NovoThirteen

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
R/0020	Renewal of the marketing authorisation.	23/03/2017	24/05/2017	SmPC, Annex II, Labelling and PL	
II/0018	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/03/2017		SmPC, Annex II, Labelling and PL	The MAH updated the SmPC: - Section 4.4 to reflect that on-demand treatment was used in the extension study F13CD-3720: The on-demand treatment of acute bleeds or breakthrough bleeds with NovoThirteen was allowed per protocol in the

[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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					late phase clinical development programme. One patient was treated on demand in a phase 3b extension study (F13CD-3720). Also, on-demand treatment is followed in a non-interventional post-authorisation safety study (NN1841-3868). Until further results are available, alternative treatment should be considered in such situations. - Section 5.1 to update the bleeding rate: In the F13CD-1725 extension trial F13CD-3720, the age-adjusted rate of bleeds that required treatment with a FXIII-containing product was estimated to be 0.021 bleeds per subject year with a 95% CI of [0.0062; 0.073] (model-based estimate corresponding to a mean age of the trial population of 31.0 years). The crude bleeding rate in the two trials, F13CD-1725 and F13CD-3720, not adjusted for age, were 0.138 and 0.043 respectively, corresponding to a total of 13 bleeds over 223 subject-years and a pooled rate of 0.058. - Section 5.2 to update the half-life: The half-life of NovoThirteen was assessed in the F13CD-1725 trial from a limited blood sampling scheme at 1 hour, 14 and 28 days post dose. Based on FXIII activity measured by the Berichrom assay in patients with congenital FXIII deficiency, a geometric mean half-life of 11.8 days was estimated.
PSUSA/10034 /201607	Periodic Safety Update EU Single assessment - catridecacog	09/02/2017	n/a		PRAC Recommendation - maintenance
IA/0019	B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation	28/11/2016	n/a		

IB/0017/G	This was an application for a group of variations. 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	11/11/2016	n/a		
II/0015	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	15/09/2016	n/a		
II/0013	To update the SmPC section 4.8 Undesirable effects to reflect information that in a post-authorisation safety study transient non-neutralising antibodies were seen in a child with congenital FXIII deficiency after several years of treatment with NovoThirteen. In Annex II the MAH applied for a correction of an omission related to QRD template version 9.1. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/05/2016	24/05/2017	SmPC and Annex II	
IB/0014	B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	22/04/2016	n/a		

II/0012/G	This was an application for a group of variations. 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 C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	01/04/2016	n/a		
PSUSA/10034 /201507	Periodic Safety Update EU Single assessment - catridecacog	11/02/2016	n/a		PRAC Recommendation - maintenance
IB/0009	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	01/10/2015	n/a		
IB/0010	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	10/08/2015	n/a		
IB/0007	To extend the shelf life of the primary and secondary reference materials of the active substance from 5 to 10 years. B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	16/02/2015	n/a		

PSUSA/10034 /201407	Periodic Safety Update EU Single assessment - catridecacog	12/02/2015	n/a		PRAC Recommendation - maintenance
IB/0005/G	This was an application for a group of variations. B.I.d.1.a.1 - Stability of AS - Change in the re-test period/storage period - Reduction B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	17/10/2014	n/a		
PSUV/0004	Periodic Safety Update	11/09/2014	n/a		PRAC Recommendation - maintenance
PSUV/0003	Periodic Safety Update	06/03/2014	n/a		PRAC Recommendation - maintenance
II/0002	Extension of indication to include the treatment of bleeding in children with congenital factor XIII A-subunit deficiency below 6 years of age. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated regarding posology recommendations, as well as safety, efficacy and pharmacokinetics information in this patient population. In addition, section 6.6 of the SmPC is updated in order to add a recommendation for the dilution of the reconstituted product for patients less than 24 kg. The Package Leaflet is updated in accordance. Furthermore, the PI is being brought in line with the latest QRD template version 9.0. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	23/01/2014	21/02/2014	SmPC, Annex II and PL	Please refer to the Scientific Discussion NovoThirteen EMEA/H/C/002284/II/0002.

IG/0280	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	17/04/2013	n/a		