Carbaglu

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
IAIN/0046/G	This was an application for a group of variations. 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 -	09/12/2024		SmPC, Annex II, Labelling and PL	

[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).

	Not including batch control/testing A.1 - Administrative change - Change in the name and/or address of the MAH				
II/0045	Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to include a proposed dose adjustment for patients with impaired renal function based on final results from study RCD-P0-027; this is a Phase I, multicenter, open-label, parallel-group adaptive pharmacokinetic single dose study of oral Carbaglu in subjects with normal and varying degrees of impaired renal function. The Package Leaflet is updated accordingly. The RMP version 2.3 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in Annex II and Labelling, and to bring the PI in line with the latest QRD template version 10.3. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/06/2023	05/07/2024	SmPC, Annex II and PL	Based on the review of the data, the CHMP concluded that the dose of Carbaglu must be reduced in patients with renal impairment. For more information, please refer to the Summary of Product Characteristics.
IA/0043/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	19/03/2021	n/a		
IA/0042	B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative	27/10/2020	n/a		

	composition - Solid pharmaceutical forms				
PSUSA/564/202001	Periodic Safety Update EU Single assessment - carglumic acid	01/10/2020	n/a		PRAC Recommendation - maintenance
IG/1085/G	This was an application for a group of variations. A.1 - Administrative change - Change in the name and/or address of the MAH A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release 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)	16/05/2019	23/04/2020	SmPC, Annex II, Labelling and PL	
N/0039	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/02/2019	23/04/2020	PL	
N/0037	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/07/2018	23/04/2020	Labelling and PL	
IAIN/0036	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	22/05/2018	n/a		
IB/0035	B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an	15/05/2018	n/a		

	ASMF				
IA/0034	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	21/02/2018	n/a		
IA/0033/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.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition	08/12/2017	n/a		
IB/0032	B.II.f.1.b.2 - Stability of FP - Extension of the shelf life of the finished product - After first opening (supported by real time data)	08/09/2017	11/01/2018	SmPC, Annex II, Labelling and PL	
IG/0773/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	14/02/2017	11/01/2018	Annex II and PL	

IAIN/0030	B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site	16/12/2016	n/a		
IG/0686	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	12/05/2016	n/a		
PSUSA/564/201501	Periodic Safety Update EU Single assessment - carglumic acid	24/09/2015	19/11/2015	SmPC, Labelling and PL	Please refer to Carbaglu PSUSA/00000564/201501 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation.
IB/0027/G	This was an application for a group of variations. B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.2.b - Change in the specification parameters	19/08/2015	19/11/2015	SmPC and PL	

	and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products B.II.e.6.a - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that affects the product information B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier				
N/0025	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	31/03/2015	19/11/2015	PL	
IG/0535	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	06/03/2015	n/a		
IB/0023/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	25/06/2014	n/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.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 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				
IG/0393	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	20/12/2013	n/a		
IG/0392	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	19/12/2013	07/05/2014	Annex II and PL	
II/0020	To introduce an alternative manufacturer of the active substance supported by an active substance master file. B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS -	19/09/2013	n/a		

	Introduction of a new manufacturer of the AS that is supported by an ASMF				
IB/0018	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)	24/04/2013	07/05/2014	SmPC	
IA/0019	A.7 - Administrative change - Deletion of manufacturing sites	19/02/2013	n/a		
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	31/08/2012	07/05/2014	PL	
IA/0016	C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV	15/08/2011	n/a	Annex II	
IB/0015/G	This was an application for a group of variations. 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.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place	02/08/2011	n/a		

II/0013	This variation concerns an extension of indication of Carbaglu to add the treatment of hyperammoniemia due to isovaleric acidaemia, methylmalonic acidaemia and propionic acidaemia. The Package Leaflet has been amended accordingly. In addition the MAH also took opportunity to bring the SmPC, Package Leaflet and Labelling in line with the latest QRD template and to update contact details of local representatives. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	14/04/2011	27/05/2011	SmPC, Labelling and PL	The scientific discussion of the CHMP assessment report will be published.
IB/0014/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.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	15/04/2011	n/a		
IA/0012	IA_39_Change/addition of imprints, bossing or other markings	21/09/2009	n/a	SmPC	

R/0011	Renewal of the marketing authorisation.	24/01/2008	20/05/2008	SmPC, Labelling and PL	Based on the review of the available information the CHMP is of the opinion that the quality, the safety and the efficacy of this medicinal product continues to be adequately and sufficiently demonstrated and therefore considers that the benefit/risk profile of Carbaglu continues to be favourable. The CHMP was also of the opinion that the renewal can be granted with unlimited validity.
IA/0010	IA_01_Change in the name and/or address of the marketing authorisation holder IA_05_Change in the name and/or address of a manufacturer of the finished product	24/09/2007	n/a	SmPC, Annex II, Labelling and PL	
IA/0009	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	18/06/2007	n/a		
S/0008	Annual re-assessment.	27/04/2006	26/06/2006	Annex II	Since all specific obligations stated in Annex II.C of the Opinion dated 21 April 2005 have been fulfilled, there are no remaining grounds for the Marketing Authorisation to remain under exceptional circumstances.
II/0006	Update of Summary of Product Characteristics	17/03/2005	27/04/2005	SmPC	Udate in section 5.2 of the Summary of Product Characteristics, further to the completion of the clinical study on the disposition of radiolabelled carglumic acid in three healthy volunteers.
II/0005	Update of Summary of Product Characteristics and Package Leaflet	17/03/2005	27/04/2005	SmPC and PL	Udate to sections 4.3, 4.6 and 5.3 of the Summary of Product Characteristics (SPC) and section 2 of the Package Leaflet (PL) with the results of the reproduction toxicology study program, in compliance with the CHMP conclusions on the first annual reassessment.

S/0007	Annual re-assessment.	21/04/2005	21/04/2005		
IB/0004	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	07/12/2004	07/12/2004	SmPC, Labelling and PL	
IB/0003	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	27/09/2004	n/a	SmPC	
S/0001	Annual re-assessment.	03/06/2004	21/09/2004	Annex II and PL	The CHMP reviewed the evidence of compliance with the Specific obligations submitted by the MAH and re-assessed the benefit/risk profile for Carbaglu. On the basis of the data submitted since the Marketing Authorisation, the benefit/risk for Carbaglu in the treatment of hyperammonaemia due to N-acetylglutamate synthase deficiency remained positive. The CHMP therefore recommended the updating of the Community Marketing Authorisation for Carbaglu and that the authorisation should remain under exceptional circumstances.
IA/0002	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	05/07/2004	n/a		