NINLARO

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
IB/0048	B.II.e.z - Change in container closure system of the Finished Product - Other variation	10/09/2024		SmPC, Labelling and PL	
PSUSA/10535 /202311	Periodic Safety Update EU Single assessment - ixazomib	27/06/2024	16/08/2024	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).

					PSUSA/10535/202311.
PSUSA/10535 /202305	Periodic Safety Update EU Single assessment - ixazomib	25/01/2024	19/03/2024	SmPC, Annex II and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10535/202305.
II/0045	Submission of the Clinical Study Report (Addendum 2) for study C16019 listed as a Specific Obligation in the Annex II of the Product Information. This is a phase 3, randomized, double-blind, placebo-controlled study of single-agent oral ixazomib as maintenance therapy following autologous stem cell transplant (ASCT) for patients with newly diagnosed multiple myeloma. In addition, the MAH proposes to remove NINLARO from the list of medicines subject to additional monitoring and to remove the black triangle from the SmPC. The Annex II and Package Leaflet are updated accordingly. The RMP version 10.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and update the list of local representatives in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/09/2023	03/11/2023	SmPC, Annex II and PL	Please refer to Scientific Discussion Ninlaro-EMEA/H/C/003844/II/0045.
R/0043	Renewal of the marketing authorisation.	20/07/2023	01/09/2023		
IB/0044/G	This was an application for a group of variations. B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other	23/08/2023	05/10/2023	Annex II and PL	

	variation B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality 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 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.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 of the AS				

	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 of the AS 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 of the AS 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.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation				
PSUSA/10535 /202211	Periodic Safety Update EU Single assessment - ixazomib	08/06/2023	n/a		PRAC Recommendation - maintenance
II/0041	Submission of the final report from study NSMM-5001 (INSIGHT) listed as a Specific Obligation in the Annex II of the Product Information. This is a global, prospective, non-interventional, observational study of presentation, treatment patterns, and outcomes in multiple myeloma patients. The Annex II and the RMP (submitted version 9.0) are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI.	12/01/2023	01/09/2023	Annex II	

	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				
R/0040	Renewal of the marketing authorisation.	21/07/2022	13/09/2022		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 NINLARO, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
IB/0039	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	16/06/2022	13/09/2022	Annex II	
PSUSA/10535 /202111	Periodic Safety Update EU Single assessment - ixazomib	10/06/2022	n/a		PRAC Recommendation - maintenance
IA/0038	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	17/02/2022	n/a		
IB/0036/G	This was an application for a group of variations.	14/01/2022	n/a		

	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.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				
II/0033	C.I.11 Submission of the final report for the final analysis of OS for study C16010 fulfilling an obligation in the Annex II of the Product Information. This is a phase 3 study to evaluate efficacy and safety of ixazomib in combination with LenDex in adult patients with relapsed and/or refractory multiple myeloma. Section 4.4 is also updated to include a warning about occurrence of Stevens-Johnson syndrome. The Package Leaflet is updated accordingly. An updated RMP (version 7.0) has been submitted. The applicant also took the opportunity to update the list of local representatives. 1is recommended for approval. Amendments to the marketing authorisation In view of the data submitted with the variation, amendments to Annex(es) II and to the Risk Management Plan are recommended. The following obligation has been fulfilled, and therefore it is recommended that it be deleted from the Annex II to the Opinion:	02/12/2021	13/09/2022	Annex II	The table in Module 8b of the EPAR will be updated as follows: Scope Please refer to the Recommendations section above Summary SmPC new text Section 4.4 Cutaneous reactions Warning Added: "Stevens-Johnson syndrome has also been reported with ixazomib (see section 4.8). If Stevens-Johnson syndrome occurs, discontinue ixazomib". For more information, please refer to the Summary of Product Characteristics.

	Description Due date Postauthorisation efficacy study (PAES) C16010: To provide an interim report of overall survival at the time of the 3rd interim analysis and to provide a final report for the final analysis of OS from the phase 3, randomized, doubleblind study C16010 in adult patients with relapsed and/or refractory multiple myeloma. June 2021 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				
IB/0035	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	23/11/2021	n/a		
R/0030	Renewal of the marketing authorisation.	16/09/2021	12/11/2021	SmPC and PL	
IB/0034/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.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site	01/09/2021	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 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				
IB/0032	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	28/06/2021	12/11/2021	Annex II	
IAIN/0031/G	This was an application for a group of variations. B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits B.II.a.3.a.1 - Changes in the composition (excipients) of the finished product - Changes in components of the flavouring or colouring system - Addition , deletion or replacement	04/06/2021	n/a		
PSUSA/10535 /202011	Periodic Safety Update EU Single assessment - ixazomib	06/05/2021	n/a		PRAC Recommendation - maintenance
IA/0029/G	This was an application for a group of variations.	12/04/2021	12/11/2021	SmPC, Annex	

	A.7 - Administrative change - Deletion of manufacturing sites A.6 - Administrative change - Change in ATC Code/ATC Vet Code			II and PL	
II/0026	Update of Annex II of the Product Information and the Risk Management Plan v. 5.1 following the completion of study C16014 comparing ixazomib plus lenalidomide and dexamethasone versus placebo plus lenalidomide and dexamethasone in adult patients with newly diagnosed multiple myeloma not eligible for stem cell transplantation (SCT) in fulfilment of SOB 003. A minor editorial change is proposed to section 4.2 Posology and Method of administration, for consistency with other sections of the SmPC. In addition, an update is proposed to the local representatives information in the Package Leaflet. 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	11/03/2021	12/11/2021	SmPC, Annex II and PL	The table in Module 8b of the EPAR will be updated as follows: Scope Please refer to the Recommendations section above
II/0025	Update of the SmPC section 4.9 with additional information on Ninlaro overdose. 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	21/01/2021	12/11/2021	SmPC and PL	SmPC new text The section 4.9 Overdose has been updated as follows: Overdose has been reported in patients taking NINLARO. Symptoms of overdose are generally consistent with the known risks of NINLARO (see section 4.8). Overdose of 12 mg (taken at one time) has resulted in serious adverse

	data				events, such as severe nausea, aspiration pneumonia, multiple organ failure and death. Ixazomib is not dialyzable (see section 5.2). Overdoses were most common in patients starting treatment with NINLARO. The importance of carefully following all dosage instructions should be discussed with patients starting treatment. Instruct patients to take the recommended dosage as directed because overdose has led to deaths. For more information, please refer to the Summary of Product Characteristics.
IAIN/0027	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	07/01/2021	n/a		
R/0021	Renewal of the marketing authorisation.	17/09/2020	20/11/2020	PL	
II/0022	To update section 4.8 undesirable effects of the Ninlaro (Ixazomib) Summary of Product Characteristics (SmPC) following the adoption of the CHMP opinion in 25 June 2020 on PSUR assessment procedure EMEA/H/C/PSUSA/00010535/201911. Consequently the ADRs: acute febrile neutrophilic dermatosis, Stevens-Johnson syndrome, transverse myelitis, posterior reversible encephalopathy disorders and tumour lysis syndrome have been	12/11/2020	12/11/2021	SmPC	

	assigned frequency rare. C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH				
IAIN/0024	A.1 - Administrative change - Change in the name and/or address of the MAH	09/09/2020	20/11/2020	SmPC, Labelling and PL	
IAIN/0023/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.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.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.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	08/09/2020	n/a		

	exist per material)				
PSUSA/10535 /201911	Periodic Safety Update EU Single assessment - ixazomib	25/06/2020	25/08/2020	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10535/201911.
II/0019/G	This was an application for a group of variations. Group of variations consisting of the: C.I.11.b: Submission of the final report from study NSMM-5001 listed as a Specific Obligation in the Annex II of the Product Information. This is a global, prospective, non-interventional, observational study in multiple myeloma patients. The Annex II and the RMP (submitted version 5) are updated accordingly. C.I.11.z: Submission of an updated RMP version 5 in order to extend the due date of the Post-authorisation efficacy study (PAES) C16010 listed in Annex IID. The MAH also took the opportunity to correct a typographical error in Annex II. 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 C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	25/06/2020	25/08/2020	Annex II	This variation extended the due date for some of the post-approval commitments for Ninlaro: study C16010 from December 2019 to June 2021; study NSMM-5001 from December 2019 to July 2022 to cater for a provision of updated and more mature study data.

R/0017	Renewal of the marketing authorisation.	25/07/2019	16/09/2019		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 NINLARO, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
IAIN/0018/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 - Not including batch control/testing 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	19/08/2019	25/08/2020	Annex II and PL	
II/0014/G	This was an application for a group of variations. Group of variations consisting of a type 2 variation to include submission of final report of progression free survival (PFS) in fulfilment of SOB 004 and a type IB variation to request and extension of the due date of SOB 003. The Annex II is amended accordingly. Consequently, the RMP is updated (version 4.2). In addition, the Marketing authorisation holder (MAH)	25/07/2019	16/09/2019	Annex II	The due date of the C16014 Specific obligation study has been revised to December 2020. Moreover, the description of the specific obligation SOB 003 has been revised as follows: C16019: In order to further investigate the efficacy the MAH should provide additional OS/PFS2 data when approximately 200 death events have occurred from the Phase 3, randomized, placebo-controlled, double-blind study ixazomib in maintenance therapy in patients with multiple myeloma following SCT.

	took the opportunity to introduce minor editorial changes throughout the PI and to bring the PI in line with the latest QRD template version 10.1. 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 C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation				
PSUSA/10535 /201811	Periodic Safety Update EU Single assessment - ixazomib	14/06/2019	n/a		PRAC Recommendation - maintenance
IA/0015/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.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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.2 - Submission of a new/updated or	18/02/2019	n/a		

	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.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.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.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)				
PSUSA/10535 /201805	Periodic Safety Update EU Single assessment - ixazomib	29/11/2018	n/a		PRAC Recommendation - maintenance
R/0012	Renewal of the marketing authorisation.	26/07/2018	17/09/2018	SmPC, Annex II, Labelling and PL	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 NINLARO, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.

PSUSA/10535/201711	Periodic Safety Update EU Single assessment - ixazomib	14/06/2018	n/a		PRAC Recommendation - maintenance
IB/0011	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	17/05/2018	n/a		
IA/0010/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.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.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - 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	20/04/2018	n/a		

	procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure				
IA/0008/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.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	05/01/2018	n/a		
IB/0007	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	12/12/2017	06/07/2018	SmPC and Annex II	
PSUSA/10535 /201705	Periodic Safety Update EU Single assessment - ixazomib	30/11/2017	n/a		PRAC Recommendation - maintenance
R/0003	Renewal of the marketing authorisation.	20/07/2017	18/09/2017	SmPC, Annex II, Labelling	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

				and PL	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 NINLARO, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
IA/0006	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	18/08/2017	n/a		
IAIN/0004	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	18/07/2017	06/07/2018	SmPC and PL	
II/0002	Update of sections 4.8 and 5.1 of the SmPC to reflect the final overall survival analysis of C16010 China continuation study, a phase III study comparing ixazomib plus lenalidomide and dexamethasone versus placebo plus lenalidomide and dexamethasone in patients with relapsed and/or refractory multiple myeloma, in order to fulfil SOB (Specific Obligation) 002. Annex II.E and the RMP (version 2.1) are updated accordingly. In addition the Marketing Authorisation Holder (MAH) took the opportunity to include the date of marketing authorisation in section 9 of the SmPC, to make a small correction in the Product Information to the Finnish, German and Swedish translations. C.I.4 - Change(s) in the SPC, Labelling or PL due to	06/07/2017	18/09/2017	SmPC and Annex II	In order to fulfil specific obligation (SOB 002), the MAH submitted the final results and final overall survival (OS) results of the C16010 China continuation study. This was a randomized, double-blind, placebo-controlled Phase 3 study conducted in China (N=115) comparing ixazomib plus lenalidomide and dexamethasone versus placebo plus lenalidomide and dexamethasone in patients with relapsed and/or refractory multiple myeloma, with a similar study design and eligibility criteria than the main C16010 study. Many of the patients enrolled in the study had advanced disease with Durie-Salmon Stage III (69%) at initial diagnosis and a treatment history of receiving at least 2 prior therapies (60%) and being thalidomide refractory (63%). At the primary analysis (median follow up of 8 months and a median of 6 cycles), the median progression free survival (PFS) was 6.7 months in the Ninlaro regimen

	new quality, preclinical, clinical or pharmacovigilance data				compared to 4 months in the placebo regimen (p-value=0.035, HR=0.60). At the final analysis for OS at a median follow up of 19.8 months, overall survival (OS) was improved for patients treated in the ixazomib regimen compared with placebo [p-value=0.0014, HR=0.42, 95% CI: 0.242, 0.726]). Based on the final results of the C16010 China continuation study, the pooled safety data from the pivotal studies global C16010 and C10610 China continuation studies have been reflected in section 4.8 'Undesirable effects' of the SmPC and the frequency of the adverse drug reactions 'Herpes zoster' was therefore updated from 'uncommon' to 'common' and 'vomiting' from common to uncommon.
IB/0001/G	This was an application for a group of variations. B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	05/01/2017	n/a		