Cresemba

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
X/0042/G	This was an application for a group of variations. Extension application to add a new strength of 40 mg hard capsule to be used in paediatric patients 6 years and older grouped with a type II variation (C.I.6.a) in order to extend the indication to include	27/06/2024	22/08/2024	SmPC, Labelling and PL	Extension application to add a new strength of 40 mg hard capsule to be used in paediatric patients 6 years and older grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment of paediatric patients aged 1 year and older for Cresemba 200 mg powder, based on final results from studies 9766-CL-0107 and 9766-CL-

[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).

	treatment of paediatric patients aged 1 year and older for Cresemba 200 mg powder, based on final results from studies 9766-CL-0107 and 9766-CL-0046. Study 9766-CL-0046 is a Phase 1, open-label, multicenter study to evaluate the PK, safety and tolerability of intravenous and oral isavuconazonium sulfate in paediatric patients. This study was conducted in two sequential parts: Part 1 with three intravenous dosing cohorts, and Part 2 with two oral dosing cohorts. Study 9766-CL-0107 is a Phase 2, open-label, non-comparative, multicenter study to evaluate the safety and tolerability, efficacy, and PK of isavuconazole for the treatment of invasive aspergillosis or mucormycosis in paediatric patients aged 1 to < 18 years. As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 5.3, 6.1, 6.5 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. A revised RMP version 10 has been approved. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one Annex I_2.(c) Change or addition of a new strength/potency				0046. Study 9766-CL-0046 is a Phase 1, open-label, multicenter study to evaluate the PK, safety and tolerability of intravenous and oral isavuconazonium sulfate in paediatric patients. This study was conducted in two sequential parts: Part 1 with three intravenous dosing cohorts, and Part 2 with two oral dosing cohorts. Study 9766-CL-0107 is a Phase 2, open-label, non-comparative, multicenter study to evaluate the safety and tolerability, efficacy, and PK of isavuconazole for the treatment of invasive aspergillosis or mucormycosis in paediatric patients aged 1 to < 18 years. As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 5.3, 6.1, 6.5 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. A revised RMP version 10 has been approved.
II/0046	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	25/07/2024	n/a		
II/0045	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	11/04/2024	22/08/2024	SmPC	Table 1 (Interactions), in section 4.5 of the Cresemba SmPC was amended to improve the guidance for health care professionals in relation to the co-administration of

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				cyclophosphamide and isavuconazole. For more information, please refer to the Summary of Product Characteristics.
IB/0044	B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size	08/01/2024	n/a		
IA/0043	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	20/10/2023	n/a		
IB/0041/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.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.a.1.z - Change in the manufacturer of AS or of a	03/04/2023	n/a		

	starting material/reagent/intermediate for AS - Other variation 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.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
IB/0040/G	This was an application for a group of variations. B.II.a.z - Change in description and composition of the Finished Product - Other variation 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.6 - Administrative change - Change in ATC Code/ATC Vet Code	19/12/2022	12/01/2024	SmPC, Annex II and PL	
IA/0039	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	19/09/2022	n/a		
PSUSA/10426 /202109	Periodic Safety Update EU Single assessment - isavuconazole	22/04/2022	21/06/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10426/202109.
IB/0038	B.I.b.2.e - Change in test procedure for AS or	07/01/2022	n/a		

	starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
II/0036	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	28/10/2021	19/05/2022	SmPC and PL	
II/0035/G	This was an application for a group of variations. 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	08/07/2021	n/a		
IB/0034	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	11/06/2021	n/a		
II/0030	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/04/2021	19/05/2022	SmPC, Labelling and PL	
PSUSA/10426 /202009	Periodic Safety Update EU Single assessment - isavuconazole	09/04/2021	n/a		PRAC Recommendation - maintenance
II/0031	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	28/01/2021	19/05/2022	SmPC and PL	

IA/0032/G	This was an application for a group of variations. B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size	11/09/2020	n/a		
R/0027	Renewal of the marketing authorisation.	28/05/2020	13/08/2020	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Cresemba in the approved indications remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10426 /201909	Periodic Safety Update EU Single assessment - isavuconazole	17/04/2020	n/a		PRAC Recommendation - maintenance
IB/0029	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	06/03/2020	n/a		
N/0026	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/01/2020	23/04/2020	PL	
PSUSA/10426	Periodic Safety Update EU Single assessment -	03/10/2019	n/a		PRAC Recommendation - maintenance

/201903	isavuconazole				
II/0024/G	This was an application for a group of variations. B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	26/09/2019	23/04/2020	SmPC, Labelling and PL	
IA/0023/G	This was an application for a group of variations. B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition	07/08/2019	n/a		
PSUSA/10426 /201809	Periodic Safety Update EU Single assessment - isavuconazole	11/04/2019	n/a		PRAC Recommendation - maintenance
IAIN/0021/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 finished product, including quality control sites (excluding manufacturer for batch release)	04/04/2019	23/04/2020	Annex II and PL	

	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site 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				
T/0020	Transfer of Marketing Authorisation	08/02/2019	11/03/2019	SmPC, Labelling and PL	
IAIN/0019	A.1 - Administrative change - Change in the name and/or address of the MAH	06/02/2019	11/03/2019	SmPC, Labelling and PL	
IA/0018/G	This was an application for a group of variations. 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.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter	19/12/2018	n/a		
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/12/2018	11/03/2019	PL	
IB/0015	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	20/11/2018	11/03/2019	SmPC and PL	

PSUSA/10426 /201803	Periodic Safety Update EU Single assessment - isavuconazole	04/10/2018	n/a		PRAC Recommendation - maintenance
IB/0013	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)	30/08/2018	11/03/2019	SmPC	
IA/0014	A.7 - Administrative change - Deletion of manufacturing sites	14/08/2018	n/a		
IA/0012/G	This was an application for a group of variations. 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.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter	18/07/2018	n/a		
PSUSA/10426 /201709	Periodic Safety Update EU Single assessment - isavuconazole	12/04/2018	n/a		PRAC Recommendation - maintenance
IB/0010	B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test	04/04/2018	n/a		
IB/0009	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	04/04/2018	n/a		

IB/0008	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	04/04/2018	n/a		
PSUSA/10426 /201703	Periodic Safety Update EU Single assessment - isavuconazole	28/09/2017	n/a		PRAC Recommendation - maintenance
N/0006	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/08/2017	30/01/2018	Labelling and PL	
IA/0005/G	This was an application for a group of variations. B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits	18/07/2017	n/a		
PSUSA/10426 /201609	Periodic Safety Update EU Single assessment - isavuconazole	06/04/2017	n/a		PRAC Recommendation - maintenance
IB/0002	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	13/01/2017	30/01/2018	SmPC	MAH was requested to submit the summaries of two new studies which are updating the Environmental Risk Assessment Report. The Rapporteur conclusions state that Cresemba may pose a risk for the aquatic environment therefore updates to

					sections 5.3 and 6.6 of the current SmPC are recommended.
PSUSA/10426 /201603	Periodic Safety Update EU Single assessment - isavuconazole	29/09/2016	n/a		PRAC Recommendation - maintenance