Spinraza

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/10595 /202405	Periodic Safety Update EU Single assessment - nusinersen	16/01/2025	n/a		PRAC Recommendation - maintenance
II/0034/G	This was an application for a group of variations. Update of sections 5.1 and 5.2 of the SmPC based on	16/01/2025		SmPC and Annex II	For more information, please refer to the Summary of Product Characteristics.

[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).

	final results from study CS11 (SHINE). Update of section 5.1 of the SmPC based on interim results from study CS5 (NURTURE, 232SM201). Update of section 5.1 of the SmPC in order to relocate the updated information regarding immunogenicity from SmPC section 4.8 to section 5.1 as per applicable CHMP guidance. Update of section 5.1 of the SmPC based on the outcome of a systematic literature review (SLR) and Natural History data from an International SMA registry (ISMAR). 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.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				
II/0035	B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier	26/09/2024	n/a		

IA/0037	A.7 - Administrative change - Deletion of manufacturing sites	28/08/2024		Annex II and PL	
II/0032	Update of sections 4.4 and 4.8 of the SmPC in order to amend a warning on lumbar puncture procedure to inform about the risk of arachnoiditis, the need to confirm the diagnosis using an MRI as well as the impact of arachnoiditis on the subsequent drug administration and in order to add to add 'Arachnoiditis' to the list of adverse drug reactions (ADRs) with frequency not known, based on postmarketing review. The Package Leaflet is updated accordingly. The MAH took the opportunity to update the list of local representatives. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	30/05/2024		SmPC and PL	Update of section 4.4 to inform about the risk of arachnoiditis associated with the lumbar puncture procedure. The SmPC section 4.4 has been updated to inform that an MRI should be performed to confirm the diagnosis and the extent of the inflammation. Identification of arachnoiditis precludes the use of the injection site until local inflammation has been ruled out. Update of the section 4.8 to add to add 'Arachnoiditis' to the list of adverse drug reactions (ADRs) with frequency not known. For more information, please refer to the Summary of Product Characteristics.
IB/0033	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	30/04/2024	16/08/2024	SmPC	
PSUSA/10595 /202305	Periodic Safety Update EU Single assessment - nusinersen	11/01/2024	n/a		PRAC Recommendation - maintenance
IA/0031/G	This was an application for a group of variations. B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of	09/10/2023	n/a		

	an obsolete parameter) B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place				
II/0029	Update of section 5.3 of the SmPC in order to update non-clinical information based on final results from study P058-17-02. This is a 24-month carcinogenicity study when administered by subcutaneous injection in mouse. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	31/08/2023		SmPC	Update of section 5.3 of the SmPC in order to update non-clinical information based on final results from study P058-17-02. This is a 24-month carcinogenicity study when administered by subcutaneous injection in mouse. For more information, please refer to the Summary of Product Characteristics.
IA/0028/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.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 changes to an approved test procedure A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder	22/02/2023	n/a		

	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.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 changes to an approved test procedure B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS				
PSUSA/10595 /202205	Periodic Safety Update EU Single assessment - nusinersen	12/01/2023	n/a		PRAC Recommendation - maintenance
R/0025	Renewal of the marketing authorisation.	11/11/2021	31/01/2022	SmPC, Annex II and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Spinraza in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10595 /202105	Periodic Safety Update EU Single assessment - nusinersen	13/01/2022	n/a		PRAC Recommendation - maintenance
II/0023	Update of section 5.1 of the SmPC to include information on real-world use of nusinersen in adults. C.I.z - Changes (Safety/Efficacy) of Human and	11/11/2021	31/01/2022	SmPC	Section 5.1 has been updated to inform that findings from an analysis based on real world data support the effectiveness of nusinersen to stabilize or improve motor function in some SMA adult Type II and III patients and that safety data in the adult population are consistent with

	Veterinary Medicinal Products - Other variation				the known safety profile of nusinersen and with co-morbidities associated with the underlying disease of SMA. For more information, please refer to the Summary of Product Characteristics.
IB/0024	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	24/08/2021	n/a		
IAIN/0022/G	This was an application for a group of variations. A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release 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	10/02/2021	31/01/2022	Annex II and PL	
IB/0021	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	29/01/2021	31/01/2022	SmPC	
PSUSA/10595 /202005	Periodic Safety Update EU Single assessment - nusinersen	14/01/2021	n/a		PRAC Recommendation - maintenance
N/0019	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/08/2020	14/01/2021	PL	
PSUSA/10595	Periodic Safety Update EU Single assessment -	09/07/2020	n/a		PRAC Recommendation - maintenance

/201911	nusinersen				
IB/0017	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	17/01/2020	14/01/2021	Annex II, Labelling and PL	
PSUSA/10595 /201905	Periodic Safety Update EU Single assessment - nusinersen	16/01/2020	n/a		PRAC Recommendation - maintenance
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.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	20/09/2019	n/a		
II/0014	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	05/09/2019	n/a		
PSUSA/10595 /201811	Periodic Safety Update EU Single assessment - nusinersen	27/06/2019	23/08/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10595/201811.
II/0013/G	This was an application for a group of variations.	02/05/2019	23/08/2019	SmPC	Final results of Study CS3A, a phase 2 open-label multiple

	This was an application for a group of variations. C1.3.b (Type II): to update sections 4.8 and 5.1 of the SmPC following assessment of the final CSR for Study CS3A (Procedure number: EMA/H/C/4312/P46/007). 3xC.I.4 (Type II): to update sections 4.8 and 5.1 of the SmPC to reflect safety, efficacy, and immunogenicity data from the interim analyses of studies SM201 and CS11, and results of SM202, Part 1. 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 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.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				dose study have been submitted to assess the Efficacy, Safety, Tolerability, and Pharmacokinetics of Multiple Doses of Nusinersen (ISIS 396443) Delivered Intrathecally to Patients with Infantile-Onset Spinal Muscular Atrophy. For more details please refer to the relevant sections of the SmPC. Interim analyses from studies SM202 (EMBRACE), CS11 (SHINE) and SM201 (NURTURE) have been submitted, to update the safety, efficacy and immunogenicity data. For more details please refer to the relevant sections of the SmPC.
PSUSA/10595 /201805	Periodic Safety Update EU Single assessment - nusinersen	31/01/2019	25/03/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for

					PSUSA/10595/201805.
IB/0011	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	07/03/2019	n/a		
T/0010	Transfer of Marketing Authorisation	02/10/2018	08/11/2018	SmPC, Labelling and PL	
IB/0009	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	29/10/2018	28/11/2018	SmPC	
II/0004	Update of sections 4.4 and 4.8 of the SmPC to include new safety information related to communicating hydrocephalus. The PIL and the RMP (new version 10.0) are updated accordingly. Section 4.2 of the SmPC is updated to move an existing wording on the route of administration of the product in order to improve readability. In addition, the MAH took the opportunity to implement a change in section 5.1 of the SmPC requested by the CHMP following the outcome of procedure EMA/H/C/4312/P46. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	12/07/2018	31/08/2018	SmPC and PL	There have been reports of communicating hydrocephalus not related to meningitis or bleeding in patients treated with nusinersen in the post-marketing setting. Some patients were implanted with a ventriculo-peritoneal shunt. In patients with decreased consciousness, an evaluation for hydrocephalus should be considered. The benefits-and risks of nusinersen treatment in patients with a ventriculo-peritoneal shunt are unknown at present and the maintenance of treatment needs to be carefully considered.

PSUSA/10595 /201711	Periodic Safety Update EU Single assessment - nusinersen	14/06/2018	n/a		PRAC Recommendation - maintenance
N/0007	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/05/2018	31/08/2018	PL	
IA/0006/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.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	06/03/2018	n/a		
IB/0003	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	20/11/2017	n/a		
II/0002/G	This was an application for a group of variations. Update of sections 4.8 and 5.1 of the SmPC to reflect efficacy and immunogenicity data from the final clinical study reports for the sham-controlled study in later-onset SMA (Study CS4) and the open-label study in subjects with later-onset SMA (Study CS12) and the final update to the CS2-12 longitudinal analysis. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	02/11/2017	31/08/2018	SmPC	The final results of the sham-controlled study in later-onset SMA (Study CS4) and the open-label study in subjects with later-onset SMA (Study CS12) including the final update to the CS2-12 longitudinal analysis provide confirmation of maintenance of response to nusinersen with stability of improvement in the medium-long term. For more information, please refer to the Summary of Product Characteristics.

	data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
II/0001	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	21/09/2017	31/08/2018	SmPC and PL	