Veklury

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
II/0053/G	This was an application for a group of variations. Extension of indication to include treatment of paediatric patients who are at least 4 weeks of age and weighing at least 3 kg who do not require supplemental oxygen and who are at increased risk	25/04/2025	06/06/2025	SmPC and PL	Please refer to Scientific Discussion 'Veklury-H-C-005622/II/0053/G'

[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).

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	of progressing to severe COVID-19 for Veklury, based on final results from study GS-US-540-5823; this is a Phase 2/3 single-arm, open-label study to evaluate the safety, tolerability, pharmacokinetics, and efficacy of remdesivir in participants from birth to < 18 years of age with COVID-19. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 10 of the RMP is approved with this variation. The variation leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP). C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
II/0062	Submission of the final report from study COVID-PR (CO-US-540-6127 listed as a category 3 study in the RMP. This is a non-interventional, patient-reporting, post marketing cohort study designed to collect safety data from pregnant and recently pregnant women treated with monoclonal antibodies or antiviral drugs for mild, moderate, or severe COVID-19 at any time from the first day of the last menstrual period to the end of pregnancy. The RMP version 8.2 is updated accordingly. C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of	16/01/2025	n/a		

	change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required				
N/0063	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/12/2024	06/06/2025	Labelling and PL	
PSUSA/10840 /202405	Periodic Safety Update EU Single assessment - remdesivir (Veklury)	28/11/2024	n/a		PRAC Recommendation - maintenance
II/0061	Update sections 4.9 and 5.1 of the SmPC based on final results from study GS US 540 9053. This is a Phase 1, Partially Blinded, Randomized, Placebo- and Positive-Controlled Study to Evaluate the Effect of Remdesivir on the QT/QTc Interval in Healthy Participants. The MAH took the opportunity to make some editorial changes. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	17/10/2024	14/02/2025	SmPC	SmPC new text Update sections 4.9 and 5.1 of the SmPC based on final results from study GS US 540 9053. Overall, RDV administered at a therapeutic-equivalent dose (150 mg) and at a supratherapeutic dose (600 mg) did not affect the QTc interval beyond the defined threshold of 10 ms as per guideline ICH E14. For more information, please refer to the Summary of Product Characteristics.
II/0059/G	This was an application for a group of variations. Update of sections 4.5 and 5.2 of the SmPC in order to update drug-drug interaction information based on data from the two studies GS-US-540-6587 and GS-US-611-6409. GS-US-540-6587 is a Phase 1, open-label, single-center, fixed-sequence study to evaluate the effect of multiple-dose administration of RDV on the PK of single-dose MDZ in healthy participants, while study GS-US-611-6409 is a Phase	05/09/2024	14/02/2025	SmPC	SmPC new text Sections 4.5 and 5.2 of the SmPC are updated with the results of the studies GS-US-540-6587 and GS-US-611-6409 which evaluated Remdesivir (RDV) in-vivo drug-drug interaction with CYP3A4 and OATP1B1/B3. No clinically significant drug interactions are expected with substrates of CYP1A2, CYP3A4 (including dexamethasone), UGT1A1, MATE1, OAT3, OCT1, OATP1B1 and OATP1B3. For more information, please refer to the Summary of

	1, open-label, multicenter, single-sequence or randomized-sequence , multiple-cohort study to evaluate DDIs of ODV or RDV and probe substrates or strong inhibitors in healthy participants. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				Product Characteristics.
IA/0058	A.7 - Administrative change - Deletion of manufacturing sites	27/06/2024	n/a		
II/0054/G	This was an application for a group of variations. Update of section 5.2 of the SmPC to update pharmacokinetic information based on results from population PK study report QP-2023-1074. QP-2023-1074 is a population pharmacokinetic analysis of Sulfobutylether-β- cyclodextrin (SBECD) in adults with normal and impaired renal function following remdesivir administration. Update of section 5.2 of the SmPC to update pharmacokinetic information based on results from population PK study report CTRA-2023-1084. CTRA-2023-1084 is a population pharmacokinetic analysis for remdesivir and metabolites (GS-704277 and GS-441524) after administration of remdesivir in adults. C.I.4 - Change(s) in the SPC, Labelling or PL due to	30/05/2024	14/02/2025	SmPC	

	new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0057	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	08/05/2024	n/a		
II/0056	Update of section 5.1 of the SmPC in order to update antiviral activity information based on the final results from the nonclinical study PC-540-2048 on the antiviral activity of remdesivir against SARS-CoV-2 Omicron XBF, XBB.1.16, FL.22, XBB.2.3.2, EG.5.1, EG.1.2, BA.2.86 and XBB.1.9.2 subvariants. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	02/05/2024	14/02/2025	SmPC	SmPC new text The MAH submitted new information related to the antiviral activity of Veklury against some Omicron subvariants. The results from clinical isolates and from variants tested in the replicon system confirm the antiviral activity of remdesivir against the Omicron subvariants BA.2.86, XBF, XBB.1.16, FL.22 (XBB.1.9.1 sub-lineage), XBB.1.9.2, XBB.2.3.2, EG.5.1, and EG.1.2. The SmPC is updated accordingly. For more information, please refer to the Summary of Product Characteristics.
IB/0055	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	27/02/2024	n/a		
PSUSA/10840 /202305	Periodic Safety Update EU Single assessment - remdesivir (Veklury)	30/11/2023	n/a		PRAC Recommendation - maintenance
II/0052	Update of section 5.1 of the SmPC with non-clinical information related to the antiviral activity of Remdesivir against Omicron subvariants BF.7, BQ.1,	09/11/2023	14/02/2025	SmPC	SmPC new text Section 5.1 of the SmPC is updated with regard to the antiviral activity of remdesivir (RDV) against Omicron BF.7,

	XBB.1.5, CH.1.1. In addition, the MAH took the opportunity to implement editorial changes in the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				BQ.1, XBB.1.5, and CH.1.1 subvariants. Overall, RDV showed no decrease in susceptibility, demonstrating antiviral activity of RDV against the Omicron subvariants tested. For more information, please refer to the Summary of Product Characteristics.
II/0050	Update of sections 4.2, 4.4, 4.8 and 5.2 of the SmPC in order to address the safety of remdesivir and its metabolites in patients with hepatic impairment and to update information on hepatic and coagulation laboratory abnormalities based on final results from study GS US 540 9014: "A phase 1 open-label, adaptive, single-dose study to evaluate the pharmacokinetics of remdesivir and its metabolite(s) in subjects with normal hepatic function and hepatic impairment", listed as a category 3 study in the RMP, and on safety data from postmarketing and clinical trials experience. The Package Leaflet is updated accordingly. The RMP version 8.0 have also been updated. In addition, the MAH took the opportunity to submit Minor Linguistic Amendments (MLA) for Veklury. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/09/2023	12/10/2023	SmPC and PL	SmPC new text No dose adjustment is required in patients with mild, moderate or severe hepatic impairment. No new safety concerns or hepatoxicity were identified in patients with chronic liver disease. Participants with normal hepatic function and moderate or severe hepatic impairment did not reveal any new safety concerns. The recommendation for prothrombin time monitoring is deleted from section 4.8 of the SmPC as there has been no correlation with clinical consequences seen in the placebo controlled COVID-19 clinical trials. For more information, please refer to the Summary of Product Characteristics.
II/0044/G	This was an application for a group of variations. Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the	25/05/2023	26/06/2023	SmPC and PL	At the time of approval, data on plasma concentrations of remdesivir and its metabolites from patients with renal impairment were not available. Only patients with mild to

	SmPC in order to change posology recommendations for patients with renal impairment, update an existing warning on renal impairment and update the safety and efficacy information based on final results from studies GS-US-540-5912 and GS-US-540-9015, listed as category 3 studies in the RMP. Study GS-US-540-5912 is a Phase 3 randomised, double-blind, placebo-controlled, parallel group, multicenter study evaluating the efficacy and safety of remdesivir in participants with severely reduced kidney function who were hospitalised for COVID-19, while study GS-US-540-9015 is a Phase 1, multicenter, open-label, single-dose study to evaluate the single-dose PK of remdesivir in participants with normal and impaired renal function. The Package Leaflet is updated accordingly. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor edits to the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				moderate renal impairment were included in the Phase 3 clinical development program and received remdesivir without dose adjustment. Thus, remdesivir was not recommended for use in patients with severe renal impairment (eGFR <30 ml/min). Based on newly provided results from studies GS-US-540-9015 and GS-US-540-5912, it was concluded that no dose adjustment of remdesivir or change in treatment duration is required in patients with renal impairment, including those on dialysis. However, patients with severe renal impairment and end-stage renal disease should be closely monitored for adverse events during treatment with remdesivir. For more information, please refer to the Summary of Product Characteristics.
II/0046	Update of sections 4.6 and 5.2 of the SmPC in order to update information on pregnancy and breastfeeding based on final results from study IMPAACT 2032 listed as a category 3 study in the RMP; this is a Phase 4, prospective, open-label, non-randomised study to address PK and safety of	22/06/2023	12/10/2023	SmPC and PL	SmPC new text Submission of results of IMPAACT 2032 study (phase 4, prospective, open-label, non-randomised study sponsored by National Institute of Allergy and infectious Diseases (NIAID) to evaluate pharmacokinetics and safety of remdesivir (RDV) in pregnant and non-pregnant women of

	remdesivir in pregnant women. In addition, the MAH provided post-marketing pregnancy data and literature to support this variation. The Package Leaflet is updated accordingly. The RMP version 7.0 is acceptable. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				childbearing potential treated for COVID-19). In addition, the MAH submitted data from post-marketing experience (third pregnancy safety report) to justify new recommendation for RDV use in pregnant women. Based on the submitted data no clinically relevant differences in the pharmacokinetics of RDV and its metabolites were observed between pregnant and non-pregnant women and no dose adjustment is needed. With respect to clinical safety, limited data is available from RDV use during pregnancy (198 cases with known pregnancy outcome), in particular, during first trimester of pregnancy (12 cases with known pregnancy outcome). Consequently, RDV use during the first trimester of pregnancy cannot be recommended. On the other hand, use in second and third trimester of pregnancy may be considered in individual patients as it is well known that symptomatic COVID-19 during pregnancy is accompanied with worse clinical course of the disease, increased risk for ICU admission, mechanical ventilation and death in comparison with symptomatic nonpregnant females of reproductive age and available data from RDV use during 2nd and 3rd trimester of pregnancy do not indicate any risk. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10840 /202211	Periodic Safety Update EU Single assessment - remdesivir (Veklury)	08/06/2023	n/a		PRAC Recommendation - maintenance
II/0049	Update of section 5.1 of the SmPC in order to update preclinical data on the antiviral activity of remdesivir against the Omicron subvariants BA.2.75, BA.4.6,	25/05/2023	26/06/2023	SmPC	Remdesivir activity against Omicron variants BA.2.75, BA.4.6, BF.5, XBB, and BQ.1.1 subvariants was assessed and compared to that against the SARS-CoV-2 A lineage

	BF.5, XBB, and BQ.1.1 based on results from study PC-540-2044. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				WA1 reference strain. As a result, updates to section 5.1 of the SmPC were introduced to reflect the newly generated data on subvariant susceptibility. Overall, remdesivir showed no relevant decrease in susceptibility, demonstrating full potency against all Omicron subvariants tested to date. For more information, please refer to the Summary of Product Characteristics.
II/0045	Update of section 5.1 of the SmPC in order to update clinical virology information based on results of the phenotypic analysis of the nsp12 substitutions that emerged post-treatment in study GS-US-540-5773, including T76I, A526V, A554V, E665K, and C697F. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	16/03/2023	26/04/2023	SmPC	SmPC new text The requested phenotypic analysis of the Nsp12 substitutions that emerged post-treatment in study GS-US-540-5773 was submitted within this variation. Phenotypic analysis of Nsp12 emergent substitutions observed in participants with sequencing data available in study GS-US-540-5773 showed no significant change in RDV susceptibility. For more information, please refer to the Summary of Product Characteristics.
IB/0048	B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation	31/01/2023	26/04/2023	SmPC	To change the shelf life in section 6.3, SmPC from 3 years to 4 years.
II/0043	Update of section 5.1 of the SmPC in order to update information based on the final virology report (PC-540-2040) for study GS-US-540-9012 to fulfil the recommendation by CHMP in the procedure EMEA/H/C/005622/II/0016; this is a phase 3, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of RDV in an outpatient setting in participants with	15/12/2022	05/01/2023	SmPC	SmPC new text Update of section 5.1 of the SmPC in order to update virology data of study GS-US-540-9012. No significant changes in antiviral activity were determined (<2.3 fold change in EC50 compared to reference strain) for treatment emergent substitutions in Nsp8, Nsp 10, Nsp12, Nsp13 and Nsp 14 with one exception (the amino acid

	confirmed COVID-19 who were at risk for disease progression. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				substitution A376V in Nsp12 observed in one patient showed an EC50 fold-change of 12.6). Overall, based on the submitted data RDV maintained a similar antiviral effect in vitro. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10840 /202205	Periodic Safety Update EU Single assessment - remdesivir (Veklury)	01/12/2022	n/a		PRAC Recommendation - maintenance
II/0042	Update of section 5.1 to provide in vitro data on the antiviral activity of remdesivir against the Omicron subvariants BA.2.12.1, BA.4 and BA.5 following procedure II/0034/G based on in vitro study "Remdesivir Antiviral Activity against Omicron Subvariants BA.2.12.1, BA.4, and BA.5 in A549-hACE2-TMPRSS2 Cells". C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	10/11/2022	21/11/2022	SmPC	SmPC new text Update of 5.1 of the SmPC in order to add new data related to the antiviral activity of remdesivir against COVID-19. For the Omicron subvariants tested, BA.2.12.1, BA.4 and BA.5, remdesivir showed no decrease in susceptibility, thus supporting its use for the treatment of COVID-19 considering the previously named SARS-CoV-2 variants(in circulation at the time of this assessment). For more information, please refer to the Summary of Product Characteristics.
II/0037/G	This was an application for a group of variations. Grouped variations to update sections 4.5 and 5.2 of the SmPC to update prescribing information related to interactions with other medicinal products, effect of intrinsic factors and COVID-19 disease on the pharmacokinetics (PK) of Veklury® and its metabolites in the adult population. This variation	13/10/2022	20/10/2022	SmPC and PL	SmPC new text The PI has been updated to include more data regarding the interaction of remdesivir with other medicinal products in 4.5. In addition, new pharmacokinetic data of remdesivir in healthy volunteers and patients with COVID 19 are included in 5.2. For more information, please refer to the Summary of

	covers the Recommendations 9,11 ,12 and 13 listed at the time of the conditional marketing authorization (EMEA/H/C/005622/0000) for Veklury®. Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some linguistic amendments. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				Product Characteristics.
II/0035/G	This was an application for a group of variations. Grouped application of two Extensions of indication to include: - treatment of paediatric patients (at least 4 weeks	15/09/2022	16/09/2022	SmPC and PL	Please refer to Scientific Discussion Veklury /H/C/005622/II/0035/G.

	of age and weighing at least 3 kg) with pneumonia requiring supplemental oxygen (low- or high-flow oxygen) or other non-invasive ventilation at start of treatment, based on interim results from Study GS-US-540-5823; a phase 2/3 single-arm, open-label study to evaluate the safety, tolerability, pharmacokinetics, and efficacy of Remdesivir in participants from birth to <18 years of age with COVID-19; - treatment of paediatric patients (weighing at least 40 kg) who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID 19, based on data from 8 adolescent patients who were included in Study GS-US-540-9012, which was initially assessed by the CHMP as part of procedure II/16 (Extension of Indication to include treatment of adults). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet as well as the instructions for healthcare professionals have been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Version 5.0 of the RMP has also been submitted. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				

IA/0041	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	24/08/2022	n/a		
II/0034/G	This was an application for a group of variations. Grouping variation to update section 5.1 of the SmPC in relation to information regarding the antiviral activity of Veklury. This submission of the final results of study ACTT-1 with the final sequencing and phenotyping analysis and the full virology report including activity against variants is related to the Specific Obligation 012. Furthermore, Annex II is updated accordingly to reflect the fulfilment of the specific obligations following this submission. Finally, the MAH provided data on the alternative method (i.e., the SARS-CoV-2 replicon system) that can be utilised to allow further testing of the Nsp12 mutation A547V as requested in REC 027 that is also considered fulfilled. The Package Leaflet and the RMP (version 4.0) are updated accordingly. Furthermore, the CHMP is of the opinion that in light of all the data generated throughout all the specific obligations providing a comprehensive dataset, the benefit-risk balance of the above- mentioned medicinal product remains favourable and also considering the evidence of compliance with all specific obligations, the CHMP recommends the granting of a marketing authorisation in accordance with Article 14(1) of Regulation No 726/2004.	21/07/2022	08/08/2022	SmPC, Annex II and PL	Please refer to Scientific Discussion "Veklury EMEA/H/C/005622/II/0034/G" SmPC new text As a consequence of this variation, section 5.1 of the SmPC is updated with new virological data including the virological activity of Veklury against Omicron. Furthermore, the last specific obligation for this product is considered fulfilled and, therefore, it is deleted from Annex II. For more information, please refer to the Summary of Product Characteristics.

	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/10840 /202111	Periodic Safety Update EU Single assessment - remdesivir (Veklury)	23/06/2022	19/07/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10840/202111.
II/0036	Update of sections 4.4 and 5.1 of the SmPC in order to update information regarding the baseline serostatus of patients included in the Study GS US 540 9012 (Phase 3, randomized, double blind, placebo controlled study to evaluate RDV treatment of COVID 19 in an outpatient setting) listed as a Recommendation (number 24) within the procedure EMA/ 005622/II/0016 that led to the extension of indication of remdesivir to adults with confirmed COVID 19 who do not require supplemental oxygen and who are at increased risk of progressing to severe disease. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	16/06/2022	19/07/2022	SmPC	SmPC new text Within variation, the MAH submitted a post-hoc subgroup analysis of the primary and secondary efficacy endpoint stratified by baseline serostatus of study GS-US-540-9012. However, no conclusion can be made on efficacy in the subgroups stratified by serostatus due to the small number of patients with known serostatus and overall low event rates. No new safety signal has been identified. For more information, please refer to the Summary of Product Characteristics.
IA/0038/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	10/06/2022	n/a		

	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.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure				
IA/0039	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	09/06/2022	n/a		
R/0031	Renewal of the marketing authorisation.	24/03/2022	12/04/2022		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Veklury, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
II/0026/G	This was an application for a group of variations. Grouped variation updating sections 4.6, 5.2 and 5.3 of the SmPC in order to update information in these sections considering new nonclinical data requested at the time of the initial conditional marketing application (EMEA/H/C/005622). C.I.4 - Change(s) in the SPC, Labelling or PL due to	03/02/2022	12/04/2022	SmPC	Sections 4.6,5.2 and 5.3 of the SmPC to update reproductive information from animal studies; biotransformation with metabolization details and toxicology regarding major metabolite M27.

	new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0032	B.II.e.z - Change in container closure system of the Finished Product - Other variation	28/01/2022	n/a		
II/0016	Extension of indication to include treatment of adults who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. An update of the Risk Management Plan (RMP) (Version 3.0) has been also submitted. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	16/12/2021	20/12/2021	SmPC and PL	Please refer to Scientific Discussion EMEA/H/C/005622/II/0016
II/0028/G	This was an application for a group of variations. C.I.4. Grouping variation to Update of section 5.1 of the SmPC in order to add information related to in vitro testing reports of B.1.1.28 and B.1.617 variants with additional provision of the cell culture resistance report to further understand the antiviral activity of Remdesivir. They are listed as part of the specific obligation (SOB 012) in the Annex II of the renewal procedure EMEA/H/C/005622/R/0015 for Veklury.	16/12/2021	20/12/2021	SmPC	SmPC new text Based on in vitro testing, remdesivir retained similar antiviral activity and therefore no reduction in susceptibility (≤1.5-fold change) against clinical isolates of SARS-CoV-2 variants containing the P323L substitution in the viral polymerase including Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1) and Delta (B.1.617.2). No clinical data are available on the development of SARS-CoV 2 resistance to Remdesivir, however, in vitro data on resistance development has been provided and updated.

	C.I.13.Grouping variation for the submission of the virology reports for GS-US-540-5773 and GS-US-540-5774 studies and the submission of the ACTT-1 final viral load analysis included as part of the specific obligation (SOB 012) in the Annex II of the renewal procedure EMEA/H/C/005622/R/0015 for Veklury. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data 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				For more information, please refer to the Summary of Product Characteristics.
PSUSA/10840 /202105	Periodic Safety Update EU Single assessment - remdesivir (Veklury)	02/12/2021	n/a		PRAC Recommendation - maintenance
IB/0029	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	12/11/2021	20/12/2021	Annex II	
IG/1456	A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or	08/11/2021	n/a		

	intermediate used in the manufacture of the AS or manufacturer of a novel excipient				
II/0025/G	This was an application for a group of variations. Update of section 5.1 of the SmPC with nonclinical results following final study reports addressing the activity of remdesivir in additional cell lines and chloroquine/hydroxychloroquine antagonism (fulfilment of 3 components of the Specific Obligation SOB 012 from EMEA/H/C/005622/R/0015). In addition, the Marketing authorisation holder (MAH) took the opportunity to submit the interim results of the non-clinical studies related to the characterisation of clinical isolates and/or recombinant viruses with P323L, A97V, and A547V substitutions. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/10/2021	20/12/2021	SmPC	The interim results of the analysis of the antiviral activity of remdesivir on RdRp/Nsp12 A97V, P323L, and D484Y mutants indicates that these recombinant mutants are still susceptible to remdesivir as no significant change in EC50 values was found. Secondly, the antiviral activity of remdesivir against a nanoluciferase-expressing SARS-CoV-2 construct in a human alveolar epithelial cell line A549 expressing the human ACE2 receptor (A549-hACE2) show inhibition of in vitro replication with an EC50 value of 0.115 µM in this human alveolar cell line. The results are consistent with the results achieved in other cell types and thereby confirm the in vitro antiviral activity of remdesivir against SARS-CoV-2. Finally, the in vitro studies show that co-incubation of remdesivir with Chloroquine (CQ) or Hydroxychloroquine (HCQ) results in a reduced formation of RDV-TP in various cell types. This observed reductions in RDV-TP in the presence of CQ or HCQ indicates a potential antagonistic effect on remdesivir metabolism to its active triphosphate. SmPC new text Section 5.1 Pharmacodynamic Properties / Antiviral Activity of the SmPC is being updated to include new data on the antiviral activity of remdesivir in a human alveolar epithelial cell line (A549-hACE2). The results are consistent with the results achieved in other cell types and thereby confirm the in vitro antiviral activity of remdesivir against SARS-CoV-2. For more information, please refer to the Summary of

					Product Characteristics
IA/0027/G	This was an application for a group of variations. B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process 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.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	23/09/2021	n/a		
PSUSA/10840 /202011	Periodic Safety Update EU Single assessment - remdesivir (Veklury)	24/06/2021	20/08/2021	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10840/202011.
IB/0023	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	03/08/2021	20/12/2021	Annex II	
IA/0022	B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure	23/07/2021	n/a		
IB/0020/G	This was an application for a group of variations. B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch	08/07/2021	n/a		

	control/testing takes place B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold 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				
IB/0021/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	01/07/2021	n/a		

	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				
R/0015	Renewal of the marketing authorisation.	20/05/2021	24/06/2021	SmPC, Annex II, Labelling and PL	The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Veklury, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion. Within this procedure and update on sections 4.8, 5.1, 5.2 of the SmPC has been done to mainly reflect the update in the frequency of anaphylaxis as not know and the prothrombin time prolonged as very common; to add updated data for the ACCT1 study and study 5773;to add more distribution data plus an update of the Annex II to delete the SOBs fulfilled and to reflect on the postponing of the submission of the virology report by December 2021. PL was modified accordingly. Finally, editorial changes and a linguistic review have been also performed. The RMP has been also updated (last version 2.0)
IB/0019/G	This was an application for a group of variations.	28/05/2021	n/a		

	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place				
IB/0018/G	This was an application for a group of variations. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/05/2021	n/a		
II/0013/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.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS -	22/04/2021	n/a		

	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.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product 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 B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation				
IA/0014/G	This was an application for a group of variations. B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	21/12/2020	n/a		

	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier				
II/0012	Update of section 4.1 of the SmPC to change the indication as a result of the assessment of the final D28 mortality data by ordinal scale categories of Study COUS-540-5776 (NIAID-ACTT1), listed as a Specific Obligation ('SOB 013') in the Annex II of the Product Information, in order to confirm the efficacy and safety of remdesivir in patients on Invasive Mechanical Ventilation and Extracorporeal Membrane Oxygenation (IMV/ECMO). Consequently section 5.1 of the SmPC is also updated to reflect the final study results. Furthermore, Annex II is updated to remove the completed specific obligation. The package leaflet is updated accordingly. C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required	10/12/2020	21/12/2020	SmPC, Annex II and PL	Please refer to Scientific Discussion Veklury/H/C/005622/II/0012
IB/0010	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	30/11/2020	18/12/2020	Annex II	
IB/0011/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of	26/11/2020	18/12/2020	Annex II	

	the AS - Other variation 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.c.2.z - Change in the specification parameters and/or limits of the immediate packaging of the AS - Other variation				
IB/0009/G	This was an application for a group of variations. 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 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.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation 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.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters	26/11/2020	18/12/2020	Annex II	

	and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
IB/0008/G	This was an application for a group of variations. B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	26/11/2020	18/12/2020	Annex II	
IB/0007/G	This was an application for a group of variations. B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation 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	26/11/2020	18/12/2020	Annex II	
IB/0006	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	26/11/2020	18/12/2020	Annex II	
IB/0005	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	26/11/2020	18/12/2020	Annex II	

IB/0003/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.b.4.z - Change in the batch size (including batch size ranges) of the finished product - Other variation 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 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 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 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	26/11/2020	18/12/2020	Annex II	
IB/0002/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.b.4.z - Change in the batch size (including batch size ranges) of the finished product - Other variation 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 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 B.II.b.5.b - Change to in-process tests or limits	26/11/2020	18/12/2020	Annex II	

	applied during the manufacture of the finished product - Addition of a new test(s) and limits 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				
IB/0004	B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation	29/09/2020	18/12/2020	Annex II	
IB/0001	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	04/09/2020	18/12/2020	Annex II	