Bosulif

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/0057	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	01/03/2024	n/a		
IAIN/0056	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	16/05/2023		SmPC 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).

IA/0055	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	09/11/2022	n/a		
IA/0054	B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold	13/10/2022	n/a		
II/0050/G	This was an application for a group of variations. (Type II) C.I.4 - Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to reflect results from studies B1871039 (specific obligation) and B1871040 (post-authorisation safety study); The Package Leaflet is updated accordingly. An updated RMP (version 6.0) has also been submitted. Update of Annex II to remove the specific obligation and conversion of the conditional marketing authorisation into a marketing authorisation not subject to specific obligations. Section 5.1 of the SmPC and Section 6 of the PL are updated accordingly to remove the reference to the conditional marketing authorisation. In addition, the SmPC was updated to reflect the deletion of the product from the list of medicines subject to additional monitoring. (Type IA) A.6 - Update of the ATC code in section 5.1 of the SmPC according to the new WHO classification. In addition, the MAH took the opportunity to update	27/01/2022	07/04/2022	SmPC, Annex II and PL	Please refer to Scientific Discussion 'Bosulif-H-C-002373-II-0050/G'

	the list of local representatives for Belgium, Luxemburg, Germany and Northern Ireland in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data A.6 - Administrative change - Change in ATC Code/ATC Vet Code C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
R/0051	Renewal of the marketing authorisation.	27/01/2022	31/03/2022		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the MA for Bosulif, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion. Furthermore, the CHMP confirmed the recommendation adopted in the parallel variation II/50G (EMEA/H/C/002373 /II/0050/G) to grant for Bosulif a Marketing Authorisation no longer subject to Specific Obligations.
IB/0053/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	15/03/2022	n/a		

	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.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation				
IA/0052	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	22/12/2021	n/a		
PSUSA/10073 /202103	Periodic Safety Update EU Single assessment - bosutinib	30/09/2021	n/a		PRAC Recommendation - maintenance
II/0048	Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update safety and efficacy information based on final results from study B18711053 (a recommendation of EMEA/H/C002373/II/25/G). This is an interventional safety and efficacy study covering submission of the long-term experience results secondary endpoints (duration of MMR and CCyR, EFS and OS). The Safety Data pool is also updated with results of interventional studies, B18711048 (final CSR submitted in variation II/41) and ongoing studies B18711039 and B18711040 (listed as category 3 studies in the RMP); the Package Leaflet is updated accordingly.	22/07/2021	31/03/2022	SmPC and PL	Efficacy and safety information have been updated in the product information upon available 60 months follow up data for the study B18711053. For more information, please refer to the Summary of Product Characteristics.

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
R/0045	Renewal of the marketing authorisation.	10/12/2020	11/02/2021		
PSUSA/10073 /202003	Periodic Safety Update EU Single assessment - bosutinib	15/10/2020	14/12/2020	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10073/202003.
IB/0047/G	This was an application for a group of variations. B.I.a.3.z - Change in batch size (including batch size ranges) of AS or intermediate - Other variation 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.c.2.b - Change in the specification parameters and/or limits of the immediate packaging of the AS - 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.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation 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	11/12/2020	n/a		

	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 B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - 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				
N/0046	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/11/2020	11/02/2021	PL	
II/0043	Update of section 5.3, of the SmPC in order to update non-clinical information following the final results from the six-month transgenic rasH2 mouse carcinogenicity study, listed as a category 3 in the current approved RMP version 4.5. ; The RMP version 5.0 has also been submitted. The MAH took the opportunity to implement changes resulting from the revision of the SmPC guideline on excipients, applied in the SmPC section 4.4 and in the Package Leaflet section 2. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	03/09/2020	14/12/2020	SmPC and PL	SmPC new text: 4.4 Special warning and precautions for use Dietary sodium This medicinal product contains less than 1 mmol sodium (23 mg) per 100 mg, 400 mg, or 500 mg tablet. Patients on low sodium diets should be informed that this product is essentially 'sodium-free'. 5.3 Preclinical safety data /…/ Carcinogenicity Bosutinib was not carcinogenic in the 2-year rat and 6-month rasH2 mouse carcinogenicity studies.

					The Package Leaflet (PL) is updated accordingly. For more information, please refer to the Summary of Product Characteristics.
IB/0044/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 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 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 B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	26/08/2020	n/a		

	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
II/0041	Update of sections 4.4 and 5.2 of the SmPC with additional safety and PK data from the recently completed Phase 2 study (B1871048) following a commitment within variation EMEA/H/C/002373/II/0036 and a pooled safety data analysis performed to assess the clinical impact of reduced clearance in Asian population. The MAH takes also the opportunity to make editorial changes on the Package Leaflet C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/07/2020	14/12/2020	SmPC and PL	SmPC new text According to population pharmacokinetic analyses, Asians had a lower clearance resulting in increased exposure. Therefore, these patients should be closely monitored for adverse reactions especially in case of dose escalation. No formal studies have been performed to assess the effects of Age, gender and race demographic factors. Population pharmacokinetic analyses in patients with Ph+ leukaemia or malignant solid tumour and in healthy subjects indicate that there are no clinically relevant effects of age, gender or body weight. Population pharmacokinetic analyses revealed that Asians had a 18% lower clearance corresponding to an approximately 25% increase in bosutinib exposure (AUC). For more information, please refer to the Summary of Product Characteristics.
R/0039	Renewal of the marketing authorisation.	12/12/2019	13/02/2020		
N/0040	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/11/2019	13/02/2020	PL	
PSUSA/10073 /201903	Periodic Safety Update EU Single assessment - bosutinib	03/10/2019	n/a		PRAC Recommendation - maintenance
II/0036	Submission of a population pharmacokinetic (popPK) analysis PMAR-884 that was conducted to fulfil a	18/07/2019	n/a		

	post-authorisation measure (PAM) requested by the CHMP as part of the assessment of Bosulif for the first-line treatment of chronic myelogenous leukaemia (CML) indication (variation EMEA/H/C/002373/II/0025/G). C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
II/0037	Update of sections 4.6 and 5.3 of the SmPC based on final results from An Oral (Gavage) Study of the Effects of PF-05208763 on Pre- and Postnatal Development, Including Maternal Function in Rats listed as a category 3 study in the RMP. The Package leaflet is updated accordingly. The updated RMP version 4.5 has also been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	16/05/2019	13/02/2020	SmPC and PL	Women of childbearing potential should be advised to use effective contraception during treatment with bosutinib and for at least 1 month after the last dose and to avoid becoming pregnant while receiving bosutinib. In a rat pre and postnatal development study, there were reduced number of pups born at ≥ 30 mg/kg/day, and increased incidence of total litter loss and decreased growth of offspring after birth occurred at 70 mg/kg/day. The dose at which no adverse development effects were observed (10 mg/kg/day) resulted in exposures equal to 1.3 times and 1.0 times human exposure resulting from the clinical dose of 400 mg and 500 mg, respectively (based on unbound AUC in the respective species).
R/0035	Renewal of the marketing authorisation.	13/12/2018	18/02/2019	SmPC, Annex II, Labelling and PL	
II/0030	Submission of an updated RMP (finally agreed version 4.4) in line with changes requested by the CHMP following variation II/25/G in fulfilment of REC 014; in addition, the MAH took the opportunity to	18/10/2018	18/02/2019	Annex II	

	extend the due date of the Specific Obligation (SOB) study of the conditional marketing authorisation. Annex II has been updated accordingly. 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				
PSUSA/10073 /201803	Periodic Safety Update EU Single assessment - bosutinib	04/10/2018	n/a		PRAC Recommendation - maintenance
IB/0033/G	This was an application for a group of variations. 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.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.b.4.z - Change in the batch size (including batch size ranges) of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	10/09/2018	n/a		
T/0032	Transfer of Marketing Authorisation	11/07/2018	02/08/2018	SmPC, Labelling and	

				PL	
IA/0034	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)	11/07/2018	n/a		
X/0026	Extension application to add a new strength of 400 mg film-coated tablets Annex I_2.(c) Change or addition of a new strength/potency	22/03/2018	22/05/2018	SmPC, Annex II, Labelling and PL	
II/0025/G	This was an application for a group of variations. Extension of Indication to include treatment of adult patients with newly diagnosed Philadelphia Chromosome positive (Ph+) Chronic Phase (CP) Chronic Myelogenous Leukaemia (CML) for Bosulif based on study AV001. In addition, the MAH updated the SmPC with safety and efficacy information from studies B1871006 and B1871008. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated accordingly. Moreover, the updated RMP version 4.1 was agreed during the procedure. Furthermore, the Annex IIIA is brought in line with the latest QRD template version 10. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/02/2018	23/04/2018	SmPC, Labelling and PL	Please refer to Scientific Discussion: Bosulif H-2373-II-25-G-AR

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IA/0029	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	05/04/2018	n/a		
II/0028	Update of section 5.2 of the SmPC following further analyses of the pharmacokinetic (PK) data from Study B1871044 that has been already submitted to the EMA previously. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	15/03/2018	22/05/2018	SmPC	Following administration of a single intravenous dose of 120 mg bosutinib to healthy subjects, bosutinib had a mean (% coefficient of variation [CV]) volume of distribution of 2,331 (32) L, suggesting that bosutinib is extensively distributed to extra vascular tissue. In healthy subjects given a single intravenous dose of 120 mg bosutinib, the mean (%CV) terminal elimination half life was 35.5 (24) hours, and the mean (%CV) clearance was 61.9 (26) L/h.
R/0027	Renewal of the marketing authorisation.	14/12/2017	08/02/2018	SmPC, 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 Bosulif, subject to the Specific Obligations and Conditions as laid down in Annex II

					to the opinion.
PSUSA/10073 /201703	Periodic Safety Update EU Single assessment - bosutinib	28/09/2017	n/a		PRAC Recommendation - maintenance
R/0023	Renewal of the marketing authorisation.	26/01/2017	24/03/2017	SmPC 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 Bosulif, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
PSUSA/10073 /201603	Periodic Safety Update EU Single assessment - bosutinib	13/10/2016	08/12/2016	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10073/201603.
IAIN/0021	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	11/05/2016	08/12/2016	SmPC and PL	
IB/0020	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	01/02/2016	n/a		
R/0019	Renewal of the marketing authorisation.	19/11/2015	07/01/2016		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 Bosulif, subject to the

					Specific Obligations and Conditions as laid down in Annex II to the Opinion.
PSUSA/10073 /201503	Periodic Safety Update EU Single assessment - bosutinib	24/09/2015	23/11/2015	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10073/201503.
II/0018	Update of section 5.2 of the SmPC in order to update the Pharmacokinetic properties information after analysis of final study report for study B1871044 (open label, randomised, 2-period crossover study to evaluate absolute bioavailability of bosutinib in healthy subjects) in fulfilment of MEA 005.2; in addition, the Marketing authorisation holder (MAH) took the opportunity to correct minor errors in the Package Leaflet, to combine the SmPC of the 100 mg and 500 mg presentations and to bring the PI in line with the latest QRD template version 9.1. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/10/2015	07/01/2016	SmPC, Annex II and PL	Following administration of a single dose of bosutinib (500 mg) with food in healthy subjects, the absolute bioavailability was 34%.
II/0014/G	This was an application for a group of variations. Update of section 4.5 of the SmPC in order to include further information related to concomitant use of Bosulif with CYP3A inhibitors based on the results of Study B1871041, and in order to reflect the results of Study B1871043 submitted to fulfil MEA 003.2 and undertaken to investigate the drug interaction potential with regard to bosutinib being a P-gp	23/07/2015	23/11/2015	SmPC and PL	In a study of 20 healthy subjects, in whom a single dose of 125 mg aprepitant (a moderate CYP3A inhibitor) was co administered with a single dose of 500 mg bosutinib under fed conditions, aprepitant increased bosutinib Cmax by 1.5-fold, and bosutinib AUC in plasma by 2.0-fold, as compared with administration of bosutinib alone. In a study of 27 healthy subjects, in whom a single dose of 500 mg bosutinib was co-administered with a single dose of 150 mg dabigatran etexilate mesylate (a P-glycoprotein (P-

	inhibitor. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and Package Leaflet. A revised RMP version 3.1 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.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				gp) substrate) under fed conditions, bosutinib did not increase Cmax or AUC of dabigatran in plasma, as compared with administration of dabigatran etexilate mesylate alone. The study results indicate that bosutinib does not exhibit clinically relevant P gp inhibitory effects.
N/0015	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/06/2015	23/11/2015	PL	
IB/0016/G	This was an application for a group of variations. 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.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	19/05/2015	n/a		
PSUSA/10073	Periodic Safety Update EU Single assessment -	12/03/2015	n/a		PRAC Recommendation - maintenance

/201409	bosutinib				
R/0010	Renewal of the marketing authorisation.	18/12/2014	26/02/2015		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 Marketing Authorisation for BOSULIF, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
IB/0011	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	13/01/2015	n/a		
IB/0013	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)	23/12/2014	23/11/2015	SmPC	
II/0008	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/10/2014	26/02/2015	SmPC	
PSUV/0007	Periodic Safety Update	09/10/2014	n/a		PRAC Recommendation - maintenance
IB/0009	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	18/08/2014	n/a		
II/0001	Update of sections 4.2, 4.4 and 5.2 of the SmPC further to the results of study B1871020 in patients	22/05/2014	23/06/2014	SmPC and PL	Based on population pharmacokinetic modelling, a daily dose of 400 mg in patients with moderate renal impairment

	with renal impairment conducted as a post-authorisation measure (MEA 006) and population pharmacokinetic modelling. The Package Leaflet is updated accordingly. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				and a daily dose of 300 mg in patients with severe renal impairment are predicted to result in a similar AUC to that seen in patients with normal renal function receiving 500 mg daily. Consequently, in patients with moderate renal impairment (CrCL 30 to 50 mL/min, calculated by the Cockroft-Gault formula), the recommended dose of bosutinib is 400 mg daily (see sections 4.4 and 5.2). In patients with severe renal impairment (CrCL <30 mL/min, calculated by the Cockroft-Gault formula), the recommended dose of bosutinib is 300 mg daily (see sections 4.4 and 5.2). Dose escalation to 500 mg once daily for patients with moderate renal impairment or to 400 mg once daily in patients with severe renal impairment may be considered in those who did not experience severe or persistent moderate adverse reactions, under any of the following circumstances. Long-term treatment with bosutinib may result in a clinically significant decline in renal function in CML patients. It is important that renal function is assessed prior to treatment initiation and closely monitored during therapy with bosutinib, with particular attention to those patients exhibiting risk factors for renal dysfunction, including concomitant use of medicinal products with potential for nephrotoxicity, such as diuretics, ACE inhibitors, angiotensin receptor blockers and nonsteroidal anti-inflammatory drugs (NSAIDs).
IB/0006	B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes	22/05/2014	23/06/2014	SmPC, Labelling and PL	

IB/0005	B.I.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation	13/05/2014	n/a		
PSUV/0003	Periodic Safety Update	10/04/2014	n/a		PRAC Recommendation - maintenance
R/0002	Renewal of the marketing authorisation.	21/11/2013	20/02/2014	SmPC, Annex II 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 Bosulif, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion. The product information has been updated in line with QRD template version 9. The details of the local representative in Croatia have been added in the package leaflet.