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
II/0013/G	This was an application for a group of variations. 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	02/05/2019		SmPC	Final results of Study CS3A, a phase 2 open-label multiple 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

[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).

	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				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	06/03/2018	n/a		

	and/or limits of the finished product - Tightening of specification limits				
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 data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	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.
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	