



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Spravato

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/10825 /202203	Periodic Safety Update EU Single assessment - esketamine (for centrally authorised product only)	13/10/2022	09/12/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s) for PSUSA/10825/202203.
IAIN/0015	B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g.	23/08/2022	09/12/2022	SmPC, Labelling and	

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).



	tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes			PL	
IB/0013	To extend the due date for a phase 3 study in the RMP. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	20/05/2022	n/a		To extend the due date for a phase 3 study in the RMP.
II/0012	Update to the SmPC Section 4.2, and Section 5.1, based on the findings in Chinese subjects from a recently completed efficacy Phase 3 Study in adult with treatment-resistant depression. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	12/05/2022	09/12/2022	SmPC	Update to the SmPC Section 4.2, and Section 5.1, based on the findings in Chinese subjects from a recently completed efficacy Phase 3 Study in adult with treatment-resistant depression. This update can be justified by the results of the completed Phase 3 study ESKETINTRD3006.
PSUSA/10825 /202109	Periodic Safety Update EU Single assessment - esketamine (for centrally authorised product only)	07/04/2022	n/a		PRAC Recommendation - maintenance
PSUSA/10825 /202103	Periodic Safety Update EU Single assessment - esketamine (for centrally authorised product only)	30/09/2021	n/a		PRAC Recommendation - maintenance
IB/0008	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	21/06/2021	n/a		
IB/0009	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	04/05/2021	24/06/2022	SmPC, Annex II and PL	

PSUSA/10825 /202009	Periodic Safety Update EU Single assessment - esketamine (for centrally authorised product only)	09/04/2021	n/a		PRAC Recommendation - maintenance
II/0004	<p>To update the Spravato Product Information at section 4.2 to replace the current dosing recommendation in patients with Japanese ancestry with a statement that efficacy of Spravato in Japanese patients has been studied but not established and to add information describing the study in section 5.1. The removal of the dosing recommendation for these patients is justified by the results of the completed Phase 2 study 54135419TRD2005.</p> <p>The MAH took also the opportunity to update the Product information according to latest QRD template (v. 10.1)</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>	28/01/2021	26/02/2021	SmPC	<p>Please refer to Scientific Discussion 'Product Name-H-C-Product Number-II-Var.No'</p> <p>SmPC new text</p> <p>Further to the results of the completed Phase 2 study 54135419TRD2005, the PI has been updated to remove the current dosing recommendation in patients with Japanese ancestry with a statement that efficacy of Spravato in Japanese patients has been studied but not established in section 4.2 and to add also information describing the study in section 5.1.</p> <p>For more information, please refer to the Summary of Product Characteristics.</p>
IB/0007	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	17/02/2021	n/a		
II/0001/G	<p>This was an application for a group of variations.</p> <p>C.I.6(a): Extension of Indication to include a new indication for Spravato: Spravato, co-administered</p>	10/12/2020	04/02/2021	SmPC, Annex II, Labelling and PL	<p>Please refer to Scientific Discussion 'Spravato-H-C-Product Number-II-Var.No'</p> <p>The group of variations requested amendments to the Summary of Product Characteristics, Annex II, Labelling,</p>

	<p>with oral antidepressant therapy, is indicated in adults with a moderate to severe episode of major depressive disorder, as acute short term treatment, for the rapid reduction of depressive symptoms, which according to clinical judgement constitute a psychiatric emergency (see section 5.1 for a description of the population studied).</p> <p>As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 6.5 of the SmPC are updated. The RMP version 2.5 has also been agreed.</p> <p>B.II.e.5.a.2: Addition of a new pack size (multipack) of 24 nasal spray devices (multipack of 8 packs of 3 nasal spray devices) corresponding to 4 weeks of treatment in the new indication.</p> <p>The Package Leaflet and labelling are updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to clarify the wording in Annex II.D.</p> <p>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 C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one</p>				<p>Package Leaflet and Annex IV and to the Risk Management Plan (RMP).</p> <p>Extension of Indication to include a new indication for Spravato as follows: "Spravato, co-administered with oral antidepressant therapy, is indicated in adults with a moderate to severe episode of major depressive disorder, as acute short term treatment, for the rapid reduction of depressive symptoms, which according to clinical judgement constitute a psychiatric emergency (see section 5.1 for a description of the population studied)"</p> <p>Addition of a new pack size (multipack) of 24 nasal spray devices (multipack of 8 packs of 3 nasal spray devices) corresponding to 4 weeks of treatment in the new indication.</p> <p>As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 6.5 of the SmPC are updated. The RMP version 2.5 has also been agreed.</p> <p>The Package Leaflet and labelling are updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to clarify the wording in Annex II.D.</p> <p>Changes were also made to the PI to bring it in line with the current Agency/QRD template, SmPC guideline and other relevant guideline(s) [e.g. Excipients guideline, storage conditions, Braille, etc...], which were reviewed and accepted by the CHMP.</p> <p>In addition, the list of local representatives in the PL has been revised to amend contact details for the representatives of Hungary.</p>
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PSUSA/10825 /202003	Periodic Safety Update EU Single assessment - esketamine (for centrally authorised product only)	01/10/2020	n/a		PRAC Recommendation - maintenance
IA/0005	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	24/09/2020	n/a		
IB/0003	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)	21/07/2020	04/02/2021	SmPC	