Natpar

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
II/0047/G	This was an application for a group of variations. B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.IV.1.a.1 - Change of a measuring or administration	26/01/2023		SmPC, Annex II, Labelling and PL	The SmPC section 6.6, Labelling and Package Leaflet have been updated as follows: Removal of the references and text related to the Ypsomed Clickfine pen needle approved with variation II/33/G (see above). Annex II have been updated as follows:

[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).

	device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking B.II.e.1.b.2 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Sterile medicinal products and biological/immunological medicinal products				Removal of the condition related to bi-layer bromobutyl rubber septum and Ypsomed Clickfine pen needle that had been approved with variation II/33/G (see above).
N/0048	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/01/2023		PL	
PSUSA/10591 /202204	Periodic Safety Update EU Single assessment - parathyroid hormone	01/12/2022	n/a		PRAC Recommendation - maintenance
IB/0044	B.I.a.1.f - Change in the manufacturer of AS or of 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	25/07/2022	n/a		
II/0033/G	This was an application for a group of variations. B.IV.1.a.3 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Spacer device for metered dose inhalers or other device which may have a significant impact on the delivery of the AS B.II.e.1.b.2 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Sterile medicinal products and	21/07/2022		SmPC, Annex II, Labelling and PL	The SmPC section 6.6 and the labelling have been updated to refer to the Ypsomed Clickfine pen needles. Annex II section D "obligation to conduct post-authorisation measures" has been updated to reflect the above-mentioned condition. The package leaflet has been updated to refer to the Ypsomed Clickfine pen needles and update the instructions for use.

	biological/immunological medicinal products B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol				
PSUSA/10591 /202110	Periodic Safety Update EU Single assessment - parathyroid hormone	10/06/2022	n/a		PRAC Recommendation - maintenance
IB/0043	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	09/06/2022	n/a		
IB/0041	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	20/05/2022	n/a		
IA/0040	A.7 - Administrative change - Deletion of manufacturing sites	13/04/2022	n/a		
R/0034	Renewal of the marketing authorisation.	27/01/2022	22/03/2022		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Natpar, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.

II/0035	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	10/03/2022	n/a		
IAIN/0038	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	10/02/2022	n/a		
II/0030/G	This was an application for a group of variations. Submission of the clinical study reports of the following two studies: • SHP634-402 - A Phase 4, Open-Label, Single-Center Clinical Study of Extended use of rhPTH(1-84) in Hypoparathyroidism • SHP634-404 - An Open-label Study Investigating the Safety and Efficacy of rhPTH(1-84) in Subjects with Hypoparathyroidism. 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	16/12/2021	n/a		n/a
IAIN/0036	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	14/12/2021	22/03/2022	Annex II and PL	

PSUSA/10591 /202104	Periodic Safety Update EU Single assessment - parathyroid hormone	02/12/2021	n/a		PRAC Recommendation - maintenance
T/0032	Transfer of Marketing Authorisation	13/09/2021	19/10/2021	SmPC, Labelling and PL	
PSUSA/10591 /202010	Periodic Safety Update EU Single assessment - parathyroid hormone	10/06/2021	n/a		PRAC Recommendation - maintenance
R/0027	Renewal of the marketing authorisation.	25/02/2021	15/04/2021		
II/0026	Submission of the final results of study PAR-C10-008; a long-term open-label study investigating the safety and tolerability of a rhPTH[1-84] for the treatment of adults with hypoparathyroidism – a clinical extension study (RACE). Update of SmPC section 5.1 to reflect 72 months data from the study. Update of the RMP (version 3.1) with the completed study results, to remove this study as an additional pharmacovigilance activity and to align with the GVP module V Rev 2. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	11/03/2021	19/10/2021	SmPC	The study results show durability of the physiological effects of Natpar over 72 months of treatment.
PSUSA/10591 /202004	Periodic Safety Update EU Single assessment - parathyroid hormone	26/11/2020	n/a		PRAC Recommendation - maintenance
PSUSA/10591 /201910	Periodic Safety Update EU Single assessment - parathyroid hormone	14/05/2020	n/a		PRAC Recommendation - maintenance

IB/0024/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.IV.1.z - Change of a measuring or administration device - Other variation	30/04/2020	15/04/2021	SmPC, Labelling and PL	
R/0022	Renewal of the marketing authorisation.	27/02/2020	17/04/2020		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Natpar, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
II/0020/G	This was an application for a group of variations. B.II.b.3.b - Change in the manufacturing process of the finished or intermediate product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product B.II.b.4.c - Change in the batch size (including batch size ranges) of the finished product - The change requires assessment of the comparability of a biological/immunological medicinal product or a new bioequivalence study	20/02/2020	n/a		

II/0021	B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product	14/11/2019	n/a		
PSUSA/10591 /201904	Periodic Safety Update EU Single assessment - parathyroid hormone	31/10/2019	n/a		PRAC Recommendation - maintenance
II/0013/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.IV.1.c - Change of a measuring or administration device - Addition or replacement of a device which is an integrated part of the primary packaging	25/07/2019	17/04/2020	SmPC, Labelling and PL	
II/0018/G	This was an application for a group of variations. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	18/07/2019	17/04/2020	SmPC, Annex II, Labelling and PL	
PSUSA/10591 /201810	Periodic Safety Update EU Single assessment - parathyroid hormone	16/05/2019	n/a		PRAC Recommendation - maintenance
R/0016	Renewal of the marketing authorisation.	28/02/2019	29/04/2019		The CHMP, having reviewed the available information on

					the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Natpar, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
II/0015	B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol	17/01/2019	n/a		
PSUSA/10591 /201804	Periodic Safety Update EU Single assessment - parathyroid hormone	15/11/2018	15/01/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10591/201804.
IB/0012	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	09/11/2018	n/a		
IAIN/0014/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	24/09/2018	15/01/2019	SmPC, Annex II, Labelling and PL	
N/0011	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/08/2018	15/01/2019	PL	

IB/0009/G	This was an application for a group of variations. B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.a.4.f - Change to in-process tests or limits applied during the manufacture of the AS - Addition or replacement of an in-process test as a result of a safety or quality issue B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	11/07/2018	n/a		
PSUSA/10591 /201710	Periodic Safety Update EU Single assessment - parathyroid hormone	17/05/2018	n/a		PRAC Recommendation - maintenance
R/0007	Renewal of the marketing authorisation.	22/02/2018	19/04/2018		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Natpar, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
II/0005	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/01/2018	19/04/2018	SmPC	The Marketing Authorisation Holder provided interim results for Study 2 (PAR-C10-008; RACE); a long-term, open-label extension study of daily subcutaneous dosing of Natpar in hypoparathyroidism patients who completed prior studies with Natpar.

					A total of 49 patients were enrolled in the study. Patients received doses of 25 micrograms, 50 micrograms, 75 micrograms or 100 micrograms/day for up to approximately 60 months (mean 1161 days, range 41 to 1820 days). The results demonstrate durability of the physiological effects of Natpar over 60 months including maintenance of mean albumin-corrected serum calcium levels (n=49, 2.11 ±19 mmol/L), a decrease from baseline in urinary calcium excretion (n= 47, 2.23 ± 5.9 mmol/24 h), a decrease in serum phosphate (n= 49, 0.29 ±28 mmol/L) and the maintenance of normal calcium phosphate product (n=49, <4.4mmol2/L2).
II/0004/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.a.4.d - Change to in-process tests or limits applied during the manufacture of the AS - Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the AS B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement	14/12/2017	n/a		

	or addition) for the AS or a starting material/intermediate				
II/0006	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	30/11/2017	n/a		
IB/0001/G	This was an application for a group of variations. B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	10/08/2017	n/a		
IB/0002	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	08/08/2017	n/a		
IAIN/0003/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	14/06/2017	19/04/2018	Annex II and PL	