EMA/381727/2020

Kolbam

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
N/0033	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/03/2020		Labelling and PL	
PSUSA/10182 /201903	Periodic Safety Update EU Single assessment - cholic acid (CTX, AMACR or cholesterol 7α-hydroxylase deficiency indication)	17/10/2019	16/12/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for

[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).

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					PSUSA/10182/201903.
II/0028	Update of section 5.1. of the SmPC based on the submission of the final report from study CAC-002-01, listed as a category 3 study in the RMP. This is a Phase 3, open-label, single arm, non-randomized study investigating cholic acid in the treatment of subjects with inborn errors of bile acid metabolism. The study was a continuation study that included eligible subjects who had previously received cholic acid in studies CAC-91-10-10 or CAC-001-01 as well as newly diagnosed subjects. In addition, the MAH also took the opportunity to make editorial changes and to correct typographical mistakes throughout the product information. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	14/11/2019		SmPC	Efficacy data from study CAC-002-01 were comparable to Study CAC-91-10-10. Among the subgroup of patients with CTX (n=8), 3 transitioned from CAC-91-10-10 and were on cholic acid treatment at study start. The remaining 5 patients were treatment naïve. Urinary bile acids were normal for all patients (100%) at baseline and worst post-baseline assessments, and for most patients (88%) at the best post-baseline assessment; 1 patient (12%) had a slight elevation of urinary bile acids at best post-baseline assessment. Serum transaminases were below the ULN for most patients (71-100%) at baseline and for most patients (86%) at the worst post-baseline assessment and for all patients (100%) at the best post-baseline assessment. According to all submitted data, Kolbam was shown to be generally effective in maintaining all studied parameters in the normal range for CTX patients. Safety data revealed no deaths and SAEs considered to be drug related. In general, AEs were mild to moderate. Overall, the study confirmed the known safety profile of Kolbam observed in previous studies.
S/0029	4th annual re-assessment.	19/09/2019	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation under exceptional circumstances of Kolbam should be maintained.
PSUSA/10182 /201803	Periodic Safety Update EU Single assessment - cholic acid (CTX, AMACR or cholesterol 7α-hydroxylase deficiency indication)	04/10/2018	n/a		PRAC Recommendation - maintenance

PSUSA/10182 /201709	Periodic Safety Update EU Single assessment - cholic acid (CTX, AMACR or cholesterol 7α-hydroxylase deficiency indication)	12/04/2018	n/a		PRAC Recommendation - maintenance
S/0025	2nd Annual re-assessment	22/03/2018	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Kolbam should be maintained.
IA/0026/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material)	11/01/2018	n/a		
PSUSA/10182 /201703	Periodic Safety Update EU Single assessment - cholic acid (CTX, AMACR or cholesterol 7α-hydroxylase deficiency indication)	28/09/2017	n/a		PRAC Recommendation - maintenance
S/0020	1st Annual Re-assessment	21/04/2017	n/a		The CHMP, having reviewed the evidence of compliance

					with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that Marketing Authorisation of Kolbam should be maintained.
PSUSA/10182 /201609	Periodic Safety Update EU Single assessment - cholic acid (CTX, AMACR or cholesterol 7α-hydroxylase deficiency indication)	06/04/2017	n/a		PRAC Recommendation - maintenance
IB/0022	B.I.z - Quality change - Active substance - Other variation	22/12/2016	n/a		
IB/0018	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	09/12/2016	n/a		
IB/0019	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	07/12/2016	10/11/2017	SmPC	
PSUSA/10182 /201603	Periodic Safety Update EU Single assessment - cholic acid (CTX, AMACR or cholesterol 7α-hydroxylase deficiency indication)	29/09/2016	n/a		PRAC Recommendation - maintenance
IB/0017/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.a.1.f - Change in the manufacturer of AS or of a	21/09/2016	n/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				
IAIN/0015/G	This was an application for a group of variations. 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	02/06/2016	04/01/2017	Annex II and PL	
IAIN/0014	A.1 - Administrative change - Change in the name and/or address of the MAH	11/01/2016	04/01/2017	SmPC, Labelling and PL	
PSUSA/10182 /201504	Periodic Safety Update EU Single assessment - cholic acid (CTX, AMACR or cholesterol 7α-hydroxylase deficiency indication)	08/10/2015	n/a		PRAC Recommendation - maintenance
T/0011	Transfer of Marketing Authorisation	04/05/2015	05/06/2015	SmPC, Labelling and PL	
PSUSA/10182 /201410	Periodic Safety Update EU Single assessment - cholic acid (CTX, AMACR or cholesterol 7α-hydroxylase deficiency indication)	07/05/2015	n/a		PRAC Recommendation - maintenance

IB/0006/G	This was an application for a group of variations. B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products 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.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits	23/02/2015	n/a		
IAIN/0009	B.II.a.1.a - Change or addition of imprints, bossing or other markings including replacement, or addition of inks used for product marking - Changes in imprints, bossing or other markings	02/12/2014	05/06/2015	SmPC and PL	
IAIN/0007/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging	02/12/2014	05/06/2015	Annex II and PL	

	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				
IA/0008	A.7 - Administrative change - Deletion of manufacturing sites	01/12/2014	n/a		
IB/0005	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	18/11/2014	n/a		
T/0004	Transfer of Marketing Authorisation	28/08/2014	11/09/2014	SmPC, Labelling and PL	
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	09/09/2014	n/a		
IAIN/0002	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	18/08/2014	n/a		
IAIN/0001	A.2.a - Administrative change - Change in the (invented) name of the medicinal product for CAPs	06/08/2014	11/09/2014	SmPC, Annex II, Labelling and PL	