Thyrogen

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/0118	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/07/2024	13/01/2025	PL	
IB/0117/G	This was an application for a group of variations. B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement	17/05/2024	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).

	or addition) for the AS or a starting material/intermediate 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				
N/0116	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/01/2024	10/05/2024	PL	
IA/0115	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	16/10/2023	n/a		
IA/0114	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	08/09/2023	n/a		
IAIN/0113	A.1 - Administrative change - Change in the name and/or address of the MAH	04/04/2023	10/05/2024	SmPC, Labelling and PL	
IA/0112/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites	22/02/2023	n/a		

	(excluding manufacturer for batch release)				
PSUSA/2940/202111	Periodic Safety Update EU Single assessment - thyrotropin alfa	07/07/2022	n/a		PRAC Recommendation - maintenance
II/0109/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.c.1.b - Change in immediate packaging of the AS - Qualitative and/or quantitative composition for sterile and non-frozen biological/immunological ASs 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	10/02/2022	n/a		
N/0110	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/11/2021	10/05/2024	PL	
IB/0108/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 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	02/09/2021	n/a		

	control/testing takes place				
IB/0107	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/11/2020	15/11/2021	SmPC and PL	
II/0106	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		
IA/0105/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) A.7 - Administrative change - Deletion of manufacturing sites	12/12/2019	14/12/2020	Annex II and PL	
PSUSA/2940/ 201811	Periodic Safety Update EU Single assessment - thyrotropin alfa	25/07/2019	23/09/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2940/201811.
II/0104/G	This was an application for a group of variations. B.I.b.1.e - Change in the specification parameters	25/07/2019	n/a		

	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.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				
II/0102	Update of sections 4.4 and 5.1 of the SmPC with long term follow-up results from studies HiLo and ESTIMABL1. Additionally, the sodium content provision wording in the Package Leaflet is aligned to the Annex to the European Commission guideline on "Excipients in the labelling and package leaflet of medicinal products for human use" (SANTE-2017-11668). The MAH further made editorial changes throughout the Product Information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	27/06/2019	23/09/2019	SmPC, Labelling and PL	The long term follow-up data in ESTIMABL1 and HiLo confirmed similar outcomes for patients in all four treatment groups (patients treated with Thyrogen or thyroid hormone withdrawal in combination with either low or high activity radioactive iodine). For more information please refer to the Summary of Product Characteristics.
IA/0101	A.7 - Administrative change - Deletion of manufacturing sites	14/02/2019	n/a		
IG/1003	A.1 - Administrative change - Change in the name and/or address of the MAH	20/12/2018	23/09/2019	SmPC, Labelling and PL	
II/0099/G	This was an application for a group of variations.	11/10/2018	n/a		

	B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method B.II.d.1.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				
IB/0098	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	31/08/2018	n/a		
IB/0097	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	21/08/2018	n/a		
IB/0096/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	09/05/2018	n/a		
N/0095	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/01/2018	23/09/2019	Labelling and 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		
IA/0094/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.d.2.b - Change in test procedure for the finished product - Deletion of a test procedure if an alternative method is already authorised	01/12/2017	n/a		
N/0092	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/08/2017	23/09/2019	PL	
II/0090	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	01/06/2017	n/a		
IA/0091/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	31/03/2017	n/a		

	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
II/0088	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	23/02/2017	n/a		
N/0089	Update of the package leaflet with revised contact details of the local representatives for Bulgaria and Spain. In addition, the MAH took the opportunity to make editorial changes in the Romanian package leaflet. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/01/2017	23/09/2019	PL	
IB/0087	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	04/10/2016	n/a		
IB/0086/G	This was an application for a group of variations. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation	22/08/2016	n/a		
PSUSA/2940/ 201511	Periodic Safety Update EU Single assessment - thyrotropin alfa	07/07/2016	n/a		PRAC Recommendation - maintenance

IB/0085	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	05/07/2016	n/a		
II/0083	Update of section 4.8 of the SmPC to amend the frequencies of paraesthesia and diarrhoea (from common to uncommon adverse reactions) and to add influenza, ageusia, dysgeusia and neck pain as uncommon adverse reactions based on a review of the Company Core Data Sheet. In addition, some amendments were made to reflect the MedDRA preferred terms. The Package Leaflet was updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to bring the PI in line with the latest QRD template and to introduce minor editorial changes. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/05/2016	15/07/2016	SmPC, Annex II, Labelling and PL	Based on the review of the company core data sheet, the MAH noted that the adverse reaction table was comprised of all adverse reactions regardless of relatedness. The company core data sheet and SmPC section 4.8 have therefore been revised to reflect only the adverse events determined to be related to Thyrogen, which meant that the frequency for paraesthesia and diarrhoea has been updated from common to uncommon and influenza, ageusia, dysgeusia and neck pain are added as uncommon adverse reactions. In addition, some amendments were made to reflect the MedDRA preferred terms. The Package Leaflet was updated accordingly and the PI was brought in line with the latest QRD template.
IB/0084/G	This was an application for a group of variations. 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.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	28/04/2016	n/a		

IB/0081	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	20/10/2015	n/a		
II/0079/G	This was an application for a group of variations. B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing 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	23/07/2015	15/07/2016	SmPC, Labelling and PL	
IB/0080	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	24/06/2015	n/a		

IB/0078	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	13/03/2015	n/a		
IB/0077	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	17/02/2015	n/a		
IB/0076	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	19/01/2015	n/a		
II/0071	Change in test procedure for the finished product 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	18/12/2014	n/a		Change in test procedure for the finished product
IB/0075/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.c.1.z - Change in immediate packaging of the AS - Other variation B.I.c.1.z - Change in immediate packaging of the AS - Other variation	15/12/2014	n/a		
IA/0074/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or	15/12/2014	n/a		

	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				
IA/0073/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 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 B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	15/12/2014	n/a		
IB/0072	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	13/11/2014	n/a		
IB/0070	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	02/10/2014	n/a		

IB/0069	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	08/05/2014	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		
IB/0067	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	06/12/2013	n/a		
N/0066	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/10/2013	15/07/2016	PL	
IB/0062/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	24/04/2013	n/a		

IG/0283	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/03/2013	n/a		
IA/0063/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 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	19/03/2013	n/a		
IA/0064	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/0061	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)	22/01/2013	n/a		

II/0059	Update of section 4.1 of the SmPC in order to recommend the use of Thyrogen with a range of 30-100 mCi 131I for postoperative thyroid remnant ablation, as opposed to the currently approved 100 mCi 131I, based on the results of two published studies (HiLo and ESTIMABL). Sections 4.4, 4.5 and 5.1 are updated accordingly to amend relevant existing warnings and to include information from the two studies. In addition, the MAH took the opportunity to make minor editorial amendments in the SmPC and to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 8.1. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	18/10/2012	22/11/2012	SmPC, Annex II, Labelling and PL	Please refer to the Scientific Discussion Thyrogen-H-C-220-II-59.
IB/0060	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	09/11/2012	n/a		
II/0057	Change to the control of the active substance 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	24/05/2012	n/a		

N/0058	Update in the local representative for Spain in the Package Leaflet. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	25/04/2012	22/11/2012	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		
II/0052	Changes to the manufacture 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	22/09/2011	22/09/2011		
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	21/09/2011	n/a		

	from an already approved manufacturer				
IA/0053/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.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	16/09/2011	n/a		
II/0051	Update of section 4.8 of the SmPC to include stroke as an adverse reaction based on post-marketing data. The PL and the RMP have been updated accordingly. In addition, minor changes were made to sections 4.4 and 5.3 of the SmPC and to the PL to improve comprehension of the document, the PSUR statement was deleted from Annex II, the list of local representatives in the PL was updated and changes were made throughout the PI to bring it in line with the latest version of QRD template (v 7.3.1, March 2010). C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	21/07/2011	24/08/2011	SmPC, Annex II and PL	Following two reports of stroke in women after Thyrogen administration and an additional earlier similar report, the Product Information was updated to include stroke as an Adverse Drug Reaction of Thyrogen. As all reports came from the post-marketing setting, the frequency of stroke can only be indirectly inferred, but it is expected that stroke only occurs very rarely after Thyrogen administration.
IB/0050	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	23/05/2011	n/a		

II/0049/G	This was an application for a group of variations. Additional sites for the manufacture and control of the drug product B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for biological/immunological medicinal products. B.II.b.2.b.2 - Change to batch release arrangements and quality control testing of the FP - Including batch control/testing	17/02/2011	28/02/2011		
IB/0048	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	22/07/2010	n/a		
II/0046	Changes to the manufacturing process of the drug 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	24/06/2010	06/07/2010		
IA/0047	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	28/04/2010	n/a	Annex II	

II/0044	Change to storage conditions for the drug substance Change(s) to shelf-life or storage conditions	21/01/2010	27/01/2010		
II/0038	Extension of Indication The scope of this variation is to extend the ablation of thyroid tissue remnants indication of Thyrogen from low risk patients to patients who have undergone a near-total or total thyroidectomy for well-differentiated thyroid cancer and who do not have evidence of distant metastatic thyroid cancer. As a consequence, changes were made to sections 4.1, 4.4, 4.8 and 5.1 of the Summary of Product Characteristics. Annex II has been updated to include the agreed version of the RMP and the change to the PSUR cycle. Minor editorial changes were made to the Labelling. The Package Leaflet was updated in accordance with the SPC and to update the list of local representatives. Extension of Indication	19/11/2009	20/01/2010	SmPC, Annex II and PL	Please refer to Scientific Discussion: Thyrogen H-220-II-38 AR.
R/0042	Renewal of the marketing authorisation.	22/10/2009	15/01/2010	PL	
IA/0045	To change an in process control test. IA_31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	24/11/2009	n/a		

II/0041	Change to the manufacturing process of the drug substance. Change(s) to the manufacturing process for the active substance	24/09/2009	08/10/2009		
IA/0043	IA_16_b_Submission of new TSE certificate relating to active substance - other substances	24/08/2009	n/a		
II/0039	Change to the drug substance manufacturing process. Changes to the control and specifications of the drug substance and drug product Change(s) to the test method(s) and/or specifications for the active substance	23/04/2009	07/05/2009		
IB/0040	IB_31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	07/05/2009	n/a		
II/0037	Update of sections 4.2 and 4.4 of the SPC with information on the use in geriatric patients. The Package Leaflet is updated accordingly. Update of Summary of Product Characteristics and Package Leaflet	19/02/2009	07/04/2009	SmPC and PL	Further to the review of efficacy and safety data in geriatric patients, the following wording has been agreed by the CHMP in section 4.2 (Posology and Method of administration) and 4.4 (Special warnings and precautions of use) of the SPC: Section 4.2 Geriatric population Results from controlled trials indicate no difference in the safety and efficacy of Thyrogen between adult patients less than 65 years and those greater than 65 years of age, when Thyrogen is used for diagnostic purposes. No dose adjustment is necessary in the elderly population

					(see section 4.4). Section 4.4 Careful evaluation of benefit-risk relationships should be assessed for Thyrogen administration in high risk elderly patients who have heart disease (e.g. valvular heart disease, cardiomyopathy, coronary artery disease, and prior or current tachyarrhythmia) and have not undergone thyroidectomy. The Package Leaflet has been updated accordingly.
IB/0036	IB_38_c_Change in test procedure of finished product - other changes	16/12/2008	n/a		
II/0035	Changes to the stopper for Thyrogen vials and to the treatment of glass containers. Change(s) to the manufacturing process for the finished product	23/10/2008	27/10/2008		
N/0034	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/06/2008	n/a	PL	
IB/0033	IB_37_a_Change in the specification of the finished product - tightening of specification limits IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	15/04/2008	n/a		
II/0031	Change(s) to the manufacturing process for the active substance	15/11/2007	26/11/2007		
II/0030	Update of Summary of Product Characteristics and Package Leaflet	19/07/2007	04/10/2007	SmPC and PL	The MAH is amending the SPC following receipt of safety reports and review of published information on use of

					Thyrogen in dialysis-dependant, end-stage renal disease patients (ESRD). In addition, further clarification to stress that the 2 doses of Thyrogen must be taken 24 hours apart is added to the carton for 2 vials (item 4) and the package leaflet (under information for health care professionals).
II/0028	Update of Summary of Product Characteristics, Labelling and Package Leaflet	16/11/2006	09/01/2007	SmPC, Annex II, Labelling and PL	Minor updates to the SPC and PL which include clarifications on the appropriate timepoint for scintigraphy (Section 4.2), information on overdose (Section 4.9) and the ATC code (Section 5.1). Updates to sections 4.4, 4.6, 4.7 of the SPC to improve readability.
II/0029	Change(s) to the manufacturing process for the finished product	16/11/2006	21/11/2006		
II/0026	Change(s) to the test method(s) and/or specifications for the finished product	27/04/2006	03/05/2006		
N/0027	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/01/2006	n/a	PL	
IB/0025	IB_38_c_Change in test procedure of finished product - other changes	30/11/2005	n/a		
II/0024	Change(s) to the manufacturing process for the active substance	13/10/2005	19/10/2005		
II/0023	Change(s) to the manufacturing process for the active substance	21/04/2005	25/04/2005		

R/0021	Renewal of the marketing authorisation.	15/12/2004	16/03/2005	SmPC, Annex II, Labelling and PL	
II/0018	Extension of Indication	20/01/2005	23/02/2005	SmPC and PL	Please refer to the Scientific discussion: EMEA-H-220-II-18-AR.
II/0020	Change(s) to the test method(s) and/or specifications for the active substance	20/01/2005	31/01/2005		
II/0019	Change(s) to the manufacturing process for the active substance	20/01/2005	31/01/2005		
IB/0022	IB_30_b_Change in supplier of packaging components - replacement/addition	27/01/2005	n/a		
II/0016	Change(s) to the manufacturing process for the active substance	18/11/2004	24/11/2004		
II/0017	Change(s) to the test method(s) and/or specifications for the active substance	21/10/2004	28/10/2004		
N/0015	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/07/2004	n/a	PL	
II/0013	Change(s) to the test method(s) and/or specifications for the active substance Change(s) to the test method(s) and/or specifications for the finished product	25/09/2003	30/09/2003		
N/0014	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/07/2003	28/08/2003	PL	

II/0011	Extension of Indication	19/03/2003	26/06/2003	SmPC and PL	
II/0012	Change(s) to the manufacturing process for the active substance	22/05/2003	02/06/2003		
I/0010	14_Change in specifications of active substance 24_Change in test procedure of active substance 15a_Change in IPCs applied during the manufacture of the product	19/09/2002	27/09/2002		
II/0009	Change(s) to the test method(s) and/or specifications for the active substance	30/05/2002	04/06/2002		
N/0007	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/12/2001	19/02/2002	PL	
I/0008	03_Change in the name and/or address of the marketing authorisation holder	07/12/2001	n/a	SmPC, Labelling and PL	
II/0005	Update of Summary of Product Characteristics and Package Leaflet	27/06/2001	16/10/2001	SmPC, Labelling and PL	
II/0006	Quality changes	19/09/2001	08/10/2001		
I/0003	24_Change in test procedure of active substance 25_Change in test procedures of the medicinal product	14/12/2000	07/05/2001		
I/0002	24_Change in test procedure of active substance 25_Change in test procedures of the medicinal product	14/12/2000	07/05/2001		

I/0001	25_Change in test procedures of the medicinal product	19/10/2000	07/05/2001		
I/0004	26_Changes to comply with supplements to pharmacopoeias	14/02/2001	14/02/2001		