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/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	15/12/2022	09/01/2023	SmPC	

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

	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				
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		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 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	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 considered in agreement with the data already in the product information.

	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				
IB/0008/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.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	15/10/2022	15/11/2022	Annex II	
PSUSA/10973 /202202	Periodic Safety Update EU Single assessment - sotrovimab (Xevudy)	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	01/09/2022	n/a		

	site				
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 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	21/07/2022	22/07/2022	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.2.12.1 (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, 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	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.