Zolgensma

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
PSUSA/10848 /202305	Periodic Safety Update EU Single assessment - onasemnogene abeparvovec	25/01/2024	25/03/2024	SmPC, Annex II and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10848/202305.
IB/0049/G	This was an application for a group of variations.	12/03/2024	n/a		

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

	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.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.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.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 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 A.7 - Administrative change - Deletion of manufacturing sites				
IB/0048	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	29/01/2024	n/a		
IB/0047	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	04/01/2024	n/a		

IB/0046	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	06/12/2023	25/03/2024	SmPC	
IB/0045/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 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.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	19/10/2023	n/a		
II/0040	Update of section 4.4 of the SmPC in order to add a new warning and precaution capturing the theoretical risk of tumorigenicity as a result of vector integration and to include a new statement indicating random instances of vector integration are possible; based on final results from studies 2220205 and 2220117, and literature. The Package Leaflet is updated accordingly. The RMP version 3 has also been submitted.	14/09/2023	25/03/2024	SmPC and PL	Update of section 4.4 of the SmPC to add a new warning and precaution capturing the theoretical risk of tumorigenicity as a result of vector integration.

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IAIN/0044/G	This was an application for a group of variations. B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing 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 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 B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site 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	29/08/2023	25/03/2024	Annex II and PL	
IB/0042/G	This was an application for a group of variations.	25/08/2023	n/a		

	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 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 storage site of MCB and/or WCB B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.1.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.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS				
IB/0039/G	This was an application for a group of variations. B.II.f.1.e - Stability of FP - Change to an approved stability protocol B.II.f.1.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.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	25/05/2023	25/03/2024	SmPC	

	data B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol B.II.c.2.b - Change in test procedure for an excipient - Deletion of a test procedure if an alternative test procedure is already authorised 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 procedure is already authorised				
IA/0041/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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 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 procedure is already authorised A.7 - Administrative change - Deletion of manufacturing sites B.II.d.2.b - Change in test procedure for the finished product - Deletion of a test procedure if an	23/05/2023	n/a		

	alternative method is already authorised				
II/0036/G	This was an application for a group of variations. B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method	30/03/2023	n/a		
IB/0038	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	15/03/2023	n/a		
IB/0037/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	15/03/2023	n/a		

	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation				
II/0033/G	This was an application for a group of variations. Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to introduce additional guidance on liver function laboratory tests and monitoring before and after infusion and update information based on new safety information on the topic of acute liver failure (ALF) following two reports of fatal ALF. Update of sections 4.2 and 4.4 of the SmPC in order to provide additional guidance relevant to patient's overall health status prior to dosing and to strengthen the existing description and guidance on systemic immune response. Update of the section 4.4 of the SmPC in order to indicate prompt attention to thrombotic microangiopathy (TMA) and to reflect the risk of life-threatening or fatal outcomes. The RMP version 2.2 has also been approved. 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	26/01/2023	03/03/2023	SmPC, Annex II and PL	For more information, please refer to the Summary of Product Characteristics

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/10848 /202205	Periodic Safety Update EU Single assessment - onasemnogene abeparvovec	12/01/2023	n/a		PRAC Recommendation - maintenance
IAIN/0035	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	14/11/2022	03/03/2023	Annex II and PL	
II/0034/G	This was an application for a group of variations. B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method B.II.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	10/11/2022	n/a		
II/0031	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	10/11/2022	n/a		

T/0029	Transfer of Marketing Authorisation	11/07/2022	02/09/2022	SmPC, Labelling and PL	
PSUSA/10848 /202111	Periodic Safety Update EU Single assessment - onasemnogene abeparvovec	23/06/2022	25/08/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10848/202111.
IB/0030/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.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation 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	22/07/2022	n/a		
II/0028/G	This was an application for a group of variations. B.II.d.1.f - Change in the specification parameters and/or limits of the finished product - Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product A.7 - Administrative change - Deletion of manufacturing sites	21/07/2022	n/a		

IB/0027	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	20/05/2022	n/a		
II/0024	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	19/05/2022	25/08/2022	Annex II	
II/0020/G	This was an application for a group of variations. B.II.g.2 - Introduction of a post approval change management protocol related to the finished product B.II.b.1.d - Replacement or addition of a manufacturing site for the FP - Site which requires an initial or product specific inspection 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	19/05/2022	25/08/2022	Annex II	
R/0021	Renewal of the marketing authorisation.	24/03/2022	17/05/2022	SmPC, Annex II and PL	The CAT/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 CAT/CHMP considered that, as all specific obligations have been

					fulfilled, there are no remaining grounds for the MA to remain conditional and therefore recommends the granting of the MA no longer subject to specific obligations for Zolgensma.
IB/0022	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	01/03/2022	n/a		
IB/0025/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.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.II.h.z - Adventitious Agents Safety - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	14/02/2022	n/a		
IB/0023	B.II.d.2.z - Change in test procedure for the finished product - Other variation	07/02/2022	n/a		
II/0019/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	27/01/2022	n/a		

	finished product, including quality control sites (excluding manufacturer for batch release) B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.d.2.z - Change in test procedure for the finished product - Other variation B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality 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				

PSUSA/10848 /202105	Periodic Safety Update EU Single assessment - onasemnogene abeparvovec	13/01/2022	n/a		PRAC Recommendation - maintenance
II/0017/G	This was an application for a group of variations. 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.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)	14/10/2021	n/a		
II/0015	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/10/2021	20/04/2022	SmPC	
IA/0016/G	This was an application for a group of variations. 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 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	12/07/2021	20/04/2022	Annex II	

	intermediate used in the manufacture of the AS or manufacturer of a novel excipient 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				
PSUSA/10848 /202011	Periodic Safety Update EU Single assessment - onasemnogene abeparvovec	10/06/2021	n/a		PRAC Recommendation - maintenance
IB/0014	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	03/06/2021	n/a		
R/0012	Renewal of the marketing authorisation.	25/03/2021	18/05/2021	SmPC, Annex II and PL	
II/0008	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/02/2021	31/03/2021	SmPC and PL	The Product information has been updated following 5 cases of thrombotic microangiopathy (TMA) reported within approximately a week (up to 11 days) after Zolgensma administration. TMA is an acute and life-threatening condition characterised by thrombocytopenia, haemolytic anaemia and acute kidney injury that can resolve with timely and proper intervention. In addition to a warning in section 4.4 and addition of TMA in section 4.8, section 4.2 of the SmPC has been updated to include baseline measurements of creatinine and blood count to provide individual baseline values in case of suspected TMA. If patients show clinical signs, symptoms or laboratory findings consistent with TMA, it is recommended that a specialist is consulted immediately to manage TMA

					as clinically indicated. Caregivers should be informed about signs and symptoms of TMA and should be advised to seek urgent medical care if such symptoms occur.
PSUSA/10848 /202005	Periodic Safety Update EU Single assessment - onasemnogene abeparvovec	28/01/2021	26/03/2021	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10848/202005.
II/0009/G	This was an application for a group of variations. 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 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	28/01/2021	n/a		
II/0007/G	This was an application for a group of variations. B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer B.I.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	28/01/2021	n/a		

IA/0011/G	This was an application for a group of variations. 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 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 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.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.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 B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	13/11/2020	n/a		

	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure				
II/0006	B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol	12/11/2020	n/a		
IAIN/0010	A.1 - Administrative change - Change in the name and/or address of the MAH	15/10/2020	26/03/2021	SmPC, Labelling and PL	
II/0003/G	This was an application for a group of variations. 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 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.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	15/10/2020	n/a		

IB/0002	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	12/08/2020	n/a		
IB/0004	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	05/08/2020	26/03/2021	SmPC, Labelling and PL	
IB/0001/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 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	02/07/2020	n/a		