Plenadren

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/0039/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	06/12/2022		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).

	responsible for batch release				
II/0038	Update of section 4.4 of the SmPC in order to add a warning on pheochromocytoma crisis. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to implement other minor editorial corrections in the Annexes. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/10/2022		SmPC, Annex II, Labelling and PL	Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.
IAIN/0037	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	14/03/2022		Annex II and PL	
T/0036	Transfer of Marketing Authorisation	21/12/2021	20/01/2022	SmPC, Labelling and PL	
IA/0035	A.7 - Administrative change - Deletion of manufacturing sites	04/10/2021	n/a		
IA/0033/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.5.b - Administrative change - Change in the name	05/02/2021	n/a		

	and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) 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				
PSUSA/9176/ 201911	Periodic Safety Update EU Single assessment - hydrocortisone (for centrally authorised products for adrenal insufficiency, congenital adrenal hyperplasia, modified-release formulations)	11/06/2020	n/a		PRAC Recommendation - maintenance
IAIN/0031/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.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site	14/08/2019	n/a		
IA/0030/G	This was an application for a group of variations. 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.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch	19/12/2018	n/a		

	control/testing takes place 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.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier				
IA/0029	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	28/06/2018	n/a		
IB/0028/G	This was an application for a group of variations. B.II.e.5.b - Change in pack size of the finished product - Deletion of a pack size(s) C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	15/05/2018	31/01/2019	SmPC, Labelling and PL	
IAIN/0027/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.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site	27/02/2018	n/a		
IAIN/0026	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP -	16/02/2018	31/01/2019	Annex II and PL	

	Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing				
II/0024	Submission of an updated RMP (version 3.1) in order to submit protocol amendments of the SHP 617-400 (EU-AIR) study – A European multicentre, multi-country, post-authorisation, observation study (registry) of patients with chronic adrenal insufficiency (category 3); additionally, the opportunity is being taken to implement a change agreed by the PRAC/CHMP as part of the assessment of MEA 005.3 in July 2016 and remove from the RMP the reference to study SHP617-404 (SWE-DUS), a Category 3 study to monitor off-label use of Plenadren to evaluate physician prescribing patterns. C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required	26/10/2017	n/a		
PSUSA/9176/ 201611	Periodic Safety Update EU Single assessment - hydrocortisone (for centrally authorised products for adrenal insufficiency, congenital adrenal hyperplasia, modified-release formulations)	09/06/2017	n/a		PRAC Recommendation - maintenance
IA/0025	B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP -	07/04/2017	n/a		

	Replacement/addition of a site where batch control/testing takes place				
II/0022	To update the SmPC section 4.8 (Undesirable Effects) and PIL section 4 (Possible side effects) of the Plenadren 5mg and 20 mg (hydrocortisone) modified release tablets. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/10/2016	21/09/2017	SmPC and PL	
R/0020	Renewal of the marketing authorisation.	23/06/2016	08/08/2016	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 Plenadren in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
II/0021	Update of sections 4.4 and 4.8 of the SmPC in order to add acute adrenocortical insufficiency as a new ADR based on post marketing experience and to include a relevant warning towards alignment with the Company Core Data Sheet. The Package Leaflet is updated in accordance. In addition, section 4.2 has been updated to replace parenteral administration of hydrocortisone with intravenous administration in line with currently published guidelines. Moreover, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial changes in the SmPC and Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to	26/05/2016	08/08/2016	SmPC and PL	In this variation the MAH has included information on acute adrenal insufficiency in the Product Information to explain that the acute adrenal insufficiency may develop in patients with known adrenal insufficiency who are on inadequate daily doses or in situations with increased cortisol need. Events have been reported in patients treated with Plenadren. Adrenal crisis can develop in patients with acute adrenal insufficiency. Therefore, patients should be advised of the signs and symptoms of acute adrenal insufficiency and of adrenal crisis and the need to seek immediate medical attention. During acute adrenal crisis parenteral, preferably intravenous administration of hydrocortisone in high doses, together with sodium chloride 9 mg/ml (0.9%) solution for infusion, should be administered according to

	new quality, preclinical, clinical or pharmacovigilance data				current treatment guidelines.
PSUSA/9176/ 201511	Periodic Safety Update EU Single assessment - hydrocortisone (for centrally authorised products for adrenal insufficiency, congenital adrenal hyperplasia, modified-release formulations)	13/05/2016	n/a		PRAC Recommendation - maintenance
IA/0019	B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	29/02/2016	n/a		
IG/0603/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	03/12/2015	11/05/2016	SmPC, Annex II, Labelling and PL	
IG/0621	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	16/10/2015	n/a		
PSUSA/9176/ 201411	Periodic Safety Update EU Single assessment - hydrocortisone (for centrally authorised products for adrenal insufficiency, congenital adrenal hyperplasia, modified-release formulations)	07/05/2015	n/a		PRAC Recommendation - maintenance

PSUV/0013	Periodic Safety Update	10/07/2014	n/a		PRAC Recommendation - maintenance
IAIN/0014	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	02/07/2014	n/a		
IAIN/0012/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV and/or QPPV contact details and/or back-up procedure C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) in the safety database and/or major contractual arrangements for the fulfilment of PhV obligations, and/or change of the site undergoing PhV activities C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the PhV system	05/02/2014	n/a		
IB/0011/G	This was an application for a group of variations. 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 B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g.	10/07/2013	20/11/2013	SmPC, Labelling and PL	

	tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes 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 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 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 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				
IA/0010	B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	13/05/2013	n/a		
IAIN/0009/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the	17/04/2013	n/a		

	back-up procedure of the QPPV C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system				
IAIN/0008	B.II.b.2.b.1 - Change to batch release arrangements and quality control testing of the FP - Not including batch control/testing	07/11/2012	20/11/2013	Annex II and PL	
IA/0007/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	24/10/2012	n/a		
IAIN/0005	C.I.9.i - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) to a	13/09/2012	n/a		

	DDPS following the assessment of the same DDPS in relation to another medicinal product of the same MAH				
IB/0004	C.I.8.b - Introduction of a new Pharmacovigilance system - which has been assessed by the relevant NCA/EMA for another product of the same MAH	13/08/2012	n/a		
IB/0002	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)	24/05/2012	29/10/2012	SmPC	
T/0001	Transfer of Marketing Authorisation	10/02/2012	26/03/2012	SmPC, Labelling and PL	