EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EVARREST

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/G	This was an application for a group of variations. 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 C.I.4 - Change(s) in the SPC, Labelling or PL due to	23/02/2017	29/03/2017	SmPC, Annex II, Labelling and PL	Based on the review of the submitted studies, section 4.2 of the Summary of Product Characteristics (SmPC) was updated to reflect that the dose to be applied is governed by variables including, but not limited to, the type of surgical intervention, the size of the area and the mode of intended application, and the number of applications. Section 5.1 of the SmPC has been amended to reflect that the presented efficacy data supported the authorised indication. In addition section 4.8 (SmPC) has been

[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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	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 C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				updated to provide further safety information related to pulmonary embolism, deep vein thrombosis and increase of anti-thrombin antibodies. The tabulated list of adverse drug reactions (ADRS) was amended to add operative haemorrhage and anastomotic haemorrhage as uncommon ADRs and to update the frequencies of blood fibrinogen increased and post-procedural haemorrhage ADRs from “common” to “uncommon”. The Package Leaflet was updated in line with the SmPC.
PSUSA/10297 /201606	Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin	12/01/2017	n/a		PRAC Recommendation - maintenance
IB/0025	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	23/09/2016	n/a		
PSUSA/10297 /201512	Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin	07/07/2016	n/a		PRAC Recommendation - maintenance
II/0018	B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	01/04/2016	n/a		
IB/0020/G	This was an application for a group of variations. 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.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting	29/03/2016	n/a		

	material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process				
IB/0022	B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)	08/03/2016	n/a		
IB/0021/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.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	24/02/2016	n/a		
PSUSA/10297 /201506	Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin	14/01/2016	n/a		PRAC Recommendation - maintenance
II/0016	B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method	10/12/2015	n/a		
IB/0017	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	27/11/2015	n/a		

	corresponding test method				
IB/0019/G	This was an application for a group of variations. 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 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	28/10/2015	n/a		
IB/0015	B.II.b.5.f - Change to in-process tests or limits applied during the manufacture of the finished product - Addition or replacement of an in-process test as a result of a safety or quality issue	16/10/2015	n/a		
II/0012/G	This was an application for a group of variations. 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 biological/immunological product 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.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process	24/09/2015	22/09/2016	Annex II	

	of the AS B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol				
IB/0013	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	10/09/2015	n/a		
IA/0011	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	30/04/2015	n/a		
II/0008	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	23/04/2015	n/a		

PSUSA/10103 /201409	Periodic Safety Update EU Single assessment - human fibrinogen, human thrombin (sealant matrix)	10/04/2015	n/a		PRAC Recommendation - maintenance
N/0009	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	02/03/2015	22/09/2016	Labelling	
IB/0007/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 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	06/01/2015	n/a		
II/0002/G	This was an application for a group of variations. Addition of a new size of Evarrest sealant matrix. As a consequence changes are introduced in the manufacturing process of the active substance and finished product . A.4 - Administrative change - Change in the name 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 A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder	20/11/2014	19/02/2015	SmPC, Labelling and PL	Addition of a new size of Evarrest sealant matrix. As a consequence changes are introduced in the manufacturing process of the active substance and finished product.

	or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient 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 B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.II.a.3.b.3 - Changes in the composition (excipients) of the finished product - Other excipients - Change that relates to a biological/immunological product B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits 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.z - Change in control of excipients in the Finished Product - Other variation B.II.c.z - Change in control of excipients in the Finished Product - Other variation B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure				
PSUV/0004	Periodic Safety Update	09/10/2014	n/a		PRAC Recommendation - maintenance
II/0003/G	This was an application for a group of variations. to add a site responsible for batch testing of the finished product. B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	25/09/2014	n/a		
II/0001	Addition of an in-process control in the manufacturing process of the finished product. B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability	20/02/2014	19/02/2015	SmPC and PL	