Revestive

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
PSUSA/9305/ 202408	Periodic Safety Update EU Single assessment - teduglutide	10/04/2025	n/a		PRAC Recommendation - maintenance
IA/0065/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	19/09/2024	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).

II/0064	Update of section 4.4 of the SmPC in order to add the recommendation of upper GI endoscopy or other imaging before and during the treatment with teduglutide as a precaution to 'Gastrointestinal neoplasia including hepatobiliary tract' based on the cumulative review of literature. Furthermore, section 4.8 is updated with information about location of the small intestinal polyps. In addition, the MAH took the opportunity to introduce minor editorial changes and to bring the PI in line with the latest QRD template. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	04/07/2024		SmPC	The MAH has evaluated the safety signal (small intestinal polyps and evaluation of the need to perform upper GI endoscopy") for teduglutide and propose to include need for upper endoscopy in the SmPC. The evaluation of the safety signal regarding teduglutide and small intestinal polyps and the need for monitoring of upper GI was initiated following a published scientific paper (de Dreuille et al. 2023). This observational, retrospective study included 35 adult teduglutide treated SBS patients for more than or equal to one year between 2009 and 2022. Out of 35 patients, 10 (28%) patients were identified with polypoid lesions. The polyps were observed 11 to 66 months after teduglutide initiation. In 8 out of the 10 patients, the lesion was found in the small bowel (the duodenal bulb (n=4), duodenum (n=1), ampulla (n=1), and distal jejunum (n=2)). The publication highlighted the importance of performing follow-up upper and lower GI endoscopy in short bowel syndrome patients treated with teduglutide and the potential need to make changes to the recommendations with respect to treatment initiation and follow-up. Based on the evidence from various sources, the need for inclusion of further instructions to perform an upper GI monitoring in section 4.4 as well as the update of section 4.8 of the product information for teduglutide are endorsed.
PSUSA/9305/ 202308	Periodic Safety Update EU Single assessment - teduglutide	11/04/2024	n/a		PRAC Recommendation - maintenance
IB/0063	B.I.z - Quality change - Active substance - Other variation	14/03/2024	n/a		

II/0054/G	This was an application for a group of variations. Extension of indication to include patients from 4 months corrected gestational aged 1 year and above. Consequently sections 4.1, 4.2, 4.8, 5.1 and 5.2 are updated. The Package leaflet is updated accordingly. RMP Version 9.2 has also been submitted. Update of annex II to amend the date of completion of the post authorisation study to Q2 2032. The MAH took the opportunity to also amend local representatives. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	26/04/2023	19/06/2023	SmPC, Annex II and PL	Please refer to Scientific Discussion 'Revestive-H-C-002345-II-0054-G'
PSUSA/9305/ 202208	Periodic Safety Update EU Single assessment - teduglutide	16/03/2023	n/a		PRAC Recommendation - maintenance
IAIN/0061/G	This was an application for a group of variations. B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing A.1 - Administrative change - Change in the name and/or address of the MAH	28/02/2023	19/06/2023	SmPC, Annex II, Labelling and PL	

IB/0059	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	11/08/2022	n/a		
N/0058	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	25/07/2022	19/06/2023	PL	
T/0057	Transfer of Marketing Authorisation	22/03/2022	17/05/2022	SmPC, Labelling and PL	
PSUSA/9305/ 202108	Periodic Safety Update EU Single assessment - teduglutide	07/04/2022	n/a		PRAC Recommendation - maintenance
II/0055	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	07/04/2022	n/a		
II/0053	Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update the Product information with results from two studies included in the paediatric investigation plan (PIP). Study SHP633-301 was performed to evaluate the safety, efficacy/pharmacodynamics (PD), and pharmacokinetics (PK) of teduglutide in infants 4 to 12 months gestational age with short bowel syndrome (SBS) and who are dependent on	11/11/2021	16/12/2021	SmPC and PL	Please refer to Scientific Discussion 'Revestive-H-C-002345-II-0053' In a completed clinical trial (SHP633-301) in paediatric subjects aged 4 to 12 months corrected gestational age with short bowel syndrome (SBS) dependent on parenteral support (PS), a total of 10 subjects were randomized to the teduglutide arm (n=5) and Standard of Care arm (SOC, n=5), of which 8 subjects completed the study. Overall, results showed a relatively higher number of subjects

	parenteral support. The second study is a paediatric population PK model including data from study SHP633-301. The Package Leaflet was updated accordingly. In addition, the MAH took the opportunity to make editorial changes to section 4.5 of the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				achieving clinically meaningful reductions in PS nutrition volume, caloric intake and a higher percentage of the average reductions in PS calories, daily infusion time an number of days per week in PS usage within the teduglutide arm than the SOC arm. No subject achieved enteral autonomy during the study. Adverse events reported in the study were consistent with the safety profile seen in the previous paediatric studies and no new safety issues were identified. Population pharmacokinetics (PK) and PK/PD modelling and simulation of teduglutide demonstrated Cmax similarity across age groups (4 months to 17 years) supporting 0.05 mg daily dosing in pediatric subjects who are 4 months to less than 1 year of age. A 50% dosage reduction is recommended in paediatric patients with moderate to severe renal impairment and end stage renal disease (ESRD) as adult patients with same degrees of renal impairment. Currently available data in children below 1 year are described in section 5.1 and 5.2, but no recommendation on a posology can be made. Long-term safety data are not yet available for the paediatric population. For more information, please refer to the Summary of Product Characteristics.
II/0052/G	This was an application for a group of variations. 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	22/04/2021	n/a		

	B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits				
PSUSA/9305/ 202008	Periodic Safety Update EU Single assessment - teduglutide	09/04/2021	n/a		PRAC Recommendation - maintenance
PSUSA/9305/ 201908	Periodic Safety Update EU Single assessment - teduglutide	26/03/2020	20/05/2020	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/9305/201908.
II/0050	Submission of an updated RMP version 9 in order to update the list of safety concerns. In addition, as advised during procedure EMEA/H/C/PSA/S/0023, an updated protocol for study TED-R13-002 (adding a minor editorial clarification), version 6.0 is provided. The requested variation proposed amendments 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	16/01/2020	n/a		Based on a cumulative review of safety data (from post-marketing, clinical studies and literature), antibody response in patients exposed to teduglutide is minimal and there is no significant association of formation of antibodies with events of hypersensitivity or lack of efficacy. For CRP, based on a cumulative review of safety data, there is no evidence to suggest a clinically significant increase in CRP is attributable to teduglutide. Patients with SBS are at risk for non-specific CRP elevations due to increased risk of inflammatory states including environmental infections, central line infections and Crohn's disease exacerbations. As a consequence, the important identified risk "Occurrence of anti-teduglutide antibodies, cross reactivity with GLP-2 and occurrence of anti-ECP antibodies" and the important potential risk "Increased CRP" were deleted from the RMP. In addition, important identified risks were renamed for clarity to "Biliary events", "Pancreatic events" and "Intestinal polyps" and an editorial clarification to study protocol TED-R13-002 was made.
IAIN/0047	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP -	10/05/2019	n/a		

	Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing				
PSUSA/9305/ 201808	Periodic Safety Update EU Single assessment - teduglutide	14/03/2019	n/a		PRAC Recommendation - maintenance
II/0043	Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC based on the final CSR of study TED-C14-006 (a 24-Week Double-blind, Safety, Efficacy, and Pharmacodynamic Study Investigating Two Doses of Teduglutide in Pediatric Subjects Aged 1 Year Through 17 Years With Short Bowel Syndrome who are Dependent on Parenteral Support); this is a category 3 study in the RMP. The Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/12/2018	31/01/2019	SmPC and PL	Please refer to Scientific Discussion "EMEA/H/C/000687/II/0043"
II/0045	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	20/09/2018	n/a		
IA/0044/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites	28/05/2018	n/a		

	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				
PSUSA/9305/ 201708	Periodic Safety Update EU Single assessment - teduglutide	08/03/2018	n/a		PRAC Recommendation - maintenance
IAIN/0042/G	This was an application for a group of variations. A.1 - Administrative change - Change in the name and/or address of the MAH B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	22/01/2018	23/01/2019	SmPC, Annex II, Labelling and PL	
IB/0041/G	This was an application for a group of variations. B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data) B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	04/01/2018	23/01/2019	SmPC	
II/0037	Update of section 4.2 of the SmPC in order to maintain recommended treatment length of 6 months with the addition that there might be late-responders for whom an extended evaluation period of 12 month is appropriate based on literature	14/09/2017	19/10/2017	SmPC	Limited data from clinical studies have shown that some patients may take longer to respond to treatment (i.e., those who still have presence of colon in continuity or distal/terminal ileum); if no overall improvement is achieved after 12 months, the need for continued

	references. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				treatment should be reconsidered.
PSUSA/9305/ 201702	Periodic Safety Update EU Single assessment - teduglutide	28/09/2017	n/a		PRAC Recommendation - maintenance
R/0038	Renewal of the marketing authorisation.	21/04/2017	23/06/2017	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Revestive in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
X/0029	Annex I_2.(c) Change or addition of a new strength/potency	21/04/2017	23/06/2017	SmPC, Labelling and PL	
II/0036/G	This was an application for a group of variations. Submission of 7 non-clinical study reports comprising the in vitro pharmacodynamic study 19498 and the pharmacokinetic studies 8248957, 8248958, TED-P10-007, P10-005, XGW00009, V7674M-SHP633; the final study report of the 2-year mouse carcinogenicity study P09-002/8214171 was also submitted at CHMP request. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered	18/05/2017	n/a		

	elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
II/0035	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	23/03/2017	n/a		
II/0032	Update of sections 4.3, 4.4, and 4.8 of the SmPC in order to update the safety information in line with the updated CCDS following review of the MAH's safety database. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make minor editorial	23/03/2017	23/06/2017	SmPC and PL	Revestive is contraindicated in patients with a history of malignancies in the gastrointestinal tract, including the hepatobiliary system and pancreas within the last five years. Fluid overload has been observed in clinical trials. Fluid overload adverse events occurred most frequently during the first 4 weeks of therapy and decreased over time.

	changes in section 5.1 of the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				Congestive heart failure has been observed in clinical trials. The most commonly reported adverse reactions were abdominal pain and distension (45%), respiratory tract infections (28%) (including nasopharyngitis, influenza, upper respiratory tract infection, and lower respiratory tract infection), nausea (26%), injection site reactions (26%), headache (16%), and vomiting (14%). Based on integrated data from two trials in adults with SBS (a 6 month randomised placebo controlled trial, followed by a 24 month open label trial), the development of anti teduglutide antibodies in subjects who received subcutaneous administration of 0.05 mg/kg teduglutide once daily was 3% (2/60) at Month 3, 17% (13/77) at Month 6, 24% (16/67) at Month 12, 33% (11/33) at Month 24, and 48% (14/29) at Month 30. Injection site reactions occurred in 26% of SBS patients treated with Revestive, compared to 5% of patients in the placebo arm. The reactions included injection site haematoma, injection site erythema, injection site pain, injection site swelling and injection site haemorrhage. The majority of reactions were moderate in severity and no occurrences led to drug discontinuation.
PSUSA/9305/ 201608	Periodic Safety Update EU Single assessment - teduglutide	09/03/2017	n/a		PRAC Recommendation - maintenance
II/0034	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	26/01/2017	n/a		
IB/0031/G	This was an application for a group of variations.	28/10/2016	23/06/2017	SmPC, Labelling and	

	B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes			PL	
PSUSA/9305/ 201602	Periodic Safety Update EU Single assessment - teduglutide	29/09/2016	n/a		PRAC Recommendation - maintenance
T/0030	Transfer of Marketing Authorisation from NPS Pharma Holdings Limited to Shire Pharmaceuticals Ireland Limited. Transfer of Marketing Authorisation	01/08/2016	25/08/2016	SmPC, Labelling and PL	
II/0020	Extension of Indication to include the treatment of patients aged 1 year and above with short bowel Syndrome who are stable following a period of intestinal adaptation. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	26/05/2016	29/06/2016	SmPC, Annex II and PL	Please refer to the scientific discussion Revestive EMEA/H/C/002345/II/20 for further information.
IAIN/0028	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP -	28/06/2016	25/08/2016	Annex II and	

	Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing			PL	
PSUSA/9305/ 201508	Periodic Safety Update EU Single assessment - teduglutide	17/03/2016	n/a		PRAC Recommendation - maintenance
IB/0026/G	This was an application for a group of variations. B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	12/02/2016	n/a		
IAIN/0024	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	09/12/2015	n/a		
IA/0022/G	This was an application for a group of variations. B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.II.c.3.a.1 - Change in source of an excipient or reagent with TSE risk - From TSE risk material to vegetable or synthetic origin - For excipients or	28/10/2015	n/a		

	reagents NOT used in the manufacture of a biol/immunol AS or in a biol/immunol medicinal product				
PSUSA/9305/ 201502	Periodic Safety Update EU Single assessment - teduglutide	10/09/2015	n/a		PRAC Recommendation - maintenance
IAIN/0021	A.1 - Administrative change - Change in the name and/or address of the MAH	20/08/2015	11/11/2015	SmPC, Labelling and PL	
IAIN/0019	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	16/07/2015	n/a		
IAIN/0018/G	This was an application for a group of variations. B.II.d.2.f - Change in test procedure for the finished product - To reflect compliance with the Ph. Eur. and remove reference to the outdated internal test method and test method number B.II.b.2.z - Change to importer, batch release arrangements and quality control testing of the FP - Other variation B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits B.II.d.1.h - Change in the specification parameters and/or limits of the finished product - Update of the dossier to comply with the provisions of an updated general monograph of the Ph. Eur. for the finished	25/06/2015	n/a		

	product				
II/0009	Submission of the revised RMP (version 6.4) in order to include the results of long-term study CL0600-021 and to include updated review of non-clinical risks, clinical exposure data and post-marketing exposure data. 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	21/05/2015	n/a		
II/0016	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	26/03/2015	n/a		
PSUSA/9305/ 201408	Periodic Safety Update EU Single assessment - teduglutide	12/03/2015	n/a		PRAC Recommendation - maintenance
N/0015	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/01/2015	11/11/2015	PL	
IB/0012/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	26/11/2014	11/11/2015	SmPC, Annex II, Labelling and PL	

	stability protocol B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product B.II.f.1.e - Stability of FP - Change to an approved stability protocol A.7 - Administrative change - Deletion of manufacturing sites				
IA/0013/G	This was an application for a group of variations. B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.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.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	19/11/2014	n/a		
PSUV/0008	Periodic Safety Update	09/10/2014	n/a		PRAC Recommendation - maintenance
IB/0011	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	08/09/2014	n/a		
IB/0010	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	20/08/2014	n/a		

II/0006	Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC with the results of a long term open label study on safety, tolerability and efficacy as requested in Annex II of the MA. The Package Leaflet is updated accordingly. Furthermore, the PI is being brought in line with the latest QRD template version 9.0. The requested variation proposed amendments to the Summary of Product Characteristics, Annex II and Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/05/2014	15/12/2014	SmPC, Annex II and PL	Following the results of a long-term open label study no new safety signals have been identified in patients exposed to 0.05 mg/kg/day of Revestive for up to 30 months and no clinically relevant mean increases of C-reactive protein from baseline were observed. However, due to the relative high occurrence of gastrointestinal polyps in patients who were treated with Revestive for one to two years, a recommendation to perform follow-up colonoscopies (or alternative imaging) during the first two years of treatment has been included in the product information. Long-term treatment showed continued and/or improved response for up to 2.5 years of continuous therapy and acknowledging that specialized care is customary and SBS patient's response is monitored versus any potential risks of further treatment a recommendation for continuous treatment for patients who have weaned off parenteral nutrition was added in 4.2 of the SmPC.
PSUV/0005	Periodic Safety Update	10/04/2014	n/a		PRAC Recommendation - maintenance
IG/0421	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	21/03/2014	n/a		
IAIN/0004/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP -	20/12/2013	15/12/2014	SmPC, Annex II and PL	

	Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing C.I.12 - Inclusion or deletion of black symbol and explanatory statements for medicinal products in the list of medicinal products that are subject to additional monitoring				
T/0003	Transfer of Marketing Authorisation from Nycomed Danmark ApS to NPS Pharma Holdings Limited. Transfer of Marketing Authorisation	13/09/2013	09/10/2013	SmPC, Labelling and PL	
IG/0293	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/04/2013	n/a		
IG/0219	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	25/09/2012	n/a		