Vyxeos liposomal

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/0043	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)	23/04/2024		SmPC	
IB/0042/G	This was an application for a group of variations.	10/04/2024	n/a		

[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).

	B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.z - Quality change - Active substance - Other variation 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/0044/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	05/04/2024	n/a		
IA/0041/G	This was an application for a group of variations. B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	14/12/2023	n/a		

	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process				
IAIN/0040	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	20/10/2023	n/a		
R/0037	Renewal of the marketing authorisation.	30/03/2023	05/06/2023	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Vyxeos liposomal in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IB/0039	B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method	12/05/2023	n/a		
PSUSA/10701 /202208	Periodic Safety Update EU Single assessment - daunorubicin / cytarabine	16/03/2023	n/a		PRAC Recommendation - maintenance
IB/0033	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	20/12/2022	n/a		
IA/0038	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	11/11/2022	n/a		

IB/0036/G	This was an application for a group of variations. B.II.f.z - Stability of FP - 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)	10/11/2022	05/06/2023	SmPC	
IA/0034/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.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.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	17/10/2022	n/a		
IB/0032	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	13/10/2022	n/a		
II/0030	Update of sections 4.2, 4.4 and 5.2 of the SmPC to amend information and delete the existing warning for patients with renal impairment based on the final results from study CPX351-102 (PMR2): a phase 1, open-label, PK and safety study to evaluate the potential impact of renal impairment on the pharmacokinetics and safety of CPX-351	21/07/2022	05/06/2023	SmPC	

	(Daunorubicin and Cytarabine) liposome for injection treatment in adult patients with hematologic malignancies. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0031/G	This was an application for a group of variations. 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.III.1.a.5 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate of a non-sterile AS that is to be used in a sterile medicinal product, where water is used in the last steps of the synthesis and the material is not claimed to be endotoxin free	05/07/2022	n/a		
II/0028/G	This was an application for a group of variations. B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change	12/05/2022	n/a		

	outside the approved specifications limits range				
II/0018/G	This was an application for a group of variations. Update of sections 4.4, 4.8, 5.1 and 5.2 of the SmPC to include relevant information in paediatric patients based on results from the paediatric clinical study AAML1421. The Package leaflet is updated accordingly. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	24/03/2022	02/06/2022	SmPC, Annex II and PL	Please refer to Scientific Discussion 'Vyxeos Liposomal-H-discussioC-0004282-II-0018'
IB/0029/G	This was an application for a group of variations. B.II.f.1.e - Stability of FP - Change to an approved stability protocol B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation	22/03/2022	02/06/2022	SmPC	PI was updated to reflect extension of shelf life of finished product from 24 months to 30 months
PSUSA/10701 /202108	Periodic Safety Update EU Single assessment - daunorubicin / cytarabine	10/03/2022	n/a		PRAC Recommendation - maintenance
II/0017	Submission of a final CSR for post-marketing observational study of Vyxeos liposomal to assess the incidence of infusion-related reactions in adult	02/12/2021	n/a		

	patients. The primary objective of this study is to assess the nature, incidence, and severity of infusion-related reactions during and for up to one day following the last infusion of a five-day induction course in patients treated with the product. The secondary objective is to assess this information during and for up to one day following the last infusion of a five-day induction course in patients treated with Vyxeos. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
IB/0026/G	This was an application for a group of variations. B.II.f.z - Stability of FP - Other variation B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	29/11/2021	n/a		
IB/0025	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	18/10/2021	n/a		
IA/0024/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	12/07/2021	n/a		

	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 B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.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.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure				
IA/0023/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	25/05/2021	n/a		
IA/0022/G	This was an application for a group of variations.	23/04/2021	n/a		

	B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change				

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IA/0021/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 control/testing takes place 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.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits	11/03/2021	n/a		
II/0019	B.II.d.1.f - Change in the specification parameters and/or limits of the finished product - Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product	11/03/2021	n/a		

PSUSA/10701 /202008	Periodic Safety Update EU Single assessment - daunorubicin / cytarabine	11/03/2021	n/a		PRAC Recommendation - maintenance
IB/0015	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	06/01/2021	02/06/2022	SmPC, Annex II and PL	
II/0014	Update of the section 5.1 of the SmPC to reflect the 5-years overall survival data from the Follow-Up Phase of the Phase 3 Study CPX310-301. Additionally, the MAH has introduced minor editorial changes in the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/11/2020	02/06/2022	SmPC, Annex II and PL	SmPC new text 60 Month Follow-up phase of Study 301, a Phase 3 randomised, multicentre, open-label, parallel-arm, superiority study which evaluated Vyxeos liposomal vs. a standard combination of cytarabine and daunorubicin (7+3) in 309 patients between 60 to 75 years of age with untreated high-risk AML. The 60-month overall survival rate was higher for the Vyxeos treatment arm (18%) versus the 7+3 treatment arm (8%); the hazard ratio was 0.70 (95% CI: [0.55, 0.91]). For more information, please refer to the Summary of Product Characteristics.
II/0012/G	This was an application for a group of variations. B.II.b.3.b - Change in the manufacturing process of the finished or intermediate product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	10/09/2020	n/a		

PSUSA/10701 /202002	Periodic Safety Update EU Single assessment - daunorubicin / cytarabine	03/09/2020	n/a		PRAC Recommendation - maintenance
IA/0013/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 control/testing takes place B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place 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.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	06/07/2020	n/a		
IAIN/0010	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	13/03/2020	n/a		
PSUSA/10701 /201908	Periodic Safety Update EU Single assessment - daunorubicin / cytarabine	13/02/2020	n/a		PRAC Recommendation - maintenance
IA/0009	B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP -	28/01/2020	n/a		

	Replacement/addition of a site where batch control/testing takes place				
IA/0008/G	This was an application for a group of variations. B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	10/01/2020	n/a		
IAIN/0007	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	30/10/2019	n/a		
IAIN/0004	A.2.a - Administrative change - Change in the (invented) name of the medicinal product for CAPs	25/10/2019	28/08/2020	SmPC, Labelling and PL	
PSUSA/10701 /201902	Periodic Safety Update EU Single assessment - daunorubicin / cytarabine	05/09/2019	n/a		PRAC Recommendation - maintenance
IB/0003	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/08/2019	28/08/2020	SmPC and PL	
IA/0001	B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved	29/03/2019	n/a		

	manufacturer				