Erivedge

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
N/0053	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/03/2023		PL	
PSUSA/10140 /202101	Periodic Safety Update EU Single assessment - vismodegib	02/09/2021	n/a		PRAC Recommendation - maintenance

[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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000

R/0050	Renewal of the marketing authorisation.	22/04/2021	01/07/2021	Annex II, Labelling and PL	
IA/0051/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 control/testing takes place	22/03/2021	n/a		
PSUSA/10140 /202001	Periodic Safety Update EU Single assessment - vismodegib	03/09/2020	n/a		PRAC Recommendation - maintenance
II/0046	Update of the Educational Materials provided as part of the Erivedge Pregnancy Prevention Program, following conclusion of PSUSA/00010140/201901. Annex IID is updated accordingly. Additionally, RMP v14.0 is submitted. Furthermore, section 4.4 of the SmPC is updated to remove the warning on cutaneous squamous cell carcinoma. The MAH also took the opportunity to update the Package Leaflet with the recommended wording on sodium content. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	03/09/2020	01/07/2021	SmPC, Annex II and PL	

IA/0049/G	This was an application for a group of variations. 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.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 exist per material) 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)	29/06/2020	n/a		
IA/0048	B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier	20/05/2020	n/a		

IB/0045/G	This was an application for a group of variations. 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 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.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.I.b.1.d - Change in the specification parameters	13/03/2020	n/a		

	and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation 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.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.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.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.c.z - Container closure system of the AS - Other variation B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol				
PSUSA/10140 /201901	Periodic Safety Update EU Single assessment - vismodegib	19/09/2019	11/11/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10140/201901.
IA/0043/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	13/03/2019	n/a		
IAIN/0042	C.I.12 - Inclusion or deletion of black symbol and explanatory statements for medicinal products in the list of medicinal products that are subject to additional monitoring	18/12/2018	11/11/2019	SmPC and PL	

PSUSA/10140 /201801	Periodic Safety Update EU Single assessment - vismodegib	20/09/2018	22/11/2018		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10140/201801.
IA/0041	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	09/08/2018	n/a		
II/0039/G	This was an application for a group of variations. C.I.4 Update of SmPC section 4.4 in order to update the special warnings and precautions for use on the effects of post-natal development and 4.8 in order to include a new adverse event (precocious puberty) observed in children in post marketing. C.I.11.z To submit the final study report for observational study ML28296 (post approval commitment MEA 18) and reflect the newly available information in the RMP which is updated to version 13.0. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some editorial changes in the product information and update the local representative for Malta. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing	12/07/2018	22/11/2018	SmPC and PL	Following two case events of precocious puberty listed in the Roche Safety Database from the Investigator-Sponsored Trial ML28353 in paediatric patients with medulloblastoma, the MAH prepared an assessment of precocious puberty in paediatric patients after the administration of Erivedge. Based upon the strength of evidence in the two cases, which is supported by a positive temporal association and a plausible mechanism, it is considered that precocious puberty is causally associated with vismodegib administration in paediatric patients and reported as new adverse drug reaction in section 4.8 of the SmPC with a frequency "not known". Due to the long drug elimination half-life, this may occur or progress after drug discontinuation. Section 4.4 of the SmPC on the effects on post-natal development is updated accordingly.

	authorisation, including the RMP - Other variation				
IG/0949/G	This was an application for a group of variations. 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)	04/06/2018	n/a		
T/0037	Transfer of Marketing Authorisation	20/02/2018	15/03/2018	SmPC, Labelling and PL	
IA/0036/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	20/12/2017	n/a		
IB/0035/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	04/12/2017	n/a		

	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
PSUSA/10140 /201701	Periodic Safety Update EU Single assessment - vismodegib	01/09/2017	n/a		PRAC Recommendation - maintenance
IB/0034	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	07/06/2017	n/a		
II/0032	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	21/04/2017	09/10/2017	SmPC and PL	
IB/0031/G	This was an application for a group of variations. B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a	30/11/2016	n/a		

	re-test period/storage period supported by real time data B.I.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation				
II/0025/G	This was an application for a group of variations. Update of sections 4.4, 4.6, 4.8 and 5.1 of the SmPC in order to update safety and efficacy information in the product information after finalisation of study MO25616 (SOB013). Considering the fulfilment of the specific obligations a marketing authorisation not subject to specific obligations is recommended to be granted instead of the conditional MA. Data from the same study also fulfilled the analysis required in MEA 005 regarding evaluation of the time for washout of vismodegib after treatment discontinuation and in MEA008 regarding reporting of adverse events. The Package Leaflet and the RMP (Version 10.1) are updated accordingly. Furthermore the Marketing authorisation holder (MAH) has taken the opportunity to update the RMP (version 10.1) based on the results from nonclinical studies assessed within variation EMEA/H/C/002602/II/21 and to propose deletion of hyponatraemia as an important potential risk in the RMP (version 10.1) and as an ADR in the EU Product Information as discussed in previous PSUR (EMEA/H/C/PSUSA/00010140/201407).	15/09/2016	14/11/2016	SmPC, Annex II and PL	Please refer to the published assessment report Erivedge-2602-II-0015/G.

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation				
IB/0030	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)	11/11/2016	09/10/2017	SmPC	
PSUSA/10140 /201601	Periodic Safety Update EU Single assessment - vismodegib	15/09/2016	11/11/2016	SmPC and Annex II	Please refer to Erivedge EMEA/H/C/PSUSA/00010140/201601 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation.
II/0029	Update of sections 4.2, 4.4 and 4.8 of the SmPC with additional information to describe the risk of epiphyses premature fusion in paediatric patients. The PL and RMP (new version v.11.0) have been updated accordingly. The MAH has also taken the opportunity to include an editorial change in section 5.2. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	15/09/2016	11/11/2016	SmPC and PL	Three cases of premature fusion in children 2-8 years have been identified in the reported data. A temporal pattern was suggestive of a causal relationship, and a more probable alternative explanation was lacking. Precocious puberty, a possible consequence of CNS tumors and radiation, was only described in one patient. Based on this data section 4.4 of the SmPC is updated to warn that premature fusion of the epiphyses has been reported in patients exposed to Erivedge. Due to the long drug elimination half-life, fusion may occur or progress after drug discontinuation. Section 4.8 is updated to add Epiphyses premature fusion as a new adverse event with a frequency category of unknown as it cannot be estimated

					from the available data. Section 4.2 is updated to remove that "no data are available" under the paediatric population sub-heading. The RMP is updated to upgrade the important risk on postnatal development from potential to identified since the risk of epiphyses premature fusion initially observed in animals has now been observed in patients.
IB/0028	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	14/06/2016	11/11/2016	SmPC, Labelling and PL	
R/0023	Renewal of the marketing authorisation.	01/04/2016	26/05/2016		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 Erivedge, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
IA/0026/G	This was an application for a group of variations. 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.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	26/04/2016	n/a		
IG/0667/G	This was an application for a group of variations.	08/04/2016	n/a		

	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.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 exist per material)				
II/0021	Update of sections 4.6 and 5.3 of the SmPC in order to update the information on vismodegib effects on fertility (MEA002). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	17/03/2016	26/05/2016	SmPC, Annex II, Labelling and PL	Human female fertility may be irreversibly compromised by treatment with Erivedge. Reversibility of fertility impairment is unknown. Fertility impairment in human males is not expected. In the dedicated 26-week vismodegib rat fertility study, the absolute weights of the seminal vesicles were significantly increased. After recovery, organ weights to the terminal body weight were also significantly increased for the epididymis, cauda epididymis, testes, seminal vesicles and prostate. No effects on male reproductive organs or on male fertility endpoints, including percent motile sperm, were observed at 100 mg/kg/day at the end of dosing or recovery phase (corresponding to 1.3-fold of the steady-state AUC0-24h at the recommended human dose). In addition, in the vismodegib general toxicity studies up to 26-week in sexually mature rats and dogs, no effects on

					male reproductive organs were observed. Increased number of degenerating germ cells and hypospermia in sexually immature dogs observed at ≥ 50 mg/kg/day in the 4-week general toxicity study was of undetermined relationship to vismodegib. In the dedicated 26-week vismodegib rat fertility study, vismodegib-related effects on female reproductive organs were observed at 100 mg/kg/day immediately after treatment discontinuation, including decreased implantations, increased percent preimplantation loss, and decreased number of dams with viable embryos. Similar findings were not observed after a 16 week recovery period. No correlative histopathologic changes were observed. The exposure in female rats at 100 mg/kg corresponds to 1.2-fold of the steady-state AUC0-24h at the recommended human dose. In addition, in the vismodegib general 26-week toxicity study, decreased number of corpora lutea was observed at 100 mg/kg/day; the effect was not reversed by the end of an 8 week recovery period.
PSUSA/10140 /201507	Periodic Safety Update EU Single assessment - vismodegib	11/02/2016	n/a		PRAC Recommendation - maintenance
IB/0022	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)	22/01/2016	26/05/2016	SmPC	
PSUSA/10140 /201501	Periodic Safety Update EU Single assessment - vismodegib	10/09/2015	n/a		PRAC Recommendation - maintenance

IG/0573	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	01/07/2015	n/a		
IAIN/0018	B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer	01/07/2015	n/a		
R/0016	Renewal of the marketing authorisation.	26/03/2015	27/05/2015	Annex II	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 Erivedge, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
II/0015/G	This was an application for a group of variations. 1. Following the review of the GP28465 study report, update of SmPC section 4.3 to delete the contraindication with St John's wort, 4.4 to delete warning regarding concomitant treatment with strong CYP inducers and 4.5 to update the effects of concomitant medicinal products on vismodegib. The PL was updated accordingly. In addition, the RMP has been updated to reflect the newly generated clinical pharmacology data. This variation fulfils MEA 004.	26/03/2015	05/05/2015	SmPC and PL	

	2. Following the review of the GP27839 study report as well as new clinical PK and PK modelling data generated since the initial marketing authorization, update of SmPC section 4.2 regarding the posology information for patients with hepatic and renal impairment and section 5.2 to reflect the new PK data generated in patients with hepatic and renal impairment. In addition the RMP has been updated to reflect the newly generated data in patients with hepatic and renal impairment. This variation fulfils MEA 007. 3. Submission of a summary document outlining new non-clinical, clinical PK data generated since the initial marketing authorization to complement the existing oral contraceptive drug-drug interaction data. This variation fulfils MEA 006. The requested group of variations proposed amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP). 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 C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				

PSUSA/10140 /201407	Periodic Safety Update EU Single assessment - vismodegib	12/02/2015	n/a		PRAC Recommendation - maintenance
II/0008	Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information from the pooled safety population, a final SHH4476g pivotal study and an interim analysis of study MO25616. The Annex II is being updated to delete the relevant specific obligation. 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	18/12/2014	05/05/2015	SmPC, Annex II and PL	In this variation the MAH updated frequencies of some side effects including dyspepsia (upset stomach or indigestion) rash, pain (in general) or pain in arms and legs from common to very common based on an analysis of the available safety information.
IA/0014/G	This was an application for a group of variations. B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products	26/11/2014	n/a		
IG/0497	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	18/11/2014	n/a		
IB/0010	B.I.d.1.a.4 - Stability of AS - Change in the re-test	15/10/2014	n/a		

	period/storage period - Extension or introduction of a re-test period/storage period supported by real time data				
IB/0011	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	08/10/2014	n/a		
PSUV/0007	Periodic Safety Update	11/09/2014	n/a		PRAC Recommendation - maintenance
IA/0009/G	This was an application for a group of variations. B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits 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 control/testing takes place B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	04/08/2014	n/a		

R/0006	Renewal of the marketing authorisation.	25/04/2014	19/06/2014		
II/0005	Update of section 4.5 of the SmPC further to the results of an in vitro study that evaluated whether vismodegib is a substrate for or an inhibitor of OATP1B1 and OATP1B3 (MEA 001). The Package Leaflet is updated accordingly. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	22/05/2014	05/05/2015	SmPC and PL	In vitro, vismodegib is an inhibitor of OATP1B1. It cannot be excluded that vismodegib may increase the exposure to substrates of OATP1B1, e.g. bosentan, glibenclamide, repaglinide, valsartan and statins. In particular, caution should be exercised if vismodegib is administered in combination with any statin.
PSUV/0004	Periodic Safety Update	06/03/2014	n/a		PRAC Recommendation - maintenance
IA/0002/G	This was an application for a group of variations. 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	11/11/2013	n/a		
IAIN/0001	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	18/09/2013	n/a		