Myozyme

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
IA/0066/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	21/09/2017	n/a		
II/0063/G	This was an application for a group of variations.	14/09/2017	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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	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.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.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				
N/0065	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/09/2017		Labelling and PL	
IB/0064/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.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.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	18/08/2017	n/a		

	product - Minor changes to an approved test procedure				
PSUSA/86/201609	Periodic Safety Update EU Single assessment - alglucosidase alfa	18/05/2017	10/07/2017	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/86/201609.
N/0061	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/02/2017	10/07/2017	PL	
IB/0059	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)	12/01/2017	n/a		
IB/0058	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	26/09/2016	n/a		
II/0057/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.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	19/05/2016	n/a		
II/0056	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	17/03/2016	n/a		

	which may have a significant impact on the medicinal product and is not related to a protocol				
IA/0055	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	12/11/2015	n/a		
II/0053	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	21/05/2015	n/a		
IA/0054/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	20/05/2015	n/a		
II/0052	Submission of the revised RMP version 7.5 including the new version of the Physician Guide (Safety Information Packet version 8.2), a proposed study protocol for an effectiveness measure of the updated safety information packet and other minor amendments in accordance with the PRAC recommendation following the last PBRER assessment (EMEA/H/C/000636/PSUV/0049).	26/02/2015	n/a		

	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				
IB/0051	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	14/05/2014	n/a		
PSUV/0049	Periodic Safety Update	08/05/2014	n/a		PRAC Recommendation - maintenance
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		
IB/0047	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	07/01/2014	n/a		
II/0041	Update of sections 4.1 and 5.1 of the SmPC in order to include relevant clinical data from several clinical trials and from other analyses of late-onset Pompe disease patients treated with Myozyme. The Package Leaflet was updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is being brought in line with the	21/11/2013	18/12/2013	SmPC, Annex II, Labelling and PL	The MAH provided clinical data based on five observational studies evaluating motor and respiratory functions of LOPD patients treated by ERT and one observational study evaluating the impact of ERT on survival in adult with LOPD. These new observational data present a clinically relevant efficacy trend in the treatment effect of Myozyme on overall survival, motor functions and respiratory status in patients with late-onset Pompe disease. The CHMP considered this information to be of importance to the

	latest QRD template version 9.0. The requested variation proposed amendments to the Summary of Product Characteristics, 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				prescriber and an update of section 5.1 and consequently that of section 4.1 is warranted. The benefit/risk of Myozyme remains unchanged. Please refer to the scientific discussion in the assessment report for EMEA/H/C/000636/II/0041.
IA/0048	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		
II/0046	Update of sections 4.4 and 4.8 of the SmPC in order to update the information with clinical data available from studies AGLU03707 and AGLU03807 as per Article 46 of the Paediatric Regulation 1901/2006, and from post-marketing experience. The Package Leaflet is updated accordingly. The requested variation proposed amendments to the Summary of Product Characteristics and Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	21/11/2013	18/12/2013	SmPC and PL	This variation updates the PI of Myozyme with the information that the use of immunosuppressive agents may increase this risk of developing infections that can be serious, as supported by two clinical studies provided by the MAH. In addition, the review of post-marketing cases shows that a combination and a recurrence of the events of fever, chills, myalgia, arthralgia, pain, fatigue and/or flu-like illness have been reported in some patients treated with Myozyme. Therefore, further details on the occurrence of these events in the product information of Myozyme were included in the SmPC. The PIL was updated accordingly.
II/0045	Changes in the manufacturing process of the active substance. B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the	21/11/2013	n/a		

	manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol				
IG/0283	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/03/2013	n/a		
IA/0043/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 supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer	15/03/2013	n/a		
IA/0042	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	08/03/2013	n/a		
IB/0040	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol	20/12/2012	18/12/2013	SmPC	
II/0039/G	This was an application for a group of variations. - to register a new reference standard for use in the production of Myozyme (alglucosidase alfa).	20/09/2012	n/a		

	- to update the release specification for the Drug Substance binding assay to reflect the implementation of the new reference standard. 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				
N/0038	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/07/2012	18/12/2013	PL	
II/0037	To register an additional quality control testing site for in vitro virus testing of Myozyme DP. B.II.b.2.z - Change to batch release arrangements and quality control testing of the FP - Other variation	21/06/2012	21/06/2012		
II/0035	This was an application for a single variation procedure to apply changes in a test procedure, rhGAA Afinity Binding Assay, for the active substance, Alglucosidase Alfa. 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	24/05/2012	n/a		

	biological reagent for a biological AS				
N/0036	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/04/2012	n/a	PL	
IB/0034/G	This was an application for a group of variations. B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer 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	07/02/2012	n/a		
IB/0031/G	This was an application for a group of variations. 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.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	21/12/2011	n/a		

	B.II.b.3.a - Change in the manufacturing process of the finished product - Minor change in the manufacturing process of an immediate release solid oral dosage form or oral solutions				
IB/0033	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)	13/12/2011	n/a		
IB/0029	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	29/11/2011	n/a		
IG/0122	To update the Detailed Description of the Pharmacovigilance System (DDPS) to version 9, to include a change in the major contractual arrangements. 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	25/11/2011	n/a		
II/0027	Update of section 4.8 of the SmPC to include the ADRs 'nephrotic syndrome', 'proteinuria', 'stridor' and 'vasoconstriction', and section 4.4 of the SmPC to amend the existing warning related to 'nephrotic syndrome'. The Package Leaflet has been amended accordingly. In addition, the MAH took the	20/10/2011	22/11/2011	SmPC, Annex II, Labelling and PL	The MAH has submitted an analysis of post-marketing cases of nephrotic syndrome and proteinuria (from the International Birth Date, 29 March 2006 to March 2011), and stridor and vasoconstriction (from 29 March 2006 to 28 June 2011).

	opportunity to update the RMP version number in annex II to reflect the latest version agreed with CHMP (version 6), to make editorial changes to the annexes and to update the contact details in the list of local representatives in the Package Leaflet. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				Reports of immune-mediated reactions in patients treated with Myozyme remain "uncommon" (<1/100; ≥1/1000). Cases suggestive of immune-mediated reactions included reports of nephrotic syndrome, proteinuria, haematuria, skin lesion, skin necrosis, arthralgia, myalgia, arthropathy, lymphadenopathy, serum sickness, and type III immune complex mediated reaction. Proteinuria was observed in 5 patients, 3 of whom developed nephrotic syndrome associated with high antibody titres (≥ 102,400). Among the patients with nephritic syndrome, 1 was male and 2 were female; 1 was an infant and 2 were adults. Renal biopsy in these 3 patients stained positive with rhGAA antibody consistent with immune complex deposition, thus confirming the previously recognized potential risk of immune-mediated reactions to be an identified risk. As further support identifying nephrotic syndrome as a risk of treatment with alglucosidase alfa, all 3 patients improved following treatment interruption. From the International Birth Date of 29 March 2006 through 28 June 2011, cumulatively 3 patients experienced stridor in addition to other IARs that occurred during infusion. The events resolved in all cases upon infusion interruption, administration of corticosteroids and or administration of epinephrine. One patient with a report of vasoconstriction was identified with concomitant IARs of abdominal pain, asystole, bradycardia, bronchoconstriction, extensive erythema, gastroenteritis and oedema. Infusion reactions were managed with infusion schedule adjustments,

					premedications, slower rates and preparation of the infusion from a different batch. Based on the data provided, the CHMP agreed with the proposed inclusion of the ADRs 'nephrotic syndrome', 'proteinuria', 'stridor', 'vasoconstriction' and related safety information in Sections 4.4, 4.8 of the Summary of Product Characteristics, and relevant sections of the Package Leaflet. The Risk Management Plan and the Myozyme Safety Package have been updated in line with these conclusions. The known benefit/risk profile of Myozyme remains favourable.
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/0028/G	This was an application for a group of variations. 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.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	07/09/2011	n/a		

	DD C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities 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				
IA/0026	A.7 - Administrative change - Deletion of manufacturing sites	23/08/2011	n/a		
R/0024	Renewal of the marketing authorisation.	16/12/2010	21/02/2011	SmPC, Annex II, Labelling and PL	
II/0022	Change in manufacturing process of the Active Substance. 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	23/09/2010	29/09/2010		
IB/0023	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	31/08/2010	n/a	SmPC, Annex II, Labelling and PL	
IA/0025	B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished	26/08/2010	n/a		

	product - Tightening of in-process limits				
IB/0021	Changes in test procedure for the finished product. B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	09/06/2010	n/a		
IA/0020/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 supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release)	28/05/2010	n/a	Annex II	
IA/0019	Deletion of a manufacturer site A.7 - Administrative change - Deletion of manufacturing sites	30/04/2010	n/a	Annex II	
IA/0018	IA_31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	17/12/2009	n/a		
II/0007	Update of section 4.1 of the Summary of Product Characteristics to amend the statement on the benefits of Myozyme in Late-onset Pompe Disease patients.	22/10/2009	28/10/2009	SmPC and PL	Please refer to Scientific Discussion: Myozyme-H-C-636-II-07

	Update of Summary of Product Characteristics				
IA/0017	IA_28_Change in any part of primary packaging material not in contact with finished product	01/09/2009	n/a		
II/0013	Update of Sections 4.6 and 5.3 of the SPC and the corresponding sections in the PL with the results of toxicological studies on animals. Editorial changes in the German, Finnish, and Greek languages. Update of Summary of Product Characteristics and Package Leaflet	23/07/2009	21/08/2009	SmPC and PL	The MAH has submitted following the request from the CHMP the results of non-clinical toxicological studies and the effect of the product on pregnant animals. The results have been reflected in the SPC section 4.6 on "Pregnancy and Lactation" regarding reproductive toxicity in animals. The wording is a follows: "Pregnancy There are no data from the use of alglucosidase alfa in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). The potential risk for humans is unknown. Myozyme should not be used during pregnancy unless clearly necessary." Section 5.3 on "Preclinical safety data" regarding the results of the early embryonic and embryofoetal development in mice and rabbits was also amended. Treatment related cases of abortion in animals when coadministered with diphenhydramine were also reported. In the Package Leaflet the information to stop breast-feeding while taking the product was added. The final wording is as follows: "5.3 Preclinical safety data Preclinical data reveal no special hazards for humans based

					on studies of safety pharmacology, single and repeat dose toxicity. No significant adverse findings on embryofoetal development were observed in a mouse and a rabbit embryofoetal study and no significant adverse findings were observed in a mouse fertility and early embryonic development study. In the rabbit embryofoetal development study, following administration of Myozyme (10-40 mg/kg/day) with coadministration of diphenhydramine, a treatment-related increase in the incidence of abortions and early delivery was observed. This effect was partly attributable to maternal toxicity, as a significant decrease in feed consumption and body weight gain was observed. "
II/0016	Change(s) to the manufacturing process for the finished product Change(s) to the manufacturing process for the finished product	23/07/2009	29/07/2009		
II/0014	Change to the manufacturing process for the active substance Change(s) to the manufacturing process for the active substance	25/06/2009	01/07/2009		
IB/0015	IB_31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	13/05/2009	n/a		
II/0012	MAH proposes to add an additional site for the manufacture of active substance.	19/02/2009	23/02/2009	Annex II	

	Change(s) to the manufacturing process for the active substance				
II/0010	To update section 4.8 of the SPC and section 4 of the Package Leaflet by adding safety information on Infusion Associated Reactions (IARs). Additionally, the SPC, Labelling and Package Leaflet are updated according to the QRD requirements and section 6 of the Package Leaflet was amended with the updated list of local representatives. Finally, a minor linguistic correction was included in the Hungarian version of the SPC. Update of Summary of Product Characteristics, Labelling and Package Leaflet	22/01/2009	20/02/2009	SmPC, Labelling and PL	This variation changed section 4.8 of the SPC to include infusion associated reactions reported from worldwide post-marketing sources, as requested by the CHMP in the assessment report of FU2 029.
IB/0011	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	05/02/2009	n/a	SmPC	
II/0008	Updated changes of specification for Drug Substance Change(s) to the test method(s) and/or specifications for the active substance	20/11/2008	28/11/2008		
II/0005	Update of safety and efficacy information for infantile onset patients with data from long-term treatment based on final study reports. Sections 4.4, 4.8 and 5.1 of the SPC and the relevant sections of the Package Leaflet have been updated. In addition, minor changes were made to sections 4.6 and 4.7 of the SPC in accordance with QRD template. One minor clarification was implemented in the Labelling	25/09/2008	30/10/2008	SmPC, Annex II, Labelling and PL	The CHMP variation Assessment Report will be published as part of the EPAR following review and deletion of confidential information.

	of the outer carton. The Romanian local representatives contact details have been amended in the Package Leaflet. In addition, an update of the Detailed Description of Pharmacovigilance System (DDPS) has been submitted within this variation. Update of Summary of Product Characteristics, Labelling and Package Leaflet				
IA/0009	IA_08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing	16/10/2008	n/a	Annex II and PL	
II/0006	The Marketing Authorisation Holder applied to make a number of amendments to the specification for the active substance, arising from earlier commitments. In addition a consequential change will be made to the specification for the finished product. Change(s) to the test method(s) and/or specifications for the active substance	26/06/2008	15/07/2008		
IB/0004	IB_13_b_Change in test proc. for active substance - other changes (replacement/addition)	14/11/2007	n/a		
II/0002	Update of the Summary of Products Characteristics, Labelling and Package Leaflet in accordance to the new QRD template 7.2 and include the changes to the PL following the User readability testing in accordance with the EU readability guideline. Update of the contact details of Romanian and Bulgarian	19/07/2007	09/10/2007	SmPC, Annex II, Labelling and PL	This was a variation which mainly dealt with the update of the package Leaflet in accordance with the EU readability guideline. The MAH used this opportunity to also make editorial amendments to the SPC according to the QRD Template Version 7.2, to update the Annex II providing the updated information regarding the Pharmacovigilance

	local representatives. The Annex II has also been amended to include the latest wording to reflect the information on the PhV system and RMP. Update of Summary of Product Characteristics, Labelling and Package Leaflet				system in place as well as the Risk Management Plan. The contact details of the local representatives of the Package leaflet of Bulgaria and Romania have also been included.
II/0003	Change(s) to the manufacturing process for the finished product	19/07/2007	01/08/2007		
II/0001	This variation relates to an update of sections 4.4 and 4.8 of the Summary of Product Characteristics (SPC) as a consequence of reports of serious cases of anaphylaxia. Corresponding sections of the Package Leaflet (PL) have been updated accordingly. In addition, minor changes were included in the list of local representatives. Update of Summary of Product Characteristics and Package Leaflet	28/06/2006	28/07/2006	SmPC and PL	4 cases of serious infusion adverse reactions (IARs) were reported in March and April 2006 with Myozyme: · 2 cases of serious IARs in late-onset patients (one angioedema, severe; and one anaphylactoid reaction, severe), and both have been withdrawn from their ongoing study; · as well as 2 cases of serious IARs in infantile-onset patients (both with anaphylaxis, one life-threatening and the other, moderate), and both will probably continue with their treatment due to the life-threatening nature of their disease. None of these events was due to an inappropriate infusion rate or dose. During the clinical trials, 4 female patients experienced serious oedema-IARs while receiving 20 mg/kg Myozyme. Three of the 4 patients had late-onset Pompe disease with a mean age at time of IAR occurrence of 33.3 years (age range 29 to 39 years). The remaining patient was a 25-month-old with infantile-onset Pompe disease. Events of oedema by MedDRA preferred term included periorbital oedema, swollen tongue, face oedema,

					and oedema peripheral (1 patient each). The time of onset was either during the infusion (2 cases) or 1.5 and 2 h following completion of the injection (2 cases). All patients continued to receive Myozyme, either at lower doses and/or with premedication, with either no reaction or reduced intensity reactions. There had also been 1 case of oedema-IAR with Pharming rhGAA 10 mg/kg in a late-onset Pompe disease patient. In addition, previous to the granting of the MA, there were 4 cases of serious anaphylactic/anaphylactoid-IARs with bronchospasm, decreased oxygen saturation and/or hypotension. All 4 patients were females with infantile-onset Pompe disease receiving Myozyme at a dose of 20 mg/kg QOW. At time of IAR occurrence, mean age of patients was 13 months (age range 5 to 25 months). All patients continued to receive Myozyme, except one. Myozyme is contra-indicated in patients with a hypersensitivity (anaphylactic reaction) to the active substance or