IMVANEX in the active immunisation against smallpox and disease caused by vaccinia virus, the MAH shall provide yearly updates on any new information concerning the safety and efficacy of IMVANEX. The benefit risk profile of Imvanex remains positive.
II/0106	B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	14/11/2024	n/a		
IB/0109/G	This was an application for a group of variations.	01/10/2024	n/a		

	A.7 - Administrative change - Deletion of manufacturing sites 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				
II/0108	Extension of indication to include active immunisation of adolescents from 12 to 17 years of age for IMVANEX based on interim results from study DMID 22-0020. This is a Phase 2 randomised open label multicentre trial to inform Public Health strategies involving the use of MVA-BN vaccine for mpox. As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC and Annex II.E are updated. The Package Leaflet is updated in accordance. Furthermore, the PI is brought in line with the latest QRD template version 10.4. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	19/09/2024	19/09/2024	SmPC, Annex II and PL	Please refer to Scientific Discussion Imvanex-EMEA/H/C/002596/II/0108
PSUSA/10119 /202401	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	05/09/2024	n/a		PRAC Recommendation - maintenance
II/0104/G	This was an application for a group of variations. B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for	25/07/2024	19/09/2024	SmPC, Labelling and PL	

	biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site 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.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier B.II.b.z - Change in manufacture of the Finished Product - Other variation B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes				
II/0100	Update of section 5.1 of the SmPC in order to add vaccine effectiveness data based on the IMVANEX vaccine effectiveness data in real-world use during the 2022 mpox outbreak. The RMP version 10.2 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.4. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/07/2024	19/09/2024	SmPC, Annex II and PL	SmPC section 5.1 Vaccine effectiveness In real-world observational studies conducted in vaccine-eligible individuals (according to local recommendations), vaccine effectiveness against mpox disease was demonstrated at least 14 days after vaccination, with adjusted vaccine effectiveness estimates ranging from 35% (95% CI, -2-59) to 89% (95% CI, 76-95) after one IMVANEX dose and from 66% (95% CI, 47-78) to 90% (95% CI, 86-92) after two IMVANEX doses. Impact on hospitalisation In a surveillance study conducted from May 2022 to May

					2023 in the US, IMVANEX was shown to reduce the risks of mpox-related hospitalisation. Compared with unvaccinated mpox patients, the odds of hospitalisation were 0.27 (95% CI, 0.08-0.65) after one IMVANEX dose, and 0.20 (95% CI, 0.01 0.90) after two IMVANEX doses. The estimated relative risk reduction was 73% after one IMVANEX dose and 80% after two IMVANEX doses. For more information, please refer to the Summary of Product Characteristics.
IB/0105/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	09/07/2024	n/a		
PSUSA/10119 /202307	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	21/03/2024	16/05/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10119/202307.
IB/0102/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.a.4.c - Change to in-process tests or limits	29/04/2024	n/a		

	applied during the manufacture of the AS - Deletion of a non-significant in-process test				
IA/0101/G	This was an application for a group of variations. B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient	26/02/2024	n/a		
S/0095	10th annual re-assessment.	22/02/2024	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of IMVANEX should be maintained.
IB/0099	B.I.b.z - Change in control of the AS - Other variation	26/01/2024	n/a		
IB/0097	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	09/11/2023	n/a		
IA/0098	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	30/10/2023	n/a		

IB/0094	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	21/09/2023	n/a		
IB/0093/G	This was an application for a group of variations. B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	05/09/2023	n/a		
PSUSA/10119 /202301	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	31/08/2023	n/a		PRAC Recommendation - maintenance
IB/0092/G	This was an application for a group of variations. B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	01/08/2023	n/a		
IA/0090	A.7 - Administrative change - Deletion of manufacturing sites	19/04/2023	n/a		
II/0084/G	This was an application for a group of variations. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial	16/03/2023	n/a		

	change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS A.7 - Administrative change - Deletion of manufacturing sites				
II/0081	Submission of an updated RMP version 9.3 in order to update the safety specifications in line with extension of the indication to "active immunisation against smallpox, monkeypox and disease caused by vaccinia virus in adults", update the missing information from the list of safety concerns, differentiate routine pharmacovigilance activities and additional pharmacovigilance activities, addition of non-BN sponsored clinical study SEMVAc to additional pharmacovigilance activities and deletion of paediatric study POX-MVA-035 upon request by PRAC following the assessment of procedure II/76. 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	16/03/2023	n/a		
PSUSA/10119 /202207	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	16/03/2023	n/a		PRAC Recommendation - maintenance

IAIN/0089/G	This was an application for a group of variations. B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes	15/03/2023	22/09/2023	SmPC, Labelling and PL	
IB/0088/G	This was an application for a group of variations. B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation A.7 - Administrative change - Deletion of manufacturing sites	20/02/2023	n/a		
IB/0087	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	14/02/2023	n/a		
IB/0083	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	03/02/2023	n/a		
II/0079	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	26/01/2023	n/a		

N/0086	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/12/2022	22/09/2023	Labelling	
IB/0085	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	21/12/2022	n/a		
IB/0082	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	29/11/2022	n/a		
S/0077	Annual re-assessment.	10/11/2022	n/a		
IB/0078/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.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	21/10/2022	22/09/2023	SmPC and PL	Shelf-life update
PSUSA/10119 /202201	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	01/09/2022	n/a		PRAC Recommendation - maintenance

II/0076	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	21/07/2022	22/07/2022	SmPC, Labelling and PL	
II/0075/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.e.1.z - Change in immediate packaging of the finished product - Other variation B.II.c.z - Change in control of excipients in the Finished Product - Other variation B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	21/07/2022	n/a		
IB/0073/G	This was an application for a group of variations. B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New	13/04/2022	n/a		

	storage site of MCB and/or WCB				
PSUSA/10119 /202107	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	10/03/2022	n/a		PRAC Recommendation - maintenance
IB/0072	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	22/12/2021	n/a		
S/0069	Annual re-assessment.	11/11/2021	n/a		
IAIN/0070	C.I.3.a - 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 - Implementation of wording agreed by the competent authority	01/10/2021	22/07/2022	Annex II	
PSUSA/10119 /202101	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	02/09/2021	n/a		PRAC Recommendation - maintenance
IB/0067	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	26/08/2021	n/a		
IB/0068	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	25/08/2021	n/a		

II/0064	B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product	01/07/2021	n/a		
IB/0063	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	10/05/2021	n/a		
IB/0065	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	04/05/2021	n/a		
PSUSA/10119 /202007	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	11/03/2021	n/a		PRAC Recommendation - maintenance
IB/0061	B.II.f.z - Stability of FP - Other variation	18/12/2020	n/a		
IA/0062	B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	17/12/2020	n/a		
IA/0060/G	This was an application for a group of variations. B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test	11/12/2020	n/a		

	procedure is already authorised B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method 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.b.1.b - Change in the specification parameters and/or limits of an AS, starting				

	material/intermediate/reagent - Tightening of specification limits 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.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits 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.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits				
IB/0058/G	This was an application for a group of variations. 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.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor	09/12/2020	n/a		

	changes to an approved test procedure				
II/0055	B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product	26/11/2020	n/a		
II/0050	B.I.a.1.d - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New manufacturer of material for which an assessment is required of viral safety and/or TSE risk	19/11/2020	n/a		
IAIN/0059/G	This was an application for a group of variations. B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation 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	18/11/2020	16/04/2021	SmPC and PL	
S/0054	Annual re-assessment.	12/11/2020	n/a		
II/0049	B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol	01/10/2020	16/04/2021	SmPC and PL	As a result of this variation, sections 2 and 4.3 of the SmPC are being updated to reflect the newly added trace residue of ciprofloxacin. In addition, the list of residues traces in the SmPC section 2 has been updated with the following compounds chicken protein, benzonase, and gentamicin, which were already mentioned in section 4.3. The company takes the opportunity to correct section 2 to align the contents with section 4.3. The Package Leaflet (PL) is

					updated accordingly in section 2 and 6. In addition, update of section 4.4, including the traceability statement, and Annex II according to the current QRD template together with the inclusion of the statement for sodium as an excipient, according to the excipient guideline, were implemented.
IB/0052	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	17/09/2020	n/a		
IB/0051	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	14/09/2020	n/a		
IB/0056/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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	03/09/2020	n/a		
II/0047/G	This was an application for a group of variations. B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS -	03/09/2020	n/a		

	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.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product 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				
PSUSA/10119 /202001	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	03/09/2020	n/a		PRAC Recommendation - maintenance
IB/0053/G	This was an application for a group of variations. B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS	01/09/2020	n/a		
IB/0048	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	08/06/2020	16/04/2021	SmPC and PL	
IB/0043	B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition	23/04/2020	n/a		

IAIN/0046	A.1 - Administrative change - Change in the name and/or address of the MAH	10/04/2020	16/04/2021	SmPC, Labelling and PL	
IAIN/0044/G	This was an application for a group of variations. B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits 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.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.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.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor	10/04/2020	n/a		

	changes to an approved test procedure				
PSUSA/10119 /201907	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	13/02/2020	n/a		PRAC Recommendation - maintenance
S/0041	6th annual re-assessment	14/11/2019	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of IMVANEX should be maintained.
PSUSA/10119 /201901	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	05/09/2019	n/a		PRAC Recommendation - maintenance
II/0036	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	11/04/2019	09/03/2020	SmPC and PL	Imvanex was compared to ACAM2000 (a 'second generation' live attenuated smallpox vaccine produced in cell culture and licenced in the United States of America) in a randomized, open-label non-inferiority clinical trial in healthy adults (US military personnel) aged 18 to 42 years and who were naïve to smallpox vaccine (Study POX-MVA-006). A total of 433 subjects were randomized in a 1 : 1 ratio to receive either two doses of Imvanex followed by a single dose of ACAM2000 at four weeks intervals or to receive a single dose of ACAM2000. ACAM2000 was administered via scarification. The first co-primary endpoint compared vaccinia-specific neutralizing antibody responses at the peak visits (Day 42 after first vaccination for Imvanex where the subjects received two doses according to the standard vaccination

					schedule and Day 28 for ACAM2000). Imvanex induced a peak neutralizing antibody geometric mean titer (GMT) of 153.5 (n = 185; 95% CI 134.3, 175.6), which was non-inferior to the GMT of 79.3 (n = 186; 95% CI 67.1, 93.8) obtained after scarification with ACAM2000. The second co-primary endpoint evaluated if vaccination with Imvanex (n = 165) prior to administration of ACAM2000 results in an attenuation of the cutaneous reaction to ACAM2000 (n = 161) as measured by maximum lesion area in mm2. At day 13-15, the median maximum lesion area for subjects who were administered ACAM2000 was 75mm2 (95% CI 69.0, 85.0) and for those who received Imvanex it was 0.0 (95% CI 0.0, 2.0).
II/0035	Update of sections 4.4 and 4.8 of the SmPC in order to reflect the final results of study POX-MVA-037 (phase II, randomised, open-label, multicentre trial designed to evaluate the safety and immunogenicity of IMVANEX (MVA-BN smallpox vaccine) when increasing the dose or the number of injections compared with the standard 2-dose regimen in a population of adult, vaccinia naive, immunocompromised subjects with human immunodeficiency virus (HIV) infection), listed as a category 3 study in the RMP (described as post authorisation MEA 007); The RMP version 7.1 has also been submitted. Moreover, the PI is brought in line with the latest QRD template version 10. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/03/2019	09/03/2020	SmPC and PL	Data have been generated in HIV infected individuals with CD4 counts ≥100 cells/µl and ≤750 cells/µl. Lower immune response data have been observed in HIV infected individuals compared to healthy individuals.

IB/0039/G	This was an application for a group of variations. B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation 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	13/03/2019	09/03/2020	SmPC, Labelling and PL	
PSUSA/10119 /201807	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	14/02/2019	n/a		PRAC Recommendation - maintenance
S/0037	5th annual re-assessment	15/11/2018	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Imvanex should be maintained.
PSUSA/10119 /201801	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	06/09/2018	n/a		PRAC Recommendation - maintenance
R/0032	Renewal of the marketing authorisation.	22/02/2018	23/04/2018		Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of IMVANEX in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10119 /201707	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	08/02/2018	n/a		PRAC Recommendation - maintenance

IB/0033	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	30/01/2018	23/04/2018	SmPC	
S/0029	Annual re-assessment.	09/11/2017	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of IMVANEX should be maintained
IB/0030	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	06/11/2017	n/a		
II/0027	B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS	14/09/2017	15/11/2017	SmPC, Labelling and PL	SmPC Section 2 and 4.8 has been updated as follows: One dose (0.5 ml) contains: Modified Vaccinia Ankara – Bavarian Nordic Live virus1 no less than 5 x 107 Inf.U * *infectious units
PSUSA/10119 /201701	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	01/09/2017	n/a		PRAC Recommendation - maintenance
IB/0026	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	11/04/2017	15/11/2017	Annex II	
PSUSA/10119	Periodic Safety Update EU Single assessment -	09/02/2017	n/a		PRAC Recommendation - maintenance

/201607	Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)				
S/0022	Annual re-assessment.	10/11/2016	06/02/2017	Annex II	The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that Marketing Authorisation of IMVANEX should be maintained. The SOB1 in Annex II of the Product Information is deleted, as the MAH has provided adequate information to reassure that assays used to measure antibody titres over time are adequately validated.
IB/0025/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.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	11/01/2017	n/a		
IB/0024	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	23/11/2016	15/11/2017	SmPC	
PSUSA/10119 /201601	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	02/09/2016	n/a		PRAC Recommendation - maintenance

II/0018	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/05/2016	12/08/2016	SmPC and PL	
II/0020	Update of sections 4.8 and 5.1 of the SmPC based on data from Study MVA-POX-013, a randomised, double-blind, placebo-controlled phase III trial to evaluate immunogenicity and safety of three consecutive production lots of Imvanex (MVA-BN) smallpox vaccine in healthy vaccinia-naive subjects. The Package Leaflet has been updated accordingly. The provision of the study report addresses the post-authorisation measure (PAM) ANX 003, which has been deleted accordingly in Annex II. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	21/04/2016	12/08/2016	SmPC, Annex II and PL	In the clinical study MVA-POX-013, three consecutive production lots of IMVANEX (MVA-BN) are compared. The data suggest comparable performance between lots. The combined groups 1-3 included 2119 healthy subjects and the PRNT and ELISA seroconversion rates for the pooled vaccine lots were 99.8% (95% CI: 99.5; 99.9) and 99.7% (95% CI: 99.4; 99.9), respectively. Further, the MAH has submitted an analysis of the safety data from the 3,000 subjects who were exposed across the three vaccine lots which were tested. The rates of adverse events were generally consistent across the lots. No new safety concerns are raised based on the information provided.
PSUSA/10119 /201507	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	11/02/2016	n/a		PRAC Recommendation - maintenance
S/0017	Annual re-assessment.	28/01/2016	n/a		
PSUSA/10119 /201501	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	10/09/2015	n/a		PRAC Recommendation - maintenance
IB/0016	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the	03/08/2015	18/09/2015	SmPC, Annex	

	diluted/reconstituted product			II and PL	
IB/0015	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	22/06/2015	n/a		
II/0013/G	This was an application for a group of variations. Submission of non-clinical final study reports for studies BN-PRE-2013-12 (Study for effects on embryo-fetal development by subcutaneous route in rats), BN-PRE-11-021 (Determination of the optimal dose of monkeypox for the aerosol challenge model in cynomolgus macaques and evaluation of efficacy and immunogenicity of IMVAMUNE), BN-PRE-011-022 (Correlation of neutralising antibody titers with survival of cynomolgus monkeys in the aerosol monkeypox virus challenge model), BN-PRE-11-020 (Non-inferiority of the immunogenicity of freeze-dried IMVAMUNE compared to liquid-frozen IMVAMUNE in a BALB/c mouse model), BN-PRE-11-024 (Non-inferiority of efficacy and immunogenicity of freeze-dried IMVAMUNE compared to liquid-frozen IMVAMUNE in the mouse vaccinia challenge model), BN-PRE-11-027 (Non-inferiority of efficacy and immunogenicity of freeze-dried IMVAMUNE compared to liquid-frozen IMVAMUNE in a mouse ectromelia challenge model). C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	26/03/2015	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 C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
PSUSA/10119 /201407	Periodic Safety Update EU Single assessment - Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara)	12/02/2015	n/a		PRAC Recommendation - maintenance
IB/0012	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	15/12/2014	18/09/2015	SmPC, Labelling and PL	
S/0010	1st Annual Re-assessment.	20/11/2014	n/a		The CHMP, having reviewed the evidence on compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of Imvanex, concluded that Marketing Authorisation of Imvanex should be maintained.
II/0008/G	This was an application for a group of variations.	25/09/2014	18/09/2015	SmPC, Labelling and	to introduce an alternative storage temperature of the finished product at -80°C. The shelf-life of the finished

	to introduce an alternative storage temperature of the finished product at -80°C. The shelf-life of the finished product stored at -80°C is 5 years. 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.c - Stability of FP - Change in storage conditions for biological medicinal products, when the stability studies have not been performed in accordance with an approved stability protocol			PL	product stored at -80°C is 5 years.
IB/0009	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	03/09/2014	n/a		
PSUV/0007	Periodic Safety Update	26/06/2014	22/08/2014	SmPC and PL	Please refer to IMVANEX PSUV-07 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation.
II/0004/G	This was an application for a group of variations. Update of Section 4.8 of the SmPC to reflect pooled safety data from completed clinical trials. The PL 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	26/06/2014	22/08/2014	SmPC and PL	Based on the results of a completed Clinical Study POX MVA 030 and a pooling of ADRs from all Imvanex studies, the MAH proposed changes to the Product Information (PI). Information was updated to amend the number of studies making up the source of the pooled Safety information and the number of patients constituting the dataset in the SmPC. The frequency of a number of adverse events was re-assigned based on the new figures. 'Chest pain' was added to the list of Side Effects observed with Imvanex.

IB/0006	B.I.a.3.e - Change in batch size (including batch size ranges) of AS or intermediate - The scale for a biological/immunological AS is increased/decreased without process change (e.g. duplication of line)	04/03/2014	n/a		
IB/0005/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.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.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.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.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement	23/01/2014	n/a		

	or addition) for the AS or a starting material/intermediate 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.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/0003	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	20/12/2013	n/a		
IAIN/0002	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	09/12/2013	n/a		
IAIN/0001	C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV and/or QPPV contact details and/or back-up procedure	06/09/2013	n/a		