Juluca

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
WS/2751/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	31/10/2024	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).

	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 A.7 - Administrative change - Deletion of manufacturing sites 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 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.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.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				

WS/2620	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 4.6 of the SmPC in order to update information about the use of DTG-containing regimens in pregnancy and at conception based on final results from non-interventional Tsepamo study and the Eswatini Birth Outcomes Surveillance study. In addition, data from other cohort studies and pregnancy registries, including the APR, DOLOMITE-EPPICC (Study 208613) and DOLOMITE-NEAT-ID Network study (Study 208759) both listed as category 3 studies in the RMP; and the US Chart Review (Study 212976) as well as data from literature are included. DOLOMITE-EPPICC (Study 208613) is a non-interventional study to assess "real-world" maternal and foetal outcomes following DTG use during pregnancy and to describe patterns of DTG utilization; DOLOMITE NEAT ID Network Study (208759) is a non-interventional, multi-site observational study to define the safety and effectiveness of dolutegravir use in HIV positive pregnant women. In addition, the MAH took the opportunity to implement editorial changes to sections 4.4 and 4.5 of the SmPC. The package leaflet is updated accordingly. The RMP version 19.0 (Tivicay), version 23.1 (Triumeq), version 5.0 (Dovato) and version 8.0 (Juluca) have also been submitted.	31/10/2024		SmPC and PL	SmPC new text At the light of the updated information about the use of dolutegravir (DTG)-containing regimens in pregnancy and at conception based on final results from two large non-interventional studies (Tsepamo and Eswatini Birth Outcomes Surveillance studies), data from other cohort studies and pregnancy registries (including the Antiretroviral Pregnancy Registry (APR), final results from DOLOMITE-EPPICC and data from ongoing DOLOMITE-NEAT-ID Network study), the US Chart Review as well as data from literature, section 4.6 of the SmPC has been updated. The recommendation for use of these products during pregnancy has also been amended. The package leaflet has been updated accordingly. 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				
II/0059/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.4.z - Change in the batch size (including batch size ranges) of the finished 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.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.g.1.a - Introduction of a new design space or extension of an approved design space for the finished product - One or more unit operations in the manuf. process of the FP including the resulting IPCs and/or test procedures	25/07/2024	n/a		
IA/0058	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	03/05/2024	n/a		

II/0057/G	This was an application for a group of variations. Grouped application comprising two type II variations as follows: C.I.13: Submission of the final report from study 201636 (SWORD 1) listed as a category 3 study in the RMP. This is a phase III, randomized, multicenter, parallel-group, non-inferiority study evaluating the efficacy, safety, and tolerability of switching to dolutegravir plus rilpivirine from current INI-, NNRTI-, or PI-based antiretroviral regimen in HIV-1-infected adults who are virologically suppressed. C.I.13: Submission of the final report from study 201637 (SWORD 2) listed as a category 3 study in the RMP. This is a phase III, randomized, multicenter, parallel-group, non-inferiority study evaluating the efficacy, safety, and tolerability of switching to dolutegravir plus rilpivirine from current INI-, NNRTI-, or PI-based antiretroviral regimen in HIV-1-infected adults who are virologically suppressed. The RMP version 7.0 has also been submitted. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	18/04/2024	n/a		No SmPC changes have been done as a consequence of this procedure. The group of variations resulted in amendments to the Risk Management Plan. For more information, please refer to the Summary of Product Characteristics.

II/0054	Submission of the final report from non-interventional PASS study COMBINE-2 listed as a category 3 study in the RMP. This is a real-world evidence study to evaluate effectiveness of two drug regimen, antiretroviral therapy with integrase inhibitors plus a reverse transcriptase inhibitor. The RMP version 6.1 has also been submitted in order to remove the important identified risk of ''drug resistance''. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	30/11/2023	n/a		Update of the RMP to remove “drug resistance” as an important identified risk from the DTG/RPV EU after the submission of the final report from non-interventional PASS study COMBINE-2.
PSUSA/10689 /202305	Periodic Safety Update EU Single assessment - dolutegravir / rilpivirine	30/11/2023	n/a		PRAC Recommendation - maintenance
IG/1655/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.i - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS -	10/08/2023	n/a		

	Introduction of a new site of micronisation				
WS/2458	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	01/06/2023	n/a		
IB/0050	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	14/02/2023	n/a		
R/0049	Renewal of the marketing authorisation.	10/11/2022	12/01/2023	SmPC and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Juluca in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10689 /202205	Periodic Safety Update EU Single assessment - dolutegravir / rilpivirine	01/12/2022	n/a		PRAC Recommendation - maintenance
WS/2334	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 4.6 of the SmPC in order to update information on pregnancy and breast-feeding based on supporting published medical literature data on DolPHIN-1 (Dolutegravir in pregnant HIV mothers and their neonates, NCT02245022).	22/09/2022	12/01/2023	SmPC	Section 4.6. Pregnancy Dolutegravir crosses the placenta in humans. In pregnant women living with HIV, the median foetal umbilical cord concentration of dolutegravir was approximately 1.3-fold greater compared with the maternal peripheral plasma concentration. There is insufficient information on the effects of

	The requested worksharing procedure proposed amendments 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				dolutegravir on neonates. Breast-feeding A median dolutegravir breast milk to maternal plasma ratio of 0.033 has been shown. For more information, please refer to the Summary of Product Characteristics.
WS/2323	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of the final report from study 200336 listed as a category 3 study in the RMP. This is a prospective, interventional pharmacokinetic and safety study of DTG/ABC/3TC in pregnant women. The summary of objective of this PASS study is to investigate the use of DTG during pregnancy and address the safety concerns of pregnant/breastfeeding women. The RMP versions 18.0, 20.0 and 4.0 for Tivicay, Triumeq and Juluca, respectively, have also been submitted. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	01/09/2022	n/a		
WS/2268	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	01/09/2022	12/01/2023	SmPC and PL	To update section 4.8 of the SmPC and section 4 of the PL to include the ADR “weight increased” with a frequency “common”.

	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation				
IG/1531	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/08/2022	12/01/2023	SmPC and PL	
WS/2255	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	30/06/2022	n/a		
WS/2210	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Following the finalisation of procedure EMEA/H/C/WS1810 concerning submission of EuroSIDA (category 3 PASS) study, this Type II worksharing variation was proposed to address the removal of three important risks (Dolutegravir Hypersensitivity reactions, Hepatobiliary reactions and Serious rash) from all four dolutegravir-containing product EU-RMPs; Tivicay (dolutegravir), Triumeq (dolutegravir/abacavir/lamivudine), Dovato (dolutegravir/lamivudine) and Juluca (dolutegravir/rilpivirine) - i.e. deletion of safety concerns. In addition, the MAH took opportunity to propose a harmonisation of the risks across all four	10/03/2022	n/a		

	dolutegravir-containing product EU-RMPs and other minor updates (including study details and epidemiology data). The requested worksharing procedure proposed amendments to the Risk Management Plan (RMP). C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required				
IB/0042	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	24/02/2022	12/01/2023	SmPC and PL	Update of Section 4.8 of the SmPC and Section 4 of the PL with the ADR "panic attack" following PRAC recommendation issued during the PSUR (EMEA/H/C/PSUSA/00010689/202105) for dolutegravir / rilpivirine fixed dose combination
WS/2192	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 to add "completed suicide" to the list of adverse drug reactions (ADRs) with frequency "rare" in the dolutegravir (Tivicay), dolutegravir/ abacavir/lamivudine (Triumeq) and dolutegravir/lamivudine (Dovato) following the finalisation of PSUSA procedure EMEA/H/C/PSUSA/00010075/202101 (reporting period 17 Jan 2020 to 16 Jan 2021) based on reports of completed suicide from participants exposed to	10/02/2022	12/01/2023	SmPC and PL	

	dolutegravir containing regimen in ViiV Healthcare-sponsored clinical trials. As the changes impact all dolutegravir containing products, the MAH submitted a worksharing procedure to include Dolutegravir/Rilpivirine (Juluca) product in accordance with Article 20 (worksharing procedure) of Commission Regulation (EC) 1234/2008. The Package Leaflet is updated in section 4 with a rather identical wording. The proposed wording should be as follows (identical with the suggested wording by the MAH regarding Dovato (footnote instead of brackets for the explanatory wording is acceptable to be in line with already included footnote on suicidal ideation and suicide attempt), Triumeq and Juluca. Nevertheless, the wording in section 4 for Tivicay is not exactly the same as for the other three products and should be therefore adapted accordingly). Furthermore, it could be considered to add a statement for patients in section of the PL that they should consult their doctor especially if neuropsychiatric side effects occur, since only under this condition an adequate reaction by the HCPs (knowledge of the adverse effects) is possible. C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH				

PSUSA/10689 /202105	Periodic Safety Update EU Single assessment - dolutegravir / rilpivirine	02/12/2021	n/a		PRAC Recommendation - maintenance
IB/0037	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	23/08/2021	31/01/2022	SmPC and PL	
IG/1417	A.7 - Administrative change - Deletion of manufacturing sites	03/08/2021	n/a		
PSUSA/10689 /202011	Periodic Safety Update EU Single assessment - dolutegravir / rilpivirine	10/06/2021	n/a		PRAC Recommendation - maintenance
IB/0035	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	21/05/2021	31/01/2022	SmPC, Annex II, Labelling and PL	
IA/0036	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	07/04/2021	n/a		
IB/0034	B.II.z - Quality change - Finished product - Other variation	17/03/2021	n/a		
IG/1362	A.7 - Administrative change - Deletion of manufacturing sites	22/02/2021	n/a		
IG/1332	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP -	18/01/2021	n/a		

	Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing				
PSUSA/10689 /202005	Periodic Safety Update EU Single assessment - dolutegravir / rilpivirine	14/01/2021	n/a		PRAC Recommendation - maintenance
WS/1810	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of the final report from study EuroSIDA (Study 201177) listed as a category 3 study in the RMP. This is a prospective observational cohort study to monitor and compare the occurrence of hypersensitivity reaction and hepatotoxicity in patients receiving dolutegravir (with or without abacavir) and other integrase inhibitors (with or without abacavir). Update of section 4.8 of the SmPC of Triumeq and Tivicay to include elevated bilirubin levels in combination with increased transaminases in patients treated with DTG-containing regimens (data from EuroSIDA and 14 other clinical trials), classified as 'rare' (≥1/10,000 to <1/1,000) and labelled under the SOC "Hepatobiliary disorders". In addition, the MAH updated the Package Leaflet of Triumeq and Tivicay to include increase in bilirubin levels as rare side effect. Furthermore, in line with the SmPC guideline, all laboratory findings related to hepatitis / acute hepatic failure, i.e. including ALT and AST elevations	14/01/2021		SmPC and PL	Final results of study EuroSIDA (Study 201177), a prospective observational cohort study to monitor and compare the occurrence of hypersensitivity reaction and hepatotoxicity in patients receiving dolutegravir (with or without abacavir) and other integrase inhibitors (with or without abacavir) has been submitted. In addition to the data from EuroSIDA, the MAH submitted and 14 other clinical trials to establish the incidence of clinically relevant elevated bilirubin levels in combination with increased transaminases in patients treated with DTG-containing regimens For more details please refer to section 4.8 of the SmPC and section 4 of the PI.

	currently listed under the SOC "Investigations", were moved to the SOC "Hepatobiliary disorders" in section 4.8 of the SmPC of Triumeq and Tivicay. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
II/0027	Update of sections 4.8 and 5.1 of the SmPC in order to add new information on resistance in vivo and clinical efficacy, based on final results from studies 201636 (SWORD-1) and 201637 (SWORD-2): Phase III, Randomized, Multicenter, Parallel-Group, Non-Inferiority Studies Evaluating the Efficacy, Safety, and Tolerability of Switching to Dolutegravir plus Rilpivirine from Current INSTI-, NNRTI-, or PI-Based Antiretroviral Regimen in HIV-1-Infected Adults who are Virologically Suppressed. In addition, information regarding "Changes in laboratory biochemistries" with the Week 148 data are also updated. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	17/09/2020	04/02/2021	SmPC	SmPC new text: Information on resistance in vivo and clinical efficacy is updated based on final results (Week 148) from studies 201636 (SWORD-1) and 201637 (SWORD-2). In the subjects receiving dolutegravir plus rilpivirine who met confirmed virologic failure leading to withdrawal (CVW) through Week 148, no DTG resistance was observed at the virological withdrawal timepoint being the NNRTI-associated substitutions E138E/A and M230M/L detected in some of the subjects. The studies demonstrated that treatment with dolutegravir + rilpivirine (DTG + RPV) maintained efficacy in the studied population with good rates of viral suppression for up to 3 years. For more information, please refer to the Summary of Product Characteristics.
II/0016	Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the dolutegravir -containing regimens based on the interim analysis from the	23/07/2020	04/02/2021	SmPC	Section 4.6 of the SmPC of Tivicay, Triumeq, Juluca and Dovato (dolutegravir-based products) has been updated to include safety information regarding the occurrence of neural tube defects (NTDs) with dolutegravir (DTG)-

	Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegravir. The PL is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				containing regimens based on interim analysis from a birth outcomes surveillance study being conducted in Botswana (the Tsepamo study). This is an observational cohort study focusing on the safety of antiretroviral therapy during pregnancy and was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen. The assessment of the latest results (July 2020) from the study shows a small increase of neural tube defects; 7 cases in 3,591 deliveries (0.19%; 95% CI 0.09%, 0.40%) to mothers taking dolutegravir-containing regimens at the time of conception compared to 21 cases in 19,361 (0.11%: 95% CI 0.07%, 0.17%) women exposed to non-DTG regimens at the time of conception. The SmPC has been updated to include advice for women of childbearing potential to be counselled about the potential risk of NTD with DTG, including consideration of effective contraceptive measures. In addition, a recommendation to discuss the benefits and risks of continuing DTG versus switching to another antiretroviral regimen has been added in the case when a pregnancy is confirmed in the first trimester while on DTG.
WS/1806	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	02/07/2020	n/a		

IG/1238	A.1 - Administrative change - Change in the name and/or address of the MAH	17/06/2020	04/02/2021	SmPC, Labelling and PL	
PSUSA/10689 /201911	Periodic Safety Update EU Single assessment - dolutegravir / rilpivirine	11/06/2020	n/a		PRAC Recommendation - maintenance
WS/1762	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of sections 4.3 and 4.5 of the SmPC in order to add a new contraindication in relation to the co-administration of dolutegravir with medicinal products with narrow therapeutic windows that are substrates of organic cation transporter 2 (OCT2), including but not limited to fampridine (also known as dalfampridine).The Package Leaflet is updated accordingly. In addition, the products information have been updated to reflect the following changes: - remove the drug-drug interactions for products no longer authorised in the EU (boceprevir, dofetilide, nelfinavir) - remove the inverted triangle for additional monitoring for Dovato only. Editorial changes have been made to the product information. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflets. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	06/02/2020	01/04/2020	SmPC and PL	A new contraindication is added to the Product information for dolutegravir containing products namely dolutegravir (DTG; TIVICAY), dolutegravir/abacavir/lamivudine (DTG/ABC/3TC; TRIUMEQ), dolutegravir/rilpivirine fixed dose combination (DTG/RPV FDC; JULUCA), and dolutegravir/lamivudine (DTG/3TC; DOVATO), to warn of concurrent administration of dolutegravir with medicinal products with narrow therapeutic windows, that are substrates of OCT-2, including but not limited to fampridine (also known as dalfampridine). Fampridine is a substrate of OCT2 with a narrow therapeutic index and could show an increased risk of seizures at elevated concentrations. While the proposed interaction has not been formally investigated in a drug interaction study for dolutegravir, the contradiction is accepted given the information stated in the approved product labelling for fampridine, and the understanding of dolutegravir potential to inhibit OCT2. The SmPC section 4.3 and 4.5 and the PL have been updated accordingly.

	data				
WS/1738/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 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.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.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	20/02/2020	n/a		

	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.i - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new site of micronisation 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 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.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				
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)	14/02/2020	04/02/2021	SmPC	
WS/1729	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	13/02/2020	n/a		

	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation				
IAIN/0025	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	07/02/2020	n/a		
IA/0024	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)	31/01/2020	n/a		
IA/0019	B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits	19/12/2019	n/a		
PSUSA/10689 /201905	Periodic Safety Update EU Single assessment - dolutegravir / rilpivirine	28/11/2019	n/a		PRAC Recommendation - maintenance
WS/1685	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	14/11/2019	n/a		

PSUSA/10689 /201811	Periodic Safety Update EU Single assessment - dolutegravir / rilpivirine	14/06/2019	n/a		PRAC Recommendation - maintenance
WS/1572	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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)	16/05/2019	n/a		
WS/1580	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	11/04/2019	n/a		
IA/0013	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	27/02/2019	n/a		
T/0007	Transfer of Marketing Authorisation	21/11/2018	23/01/2019	SmPC, Labelling and PL	
IB/0009/G	This was an application for a group of variations.	11/01/2019	19/11/2019	SmPC and PL	

	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - 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				
IG/1032/G	This was an application for a group of variations. B.I.a.1.i - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new site of micronisation B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	18/12/2018	n/a		
IB/0008	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	29/11/2018	19/11/2019	SmPC	
IB/0006	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	18/10/2018	n/a		
IB/0005/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 B.I.a.1.z - Change in the manufacturer of AS or of a	18/09/2018	n/a		

	starting material/reagent/intermediate for AS - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation				
IB/0002/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 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	29/08/2018	n/a		
IA/0004/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	27/07/2018	n/a		

IA/0003	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	20/07/2018	n/a		
IA/0001/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.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	17/07/2018	n/a		