Biktarvy

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
II/0059	Update of sections 4.4, 4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC in order to update information on pregnancy and dosing recommendations with polyvalent cation-containing products for pregnant individuals based on final results from study GS-US-380-5310; A Phase 1b, Open-label study to Evaluate	27/06/2024		SmPC, Labelling and PL	A clinical study was conducted in HIV-1 infected virologically suppressed pregnant adults receiving Biktarvy from the second or third trimester through postpartum. All 32 adult participants who completed the study maintained viral suppression during pregnancy, at delivery, and through Week 18 postpartum. All 29 neonate participants

[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).

	the Pharmacokinetics (PK), Safety and Efficacy of B/F/TAF in HIV-1 infected, Virologically Suppressed, Pregnant Women in their Second and Third Trimesters; study GS-US-380-3909 and the Antiretroviral Pregnancy Registry. 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				had negative/nondetectable HIV-1 PCR results at birth and/or 4 to 8 weeks of age. Exposures of bictegravir, emtricitabine and tenofovir alafenamide were lower during pregnancy. Therefore, Biktarvy may be used during pregnancy if the potential benefit justifies the potential risk to the foetus. Moreover, viral load should all the more be monitored closely in accordance with established treatment guidelines. There were no new safety findings compared to the known safety profile of Biktarvy in HIV-1 infected adults. In pregnant individuals dosage adjustments are recommended for co-administration of polyvalent cation-containing antacids, oral medications or supplements. For more information, please refer to the Summary of Product Characteristics.
IG/1722/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.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	04/04/2024	n/a		
IB/0058	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	04/03/2024	n/a		

WS/2540	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	14/12/2023	n/a		
IG/1626/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 originally approved batch size 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	23/06/2023	n/a		
IB/0053	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)	28/04/2023	19/04/2024	SmPC and PL	
IA/0055	B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect	24/04/2023	n/a		

	the product information				
IA/0054	B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure	24/04/2023	n/a		
R/0052	Renewal of the marketing authorisation.	10/11/2022	10/01/2023	SmPC and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Biktarvy in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10695 /202202	Periodic Safety Update EU Single assessment - bictegravir / emtricitabine / tenofovir alafenamide	15/09/2022	21/11/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10695/202202.
X/0040/G	This was an application for a group of variations. Annex I_2.(c) Change or addition of a new strength/potency C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	15/09/2022	21/11/2022	SmPC, Labelling and PL	Please refer to scientific discussion Biktarvy-H-C-004449-X-0040-G.
WS/2315/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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.z - Changes in the manufacturing process of the AS - Other variation	10/11/2022	n/a		

	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation				
IB/0050/G	This was an application for a group of variations. B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	08/08/2022	n/a		
IA/0049	B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information	22/06/2022	n/a		
II/0047	Update of sections 4.8 and 5.1 of the SmPC in order to include efficacy and safety data for antiretroviral therapy (ART)-naive adults based on final results from interventional studies GS-US-380-1489 (A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of GS-9883/Emtricitabine/Tenofovir Alafenamide Versus Abacavir /Dolutegravir /Lamivudine in HIV-1 Infected, Antiretroviral Treatment-Naive Adults) and GS-US-380-1490 (A Phase 3, Randomized, Double-Blind Study to Evaluate the Safety and Efficacy of GS-9883/Emtricitabine/Tenofovir Alafenamide Versus	10/06/2022	21/11/2022	SmPC	Final efficacy and safety data from studies GS-US-380-1489 and GS-US-380-1490 in ART-naive adults through 96 weeks of open-label treatment on Biktarvy (BVY) following 144 weeks of a double-blinded phase (BVY vs ABC/DTG/3TC in study GS-US-380-1489 or BVY vs DTG+F/TAF in study GS-US-380-1490) were submitted. These 5-years BVY data for subjects treated with BVY at baseline (ART-naïve subjects) and 2-years BVY data for subjects who switched from ABC/DTG/3TC or from DTG+F/TAF to BVY at the end of the double-blinded phase (i.e. virologically-suppressed subjects with a DTG-based first line regimen) demonstrate that, overall, BVY is

	Dolutegravir + Emtricitabine/Tenofovir Alafenamide in HIV-1 Infected, Antiretroviral Treatment-Naïve Adults). In addition, the MAH took this opportunity to introduce some minor administrative updates. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				associated with a long-term efficacy, without resistance emerging concern. Of note, the population of this study (and therefore the current therapeutic indication of BVY) was mainly without INSTI, FTC and TAF resistance, thus these efficacy data of BVY may not be extrapolated for the treatment of subjects who already experienced virological failure. No new safety concern emerged since the previous assessment of the Week 144 data: the long-term safety data of BVY are consistent with its known safety profile, notably as regards the hepatic and renal effects. Sections 4.8 and 5.1 of the SmPC were updated to reflect the final results from GS-US-380-1489 and GS-US-380-1490 efficacy and safety studies. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10695 /202108	Periodic Safety Update EU Single assessment - bictegravir / emtricitabine / tenofovir alafenamide	10/03/2022	n/a		PRAC Recommendation - maintenance
IB/0046	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	20/12/2021	n/a		
IB/0043/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	14/12/2021	n/a		

	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				
IG/1456	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	08/11/2021	n/a		
PSUSA/10695 /202102	Periodic Safety Update EU Single assessment - bictegravir / emtricitabine / tenofovir alafenamide	02/09/2021	n/a		PRAC Recommendation - maintenance
IAIN/0042/G	This was an application for a group of variations. B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	01/09/2021	n/a		
IG/1412	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	28/07/2021	n/a		
WS/2030	This was an application for a variation following a worksharing procedure according to Article 20 of	20/05/2021	22/10/2021	SmPC and PL	

	Commission Regulation (EC) No 1234/2008. To update section 4.4 of the SmPC and section 2 of the PL with information regarding nephrotoxicity, in alignment with the outcome of procedure EMEA/H/C/PSUSA/00010575/201911 already approved for Vemlidy. In addition, the marketing authorisation holder has taken the opportunity to introduce minor editorial changes for Biktarvy and to align the PI of all four products to the latest QRD template (v. 10.2). C.I.3.z - 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 - Other variation				
IG/1399	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	18/05/2021	n/a		
IB/0036/G	This was an application for a group of variations. B.II.e.1.b.1 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Solid, semi-solid and non-sterile liquid pharmaceutical forms B.II.e.1.b.1 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Solid, semi-solid and non-sterile liquid	15/04/2021	22/10/2021	SmPC, Labelling and PL	

	pharmaceutical forms				
PSUSA/10695 /202008	Periodic Safety Update EU Single assessment - bictegravir / emtricitabine / tenofovir alafenamide	11/03/2021	n/a		PRAC Recommendation - maintenance
PSUSA/10695 /202002	Periodic Safety Update EU Single assessment - bictegravir / emtricitabine / tenofovir alafenamide	17/09/2020	18/11/2020	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10695/202002.
II/0034	Update of section 4.8 of the SmPC in order to add the Stevens-Johnson Syndrome (SJS) to the list of adverse drug reactions (ADRs) with frequency "rare" based on an internal cumulative safety review performed by the company and prompted by a spontaneous case report of a HIV patient who experienced SJS during treatment with Biktavry. 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	29/10/2020	22/10/2021	SmPC and PL	SmPC new text: The risk of Stevens-Johnson Syndrome (SJS) is added to the list of Undesirable effects of Biktarvy with a frequency of rare. This adverse reaction was identified through post-marketing surveillance for Biktarvy. For more information, please refer to the Summary of Product Characteristics.
II/0029	Update of sections 4.2, 4.4, 4.8 and 5.2 of the SmPC in order to update the efficacy and safety data in haemodialysis patients population based on week 48 interim results from study GS-US-292-182, "A Phase 3b Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Efficacy of E/C/F/TAF Fixed Dose Combination (FDC) in HIV-1 Infected Subjects on Chronic Hemodialysis". The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement minor	17/09/2020	28/10/2020	SmPC and PL	Based on week 48 interim results from study GS-US-292-182, no dose adjustment of Biktarvy is required in adult HIV-1 patients with end stage renal disease (estimated creatinine clearance < 15 mL/minute) who are receiving chronic haemodialysis. However, Biktarvy should generally be avoided and only be used in these patients if the potential benefits are considered to outweigh the potential risks. On days of haemodialysis, administer the daily dose of

	linguistic amendments and editorial changes to the product information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				Biktarvy after completion of haemodialysis treatment. In addition, initiation of Biktarvy should be avoided in patients with estimated creatinine clearance ≥15 mL/min and < 30 mL/min, or < 15 mL/min who are not receiving chronic haemodialysis, as the safety of Biktarvy has not been established in these populations. For more information, please refer to the Summary of Product Characteristics.
IG/1278	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	27/08/2020	n/a		
II/0032	Update of sections 4.2 and 4.8 of the SmPC in order to update the efficacy and safety data in HIV-1 infected subjects aged ≥ 65 years based on week 48 interim results from study GS-US-380-4449, "A Phase 3b, Multicenter, Open-Label Study to Evaluate Switching from an Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide Fixed-Dose Combination Regimen or a Tenofovir Disoproxil Fumarate Containing Regimen to Fixed-Dose Combination of Bictegravir /Emtricitabine/Tenofovir Alafenamide in Elderly, Virologically-Suppressed, HIV-1 Infected Subjects Aged ≥ 65 Years". C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	23/07/2020	28/10/2020	SmPC	The marketing authorisation holder (MAH) presented results from a study (GS-US-380-4449) to evaluate the potential benefits of switching from elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) or a tenofovir disoproxil fumarate (TDF)-containing regimen to Biktarvy in subjects aged ≥65 years. No efficacy or safety concerns were raised on this sub-population during the MA procedure for Biktarvy but the proportion of patients from this specific population was limited. The dedicated study GS-US-380-4449 in patients > 65 y/o submitted for this current application is mainly relevant to substantiate the safety in this sub-population. Based on this, the product information has been updated to reflect the efficacy and safety data in HIV-1 infected subjects aged ≥ 65 years based on this week 48 interim results from study GS-US-380-4449, showing a similar

	data				safety profile of Biktarvy in these subjects to that in younger adults. No new safety signal has emerged. In addition, the MAH took the opportunity to make some minor editorial changes to the PI, in section 5.1 of the SmPC. For more information, please refer to the Summary of Product Characteristics.
WS/1745	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	28/05/2020	28/10/2020	PL	
IG/1236	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	04/05/2020	n/a		
II/0027	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/02/2020	28/10/2020	SmPC and Annex II	
PSUSA/10695 /201908	Periodic Safety Update EU Single assessment - bictegravir / emtricitabine / tenofovir alafenamide	13/02/2020	n/a		PRAC Recommendation - maintenance
WS/1746	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	06/02/2020	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				
IB/0025	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)	04/12/2019	28/10/2020	SmPC	
IAIN/0024	B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site	22/10/2019	n/a		
PSUSA/10695 /201902	Periodic Safety Update EU Single assessment - bictegravir / emtricitabine / tenofovir alafenamide	05/09/2019	n/a		PRAC Recommendation - maintenance
IA/0022	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	30/08/2019	n/a		
II/0008/G	This was an application for a group of variations. Update of section 4.5 of the SmPC in order to remove the recommendation for caution when methadone is co-administered with Biktarvy, based on final results from study AD-141-2321, an in vitro assessment of human Cytochrome P450 inhibition potential of GS-943389 (the sulfate metabolite, M20, of bictegravir). The Package Leaflet is updated accordingly.	27/06/2019	21/10/2019	SmPC, Annex II and PL	

	In addition, the Marketing authorisation holder (MAH) took the opportunity to remove reference to boceprevir in sections 4.4 and 4.5 of the SmPC and in the Package Leaflet as it is no longer available in the EU; as well as to introduce some minor editorial corrections throughout the SmPC and the Package Leaflet. Submission of the final report from study AD-141-2322, an in vitro assessment of the inhibition potential of GS-943389 against human P-gp and BCRP transporters. 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				
IB/0021	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	20/06/2019	n/a		
IA/0020	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	24/05/2019	n/a		
IA/0019	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	24/05/2019	n/a		

	manufacturer of a novel excipient				
WS/1566	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of section 4.8 of the SmPC following a safety review by the MAH assessing the clinical evidence of a causal association between tenofovir alafenamide-containing products and two adverse events, angioedema and urticaria. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement minor linguistic amendments and editorial changes to the Odefsey and Vemlidy products information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	02/05/2019	21/10/2019	SmPC, Annex II, Labelling and PL	Based on post-marketing surveillance data, there is sufficient evidence to consider that a causal association between tenofovir alafenamide-containing products and two adverse events, angioedema and urticaria, with the frequency uncommon. The Product information is updated accordingly.
II/0011	Update of sections 4.8 and 5.1 of the SmPC in order to update the efficacy and safety information based on the pooling of 96-week data from two randomized, double-blind, active controlled studies GS-US-380-1489 and GS-US-380-1490 in HIV-1 infected, antiretroviral treatment-naïve adults receiving Biktarvy compared with each of the comparator treatment groups (i.e. pooled Biktarvy (BVY) vs abacavir /dolutegravir /lamivudine and pooled BVY vs dolutegravir + emtricitabine/tenofovir alafenamide).	26/04/2019	21/10/2019	SmPC and PL	The week 96 analysis of the ongoing, randomized, double-blind, active controlled studies GS-US-380-1489 and GS-US-380-1490 in HIV-1 infected, treatment-naïve adults, is in line with the week 48 data, and similar conclusions could be drawn. Biktarvy is non-inferior in achieving HIV 1 RNA < 50 copies/mL when compared to abacavir/dolutegravir/lamivudine and to dolutegravir+emtricitabine/tenofovir alafenamide, respectively. The trend in favour of the dolutegravir comparator arm in subjects with baseline HIV-1 RNA >

	In addition the Marketing authorisation holder (MAH) took the opportunity to introduce some minor linguistic amendments in the SmPC and the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				100,000 copies/mL or CD4 cell count < 200 cells/µl already identified at week 48 is still apparent at week 96. Those subgroup analyses have been updated with 96-week data. No subject in any group developed treatment-emergent resistance to study drugs. The safety profile of Biktarvy at Week 96 did not differ from that at Week 48, and overall remains similar to dolutegravir+emtricitabine/tenofovir alafenamide. No new safety findings have been identified. Based on 96-week data sections 4.8 and 5.1 of the SmPC have been updated accordingly.
IB/0014	B.I.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation	13/03/2019	n/a		
IB/0013	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	13/03/2019	n/a		
IAIN/0016	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	19/02/2019	n/a		
IA/0015	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)	15/02/2019	n/a		
PSUSA/10695	Periodic Safety Update EU Single assessment -	14/02/2019	n/a		PRAC Recommendation - maintenance

/201808	bictegravir / emtricitabine / tenofovir alafenamide				
IA/0012	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	30/01/2019	n/a		
IB/0010	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	30/01/2019	n/a		
IB/0003/G	This was an application for a group of variations. B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier	30/12/2018	n/a		
IA/0009/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.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	05/12/2018	n/a		

	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				
WS/1466/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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.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	29/11/2018	n/a		
IG/1001	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)	23/11/2018	n/a		

IB/0004/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.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	23/11/2018	n/a		
IG/0995	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	24/10/2018	21/10/2019	SmPC	
T/0001	Transfer of Marketing Authorisation	26/07/2018	23/08/2018	SmPC, Labelling and PL	