Nuwiq

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
WS/2244	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of study results of study GENA-21b; a prospective, open-label, multicentre phase 3b study to assess the efficacy and safety of personalised prophylaxis with Human-cl rhFVIII in previously	13/10/2022		SmPC and PL	

[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).

	treated adult patients with severe haemophilia A to update the Adverse Drug Reactions in section 4.8 of the SmPC, based on reports from clinical trials. Section 5.1 of the SmPC has been updated to provide in-formation on a prospective open-label clinical study. For more information, please refer to the Summary of Product Characteristics. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
WS/2319	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	01/09/2022	n/a		
IG/1527/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 changes to an approved test procedure 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 A.4 - Administrative change - Change in the name	22/06/2022	n/a		

	and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
WS/2156	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 GENA-99 including the integrated analysis report of studies GENA-99, GENA-13, GENA-15, GENA-21, GENA-21b and GENA-100. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	27/01/2022	n/a		This variation includes the submission of the final reports from study GENA-99 including the integrated analysis report of studies GENA-99, GENA-13, GENA-15, GENA-21, GENA-21b and GENA-100 to provide data on the long-term immunogenicity, safety, and efficacy of simoctocog alfa in patients with haemophilia A in line with the requirements of the FVIII guideline. Please also refer to Scientific Discussion "Nuwiq-Vihuma-WS-2156"
X/0042	Extension application to add a new strength of 1500 IU for simoctocog alfa powder and solvent for solution for injection, for Intravenous use.	11/11/2021	06/01/2022	SmPC, Labelling and PL	

	The marketing authorisation holder took the opportunity to align the PI to the latest QRD template (version 10.2). Annex I_2.(c) Change or addition of a new strength/potency				
WS/2064	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	02/12/2021	n/a		
WS/2146	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS	07/10/2021	n/a		
PSUSA/10276 /202101	Periodic Safety Update EU Single assessment - simoctocog alfa	02/09/2021	n/a		PRAC Recommendation - maintenance
WS/2029	This was an application for a variation following a worksharing procedure according to Article 20 of	18/03/2021	n/a		

	Commission Regulation (EC) No 1234/2008. B.II.e.1.z - Change in immediate packaging of the finished product - Other variation				
WS/1999	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	04/03/2021	n/a		
WS/1992/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	14/01/2021	n/a		
IG/1310/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	27/11/2020	n/a		

	changes to an approved test procedure B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits				
WS/1847	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	16/07/2020	05/07/2021	SmPC, Annex II, Labelling and PL	
WS/1816	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	02/07/2020	n/a		
WS/1752	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	30/01/2020	n/a		
WS/1726	This was an application for a variation following a	28/11/2019	n/a		

	worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS				
WS/1662	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	12/09/2019	n/a		
PSUSA/10276 /201901	Periodic Safety Update EU Single assessment - simoctocog alfa	05/09/2019	n/a		PRAC Recommendation - maintenance
IG/1138/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 changes to an approved test procedure B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation	26/08/2019	n/a		
WS/1506/G	This was an application for a group of variations	25/07/2019	27/07/2020	SmPC and PL	

	following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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				
WS/1584	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB	20/06/2019	n/a		
R/0027	Renewal of the marketing authorisation.	28/02/2019	26/04/2019	Annex II and PL	
IG/1061	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	31/01/2019	n/a		
WS/1427	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.4.z - Change to in-process tests or limits	25/10/2018	n/a		

	applied during the manufacture of the AS - Other variation				
WS/1404	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method	18/10/2018	n/a		
WS/1425	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	13/09/2018	n/a		
PSUSA/10276 /201801	Periodic Safety Update EU Single assessment - simoctocog alfa	06/09/2018	n/a		PRAC Recommendation - maintenance
IG/0969/G	This was an application for a group of variations. B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method	03/08/2018	n/a		

	B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - 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.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure				
X/0020	Annex I_2.(c) Change or addition of a new strength/potency	25/01/2018	23/03/2018	SmPC, Labelling and PL	
A31/0015	Pursuant to Article 31 of Directive 2001/83/EC, Germany initiated a procedure on 6 July 2016 based on concerns resulting from the evaluation of data from pharmacovigilance activities. The PRAC was requested to assess the potential	14/09/2017	24/11/2017	SmPC and PL	Please refer to the assessment report: human coagulation factor VIII - EMEA/H/A-31/1448

	impact of the results of the SIPPET study (which concluded that recombinant factor VIII medicines had a higher incidence of inhibitor development than plasma-derived medicines), and to issue a recommendation as to whether the marketing authorisations of these products should be maintained, varied, suspended or revoked. The EMA concluded in September 2017 that there is no clear and consistent evidence of a difference in the incidence of inhibitor development between the two classes of factor VIII medicines: those derived from plasma and those made by recombinant DNA technology. Due to the different characteristics of individual products within the two classes, EMA concluded that the risk of inhibitor development should be evaluated individually for each medicine, regardless of class. The risk for each product will continue to be assessed as more evidence becomes available.				
WS/1176/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a	28/09/2017	n/a		

	biological/immunological product B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol				
II/0017/G	This was an application for a group of variations. C.I.4: Update of sections 4.2, 4.8 and 5.1 of the SmPC to reflect available data from Previously Untreated Patients (PUP) from GENA-05 (interim report) study. The Package Leaflet is updated accordingly. The RMP version 8.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the Product Information throughout to bring it in line with the Core summary of product characteristics for human plasma-derived and recombinant coagulation factor VIII products (EMA/CHMP/BPWP/1619/1999 rev. 2) and with the QRD version 10 (affects labelling only). Moreover the MAH is combining the SmPC for all strengths and updating Annex A with detailed information on the packaging. C.I.11: Submission of an updated RMP version 8.0 in order to align the content in a single harmonised	14/09/2017	24/11/2017	SmPC, Labelling and PL	The MAH provided an Interim Report on their PUP-study. Preliminary data regarding efficacy and safety is considered to be in line with previously collected data in children but should be updated, accordingly, as soon as the final study report is available. Consequently, section 4.2 of the SmPC has been updated to remove the statement that safety and efficacy of Nuwiq in previously untreated patients (PUP) have not yet been established and additional information on treatment monitoring has been added. Section 4.8 has been updated to reflect the entity of 'Hypersensitivity'. Section 5.1 has been updated with a statement that the PUP-study is ongoing. The MAH should provide an update of the SmPC with the Final Study Report.

	worldwide version for simoctocog alfa (rFVIII). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data 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				
PSUSA/10276 /201701	Periodic Safety Update EU Single assessment - simoctocog alfa	01/09/2017	n/a		PRAC Recommendation - maintenance
II/0012/G	This was an application for a group of variations. B.I.a.3.c - Change in batch size (including batch size ranges) of AS or intermediate - The change requires assessment of the comparability of a biological/immunological AS B.II.b.4.c - Change in the batch size (including batch size ranges) of the finished product - The change requires assessment of the comparability of a biological/immunological medicinal product or a new bioequivalence study B.II.e.1.b.2 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Sterile medicinal products and biological/immunological medicinal products	16/03/2017	n/a		

PSUSA/10276 /201607	Periodic Safety Update EU Single assessment - simoctocog alfa	09/02/2017	n/a		PRAC Recommendation - maintenance
PSUSA/10276 /201601	Periodic Safety Update EU Single assessment - simoctocog alfa	02/09/2016	n/a		PRAC Recommendation - maintenance
IB/0014	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	19/07/2016	n/a		
IAIN/0013/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site 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	12/07/2016	n/a		
IB/0009	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	31/03/2016	n/a		
IB/0010	B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation	23/02/2016	n/a		
PSUSA/10276 /201507	Periodic Safety Update EU Single assessment - simoctocog alfa	11/02/2016	n/a		PRAC Recommendation - maintenance
IB/0008/G	This was an application for a group of variations.	08/02/2016	n/a		

	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.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method				
IB/0006	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	11/11/2015	26/09/2016	SmPC, Labelling and PL	
IAIN/0005/G	This was an application for a group of variations. A.1 - Administrative change - Change in the name and/or address of the MAH A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release 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)	25/09/2015	26/09/2016	SmPC, Annex II, Labelling and PL	
PSUSA/10276 /201501	Periodic Safety Update EU Single assessment - simoctocog alfa	10/09/2015	n/a		PRAC Recommendation - maintenance
IB/0004/G	This was an application for a group of variations.	14/08/2015	n/a		

	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.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation				
IB/0001	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)	05/12/2014	n/a		