Xevudy

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/0027	Update of section 5.1 of the SmPC with data on the in vitro activity of sotrovimab in a pseudotyped virus assay against the Omicron HV.1 and BA.2.86 spike variants (PC-23-0165) and the Omicron HK.3 spike variant (PC-23-0179) as well as data on the in vitro activity of sotrovimab in an authentic virus assay	18/04/2024		SmPC	SmPC new text Point 5.1 of the SmPC is updated with the available information related to the antiviral activity of Xevudy against HV.1 ,BA.2.86, and HK.3 and EG.5.1 Omicron variants. For more information, please refer to the Summary of

[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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	against the SARS-COV-2 EG.5.1 variant (PC-23-0176) based on the relevant pharmacology study reports. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				Product Characteristics.
II/0026	To update sections 4.2, 4.8 and 5.2 of the SmPC in order to update information on paediatric population based on final results from study COMET-PACE (215226), a category 3 study in the RMP; this is an open-label, non-comparator, multicentre study to describe the pharmacokinetics (PK), pharmacodynamics (PD; viral load) and safety following a single intravenous or intramuscular dose of sotrovimab in paediatric participants with mild to moderate COVID-19 at high risk of disease progression. The RMP version 1.1 has also been updated. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	07/03/2024		SmPC	SmPC new text Sections 4.2, 4.8 and 5.2 of the SmPC are updated with the new information on paediatric population based on final results from study COMET-PACE (215226). The PK modelling data provided by the MAH demonstrated that the pharmacokinetics and the safety profile of sotrovimab in adolescents is comparable to adults. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10973 /202308	Periodic Safety Update EU Single assessment - sotrovimab	07/03/2024	n/a		PRAC Recommendation - maintenance
II/0024	Update of section 5.1 of the SmPC in order to include virology information based on data from various pharmacology studies on the in vitro activity of	15/02/2024		SmPC	SmPC new text The antiviral activity of sotrovimab against the SARS-CoV-2 variants named XBB.1.16, XBB.2.3, XBB.1.16.1,

	sotrovimab in a pseudotyped virus assay against the SARS-CoV-2 Omicron variants named XBB.1.16 and XBB.2.3, XBB.1.16.1, XBB.1.5.10 as well as data on the in vitro activity of sotrovimab in an authentic virus assay against the SARS-CoV-2 XBB.1.16, BA.2.75, BA.4.6 and BQ.1.1 variants. Based on the data reported in PC-23-0139, under this variation application, in addition to the proposed SmPC updates, the MAH also proposed a change to the current methodology for assessment of the in vitro neutralization potency of sotrovimab against SARS-CoV-2 variants (change in target cells used for the authentic virus neutralization assay, from the currently used Vero-TMPRSS2 cells, back to the previously used VeroE6 cells). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				XBB.1.5.10, BA.2.75, BA.4.6 and BQ.1.1 is updated in 5.1. For more information, please refer to the Summary of Product Characteristics.
IB/0023/G	This was an application for a group of variations. B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol B.II.f.1.e - Stability of FP - Change to an approved stability protocol	12/10/2023		SmPC	
IB/0022	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a	04/10/2023	n/a		

	re-test period/storage period supported by real time data				
PSUSA/10973 /202302	Periodic Safety Update EU Single assessment - sotrovimab	28/09/2023	n/a		PRAC Recommendation - maintenance
IB/0020/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.1.z - Replacement or addition of a manufacturing site for the FP - Other variation	18/09/2023	n/a		
IB/0021	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	14/09/2023	n/a		
II/0018	Update of section 5.1 of the SmPC with data on the in vitro activity of sotrovimab in a pseudotyped virus assay against the Omicron XBB.1.5 and BN.1 spike variants (PC-23-0104), the Omicron CH.1.1 spike variant (PC-23-0108) and the Omicron BR.2 and XBF spike variants (PC-23-0117), as well as data on the in vitro activity of sotrovimab in a live virus assay against the SARS-CoV-2 XBB.1.5 variant (PC-23-0106) and the CH.1.1 variant (PC-23-0118). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	31/08/2023		SmPC	SmPC new text In vitro neutralization data for omicron XBB.1.5, CH.1.1, BN.1, BR.2 and XBF are provided within this variation to update the SmPC with the new antiviral activity information for sotrovimab. Omicron BN.1 exhibits the highest resistance to in vitro neutralization by sotrovimab detected so far. As regards the other omicron lineages for which new data was provided (XBB.1.5, CH.1.1, BR.2 and XBF), XBB.1.5 and CH.1.1 exhibited the highest sotrovimab resistance. The sotrovimab resistance of XBB.1.5 appears comparable to BA.2 and BA.5. For more information, please refer to the Summary of Product Characteristics.

II/0014	Update of sections 4.4 and 5.1 of the SmPC with data on epitope conservation and activity of sotrovimab against pseudotyped virus encoding epitope variants (PC-7831-0143 v15), as well as data on the in vitro activity of sotrovimab in a pseudotyped virus assay against the Omicron BA.4.6 spike variant (PC-22-0130), the Omicron BQ.1.1 spike variant (PC-22-0142), the Omicron BQ.1, BF.7, BA.2.75.2 and XBB.1 spike variants (PC-22-0145). In addition, an editorial change is made to section 4.2 of the SmPC for increased clarity as to the settings in which sotrovimab can be administered, and to section 4.1 to advise prescribers on the activity of sotrovimab against SARS-CoV2 viral variants of concern. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	04/05/2023	26/06/2023	SmPC	The update of sections 4.4 and 5.1 of the product information is supported by data on epitope conservation and activity of sotrovimab against pseudotyped virus encoding epitope variants, as well as data on in vitro neutralization potency of sotrovimab against omicron lineages BA.2.75.2, BA.4.6, BF.7, BQ.1, BQ.1.1 and XBB.1. Based on the new data, and taking into account current knowledge as regards sotrovimab's neutralizing as well as Fc-mediated functions, it is at present considered scientifically justified to conclude that it is unlikely that sotrovimab might be expected to provide clinical benefit against certain omicron lineages currently driving the COVID-19 pandemic, such as BQ.1.1. For more information, please refer to the Summary of Product Characteristics.
IA/0016	B.II.f.1.e - Stability of FP - Change to an approved stability protocol	14/04/2023	n/a		
PSUSA/10973 /202208	Periodic Safety Update EU Single assessment - sotrovimab	16/03/2023	n/a		PRAC Recommendation - maintenance
IB/0013/G	This was an application for a group of variations. B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of	07/02/2023	n/a		

	specification limits B.I.z - Quality change - Active substance - Other variation B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits				
II/0007	Update of sections 5.1 and 5.2 of the SmPC based on final clinical study report from COMET-ICE study (214367; VIR-7831-5001); this was a phase II/III, randomised, multi-centre, double-blind, placebo-controlled study to assess the safety and efficacy of Xevudy for the treatment of patients at increased risk of progressing to severe COVID-19. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	15/12/2022	09/01/2023	SmPC	
IB/0012	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol	04/01/2023	26/06/2023	SmPC	
II/0010/G	This was an application for a group of variations. C.I.4: Update of sections 4.4 and 5.1 of the SmPC based on results from study reports PC-22-0108 on the in vitro activity of sotrovimab against Omicron spike variants encoding epitope substitutions in a pseudotyped virus assay, PC-22-0116 on the in vitro	10/11/2022	15/11/2022	SmPC	Pseudotyped virus like particles assessments indicated greater than 5-fold changes in sotrovimab EC50 values compared to wild-type against the following variant spike proteins: Omicron BA.2.75 (8.3-fold change in EC50 value). The clinical relevance of the observed decrease in in vitro neutralisation against Omicron BA.2.75 is not known. The authentic virus data for BA.2.12.1, BA.4 and BA.5, was

	activity of sotrovimab against the SARS-CoV-2 XD variant in a live virus assay, PC-22-0117 on the in vitro activity of sotrovimab against the SARS-CoV-2 Omicron BA.2.12.1, BA.4 and BA.5 variants in a live virus assay, and PC-22-0124 on the in vitro activity of sotrovimab against the Omicron BA.2.75 spike variant in a pseudotyped virus assay. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. C.I.13: Submission of the final study report PC-22-0101 on the in vivo activity of S309 encoding the hamster Fc region in a Syrian golden hamster model of SARS-CoV-2 Omicron BA.2 infection. C.I.13: Submission of the final study report PC-22-0126 on the in vivo activity of VIR-7831-WT in a Syrian golden hamster model of SARS-CoV-2 Omicron BA.5. infection. 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				considered in agreement with the data already in the product information.
IB/0008/G	This was an application for a group of variations.	15/10/2022	15/11/2022	Annex II	

	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product				
PSUSA/10973 /202202	Periodic Safety Update EU Single assessment - sotrovimab	29/09/2022	n/a		PRAC Recommendation - maintenance
IAIN/0009	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	01/09/2022	n/a		
II/0004	Submission of the final report from study PC-7831-0126 in order to fulfil the recommendation by the CHMP to submit an in vivo study in hamsters challenged with the alpha (B.1.1.7) SARS-CoV-2 variant. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	01/09/2022	n/a		
IB/0006	B.II.e.3.b - Change in test procedure for the immediate packaging of the finished product - Other changes to a test procedure (including replacement or addition)	31/08/2022	n/a		
II/0005	Update of sections 4.4 and 5.1 of the SmPC based on	21/07/2022	22/07/2022	SmPC	Pseudotyped virus like particles assessments indicated

	final results from study PC-7831-0157. This is a pharmacology study to determine the neutralisation activity of sotrovimab against SARS-CoV-2 pseudotyped virus expressing the Omicron BA.2.12.1, Omicron BA.4, or Omicron BA.5 spike proteins. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				greater than 5-fold changes in sotrovimab EC50 values compared to wild-type against the following variant spike proteins: Omicron BA.2.12.1 (16.6-fold change in EC50 value), BA.4 (21.3-fold change in EC50 value) and Omicron BA.5 (22.6-fold change in EC50 value). The clinical relevance of the observed decreases in in vitro neutralisation against Omicron BA.2.12.1, BA.4 and BA.5 is not known.
IA/0003	A.7 - Administrative change - Deletion of manufacturing sites	01/06/2022	22/07/2022	Annex II, Labelling and PL	
II/0001/G	This was an application for a group of variations. C.I.4 - Update of sections 4.4, 5.1 and 5.3 of the SmPC, to include new virology data based on the results from pharmacology studies, describing the conservation of the epitope as well as assessing any susceptibility changes due to either individual amino acid substitutions or emerging variants, including data against Omicron BA.1, BA.2 and BA.3; to include a warning to refer to the uncertainty of the clinical relevance of the observed decrease in "in vitro" neutralisation against Omicron BA.2, and include animal toxicology and pharmacology results observed from the cynomolgus monkey 2-week repeat-dose toxicology study. In addition, the MAH took the opportunity to implement editorial changes in sections 4.2, 4.8, 5.1,	22/04/2022	29/04/2022	SmPC and PL	Pseudotyped virus like particles assessments indicated greater than 5-fold changes in sotrovimab EC50 values compared to wild-type against the following variant spike proteins: Omicron BA.2 (16-fold change in EC50 value) and Omicron BA.3 (7.3-fold change in EC50 value). The reduction was of 2.7-fold and 3.3-fold for BA.1 and BA.1.1, respectively. The clinical relevance of the observed decrease in in vitro neutralisation against Omicron BA.2 is not known.

	5.2, 6.6 and 9 of the SmPC. The package leaflet is updated accordingly. A.6 - To include the ATC Code J06BD05 in Section 5.1 of the Summary of Product Characteristics (SmPC). A.6 - Administrative change - Change in ATC Code/ATC Vet Code C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				