Signifor

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/0072/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 -	16/12/2024		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/0070	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	31/10/2024	n/a		
PSUSA/9253/ 202310	Periodic Safety Update EU Single assessment - pasireotide	27/06/2024	22/08/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/9253/202310.
IA/0071	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	07/08/2024	n/a		
IA/0069/G	This was an application for a group of variations. 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 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 B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor	16/05/2024	n/a		

	changes to an approved test procedure				
IAIN/0067/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.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	04/12/2023	n/a		
IA/0066	A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient	02/08/2023	n/a		
IA/0065/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) 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)	26/07/2023	n/a		
IA/0064	A.7 - Administrative change - Deletion of manufacturing sites	20/02/2023	n/a		

IA/0063	B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test	10/01/2023	n/a		
IA/0062	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)	20/10/2022	n/a		
IA/0061	A.7 - Administrative change - Deletion of manufacturing sites	08/08/2022	21/08/2023	Annex II and PL	
IB/0060	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	10/05/2022	n/a		
IB/0059/G	This was an application for a group of variations. 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.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation A.7 - Administrative change - Deletion of manufacturing sites	04/02/2022	n/a		

	A.7 - Administrative change - Deletion of manufacturing sites B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS 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 A.7 - Administrative change - Deletion of manufacturing sites B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation				
IA/0058	A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient	15/12/2021	n/a		
IB/0055/G	This was an application for a group of variations. 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.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.e.6.b - Change in any part of the (primary)	17/11/2021	n/a		

	packaging material not in contact with the finished product formulation - Change that does not affect the product information 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.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.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.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				
IA/0057	A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient	09/11/2021	n/a		
IA/0056/G	This was an application for a group of variations. B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test	08/10/2021	n/a		

	procedure B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method				
PSUSA/9253/ 202010	Periodic Safety Update EU Single assessment - pasireotide	10/06/2021	n/a		PRAC Recommendation - maintenance
IAIN/0054/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 A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient	29/01/2021	n/a		
IB/0052/G	This was an application for a group of variations. B.II.z - Quality change - Finished product - Other variation B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	09/12/2020	n/a		

IAIN/0051/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 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	23/07/2020	12/05/2021	Annex II and PL	
IA/0050/G	This was an application for a group of variations. B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	29/05/2020	n/a		
T/0049	Transfer of Marketing Authorisation	24/04/2020	18/05/2020	SmPC, Labelling and PL	
II/0046	Update of sections 4.4 of the SmPC in order to add new warnings on cholangitis and ketoacidosis and 4.8 to add diabetic ketoacidosis to the list of adverse	14/05/2020	12/05/2021	SmPC and PL	Sections 4.4 and 4.8 of the SmPC were updated in order to add new information on cholangitis and diabetic ketoacidosis. The Package Leaflet was updated accordingly.

	drug reactions (ADRs) with frequency not known. The Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/9253/ 201910	Periodic Safety Update EU Single assessment - pasireotide	14/05/2020	n/a		PRAC Recommendation - maintenance
IB/0047/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient A.7 - Administrative change - Deletion of manufacturing sites 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 B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process	16/04/2020	n/a		

	of the AS B.I.c.z - Container closure system of the AS - Other variation				
IA/0048	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	18/03/2020	n/a		
IA/0045/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) A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	07/02/2020	n/a		

	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				
II/0041/G	This was an application for a group of variations. Submission of the final CSR from Study CSOM230B2219; a multi-center, randomized, open-label, Phase IV study to investigate the management of pasireotide-induced hyperglycaemia with incretin based therapy or insulin in adult patients with Cushing's disease or acromegaly (listed as a category 3 study in the RMP). A revised RMP version 7.1, updated in line with the revised GVP Module V, including changes to the safety concerns, was agreed during the procedure. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data 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	03/10/2019	n/a		The data provided confirms the information on pasireotide-induced hyperglycaemia which is already included in the SmPC, and therefore no further amendments to the product information are considered necessary at present.
IG/1099	A.7 - Administrative change - Deletion of manufacturing sites	24/05/2019	n/a		

PSUSA/9253/ 201810	Periodic Safety Update EU Single assessment - pasireotide	16/05/2019	n/a		PRAC Recommendation - maintenance
IA/0042/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient B.II.c.4.a - Change in synthesis or recovery of a non-pharmacopoeial or novel excipient - Minor change	03/05/2019	n/a		
IAIN/0040/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) B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	14/03/2019	n/a		
IG/0950	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)	18/06/2018	n/a		

PSUSA/9253/ 201710	Periodic Safety Update EU Single assessment - pasireotide	17/05/2018	n/a		PRAC Recommendation - maintenance
T/0037	Transfer of Marketing Authorisation	13/03/2018	12/04/2018	SmPC, Labelling and PL	
IB/0036	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	08/03/2018	n/a		
X/0030/G	This was an application for a group of variations. Annex I_2.(c) Change or addition of a new strength/potency C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	20/07/2017	18/09/2017	SmPC, Labelling and PL	
IB/0034	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)	27/07/2017	12/04/2018	SmPC	
IB/0033/G	This was an application for a group of variations. B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.b - Change in test procedure for an excipient - Deletion of a test procedure if an alternative test	11/07/2017	n/a		

	procedure is already authorised B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)				
PSUSA/9253/ 201610	Periodic Safety Update EU Single assessment - pasireotide	05/05/2017	n/a		PRAC Recommendation - maintenance
IB/0031	Change in the test procedure of the test 'Enantiomer by HPLC' for the starting material Fmoc-Tyr(Bzl)-OH used in the manufacturing process of the active substance pasireotide. The test procedure has been updated to allow better separation of the peaks FMOC-L-Tyrosin-(Bzl)-OH and FMOC-D-Tyrosin-(Bzl)-OH. In addition, the MAH took the opportunity to make editorial changes in the test method 'Identity by IR (KBr)' and in the test method 'Assay by titration'. 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	10/01/2017	n/a		
IB/0029	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	29/11/2016	n/a		
R/0028	Renewal of the marketing authorisation.	15/09/2016	18/11/2016	SmPC, Labelling and	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Signifor in the approved indication remains favourable and

				PL	therefore recommended the renewal of the marketing authorisation with unlimited validity.
II/0026	Update of sections 4.2, 4.4, 4.6, 5.1 and 5.2 in order to amend the safety information on SOM230B2126 study "A phase I, open-label, multicenter, single-dose study to evaluate the pharmacokinetics (PK) and safety of subcutaneous (sc) pasireotide in subjects with varying degrees of renal impairment compared to a matched control group of healthy volunteers". In addition, the Marketing authorisation holder (MAH) took the opportunity to make some additional editorial changes and bring the PI in line with the latest QRD template. The variation leads to amendments to the Summary of Product Characteristics, Labelling and Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	21/07/2016	18/11/2016	SmPC, Annex II, Labelling and PL	Signifor (pasireotide) is indicated for the treatment of adult patients with Cushing's disease for whom surgery is not an option or for whom surgery has failed and for the treatment of adult patients with acromegaly for whom surgery is not an option or has not been curative and who are inadequately controlled on treatment with another somatostatin analogue. Pasireotide was mainly eliminated as unchanged form in feces and urine. The purpose of this study (SOM230B2126) was to evaluate the effect of varying degrees of renal impairment on the PK and safety of pasireotide in subjects with various degrees of renal impairment compared to a matched group of healthy subjects with normal renal function. The product information has been updated to include guidance on use of pasireotide in renally impaired patients based on the final results of the clinical pharmacology study SOM230B2126 and introduce some editorial changes in accordance with the QRD template.
PSUSA/9253/ 201510	Periodic Safety Update EU Single assessment - pasireotide	13/05/2016	n/a		PRAC Recommendation - maintenance
IA/0027/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) B.II.b.5.b - Change to in-process tests or limits	03/05/2016	n/a		

	applied during the manufacture of the finished product - Addition of a new test(s) and limits				
IA/0024/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.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	04/12/2015	n/a		
N/0023	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/07/2015	07/03/2016	Labelling and PL	
IG/0578/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) 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)	01/07/2015	n/a		
IG/0559	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)	20/05/2015	n/a		

PSUSA/9253/201410	Periodic Safety Update EU Single assessment - pasireotide	07/05/2015	n/a		PRAC Recommendation - maintenance
IAIN/0020	A.1 - Administrative change - Change in the name and/or address of the MAH	02/03/2015	07/03/2016	SmPC, Labelling and PL	
X/0010	Annex I_2.(d) Change or addition of a new pharmaceutical form	25/09/2014	19/11/2014	SmPC, Labelling and PL	For further information, please refer to the Assessment Report: Signifor-H-2052-X-10-AR-en.
IG/0484/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	12/11/2014	n/a		
PSUV/0015	Periodic Safety Update	06/11/2014	n/a		PRAC Recommendation - maintenance
II/0014	Submission of the non-clinical study report for Study 1270375 which examined the expression profile of somatostatin receptor subtypes in cardiac tissues across species. The requested variation did not propose any amendments to 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	25/09/2014	n/a		

IG/0443	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)	20/08/2014	n/a		
IB/0016	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	19/08/2014	n/a		
PSUV/0011	Periodic Safety Update	08/05/2014	n/a		PRAC Recommendation - maintenance
II/0012	Update of SmPC section 4.4 to include guidance regarding monitoring of glucose metabolism in the event of dose increase. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/04/2014	19/11/2014	SmPC	After review of all available safety data regarding the increased risk of developing hyperglycaemia with pasireotide treatment, the MAH proposed to further strengthen the recommendations for glucose monitoring. The underlying mechanism for the increased risk of hyperglycaemia with pasireotide treatment has been well described. In study C2305, performed with the long-acting formulation in acromegalic patients, worsening in glucose metabolic control was observed not only after initiation of therapy but also after dose increases. Therefore the MAH proposed to amend the current wording regarding glucose monitoring in the SmPC with the recommendation to closely monitor blood glucose also after dose increase. This was endorsed by the CHMP and the wording proposed was considered acceptable. No amendment of the Package Leaflet is considered necessary. The benefit/risk balance for Signifor remains positive.
IB/0013	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	07/04/2014	n/a		

II/0008	Update of SmPC section 4.5 based on the Drug Drug Interaction (DDI) study SOM230B2127 undertaken to investigate the effect of verapamil on the pharmacokinetics of pasireotide. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/01/2014	19/11/2014	SmPC	The study undertaken demonstrates that co administration of verapamil did not affect the pharmacokinetics of pasireotide. It is considered possible to generalize the result to all P-gp inhibitors, given that verapamil is considered a strong/moderate P-gp inhibitor. However, in order to predict potential interactions involving pasireotide, the MAH is encouraged to in the future further characterise the biliary elimination of pasireotide. The results of the study do not have any impact on the benefit-risk balance of pasireotide, which remains positive.
IA/0009	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	07/11/2013	n/a		
IB/0007/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.1.c - Change in the specification parameters	26/04/2013	n/a		

	and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS				
II/0005	Update of SmPC sections 4.5 and 5.2 based on three non-clinical in vitro studies undertaken to further investigate the role of pasireotide as inhibitor of UDP-glucuronosyltransferase 1A1 (UGT1A1), multi-drug resistance-associated protein 2 (MRP2), the bile salt efflux pump (BSEP), breast cancer resistance protein (BCRP) and P-glycoprotein (P-gp). The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity of this variation to propose minor changes to the instructions for use in the Package Leaflet, to implement editorial changes in the annexes, align Annex II with the latest QRD template (version 8.3) and to update the contact details for the local representative in Malta in the Package Leaflet. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	21/03/2013	12/08/2013	SmPC, Annex II and PL	The MAH have submitted three in vitro studies that investigate the in vitro inhibitory potential of pasireotide of the enzyme UGT1A1 and the transporters BSEP, MRP2, P-gp and BCRP. The studies have been conducted with an acceptable setup and appropriate controls and concentrations have been utilised. Pasireotide was identified as an in vitro inhibitor of all investigated enzymes and transporters. However, the inhibition potency is unlikely to be of any relevance in the clinical setting and therefore no follow-up in vivo interaction studies is necessary. This variation application does not have any impact on the benefit/risk balance of Signifor which remains positive.
IB/0006	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	06/03/2013	12/08/2013	SmPC, Labelling and	

				PL	
IG/0248	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	17/12/2012	n/a		
N/0002	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/09/2012	12/08/2013	PL	
IAIN/0003/G	This was an application for a group of variations. C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD 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	13/08/2012	n/a		
IA/0001/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 of the finished product, including quality control sites (excluding manufacturer for batch release) A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished	31/05/2012	n/a		

	product, including quality control sites (excluding manufacturer for batch release) A.7 - Administrative change - Deletion of manufacturing sites 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 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				