Cerezyme

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
N/0133	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/05/2024		PL	
IB/0132	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	19/04/2024	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).

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II/0131	B.I.b.1.e - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP	15/02/2024	n/a		
PSUSA/1727/202305	Periodic Safety Update EU Single assessment - imiglucerase	11/01/2024	n/a		PRAC Recommendation - maintenance
IAIN/0129	A.1 - Administrative change - Change in the name and/or address of the MAH	03/04/2023	17/07/2023	SmPC, Labelling and PL	
PSUSA/1727/202205	Periodic Safety Update EU Single assessment - imiglucerase	12/01/2023	n/a		PRAC Recommendation - maintenance
IB/0128	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	16/11/2022	17/07/2023	SmPC and PL	
IA/0127/G	This was an application for a group of variations. 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.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)	31/08/2022	17/07/2023	Annex II	

II/0123/G	This was an application for a group of variations. 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 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 B.I.d.1.b.2 - Stability of AS - Change in the storage conditions - Change in storage conditions of biological/immunological ASs, when the stability studies have not been performed in accordance with a currently approved stability protocol B.I.b.1.e - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP 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 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.2.c - Changes in the manufacturing process of	03/03/2022	29/06/2022	Annex II	

	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.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits 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.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.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place 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 B.I.c.1.b - Change in immediate packaging of the AS - Qualitative and/or quantitative composition for sterile and non-frozen biological/immunological ASs B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a				

	biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol				
PSUSA/1727/ 202105	Periodic Safety Update EU Single assessment - imiglucerase	13/01/2022	n/a		PRAC Recommendation - maintenance
N/0125	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	05/11/2021	29/06/2022	PL	
IA/0122/G	This was an application for a group of variations. 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) 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 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	21/06/2021	29/06/2022	Annex II	
IA/0121	B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the	01/04/2021	n/a		

	dossier) - Deletion of a supplier				
IA/0120	B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter	16/12/2020	n/a		
II/0118	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	19/11/2020	n/a		
N/0119	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/10/2020	18/12/2020	PL	
IB/0117/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 C.I.7.b - Deletion of - a strength	18/02/2020	18/12/2020	SmPC, Labelling and PL	
IA/0116/G	This was an application for a group of variations. 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	13/12/2019	18/12/2020	Annex II and PL	

	or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient 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) A.7 - Administrative change - Deletion of manufacturing sites				
II/0113/G	This was an application for a group of variations. B.I.b.1.e - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP 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	07/02/2019	n/a		
PSUSA/1727/ 201805	Periodic Safety Update EU Single assessment - imiglucerase	17/01/2019	n/a		PRAC Recommendation - maintenance
IB/0115	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	15/01/2019	n/a		

IG/1003	A.1 - Administrative change - Change in the name and/or address of the MAH	20/12/2018	05/12/2019	SmPC, Labelling and PL	
IB/0112/G	This was an application for a group of variations. B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol B.II.f.1.e - Stability of FP - Change to an approved stability protocol	13/12/2018	05/12/2019	SmPC, Labelling and PL	
IB/0111/G	This was an application for a group of variations. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	12/11/2018	n/a		
IB/0108/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	14/05/2018	n/a		
IA/0109	A.7 - Administrative change - Deletion of manufacturing sites	27/04/2018	n/a		

N/0107	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/03/2018	05/12/2019	PL	
WS/1262	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	14/12/2017	n/a		
II/0105	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.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	02/11/2017	n/a		N/A
N/0104	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/08/2017	05/12/2019	PL	

IB/0103	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	27/07/2017	n/a		
IB/0101	B.II.z - Quality change - Finished product - Other variation	20/04/2017	n/a		
II/0099/G	This was an application for a group of variations. B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits 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.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 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	30/03/2017	n/a		

	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 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 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				
N/0102	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/02/2017	02/06/2017	PL	
IB/0100/G	This was an application for a group of variations. B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place	06/01/2017	n/a		

IB/0098	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	27/10/2016	n/a		
IA/0097	B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	20/09/2016	n/a		
II/0094/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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.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 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.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.1.j - Change in the manufacturer of AS or of a	14/07/2016	02/06/2017	SmPC, Annex II, Labelling and PL	

	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 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/0096/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 B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	10/05/2016	n/a		
IA/0095/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 B.I.b.2.a - Change in test procedure for AS or	23/03/2016	n/a		

	starting material/reagent/intermediate - Minor changes to an approved test procedure				
II/0093/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.b.1.e - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP	11/02/2016	n/a		
PSUSA/1727/201505	Periodic Safety Update EU Single assessment - imiglucerase	14/01/2016	n/a		PRAC Recommendation - maintenance
IB/0091	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	28/10/2015	n/a		
IB/0090	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	10/04/2015	n/a		
IA/0089	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	19/12/2014	n/a		
II/0087	Update of the RMP to reflect the results of the THEME survey, which tested the effectiveness of the	23/10/2014	28/10/2015	Annex II	The MAH updated the RMP with data from the annual pregnancy report, including data from the

	educational materials for home infusion, evaluated as MEA 040.7, and to reflect the results of the 6th annual report on the pregnancy and lactation Registry in Gaucher patients, submitted in parallel to the variation as MEA 040.8. The Annex II of the Product Information was proposed to be brought in line with the latest version of the QRD template (9.0). The requested variation proposed amendments to Annex II and to the Risk Management Plan (RMP). 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				pharmacovigilance database of the MAH and data from the Pregnancy Sub-registry. The data of the present annual report (1 June 2013 to 31 May 2014) is comparable to the previous reported year. No new safety issue has been identified. In addition, in line with the request made in the previous assessment report (MEA 040.7, CHMP conclusion adopted on 24 Jan 2014), the MAH proposes to use a questionnaire to follow-up each reported ADR as a routine pharmacovigilance activity to ensure that information is obtained on the setting in which the ADR occurred and risks associated with home infusion. The additional data submitted by the MAH are considered not to change the overall benefit/risk balance. The following point should be addressed by the MAH in the next update of the RMP: - The MAH should be aware that in Section III.3 of the RMP it is stated that the final study report of the Home Infusion Educational Material Effectiveness Tracking (THEME) Study is provided in Annex 9. However, this study report has been removed from the annex in this version of the RMP. In annex 9 of the RMP version 7.0 the pregnancy report (number 6) is provided.
IB/0086	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	17/10/2014	n/a		
IB/0088	B.I.a.3.e - Change in batch size (including batch size ranges) of AS or intermediate - The scale for a biological/immunological AS is increased/decreased without process change (e.g. duplication of line)	08/10/2014	n/a		

IB/0085/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.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.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 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	27/08/2014	n/a		
IAIN/0084	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	22/07/2014	n/a		
IB/0083	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	11/07/2014	n/a		
IA/0081	B.II.d.2.a - Change in test procedure for the finished	23/06/2014	n/a		

	product - Minor changes to an approved test procedure				
IB/0080	B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place	25/04/2014	n/a		
IB/0079	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	25/04/2014	n/a		
IG/0418	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	11/04/2014	n/a		
IA/0077	B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier	11/12/2013	n/a		
N/0076	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/11/2013	28/10/2015	PL	
IB/0075	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	25/09/2013	n/a		
IB/0072/G	This was an application for a group of variations.	19/07/2013	n/a		

	B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the currently approved batch size B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line) B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation				
IB/0074	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	21/06/2013	n/a		
IB/0073	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	13/06/2013	n/a		
IA/0071	B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information	21/05/2013	n/a		
IA/0069/G	This was an application for a group of variations. B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate	10/04/2013	n/a		

	from an already approved manufacturer B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer 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				
IG/0283	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/03/2013	n/a		
IB/0068/G	This was an application for a group of variations. B.I.a.4.f - Change to in-process tests or limits applied during the manufacture of the AS - Addition or replacement of an in-process test as a result of a safety or quality issue 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	20/03/2013	n/a		
IB/0067	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other	07/12/2012	n/a		

	changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
N/0066	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/07/2012	28/10/2015	PL	
N/0065	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/04/2012	28/10/2015	PL	
IG/0119/G	This was an application for a group of variations. B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer	07/11/2011	n/a		
IG/0104	A.7 - Administrative change - Deletion of manufacturing sites	27/09/2011	n/a		
IG/0103/G	This was an application for a group of variations. B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer	21/09/2011	n/a		

IA/0062	B.II.b.2.b.1 - Change to batch release arrangements and quality control testing of the FP - Not including batch control/testing	27/05/2011	n/a	Annex II and PL	
N/0061	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/05/2011	n/a	PL	
II/0057	C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	23/09/2010	25/10/2010	SmPC and PL	
II/0058	Update of section 4.2 of the SmPC with a statement on the possibility of home infusion for a selected population of patients. Consequently, Section 3 of the Package Leaflet was updated with a statement on the possibility of home infusion. Additionally, several minor adjustments have been implemented to bring the SmPC, labelling and package leaflet in line with the current revised QRD template. Annex II was affected. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	22/07/2010	26/08/2010	SmPC, Annex II, Labelling and PL	Based on the assessment of the submitted Healthcare Professional guidance and the patient manual and on the evaluation of identified and potential risks of home infusion, the CHMP accepted the proposal for the MAH to include the possibility of home infusion in the PI. Section 4.2 of the SmPC and section 3 of the Package Leaflet were updated accordingly.
II/0055	Changes in the manufacturing process if the active substance B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the	22/07/2010	30/07/2010		

	manufacture of a biological/immunological medicinal product and is not related to a protocol				
IB/0059	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	30/06/2010	n/a		
IB/0056	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, or amendments to reflect a Core SPC - Changes with NO new additional data are submitted by the MAH	19/06/2010	n/a	SmPC and PL	
IA/0060	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	18/06/2010	n/a		
IA/0054	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 in the manufacture of the AS	12/03/2010	n/a		
II/0049	Change to the test methods for the active sustance. Change(s) to the test method(s) and/or specifications for the active substance	19/11/2009	25/11/2009		
IA/0053	IA_31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	24/11/2009	n/a		

II/0050	Addition of the active substance manufacturing site. Change(s) to the manufacturing process for the active substance	24/09/2009	29/09/2009		
IA/0048	IA_16_b_Submission of new TSE certificate relating to active substance - other substances	15/07/2009	n/a		
II/0046	Update of sections 4.2 "Posology and method of administration", 4.4 "Special warnings and precautions for use", 4.9 "Overdose", 5.1 "Pharmacodynamic properties" of the Summary of Product Characteristics (SPC) to reflect the current knowledge on Gaucher disease and Cerezyme's efficacy mainly based on comprehensive literature review in order to ensure optimal treatment guidance. The MAH also took the opportunity to update section 2 "Qualitative and quantitative composition" and to include in section 4.8 "Undesirable effects" the adverse event 'backache'. The Package Leaflet (PL) was updated accordingly. Update of Summary of Product Characteristics and Package Leaflet	29/05/2009	30/06/2009	SmPC and PL	Data available mainly from the literature confirm the positive effect of Cerezyme on the haematological, visceral and skeletal signs and symptoms of Gaucher disease in both type 1 and type 3 patients. Dose-response analyses have shown that response to Cerezyme is dose-dependent. Current knowledge as described in literature also allowed a more comprehensive and up-to-date description of Gaucher disease and its clinical manifestations. Pulmonary hypertension is recognised as an uncommon complication in patients with Gaucher disease and is unlikely related to Cerezyme therapy based on current knowledge; pulmonary hypertension is therefore moved from section 4.4 to section 5.1. Literature analysed refers only to treatment schedules with infusions every other week. Due to the demonstration of the effectiveness and safety of this two-week schedule, the 3 times per week regimen has become obsolete and therefore was removed from the SPC. Results from two clinical studies showed that maintenance treatment with 4 weeks intervals could be a therapeutic option for some adult patients with stable residual Gaucher disease type 1, but clinical data are limited. Recommendation for the infusion administration has been

					made more informative in section 4.2 of the SPC by providing a recommendation for infusion rate only, removing the duration of infusion which is not taking into account the fact that the dose is individualised. Based on a cumulative review of the MAH safety database from May 1994 to May 2008 backache was added in section 4.8 as an uncommon adverse event. This search identified 54 adverse events (AEs) reported in 46 patients. Of these 54 AEs, 52 were considered to be related to treatment and 36 occurred within 24 hours of infusion.
IB/0047	IB_31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	07/05/2009	n/a		
II/0045	Update of Summary of Product Characteristics and Package Leaflet	20/11/2008	22/12/2008	SmPC and PL	
II/0042	Change(s) to the manufacturing process for the finished product	30/05/2008	05/06/2008		
IB/0044	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	25/04/2008	n/a		
IB/0043	IB_13_b_Change in test proc. for active substance - other changes (replacement/addition)	25/04/2008	n/a		
II/0040	Change(s) to the manufacturing process for the finished product	20/09/2007	25/09/2007		
R/0039	Renewal of the marketing authorisation.	19/07/2007	17/09/2007	SmPC, Annex II, Labelling	Based on the review of the available information the CHMP is of the opinion that the quality, the safety and the efficacy of this medicinal product continues to be adequately and

				and PL	sufficiently demonstrated and therefore considers that the benefit/risk profile of Cerezyme continues to be favourable.
IB/0041	IB_33_Minor change in the manufacture of the finished product	13/06/2007	n/a		
II/0037	Update of section 4.8 of the SPC to include "arthralgia" and "paraesthesia" as adverse reactions, as requested by the CHMP following assessment of PSUR 9 (covering the period from 1 June 2004 to 31 May 2006). Section 4 of the PL has been updated accordingly. Section 6 of the PL was updated with the local representatives in Bulgaria, Romania and Hungary was updated. Update of Summary of Product Characteristics and Package Leaflet	22/02/2007	04/04/2007	SmPC and PL	Since the approval of Cerezyme in the US in May 1994 until November 2006, a total of 52 case reports of arthralgia and 15 case reports of paraesthesia were received. Paraesthesia was sometimes suggestive of hypersensitivity and responded to treatment with antihistamines and/or corticosteroids. These uncommon adverse events have been included in section 4.8 of the SPC and in section 4 of the PL.
II/0038	Change(s) to the manufacturing process for the active substance	22/02/2007	01/03/2007		
II/0036	Change(s) to the manufacturing process for the active substance	27/07/2006	07/08/2006		
IB/0035	IB_17_b_Change in the storage conditions for the active substance	11/04/2006	n/a		
N/0034	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/12/2005	n/a	PL	
II/0033	Change(s) to the manufacturing process for the finished product	17/11/2005	22/11/2005		

II/0032	Update of or change(s) to the pharmaceutical documentation	15/09/2005	29/09/2005		
II/0031	Change(s) to the manufacturing process for the active substance	15/09/2005	29/09/2005		
II/0029	Update of Summary of Product Characteristics and Package Leaflet	17/02/2005	11/04/2005	SmPC and PL	To change section 4.4 (Special warnings and special precautions for use) of the Summary of Product Characteristics (SPC) as requested by CHMP and to include a change in the contact details of the French and Polish local representatives in the Package Leaflet (PL).
IB/0030	IB_38_c_Change in test procedure of finished product - other changes	03/03/2005	n/a		
II/0028	The Marketing Authorisation Holder Applied to amend the manufacturing process for Cerezyme. Quality changes	17/02/2005	22/02/2005		
II/0027	Quality changes	21/10/2004	25/10/2004		
IB/0024	IB_17_b_Change in the storage conditions for the active substance	14/06/2004	n/a		
II/0023	Change(s) to the manufacturing process for the finished product	03/06/2004	11/06/2004		
IA/0026	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	26/05/2004	n/a		

N/0025	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	01/05/2004	n/a	PL	
IA/0022	IA_16_b_Submission of new TSE certificate relating to active substance - other substances	30/03/2004	n/a		
II/0018	Extension of indication to include type 3 Gaucher's disease Extension of Indication	22/05/2003	28/08/2003	SmPC, Annex II and PL	
I/0020	12_Minor change of manufacturing process of the active substance	24/07/2003	n/a		
I/0019	24_Change in test procedure of active substance	24/07/2003	n/a		
I/0021	11b_Change in supplier of an intermediate compound used in manufacture of the active substance	03/07/2003	17/07/2003		
R/0017	Renewal of the marketing authorisation.	19/09/2002	11/12/2002	SmPC, Annex II, Labelling and PL	
I/0015	12_Minor change of manufacturing process of the active substance	21/03/2002	11/04/2002		
I/0016	03_Change in the name and/or address of the marketing authorisation holder	07/12/2001	26/03/2002	SmPC, Labelling and PL	
I/0013	12_Minor change of manufacturing process of the	01/03/2001	06/04/2001		

	active substance				
I/0014	26_Changes to comply with supplements to pharmacopoeias	08/02/2001	n/a		
X/0010	X-3-iii_Addition of new strength	23/09/1999	28/01/2000	SmPC, Annex II, Labelling and PL	
II/0011	Update of Summary of Product Characteristics and Package Leaflet	28/07/1999	16/11/1999	SmPC, Labelling and PL	
I/0009	12_Minor change of manufacturing process of the active substance	23/09/1999	n/a		
II/0008	Update of Summary of Product Characteristics and Package Leaflet	28/01/1999	18/06/1999	SmPC, Labelling and PL	
I/0007	15_Minor changes in manufacture of the medicinal product	23/07/1998	n/a		
I/0004	12_Minor change of manufacturing process of the active substance	25/06/1998	n/a		
I/0005	12_Minor change of manufacturing process of the active substance	25/03/1998	n/a		
I/0003	12_Minor change of manufacturing process of the active substance	25/03/1998	n/a		

I/0002	02_Change in the name of the medicinal product (either invented name of common name) 15_Minor changes in manufacture of the medicinal product	25/03/1998	n/a		
I/0001	16_Change in the batch size of finished product	25/03/1998	n/a		
N/0006	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/03/1998	15/08/1998	PL	