Evicel

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/0099	Please refer to the Recommendations section above C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	16/03/2023		SmPC and PL	Following the submission of the paediatric study BIOS-13-006, section 4.8 and 5.1 of the SmPC is up-dated to add pseudomeningocele to the list of ADRs with frequency uncommon and to update efficacy and safety information on paediatric population. Please refer to Scientific Discussion 'Product Name-H-C-

[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).

					Product Number-II-Var.No’
IAIN/0101/G	This was an application for a group of variations. B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	06/02/2023	n/a		
IAIN/0100	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	12/12/2022	n/a		
IAIN/0098	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	31/10/2022	n/a		
IAIN/0097/G	This was an application for a group of variations. B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) -	18/07/2022	n/a		

	Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP				
IAIN/0096/G	This was an application for a group of variations. B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	04/07/2022	n/a		
IAIN/0095	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	23/06/2022	n/a		
IAIN/0094	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes	04/10/2021	n/a		

	do not affect the properties of the FP				
IAIN/0093	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	02/09/2021	n/a		
IAIN/0092/G	This was an application for a group of variations. B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	05/08/2021	n/a		
IAIN/0091	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	05/08/2021	n/a		

IAIN/0090	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	02/08/2021	n/a		
IA/0089/G	This was an application for a group of variations. 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.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	15/07/2021	n/a		
IAIN/0088	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	01/02/2021	n/a		
PSUSA/10297 /202006	Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin	14/01/2021	n/a		PRAC Recommendation - maintenance
IAIN/0087	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	12/01/2021	n/a		

IAIN/0086/G	This was an application for a group of variations. B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	10/11/2020	n/a		
IA/0085	A.7 - Administrative change - Deletion of manufacturing sites	28/10/2020	16/07/2021	Annex II and PL	
IAIN/0083	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	29/05/2020	n/a		
IA/0082/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.e - Change in test procedure for the finished product - Update of the test procedure to comply	29/05/2020	n/a		

	with the updated general monograph in the Ph. Eur.				
IAIN/0081	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	08/05/2020	n/a		
II/0078	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	02/04/2020	16/07/2021	SmPC and PL	
IAIN/0080	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	16/01/2020	n/a		
PSUSA/10297 /201906	Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin	16/01/2020	n/a		PRAC Recommendation - maintenance
IAIN/0079	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	27/11/2019	n/a		
IB/0075	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	22/08/2019	n/a		

	material/intermediate				
IAIN/0076	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	15/08/2019	n/a		
IAIN/0074	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	25/07/2019	n/a		
IB/0072	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	17/07/2019	n/a		
IB/0073	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	03/07/2019	n/a		
II/0067	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	02/05/2019	n/a		
IAIN/0070	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier	10/04/2019	n/a		

	of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP				
IAIN/0069	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	02/04/2019	n/a		
IAIN/0068	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	01/04/2019	n/a		
IAIN/0066	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	01/03/2019	n/a		
PSUSA/10297 /201806	Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin	17/01/2019	n/a		PRAC Recommendation - maintenance
II/0063	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	29/11/2018	n/a		

IB/0062/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	16/11/2018	n/a		
R/0054	Renewal of the marketing authorisation.	28/06/2018	23/08/2018	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 Evicel in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
II/0059	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	26/07/2018	n/a		
PSUSA/10297 /201712	Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin	12/07/2018	n/a		Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Evicel in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IAIN/0061	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	06/06/2018	n/a		
IAIN/0060/G	This was an application for a group of variations.	06/06/2018	n/a		

	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP				
IB/0058/G	This was an application for a group of variations. B.II.z - Quality change - Finished product - Other variation B.II.z - Quality change - Finished product - Other variation	15/05/2018	n/a		
IAIN/0057	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	15/03/2018	n/a		
II/0053	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	08/02/2018	n/a		

IAIN/0055/G	This was an application for a group of variations. B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	15/01/2018	n/a		

	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier				

	of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes				

	do not affect the properties of the FP				
PSUSA/10297 /201706	Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin	11/01/2018	n/a		PRAC Recommendation - maintenance
N/0052	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/09/2017	23/08/2018	Labelling	
IAIN/0051/G	This was an application for a group of variations. B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or	18/08/2017	n/a		

	amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) -				

	Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP				
IAIN/0049	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	18/08/2017	n/a		
IB/0048	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other	16/08/2017	n/a		

	changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
PSUSA/10297 /201612	Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin	06/07/2017	n/a		PRAC Recommendation - maintenance
IA/0047/G	This was an application for a group of variations. 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 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)	28/04/2017	n/a		
IB/0045	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	25/04/2017	n/a		
IA/0046	A.7 - Administrative change - Deletion of manufacturing sites	07/04/2017	n/a		
PSUSA/10297 /201606	Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin	12/01/2017	n/a		PRAC Recommendation - maintenance
IB/0043/G	This was an application for a group of variations. B.II.z - Quality change - Finished product - Other	22/12/2016	n/a		

	variation B.II.z - Quality change - Finished product - Other variation				
IA/0042/G	This was an application for a group of variations. 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.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	19/10/2016	n/a		
II/0039	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	15/09/2016	n/a		Update of the Risk Management Plan (Version 14). The variation is not affecting the PI.
IB/0041	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	05/09/2016	n/a		
PSUSA/10297 /201512	Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin	07/07/2016	n/a		PRAC Recommendation - maintenance
IA/0038	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	22/04/2016	n/a		

	specification parameter (e.g. deletion of an obsolete parameter)				
PSUSA/10297 /201506	Periodic Safety Update EU Single assessment - human fibrinogen / human thrombin	14/01/2016	n/a		PRAC Recommendation - maintenance
IB/0036/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 material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	03/12/2015	n/a		
II/0032	Update of section 4.8 of the SmPC in order to update the frequencies from common to uncommon of ADRs regarding vascular surgery already reported in the Product Information. A minor change is introduced in section 4.2 of the SmPC. The Package Leaflet and the RMP (adopted version: 13.0) are updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	19/11/2015	24/10/2016	SmPC and PL	

II/0029/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.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol 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.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	22/10/2015	24/10/2016	SmPC, Annex II and PL	
IB/0035/G	This was an application for a group of variations.	05/10/2015	n/a		

	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				
IB/0033/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	10/09/2015	n/a		
PSUSA/1627/ 201412	Periodic Safety Update EU Single assessment - human fibrinogen, human thrombin (all pharmaceutical dose forms except for sealant matrix)	09/07/2015	n/a		PRAC Recommendation - maintenance
PSUSA/1627/ 201410	Periodic Safety Update EU Single assessment - human fibrinogen, human thrombin (all pharmaceutical dose forms except for sealant matrix)	07/05/2015	n/a		PRAC Recommendation - maintenance
IB/0028/G	This was an application for a group of variations. A.5.b - Administrative change - Change in the name	18/12/2014	n/a		

	and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) B.I.b.1.i - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Where there is no monograph in the European/National Ph. for the AS, a change in specification from in-house to a non-official/third country Ph. 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.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.e.2.d - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition or replacement of a specification parameter as a result of a safety or quality issue B.II.f.1.e - Stability of FP - Change to an approved stability protocol B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
II/0026	This variation concerned an update of section 6.6 of the SmPC with instructions regarding the use of EVICEL Fibrin Sealant applicator tips. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the ATC	23/10/2014	27/01/2015	SmPC, Annex II and PL	As part of this application, the MAH proposed to revise the EVICEL product information with instructions regarding the use of additional EVICEL Fibrin Sealant accessory tips; a 4 cm Control Tip, a 45 cm tip, and an Airless Spray Accessory. Detailed instructions for use of these accessory

	code in section 5.1 of the SmPC as well as to make minor editorial changes to the SmPC, Annex II and the Package Leaflet. 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				tips have not been included in the Product Information as it should be provided together with the devices. However, for the proposed 45 cm flexible tip, the CHMP was of the view that distance and pressure recommendations should be included in the Product Information. Under the prerequisite of compliance with distance requirements, CHMP considered the 45 cm flexible accessory tip acceptable. It can be used in both open and laparoscopic procedures, but is especially designed for the use in laparoscopic procedures. For open surgery a pressure range of 1.4 – 1.7 bar is proposed, however, the range appears unnecessarily high for laparoscopic procedures. Following life-threatening events of air/gas embolism the spray pressure used in laparoscopic procedures was limited to a maximum of 1.4 bar (Article 20 referral). No clinically relevant advantage could be demonstrated for 1.7 bar over 1.4 bar for the small distances used within laparoscopic procedures. On the other hand a pressure of 1.0 bar cannot produce a sufficient mixing of the two sealant components. It is therefore recommended to use the 45 cm flexible tip in laparoscopic procedures at a spray gas pressure of 1.4 bar. The product information has been revised accordingly.
PSUV/0027	Periodic Safety Update	08/05/2014	n/a		PRAC Recommendation - maintenance
II/0025/G	This was an application for a group of variations. Changes to the quality documentation A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used	23/01/2014	27/01/2015	SmPC, Labelling and PL	

	in the manufacture of the AS 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 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.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.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Change (replacement) to a biological/immunological/ immunochemical test method or a method using a biological reagent for a biological AS B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.e.1.b.2 - Change in immediate packaging of the finished product - Type of container - Sterile medicinal products and biological/immunological				

	medicinal products B.II.f.1.c - Stability of FP - Change in storage conditions for biological medicinal products, when the stability studies have not been performed in accordance with an approved stability protocol				
II/0023	Introduction of additional batch testing laboratory for release in EU. B.II.b.2.b.3 - Change to batch release arrangements and quality control testing of the FP - Including batch control/testing for a biol/immunol product and one of the test methods is a biol/immunol/immunochemical method	21/11/2013	n/a		
R/0022	Renewal of the marketing authorisation.	24/10/2013	20/11/2013	SmPC, Annex II, Labelling and PL	The benefit – risk balance of Evicel in the approved indications of supportive treatment in surgery where standard surgical techniques are insufficient, for improvement of haemostasis and suture support for haemostasis in vascular surgery and for suture line sealing in dura mater closure, remains positive. A further update of the Risk Management system is requested by the CHMP by 16 December 2013 as the same time with the Periodic Safety Update Report to ensure ongoing implementation of all risk minimisation measures agreed to eliminate the risk of air embolism.
II/0021	Extension of indication to include: use for "suture line sealing in dura mater closure" for Evicel. As a consequence, update of sections 4.1, 4.2, 4.3, 4.4, 4.8, and 5.1 of the SmPC in order to relevant posology, contra-indications, warnings, safety	27/06/2013	26/07/2013	SmPC, Annex II, Labelling and PL	Please refer to the Scientific Discussion Evicel-H-C-0898-II-21

	information. The Package Leaflet is updated in accordance. Furthermore, the PI is being brought in line with the latest QRD template version 9.0. Minor editorial amendments were also implemented in the PI. The requested variation proposed amendments to the SmPC, Annex II, Labelling and Package Leaflet. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
A20/0018	Pursuant to Article 20 of Regulation (EC) No. 726/2004, the European Commission requested the CHMP to re-evaluate the benefit-risk balance of the use of Evicel with a spray device in light of newly available data on the risk of life-threatening gas embolism following spray application of Evicel, and to give its opinion on measures necessary to ensure the safe and effective use of Evicel, and on whether the marketing authorisation for this product should be maintained, varied, suspended or withdrawn.	15/11/2012	13/02/2013	SmPC, Annex II and PL	Please refer to the assessment report: EMEA/H/C/000898/A-20/0018.
II/0020	Change in test procedure B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Change (replacement) to a biological/immunological/	13/12/2012	n/a		

	immunochemical test method or a method using a biological reagent for a biological AS				
IAIN/0019/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV	20/07/2012	n/a		
IB/0016	B.I.c.1.c - Change in immediate packaging of the AS - Liquid ASs (non sterile)	17/07/2012	n/a		
IB/0014	C.I.3.a - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46,	16/01/2012	26/07/2012	SmPC	Following review of PSUR 5 EMA requested to add details concerning pressure and distance for spray applications to section 6.6 of the SPC "Instructions for use, handling and

	or amendments to reflect a Core SPC - Changes with NO new additional data are submitted by the MAH				disposal" under sub header "Spray application". These parameters currently appear in section 4.4 "Special warnings and precautions for use".
IA/0013	A.1 - Administrative change - Change in the name and/or address of the MAH	07/10/2011	n/a	SmPC, Annex II, Labelling and PL	
IB/0011	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	08/07/2011	n/a		
IB/0012	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	06/07/2011	n/a	SmPC, Labelling and PL	
II/0009/G	This was an application for a group of variations. Changes to the active substance and finished product manufacture. 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	17/02/2011	08/03/2011		
II/0007/G	This was an application for a group of variations.	20/01/2011	27/01/2011		

	1. Change in active substance control method. 2. Change in active substance specification. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Change (replacement) to a biological/immunological/ immunochemical test method or a method using a biological reagent for a biological AS B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS				
IA/0010/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	17/01/2011	n/a	Annex II	
II/0006	Update of sections 4.4 and 6.6 of the Summary of Product Characteristics with regards to the risk of air embolism associated with the spray application of Evicel following the assessment of the 1st and 2nd PSUR. The Package Leaflet has been udpated	24/06/2010	06/08/2010	SmPC, Annex II and PL	In the 1st Evicel PSUR (PSU 010), two cases of air embolism have been reported following the application of Quixil (another fibrin sealant) using the spray application device with pressurised gas or air in conjunction with a pressure regulator. In the 2nd Evicel PSUR (PSU 011),

	accordingly. Furthermore, Annex II has been updated accordingly in order to include the latest version number of the RMP (version RMP-002-01). C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH				three cases of air embolism have been reported following the application of Evicel (one case) or Quixil (two cases) using the spray application device. Following the assessment of the two PSURs, the MAH was requested by the CHMP to submit a type II variation to update sections 4.4 and 6.6 of the Summary of Product Characteristics, the Risk Management Plan and to come up with a proposal of Direct Healthcare Professional Communication. The MAH has hereby submitted a type II variation. The CHMP considered this type II variation acceptable and agreed on amendments to be introduced in the Summary of Product Characteristics and the Package Leaflet, on the revised Risk Management Plan and the proposed Direct Healthcare Professional Communication.
II/0004	Change of shelf life of final product. Quality changes	18/02/2010	30/03/2010	SmPC, Labelling and PL	Change of shelf life of final product.
II/0003	Change to Thrombin drug substance manufacture. Quality changes	17/12/2009	09/02/2010		Change to Thrombin drug substance manufacture.
II/0005	Changes to QPPV	19/11/2009	15/12/2009	Annex II	The CHMP considers that the change of QPPV as described by the MAH fulfils the requirements and is considered acceptable. Consequently, Annex II has been updated with the new version number of the agreed DDPS (version 11-01-05).
II/0002	Change to active substance manufacture of Thrombin.	24/09/2009	30/09/2009		Change to active substance manufacture of Thrombin.

	Quality changes				
II/0001	Update of Summary of Product Characteristics, Labelling and Package Leaflet	19/03/2009	23/04/2009	SmPC, Annex II, Labelling and PL	Update of the instructions for use in section 6.6 of the SPC and in the Package Leaflet further to the results of an animal comparability study evaluating the functional performance of the device in laparoscopic surgery using the 35cm tip. In addition, the date of first authorisation and MA numbers were added in the PI where appropriate. The MAH also took the opportunity to make minor editorial changes.