Maviret

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/0055	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)	02/03/2023		SmPC	
PSUSA/10620 /202207	Periodic Safety Update EU Single assessment - glecaprevir / pibrentasvir	09/02/2023	n/a		PRAC Recommendation - maintenance

[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).

IB/0054	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	18/01/2023	n/a		
N/0052	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/08/2022		PL	
WS/2216	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 elsewhere in this Annex which involve the submission of studies to the competent authority	07/07/2022	n/a		
IB/0051/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.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	06/07/2022		SmPC	

SW/0050	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.
R/0048	Renewal of the marketing authorisation.	27/01/2022	22/03/2022	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Maviret in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10620 /202107	Periodic Safety Update EU Single assessment - glecaprevir / pibrentasvir	10/02/2022	n/a		PRAC Recommendation - maintenance
IB/0046	B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation	17/09/2021	n/a		
IA/0045/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	20/08/2021	n/a		
IB/0044	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing	19/08/2021	22/03/2022	Annex II	

	authorisation, including the RMP - Other variation				
IB/0043/G	This was an application for a group of variations. B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes B.II.e.5.b - Change in pack size of the finished product - Deletion of a pack size(s)	05/08/2021	22/03/2022	SmPC, Labelling and PL	
IB/0042/G	This was an application for a group of variations. B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process 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.h - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition or replacement (excl. Biol. or immunol. substance) of a specification parameter as a result of a safety or quality issue 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.a.1.a - Change in the manufacturer of AS or of a	22/06/2021	n/a		

	starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer				
X/0033/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	22/04/2021	21/06/2021	SmPC, Annex II, Labelling and PL	Please refer to the Scientific Discussion Maviret-H-C-4430-X-33.
IB/0041/G	This was an application for a group of variations. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - 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 C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	29/03/2021	n/a		
II/0039	Update of section 5.1 of the SmPC based on results from study M13-576; a non-drug interventional follow-up study to assess resistance and durability of response to AbbVie direct-acting antiviral agent (DAA) therapy (ABT-493 and/or ABT-530) in subjects who participated in Phase 2 or 3 clinical studies for	25/03/2021	21/06/2021	SmPC	SmPC new text 5.1 Pharmacodynamic properties […] Durability of Sustained Virologic Response In a long-term follow-up study (M13-576), 99.5% (374/376) of adult subjects who had achieved SVR12 in

	the treatment of chronic hepatitis C Virus (HCV) infection. The study is included as a category 3 study in the RMP, and an updated RMP version 6.0 has also been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				prior clinical studies of Maviret maintained SVR up to their last follow-up visit (median duration of follow up: 35.5 months): 100%, 99.6%, and 95.8% of subjects who had received 8, 12, and 16 weeks of Maviret therapy, respectively. Among the 2 subjects who did not maintain SVR, 1 experienced a late relapse 390 days after Maviret therapy, and the other subject experienced re-infection with a different HCV genotype. […] For more information, please refer to the Summary of Product Characteristics.
PSUSA/10620 /202007	Periodic Safety Update EU Single assessment - glecaprevir / pibrentasvir	11/02/2021	n/a		PRAC Recommendation - maintenance
II/0037	Submission of the final clinical study report from study B16-439 (Phase 3b, a Multi-Center, Randomized, Open-Label, Pragmatic Study of Glecaprevir/Pibrentasvir (G/P) +/- Ribavirin for GT1 Subjects with Chronic Hepatitis C Previously Treated with an NS5A Inhibitor + Sofosbuvir Therapy). As part of the assessment, it has been requested by the CHMP to update the SmPC with resistance data from study B16-439; section 5.1 has been updated accordingly. In addition, a minor update was included to SmPC section 4.4, to include reference to study B16-439. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	14/01/2021	16/04/2021	SmPC	Thirteen of the 177 subjects with chronic HCV GT1 infection (all virologic failures had GT1a infection) who were treatment experienced with NS5A inhibitor + SOF treated with Maviret in study B16-439 for 12 weeks (9 out of 13) or 16 weeks (4 out of 13) experienced virologic failure. Among the 13 virologic failures, treatment-emergent NS3 substitutions were observed in 4 subjects at the time of failure: A156V (n = 2) or R155W + A156G (n = 2); 3 of these 4 subjects also had Q80K at baseline and at the time of failure. Twelve of 13 virologic failures had one or more NS5A polymorphisms detected at signature amino acid positions (M28V/T, Q30E/H/N/R, L31M/V, H58D, E62D/Q, or Y93H/N) at baseline, and 10 of 13 developed additional NS5A substitutions (M28A/S/T (n = 3), Q30N (n = 1), L31M/V (n = 2), P32del (n = 1), H58D (n = 4), E62D (n = 1)) at time of treatment failure.

					For more information, please refer to the Summary of Product Characteristics.
IA/0036	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	24/06/2020	n/a		
II/0027	Update of Section 4.8 of the SmPC to add angioedema as an adverse reaction with frequency 'uncommon', based on data from the submitted final clinical study report from study M16-133, a phase 3b, single Arm, open label, multicenter study aimed to evaluate the efficacy and safety of glecaprevir (GLE)/pibrentasvir (PIB) in treatment of naïve adults with chronic Hepatitis C Virus (HCV) Genotypes 1 – 6 infection and aspartate aminotransferase to platelet ratio index (APRI) ≤ 1. The Package Leaflet is updated accordingly. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to update Annex II with regards to PSUR requirements and correct an error in the SmPC. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	30/04/2020	16/04/2021	SmPC, Annex II and PL	
IA/0035	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	10/04/2020	n/a		
IA/0034	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test	27/03/2020	n/a		

	procedure				
IAIN/0032/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 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.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.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new	06/03/2020	n/a		

	specification parameter to the specification with its corresponding test method B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS				
II/0029	Update of sections 4.2 and 5.1 of the Maviret SmPC to shorten the treatment duration in treatment-naïve subjects with compensated cirrhosis and HCV GT3 infection, from 12 to 8 weeks, based on second interim results from study M16-135: A Single Arm, Open-Label Study to Evaluate the Efficacy and Safety of Glecaprevir (GLE)/Pibrentasvir (PIB) in Treatment Naïve Adults with Chronic Hepatitis C Virus (HCV)	30/01/2020	03/03/2020	SmPC	Considering that the GT3 cirrhotic population is considered nowadays as the more difficult to treat population, it is crucial to confirm that shortening the Maviret treatment duration to 8 weeks in these patients would not be detrimental, notwithstanding that there is now retreatment option for those patients. In this study, all but 3 GT3 patient achieved SVR12 (60/63=95.2%). Only 1 GT3 patient had virological failure (relapse by W4). The patient

	Genotype 1 - 6 Infection and Compensated Cirrhosis (EXPEDITION-8). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				had no NS3 or NS5A polymorphisms at baseline. Among GT3 patients included in this study, 7 had pejorative mutations at baseline (notably, 3 had A30K; 4 had Y93H) and none experienced virological failure. Overall, the efficacy data from study M16-135 (EXPEDITION-8) support the use of Maviret for a shortened 8-week duration in all treatment-naïve patients with compensated cirrhosis, including GT3 patients
II/0031	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	13/02/2020	n/a		
PSUSA/10620 /201907	Periodic Safety Update EU Single assessment - glecaprevir / pibrentasvir	13/02/2020	n/a		PRAC Recommendation - maintenance
II/0030	Update of section 4.2 of the Maviret SmPC to improve the clarity of the dosing instruction, based on post-marketing data and pharmacokinetic simulations. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	30/01/2020	03/03/2020	SmPC	The recommended dose of Maviret is 300 mg/120 mg (three 100 mg/40 mg tablets), taken orally, once daily at the same time with food.
II/0024	Update of section 5.1 of the SmPC to include data from the final clinical report from the Phase 3 study M16-126 (ENDURANCE-5,6, A Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Glecaprevir (GLE)/Pibrentasvir (PIB) in Adults with Chronic Hepatitis C Virus (HCV) Genotype 5 or 6 Infection).	19/09/2019	03/03/2020	SmPC	The MAH submitted the final results from the ENDURANCE-5,6 study, an open-label study in 84 HCV GT5 (N=23) or 6-infected (N=61) TN or TE-PRS subjects. Subjects without cirrhosis received Maviret for 8 weeks, and subjects with compensated cirrhosis received Maviret for 12 weeks. Of the 84 subjects treated, the median age was 59 years (range 24-79); 27% had HCV genotype 5, 73% had HCV

	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				genotype 6; 54% were female, 30% were White, 68% were Asian; 90% were HCV TN; 11% had compensated cirrhosis. The overall SVR12 rate was 97.6% (82/84). The SVR12 rate was 95.7% (22/23) for GT5-infected subjects and 98.4% (60/61) for GT6-infected subjects. One TN GT5-infected subject without cirrhosis experienced relapse, and one TN GT6-infected subject with compensated cirrhosis experienced on-treatment virologic failure.
PSUSA/10620 /201901	Periodic Safety Update EU Single assessment - glecaprevir / pibrentasvir	05/09/2019	n/a		PRAC Recommendation - maintenance
II/0026	Update of section 5.1 of the SmPC in order to reflect data from two Asian regional Phase 3 studies: study M15-592 (VOYAGE-1 - A Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy and Safety of ABT-493/ABT-530 in Treatment-Naïve and Treatment-Experienced, Non-Cirrhotic Asian Adults with Chronic Hepatitis C Virus Genotype (GT) 1 to GT6 Infection With or Without Human Immunodeficiency Virus Co-Infection) and study M15-593 (VOYAGE-2 - An Open-Label Study to Evaluate the Efficacy and Safety of ABT-493/ABT-530 in Treatment-Naïve and Treatment-Experienced Asian Adults With Chronic Hepatitis C Virus Genotype (GT) 1 to GT6 Infection With Compensated Cirrhosis and With or Without Human Immunodeficiency Virus Co-Infection). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/07/2019	03/03/2020	SmPC	Genotype 3b (GT3b) is a subtype reported in a relatively small number of HCV infected patients in China and a few countries in South and Southeast Asia, but rarely outside of this region. All subjects without cirrhosis or with compensated cirrhosis received 8 or 12 weeks of Maviret, respectively, except GT3b treatment-experienced with peg-interferon, ribavirin and/or sofosbuvir (TE-PRS) subjects who received 16 weeks of Maviret. The overall SVR12 rates were 97.2% and 99.4% in VOYAGE-1 and VOYAGE-2, respectively. Among GT3b subjects without cirrhosis, a numerically lower SVR12 rate of 58.3% for treatment-naive (TN) subjects and 50% for TE-PRS subjects was observed compared to GT3a subjects without cirrhosis (92.9%). Three GT3b TN subjects experienced relapse and two GT3b TE-PRS subjects experienced on-treatment virologic failure. Among subjects with compensated cirrhosis, the overall SVR12 rate for GT3b infected subjects was 87.5% and 100% for GT3a infected subjects. One GT3b TN subject experienced relapse. In GT3b replicon, the presence of naturally occurring

					polymorphisms K30 and M31 in NS5A reduced susceptibility to pibrentasvir by 24-fold relative to the activity of pibrentasvir in genotype 3a replicon.
II/0025	Update of sections 4.2, 4.8 and 5.1 of the SmPC to shorten the treatment duration in treatment-naïve subjects with compensated cirrhosis and Hepatitis C virus GT1, 2, 4, 5, or 6 infection, from 12 to 8 weeks, based on interim results from study M16-135 (EXPEDITION-8, A Single Arm, Open-Label Study to Evaluate the Efficacy and Safety of Glecaprevir (GLE)/Pibrentasvir (PIB) in Treatment Naïve Adults with Chronic Hepatitis C Virus (HCV) Genotype 1 - 6 Infection and Compensated Cirrhosis). In addition, the marketing authorisation holder took the opportunity to revise the submission date of the final CSR for the hepatocellular carcinoma recurrence study in Annex IID, from Q2 2021 to Q2 2023. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	27/06/2019	25/07/2019	SmPC and Annex II	The safety and efficacy of Maviret given for 8 weeks in GT 1, 2, 4, 5 or 6 treatment naïve subjects with compensated cirrhosis was evaluated in a single-arm, open-label study (M16-135, EXPEDITION-8). Of the 280 subjects treated, the median age was 60 years (range: 34 to 88); 81.8% had HCV genotype 1, 10% had HCV genotype 2, 4.6% had HCV genotype 4, 0.4% had HCV genotype 5; 3.2% had HCV genotype 6; 60% were male; 9.6% were Black. The overall SVR12 rate was 97.9% (274/280). There were no virologic failures.
PSUSA/10620 /201807	Periodic Safety Update EU Single assessment - glecaprevir / pibrentasvir	28/02/2019	29/04/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10620/201807.
IB/0022/G	This was an application for a group of variations. 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)	28/03/2019	25/07/2019	SmPC	

	B.II.f.1.e - Stability of FP - Change to an approved stability protocol				
II/0021	Update of sections 4.8 and 5.1 of the SmPC in order to include results from the final study report for study M16-127 (EXPEDITION-5), a multicentre, open-label study to evaluate the efficacy and safety of glecaprevir/pibrentasvir in renally-impaired adults with chronic hepatitis C virus genotype 1-6 infection. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	14/03/2019	25/07/2019	SmPC	Sections 4.8 and 5.1 of the SmPC were updated to include data from 101 patients with renal impairment from study M16-127 (EXPEDITION-5) who were treated according to the product information recommendations. Subjects were either treatment-naïve or treatment-experienced to combinations of (peg) interferon, ribavirin, and/or sofosbuvir and received Maviret for 8, 12, or 16 weeks per approved treatment durations. Of the 101 subjects treated, the median age was 58 years (range 32-87); 53% had HCV genotype 1; 27% had HCV genotype 2; 15% had HCV genotype 3; 4% had HCV genotype 4; 59% were male; 73% were White; 80% were HCV treatment-naïve; 13% had cirrhosis and 65% had a baseline fibrosis state of F0 or F1; 7% were CKD stage 3b; 17% were CKD Stage 4, and 76% were CKD Stage 5 (all receiving dialysis); 84 subjects received 8 weeks of treatment, 13 subjects received 12 weeks of treatment, and 4 subjects received 16 weeks of treatment. The overall SVR12 rate was 97% (98/101). There were no virologic failures. The most common adverse reaction in subjects with severe renal impairment was pruritus (14.9%).
II/0012	Extension of indication to extend the Maviret indication to adolescents (from 12 to 18 years of age) with chronic hepatitis C infection, based on new clinical data from study M16-123, an open-label, multi-centre study to evaluate the pharmacokinetics, safety, and efficacy of glecaprevir/pibrentasvir in paediatric subjects with genotypes 1 - 6 chronic	31/01/2019	11/03/2019	SmPC and PL	Please refer to the Scientific Discussion – Maviret-12.

	hepatitis C virus infection (DORA), using the adult co-formulated tablets in adolescents. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IB/0019/G	This was an application for a group of variations. 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) B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	22/02/2019	n/a		
IB/0020	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	08/01/2019	n/a		

IA/0017	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	18/12/2018	n/a		
IG/1036	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	11/12/2018	11/03/2019	SmPC and PL	
IB/0016	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	29/11/2018	n/a		
PSUSA/10620 /201801	Periodic Safety Update EU Single assessment - glecaprevir / pibrentasvir	06/09/2018	n/a		PRAC Recommendation - maintenance
IB/0014/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.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other	07/08/2018	n/a		

	changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
IA/0013/G	This was an application for a group of variations. 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	13/07/2018	n/a		
T/0011	Transfer of Marketing Authorisation	23/05/2018	15/06/2018	SmPC, Labelling and PL	
II/0006/G	This was an application for a group of variations. B.I.b.1.e - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP B.I.b.1.e - Change in the specification parameters	26/04/2018	n/a		

	and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP				
II/0004	Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC in order to update information on the use of Maviret in liver or kidney transplant patients, based on new clinical data from study M13-596 (MAGELLAN-2), a post-registrational Phase 3 study listed as a category 3 study in the RMP, which evaluated the efficacy and safety of the glecaprevir/pibrentasvir regimen in adult subjects with chronic hepatitis C virus genotypes 1-6 infection, who have received a liver or renal transplant. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/03/2018	26/04/2018	SmPC and PL	A 12-week treatment duration has been evaluated and is recommended in liver or kidney transplant recipients with or without cirrhosis. The safety of Maviret was assessed in 100 post-liver or -kidney transplant recipients with genotypes 1, 2, 3, 4, or 6 chronic HCV infection without cirrhosis (MAGELLAN-2). The overall safety profile in transplant recipients was comparable to that observed in subjects in the Phase 2 and 3 studies. Adverse reactions observed in greater than or equal to 5% of subjects receiving Maviret for 12 weeks were headache (17%), fatigue (16%), nausea (8%) and pruritus (7%). The overall SVR12 rate in post-transplant subjects was 98.0% (98/100). There was one relapse and no on-treatment virologic failure. The data also indicated that the current recommendations regarding co-administration of Maviret with immunosuppressants (ciclosporin ≤100 mg/day, tacrolimus, sirolimus, everolimus, azathioprine, mycophenolic acid, prednisone, and prednisolone) are appropriate. The Package Leaflet has been updated accordingly.
IB/0009/G	This was an application for a group of variations. 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	24/04/2018	n/a		

	starting material/reagent/intermediate for AS - Other variation B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
IA/0008/G	This was an application for a group of variations. 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.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold	20/03/2018	n/a		
IA/0007/G	This was an application for a group of variations. 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	27/02/2018	n/a		
II/0003	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/02/2018	26/04/2018	SmPC and PL	

IAIN/0005/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.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.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	31/01/2018	n/a		
II/0002	Update of sections 4.8 and 5.1 of the SmPC in order to add information on clinical efficacy and safety in HCV/HIV-1 co-infected subjects, based on new clinical data from Study M14-730 (EXPEDITION-2), a post-registrational Phase 3 study which evaluated the efficacy and safety of the glecaprevir/pibrentasvir regimen in chronic HCV GT1-GT6/HIV-1 co-infected subjects who were HCV treatment-naïve or treatment-experienced. In addition, the SmPC was revised to make minor grammatical and formatting amendments and to correct errors in section 5.2.	14/12/2017	26/04/2018	SmPC	The overall safety profile in HCV/HIV-1 co-infected subjects (ENDURANCE-1 and EXPEDITION-2) was comparable to that observed in HCV mono-infected subjects. Regarding efficacy, 97.5% (1,252/1,284) of treatment-naïve (TN) subjects or treatment-experienced to combinations of interferon, peginterferon, ribavirin and/or sofosbuvir (TE-PRS) subjects who received the recommended duration achieved SVR12 overall, while 0.3% (4/1,284) experienced on-treatment virologic failure and 0.9% (11/1,262) experienced post-treatment relapse. The presence of HIV-1 co-infection did not impact efficacy. The SVR12 rate in TN

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				or TE-PRS HCV/HIV-1 co-infected subjects treated for 8 or 12 weeks (without cirrhosis and with compensated cirrhosis, respectively) was 98.2% (165/168) from ENDURANCE-1 and EXPEDITION-2. One subject experienced on-treatment virologic failure (0.6%, 1/168) and no subjects relapsed (0%, 0/166).
IB/0001	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	16/10/2017	n/a		