Jevtana

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)	02/09/2024		PL	
IA/0052/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name	25/04/2024	n/a		

[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).

	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.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				
N/0051	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/06/2023	14/03/2024	PL	
IB/0050	B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation	12/04/2023	n/a		
II/0049	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	30/03/2023	14/03/2024	SmPC and PL	With the current variation the following main amendments have been introduced in the SmPC: Section 4.4. Men should use contraceptive measures during treatment and for 4 months after cessation of treatment with cabazitaxel. Section 4.6. Due to the genotoxic risk of cabazitaxel, men should use effective method of contraception during treatment and for 4 months after cessation of treatment with cabazitaxel. Cabazitaxel is not indicated for use in women. For more information, please refer to the Summary of Product Characteristics.
T/0048	Transfer of Marketing Authorisation	05/12/2022	10/01/2023	SmPC, Labelling and	

				PL	
PSUSA/476/202106	Periodic Safety Update EU Single assessment - cabazitaxel	24/02/2022	30/05/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/476/202106.
IA/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.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	04/05/2022	n/a		
N/0046	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/12/2021	24/02/2022	PL	
IB/0044/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 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.e - Change in test procedure for AS or	23/08/2021	n/a		

	starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate A.7 - Administrative change - Deletion of manufacturing sites				
II/0043/G	This was an application for a group of variations. Update of sections 4.8 and 5.1 of the SmPC with new clinical data from CARD study - a randomized, multicenter, Phase 4 study comparing cabazitaxel at 25 mg/m2 every 3 weeks in combination with prednisone versus alternate AR-targeted agent (abiraterone or enzalutamide) for the treatment of mCRPC patients previously treated with docetaxel and who failed a prior AR-targeted agent. Section 4.4 of the SmPC is also updated in accordance with the updated annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (SANTE-2017-11668) regarding ethanol used as an excipient. The Package Leaflet is updated accordingly. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/02/2021	24/02/2022	SmPC and PL	
R/0042	Renewal of the marketing authorisation.	15/10/2020	14/12/2020	PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of

					Jevtana in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
N/0041	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	01/08/2019	14/12/2020	PL	
PSUSA/476/201806	Periodic Safety Update EU Single assessment - cabazitaxel	17/01/2019	n/a		PRAC Recommendation - maintenance
N/0039	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/01/2018	14/12/2020	PL	
II/0038	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	14/12/2017	n/a		
II/0034	Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to add information from completed study EFC11785 (Randomized, open-label multicenter study comparing cabazitaxel at 20 mg/m2 and at 25 mg/m2 every 3 weeks in combination with prednisone for the treatment of metastatic castration-resistant prostate cancer previously treated with a docetaxel-containing regimen). In addition, the MAH is proposing to modify the wording in section 4.1 of the indication from "hormone refractory" to "castration resistant" prostate cancer to reflect current terminology of the disease in the clinical practice. The RMP is updated accordingly and in accordance with the request from the latest PSUR procedure	23/02/2017	03/04/2017	SmPC	In a non-inferiority, multicenter, multinational, randomized, open label phase III study (EFC11785 study), 1200 patients with metastatic castration resistant prostate cancer, previously treated with a docetaxel-containing regimen, were randomized to receive either cabazitaxel 25 mg/m2 (n=602) or 20 mg/m2 (n=598) dose. Overall survival (OS) was the primary efficacy end-point. The study met its primary objective of demonstrating the non-inferiority of cabazitaxel 20 mg/m2 in comparison with 25 mg/m2 (see table 4). A statistically significantly higher percentage (p<0.001) of patients showed a PSA response in the 25 mg/m2 group (42.9%) compared to the 20 mg/m2 group (29.5%). A statistically significantly higher risk of PSA progression in patients with the 20 mg/m2 dose with respect to the 25 mg/m2 dose was observed (HR

	(EMEA/C/H/002018/PSUSA/000476/201506) C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				1.195; 95%CI: 1.025 to 1.393). There was no statistically difference with regards to the other secondary endpoints (PFS, tumour and pain response, tumour and pain progression, and four subcategories of FACT-P). The safety profile of cabazitaxel 25 mg/m2 observed in study EFC11785 was qualitatively and quantitatively similar to that observed in the study EFC6193. Study EFC11785 demonstrated a better safety profile for the cabazitaxel 20 mg/m2 dose. If patients continue to experience any of the reported reactions at 20 mg/m2, further dose reduction to 15 mg/m2 or discontinuation of JEVTANA may be considered. Data in patients below the 20 mg/m2 dose are limited.
PSUSA/476/201606	Periodic Safety Update EU Single assessment - cabazitaxel	26/01/2017	24/03/2017	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/476/201606.
IA/0037/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	16/02/2017	n/a		
II/0035	Update of sections 4.2 and 5.1 of the SmPC in order to add information on study TED12689 a phase 1-2 dose finding, safety and efficacy study of cabazitaxel in pediatric patients with refractory solid tumors including tumors of the central nervous system.	15/12/2016	24/03/2017	SmPC	JEVTANA was evaluated in an open label, multi-center Phase 1/2 study conducted in a total of 39 paediatric patients (aged between 4 to18 years for the phase 1 part of the study and between 3 to 16 years for the phase 2 part of the study). The phase 2 part did not demonstrate

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				efficacy of cabazitaxel as single agent in paediatric population with recurrent or refractory diffuse intrinsic pontine glioma (DIPG) and high grade glioma (HGG) treated at 30 mg/m². There is no relevant use of JEVTANA in the paediatric population. The safety and the efficacy of JEVTANA in children and adolescents below 18 years of age have not been established.
IA/0033	A.7 - Administrative change - Deletion of manufacturing sites	25/05/2016	24/03/2017	Annex II and PL	
IB/0032/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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 B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised 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	03/05/2016	n/a		

PSUSA/476/201506	Periodic Safety Update EU Single assessment - cabazitaxel	28/01/2016	04/04/2016	SmPC and PL	Please refer to Jevtana EMEA/H/C/PSUSA/00000476/201506 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation.
R/0030	Renewal of the marketing authorisation.	24/09/2015	19/11/2015	SmPC, Annex II, Labelling and PL	Based on the review of the available information the CHMP is of the opinion that the quality, the safety and the efficacy of this medicinal product continues to be adequately and sufficiently demonstrated and therefore considers that the benefit/risk profile of Jevtana continues to be favourable. The CHMP considers that the safety profile of Jevtana and in particular the risk of neutropenia and its complications, the risk of bleeding and respiratory disorders, should continue to be closely monitored. Additional safety data have been requested and are being assessed as part of the PSURs. In addition, the post-marketing study EFC11785 comparing cabazitaxel dosage of 20 mg/m² versus 25 mg/m² in combination with prednisone for the treatment of metastatic castration resistant prostate cancer previously treated with a docetaxel-containing regimen is still ongoing and the results are expected to yield important new safety and efficacy data to optimise cabazitaxel dosage. Based on the assessment of the PSURs and the results of study EFC11785 the need for additional pharmacovigilance activities and/or risk minimisation measures will be reviewed. Therefore, considering the overall safety profile of Jevtana and the need for further data, an additional renewal is recommended.
II/0028	Update of sections 4.2, 4.3, 4.4 and 5.2 of the SmPC in order to add warnings and to update the safety information on the use of cabazitaxel in patients with hepatic impairment further to the results of the	21/05/2015	22/06/2015	SmPC and PL	Information regarding the use of cabazitaxel in patients with hepatic impairment has been included in the Product Information of Jevtana further to analysis of results from a

	POP6792 phase I safety and pharmacokinetic study of cabazitaxel in advanced solid tumor patients with varying degrees of hepatic impairment (MEA 015). The MAH also took the opportunity to update the local representative for Romania in the package leaflet. 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				phase I study on safety and pharmacokinetic data.
II/0029	Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update posology, safety and pharmacokinetic information on the use of cabazitaxel in patients with solid tumours and normal, moderately- and severely-impaired renal function based on the final study report of study POP12251; the RMP is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/04/2015	22/06/2015	SmPC	Pharmacological information on use of cabazitaxel in patients with solid tumours with moderately and severely impaired and with normal renal function have been updated in the Product information after analysis of data from study POP12251.
PSUV/0025	Periodic Safety Update	09/01/2015	n/a		PRAC Recommendation - maintenance
IB/0027	B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation	09/12/2014	n/a		
IB/0026/G	This was an application for a group of variations.	27/10/2014	n/a		

	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data 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				
PSUV/0023	Periodic Safety Update	24/07/2014	18/09/2014	SmPC	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUV/0023.
IG/0454	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	17/07/2014	n/a		
II/0022	Update of sections 2, 4.2, 6.5 and 6.6 of the SmPC in order to improve the readability of the information regarding Jevtana reconstitution as requested by PRAC further to the review of a signal of medication errors leading to cases of overdose. The labelling and package leaflet have been updated accordingly. In addition, the MAH took the opportunity of this variation to update the contact details of the local representatives listed in the PL. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	20/02/2014	18/09/2014	SmPC, Labelling and PL	Further to a reported signal of medication errors leading to overdose, the MAH reviewed the company Pharmacovigilance database which identified since launch of Jevtana, 28 cases of overdose, administration errors or medication errors reported worldwide. Among these 28 cases, 14 cases had a fatal outcome. Three cases were clearly associated with cabazitaxel, reported as either an overdose or an increased cabazitaxel dose administered. Following review of these cases, there is an indication that the overdose cases are due to errors in the reconstitution of the product. Therefore, the product information was updated in order to improve the description of the product's reconstitution process.
II/0021	Submission of the final study report for study	20/02/2014	n/a		Based on the results of study TCD11068 no definitive

	TCD11068 conducted to determine the relationship between allelic variants of drug metabolism enzymes/transporters and pharmacokinetic parameters. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				conclusion on the relationship between allelic variants of genes coding for CY3A4 enzyme and cabazitaxel disposition can be drawn. No changes to the product information were considered necessary.
II/0020	Update of sections 4.2, 4.4, 4.5 and 5.2 of the SmPC in order to include information regarding the effect of CYP3A inhibitors and inducers on Jevtana based on the results of study TCD10870 conducted to address MEA 014. The MAH also discussed the effect of P-gp inhibitor on cabazitaxel in this application (MEA 018). Furthermore, the PI is being brought in line with the latest QRD template version 9.0. The MAH also made minor editorial changes to the SmPC and PL. In addition, the MAH took the opportunity to 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	23/01/2014	18/09/2014	SmPC and PL	Cabazitaxel is metabolised in the liver mainly by the CYP3A isoenzyme. CYP3A inhibitors and CYP3A inducers may affect cabazitaxel's pharmacokinetics in vivo. Therefore, the MAH carried out a drug interaction study (TCD10870) to include the risk of interaction between cabazitaxel and a strong CYP3A4 inducer (rifampicin) as well as the interaction between cabazitaxel and a strong CYP3A4 inhibitor (ketoconazole) on the pharmacokinetics of cabazitaxel in cancer patients. Cabazitaxel AUC increases about 25% when administered concomitantly with ketoconazole, whereas with rifampicin, it decreases about 17%.Therefore the concomitant administration of strong inhibitors and inducers should be avoided.The safety studies showed that the co-administration of a P-gp inhibitor with cabazitaxel was not a risk factor for CNS toxicity.
PSUV/0019	Periodic Safety Update	09/01/2014	n/a		PRAC Recommendation - maintenance
IG/0314	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	08/07/2013	n/a		

II/0017	Update of sections 4.4 and 4.8 of the SmPC in order to add a warning regarding the risk of gastrointestinal disorders further to the PRAC assessment of PSUR 4. The Package Leaflet was updated accordingly. Furthermore, the MAH took the opportunity to update the list of local representatives in the Package Leaflet in order to include Croatia. In addition, the MAH introduced minor editorial changes and implemented the latest version of the QRD template (version 9). C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH	30/05/2013	13/12/2013	SmPC, Annex II, Labelling and PL	Further to the PRAC request, the MAH performed a cumulative review of gastrointestinal perforation and haemorrhage in the company safety database. The search retrieved a total of 75 cases, 37 of which were considered for the analysis. Based on the review of the cases, the CHMP considers that available evidence is sufficient to suggest a causal or contributory relationship between gastrointestinal disorders (GI bleeding and perforation, gastritis, enterocolitis, neutropenic enterocolitis, colitis, intestinal obstruction and ileus including fatal cases) and cabazitaxel. As a consequence, sections 4.4 and 4.8 of the SmPC were updated.
IB/0016/G	This was an application for a group of variations. 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 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 currently approved batch size B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other	13/12/2012	n/a		

	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 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.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised 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.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.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting				

	material/reagent/intermediate, if an alternative test procedure is already authorised B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised 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 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.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 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 currently approved batch size				

II/0015	Update of sections 4.5 and 5.2 of the SmPC in order to reflect the results of POP6792 study Cohort 5 using midazolam as a CYP3A probe in advanced solid tumour patients with normal hepatic function (FUM 015). The MAH took the opportunity of this variation to introduce minor editorial changes in the SmPC. Furthermore, the PI is being brought in line with the latest QRD template version 8.2. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	13/12/2012	13/12/2013	SmPC and Annex II	Study POP6792, a Phase 1 safety and PK study, was designed to evaluate cabazitaxel in patients with varying degrees of hepatic impairment (cohorts 1 to 4). Additionally a separate cohort (cohort 5) in patients with normal hepatic function was included to assess the potential for drug-drug interactions (DDI) using midazolam as a CYP3A probe. The combination of a single dose of cabazitaxel with a single dose of oral midazolam altered the plasma exposure of midazolam. However, these changes are not expected to be clinically relevant. Sections 4.5 and 5.2 of the SmPC were updated to reflect the new data.
IB/0014/G	This was an application for a group of variations. B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure	07/11/2012	n/a		

	(including replacement or addition)				
IA/0013	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	15/10/2012	n/a		
IA/0012	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	08/10/2012	29/10/2012	SmPC	
II/0004/G	This was an application for a group of variations. Update of sections 4.5 and 5.2 of the SmPC in order to include the risk of interactions with OATP1B1 substrates. The Package Leaflet was updated accordingly. The MAH took the opportunity to clarify the fill volume of the concentrate and solvent vials in the Product Information as requested by the EMA. Editorial changes were also implemented in the SmPC. In addition, the MAH updated the list of local representatives in the Package Leaflet. Furthermore, the PI was brought in line with the latest QRD template version 8.1. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	19/07/2012	10/09/2012	SmPC, Annex II, Labelling and PL	Results of the in vitro Study TRE0035 conducted to assess cabazitaxel as a substrate and an inhibitor of liver uptake transporters OCT1, OATP1B1 and 1B3, concluded that the risk of interaction with OATP1B1 transporter is possible (e.g statins). Sections 4.5 and 5.2 of the SmPC were updated accordingly. Results of Study TES10884 conducted to fulfil the commitment to investigate the effect of cabazitaxel on the QTc interval (and ECG) in cancer patients did not show a QT prolongation effect of cabazitaxel and did not support an impact of cabazitaxel on ventricular repolarisation. No change to the PI is justified for the time being.

T/0011	Transfer of Marketing Authorisation	16/05/2012	15/06/2012	SmPC, Labelling and PL	Transfer of Marketing Authorisation Holder from SANOFI to Sanofi-aventis groupe.
IB/0009	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	10/05/2012	n/a		
IA/0010	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	09/05/2012	n/a		
IB/0008/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.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	12/04/2012	n/a		
IB/0007	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	12/04/2012	n/a		
IG/0147/G	This was an application for a group of variations.	29/02/2012	n/a		

	C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure 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.f - Changes to an existing pharmacovigilance system as described in the DDPS - Deletion of topics covered by written procedure(s) describing pharmacovigilance activities C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system				
IAIN/0005	A.1 - Administrative change - Change in the name and/or address of the MAH	28/02/2012	14/05/2012	SmPC, Labelling and PL	
IB/0001	B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation	27/10/2011	14/05/2012	SmPC	
IA/0002/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.b.1 - Change to batch release arrangements	24/10/2011	n/a	Annex II and PL	

	and quality control testing of the FP - Not including batch control/testing				
IG/0091	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	05/07/2011	n/a		