EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Epclusa

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/0071	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	07/08/2023		PL	
IB/0070	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)	21/04/2023		SmPC	

[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).

WS/2356	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	12/01/2023	n/a		
PSUSA/10524 /202206	Periodic Safety Update EU Single assessment - sofosbuvir / velpatasvir	12/01/2023	n/a		PRAC Recommendation - maintenance
IG/1572	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	30/11/2022	n/a		
WS/2222	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 B20-146 listed as a category 3 study in the RMP. This is a non-imposed joint post-authorisation safety study to evaluate the risk of de novo hepatocellular carcinoma in patients with compensated cirrhosis treated with direct-acting antivirals for chronic hepatitis C (HCC De Novo PASS). C.I.13 - Other variations not specifically covered	07/07/2022	n/a		

	elsewhere in this Annex which involve the submission of studies to the competent authority				
IB/0066	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	04/07/2022	n/a		
SW/0065	Post Authorisation Safety Study results - EMEA/H/C/PSR/J/0038 – Variation	24/03/2022	19/05/2022	SmPC, Annex II and PL	The observational study and the systematic review/ meta-analysis did not show an increased risk of hepatocellular carcinoma recurrence in patients treated with direct-acting antivirals. The DAA-PASS study commitment is considered fulfilled and the respective products should be removed from the list of medicines under additional monitoring.
PSUSA/10524 /202106	Periodic Safety Update EU Single assessment - sofosbuvir / velpatasvir	13/01/2022	n/a		PRAC Recommendation - maintenance
X/0056/G	This was an application for a group of variations. Annex I_2.(d) Change or addition of a new pharmaceutical form C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one Annex I_2.(c) Change or addition of a new strength/potency	11/11/2021	07/01/2022	SmPC, Labelling and PL	
WS/2157	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing	30/09/2021	07/01/2022	Annex II	

	authorisation, including the RMP - Other variation				
IG/1415	A.7 - Administrative change - Deletion of manufacturing sites	05/08/2021	n/a		
WS/2086	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	08/07/2021	07/01/2022	SmPC, Annex II, Labelling and PL	
IG/1387	B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure	18/05/2021	n/a		
IA/0057/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process 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)	13/04/2021	n/a		
IG/1381	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	06/04/2021	n/a		

	manufacturer of a novel excipient				
R/0054	Renewal of the marketing authorisation.	28/01/2021	22/03/2021	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Epclusa in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10524 /202006	Periodic Safety Update EU Single assessment - sofosbuvir / velpatasvir	14/01/2021	n/a		PRAC Recommendation - maintenance
IB/0055/G	This was an application for a group of variations. B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	29/10/2020	n/a		
WS/1915	This was an application for a variation following a worksharing procedure according to Article 20 of	29/10/2020	n/a		

	Commission Regulation (EC) No 1234/2008. Submission of the final report from study GS-US-248-0123, listed as a category 3 study in the RMP. This is a long-term observational follow-up registry of subjects who did not achieve sustained virologic response in Gilead-sponsored trials in subjects with chronic hepatitis C infection. The RMPs have also been submitted for each of the products in this work-sharing procedure (Harvoni v8.0, Epclusa v7.0 and Vosevi v4.0). C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
IG/1294	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)	01/10/2020	n/a		
X/0043/G	This was an application for a group of variations. Extension application to introduce a new strength (200/50 mg film-coated tablets). The new presentation is indicated for the treatment of chronic hepatitis C virus (HCV) infection in patients aged 6 years and older and weighing at least 17 kg. The extension application is grouped with a type II variation (C.I.6.a) to include paediatric use in	25/06/2020	25/08/2020	SmPC, Labelling and PL	

	patients aged 6 years and older and weighing at least 17 kg. Sections 4.2, 4.8, 5.1 and 5.2 of the SmPC and the Package Leaflet are updated to support the extended indication. The RMP (version 6.0) is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial updates throughout the Product Information. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one Annex I_2.(c) Change or addition of a new strength/potency				
IG/1275	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	18/08/2020	n/a		
II/0049/G	This was an application for a group of variations. B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change	16/07/2020	n/a		

	outside the approved specifications limits range B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure				
IG/1247	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)	08/05/2020	n/a		
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 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	30/04/2020	n/a		

	intermediate used in the manufacture of the AS or manufacturer of a novel excipient				
IG/1233	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	10/04/2020	n/a		
IB/0045	B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)	08/04/2020	n/a		
PSUSA/10524 /201906	Periodic Safety Update EU Single assessment - sofosbuvir / velpatasvir	30/01/2020	24/03/2020	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10524/201906.
WS/1701	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 in order to add new safety information on rash and angioedema following a cumulative review of hypersensitivity with Epclusa and Vosevi, prompted by routine pharmacovigilance and signal detection activities. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes throughout the Product Information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	16/01/2020	24/03/2020	SmPC, Annex II, Labelling and PL	The CHMP considered that "rash" should be added to the Product Information as an adverse drug reaction with the frequency "common" (i.e. may affect up to 1 in 10 people) and "angioedema" as an adverse drug reaction with the frequency "uncommon" (i.e. may affect up to 1 in 100 people).

IB/0044	B.II.b.4.z - Change in the batch size (including batch size ranges) of the finished product - Other variation	20/12/2019	n/a		
WS/1518	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 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC (Epclusa, Harvoni, Sovaldi) and 4.2, 4.4, 4.8 and 5.2 (Vosevi) in order to add new information regarding the use of the sofosbuvir-containing products in patients with renal impairment, based on final results from studies GS-US-342-4062, GS-US-337-4063 and GS-US-334-0154, listed as a category 3 study in the RMP and study GS-US-338-1125. Study GS-US-342-4062 was a phase 2, multi-centre, open-label study to evaluate the efficacy and safety of sofosbuvir/velpatasvir for 12 Weeks in subjects with chronic HCV infection who are on dialysis for end stage renal disease. Study GS-US-337-4063 was a phase 2, multi-centre, open-label study to evaluate the efficacy and safety of ledipasvir/sofosbuvir in subjects with genotype 1, 4, 5 and 6 chronic HCV infection who are on dialysis for end stage renal disease. Study GS-US-334-0154 was a phase 2b, open label study of 200 mg or 400 mg Sofosbuvir+ribavirin for 24 Weeks in Genotype 1 or 3 HCV infected subjects with renal insufficiency. Study GS-US-338-1125 was a phase 1, open-label,	19/09/2019	21/10/2019	SmPC and PL	Sofosbuvir in a fixed dose combination with ledipasvir was administered for 12 weeks to 18 patients with genotype 1 chronic hepatitis C and severe renal impairment in an open-label study (Study 0154). The safety of sofosbuvir in a fixed dose combination with either ledipasvir or velpatasvir has been studied in 154 patients with ESRD requiring dialysis (Study 4062 and Study 4063). In this setting, exposure of sofosbuvir metabolite GS-331007 is 20-fold increased, exceeding levels where adverse reactions have been observed in preclinical trials. In this limited clinical safety data set, the rate of adverse events and deaths was not clearly elevated from what is expected in ESRD patients. The CHMP considered that safety data on the use of the sofosbuvir-based products in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m2) and end stage renal disease (ESRD) requiring haemodialysis are limited. Overall, the CHMP concluded that the sofosbuvir-based products can be used in these patients with no dose adjustment when no other relevant treatment options are available.

	parallel-group, single-dose study to evaluate the pharmacokinetics of voxilaprevir in subjects with normal renal function and severe renal impairment. The Package Leaflet is updated accordingly. The RMPs have also been submitted for each of the products in this work-sharing procedure. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0042	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	08/10/2019	n/a		
PSUSA/10524 /201812	Periodic Safety Update EU Single assessment - sofosbuvir / velpatasvir	25/07/2019	23/09/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10524/201812.
WS/1613	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 4.5 of the SmPC in order to add new information regarding co-administration with atorvastatin, based on final results from study GS-US-342-4034. Study GS-US-342-4034 was a phase 1 study to evaluate the effect of sofosbuvir/velpatasvir fixed dose combination on the pharmacokinetics of atorvastatin. In addition, the Worksharing Applicant took the	25/07/2019	23/09/2019	SmPC, Annex II and PL	Based on the results of study GS-US-342-4034, the CHMP concluded that no dose adjustments are needed during co-administration of Epclusa (sofosbuvir/velpatasvir) and atorvastatin (40 mg single dose). Furthermore, based on co-administration of Epclusa (sofosbuvir/velpatasvir) and atorvastatin and earlier experience with co-administration of Vosevi (sofosbuvir/velpatasvir/voxilaprevir) and other statins, the CHMP concluded that atorvastatin may be administered with Vosevi at a dose that does not exceed atorvastatin 20 mg.

	opportunity to amend Annex II of the Product Information with regards to the due date for submission of study DAA-PASS. This study is designed to evaluate the recurrence of hepatocellular carcinoma and the date has been postponed from Q2 2021 to Q2 2023. Furthermore, the MAH implemented minor editorial updates throughout the Product Information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
WS/1523	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 4.4 and 4.5 of the SmPC in order implement new information on the use of sofosbuvir-based therapy with concomitant drugs, based on final results from study GS-US-334-2130. This was a phase I study to evaluate the effects of cytochrome P450 and drug transporter inducers on sofosbuvir and probe drug pharmacokinetics in healthy subjects. Furthermore, section 4.3 of the Sovaldi SmPC was updated in order to remove the use of rifabutin as a contraindication. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to introduce minor editorial changes throughout the Product Information.	04/07/2019	23/09/2019	SmPC and PL	Based on results from study GS-US-334-2130, effects of rifabutin and carbamazepine administration on the drug levels of sofosbuvir have been updated throughout the Product Information. With regards to the rifabutin interaction, a 28% reduction in sofosbuvir exposure was observed. Considering that reduction in sofosbuvir dose of <50% is expected to be safe in terms of potentially reduced efficacy, the CHMP concluded that the data support removal of co-administration of rifabutin as contraindication from the Sovaldi (sofosbuvir) Product Information. The contraindication is maintained for Epclusa, Harvoni and Vosevi, given the lack of data on interactions with the other active substances contained in these combination products. The data available for interactions with carbamazepine indicated that sofosbuvir levels were reduced by 48%, but the confidence interval included the 50% value. Therefore, the CHMP considered that a cautionary approach should be

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				taken and contraindication concerning co-administration of carbamazepine should be retained. Furthermore, the term "potent P-glycoprotein inducers" was replaced by "strong P-glycoprotein inducers" throughout the Product Information in line with terminology used in the EMA Guideline on the investigation of drug interactions.
IB/0038	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)	25/04/2019	20/05/2019	SmPC	
IG/1057	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)	01/03/2019	n/a		
IG/1069	C.I.3.a - 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 - Implementation of wording agreed by the competent authority	28/02/2019	20/05/2019	SmPC and PL	
IB/0032/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	29/01/2019	n/a		

	arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place				
PSUSA/10524 /201806	Periodic Safety Update EU Single assessment - sofosbuvir / velpatasvir	17/01/2019	n/a		PRAC Recommendation - maintenance
IG/1037	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/12/2018	20/05/2019	SmPC and PL	
WS/1476	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 GS-US-334-0154, listed as a category 3 study in the RMP. This is a phase 2b randomized, open-label study of 200mg or 400mg sofosbuvir + ribavirin for 24 Weeks in genotype 1 or 3 HCV-infected subjects with renal insufficiency. The RMPs have also been submitted for each of the products in this work-sharing procedure. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	29/11/2018	n/a		
PSUSA/10524	Periodic Safety Update EU Single assessment -	12/07/2018	n/a		PRAC Recommendation - maintenance

/201712	sofosbuvir / velpatasvir				
WS/1391	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 5.3 of the SmPC based on data from a 2-year rat carcinogenicity study TX-281-2030. In addition, the MAH took the opportunity to update the ATC code in line with the new classification of antivirals for treatment of HCV infections and to introduce minor linguistic amendments and typographical corrections throughout the Product Information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/06/2018	20/05/2019	SmPC and PL	Velpatasvir was not carcinogenic in the 2-year rat carcinogenicity study at exposures at least 5-times higher than human exposure.
T/0027	Transfer of Marketing Authorisation	25/04/2018	28/05/2018	SmPC, Labelling and PL	
IG/0901	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	26/03/2018	n/a		
IB/0023	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)	13/02/2018	28/05/2018	SmPC	

WS/1328/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.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	08/02/2018	n/a		
WS/1272	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation	18/01/2018	n/a		
PSUSA/10524 /201706	Periodic Safety Update EU Single assessment - sofosbuvir / velpatasvir	11/01/2018	n/a		PRAC Recommendation - maintenance
IB/0022/G	This was an application for a group of variations. B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.f.1.e - Stability of FP - Change to an approved stability protocol	09/01/2018	n/a		

IB/0019	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	15/12/2017	n/a		
WS/1246/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.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation	30/11/2017	n/a		
IG/0848/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	12/10/2017	n/a		
IG/0840/G	This was an application for a group of variations.	22/09/2017	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 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.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS 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.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS 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 specification limits				

II/0012	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/09/2017	30/10/2017	SmPC	Velpatasvir was not carcinogenic in the 6-month rasH2 transgenic mouse study at exposures at least 50 times higher than human exposure. A carcinogenicity study in rats is ongoing.
IB/0014	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	15/08/2017	n/a		
IB/0013	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	20/07/2017	n/a		
PSUSA/10524 /201612	Periodic Safety Update EU Single assessment - sofosbuvir / velpatasvir	06/07/2017	n/a		PRAC Recommendation - maintenance
IB/0011/G	This was an application for a group of variations. A.6 - Administrative change - Change in ATC Code/ATC Vet Code C.I.1.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a Union referral procedure - The product is not covered by the defined scope of the procedure but the change(s) implements the outcome of the procedure and no new additional data is required to be submitted by the MAH	25/05/2017	30/10/2017	SmPC, Annex II and PL	
IAIN/0010/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	18/04/2017	n/a		

	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				
WS/1075	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	23/03/2017	n/a		
II/0003	Update of section 5.1 of the SmPC in order to reflect on emerging clinical data from study GS-US-342-1202 investigating efficacy and safety in subjects with chronic hepatitis C virus (HCV) and human immunodeficiency virus (HIV)-1 coinfection. In addition, minor editorial changes are implemented throughout the Product Information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/02/2017	30/10/2017	SmPC and PL	The CHMP, having reviewed the results from the clinical study GS-US-342-1202, considered that section 5.1 of the SmPC should be updated with regards to the newly available data regarding patients with chronic hepatitis C and HIV co-infections. No updates to the Package Leaflet were considered necessary based on these data. An editorial update was implemented in section 2 of the Package Leaflet to align it with the existing information in the SmPC that Epclusa should be taken with food 4 hours before using a proton pump inhibitor.
WS/1104	This was an application for a variation following a worksharing procedure according to Article 20 of	16/02/2017	n/a		

	Commission Regulation (EC) No 1234/2008. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
IG/0748	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	28/11/2016	30/10/2017	SmPC and PL	
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 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.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	17/11/2016	n/a		
WS/1035/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.f - Change in the manufacturer of AS or of a	10/11/2016	n/a		

	starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.z - Change in the manufacturer of AS or of 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/0001	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	19/09/2016	n/a		