Saxenda

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
II/0036	Update of section 4.8 of the SmPC in order to add 'rash' to the list of adverse drug reactions (ADRs) with frequency common; the Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to	20/07/2023		SmPC and PL	The Product Information is updated to add rash to the list of adverse drug reactions (ADRs) with a frequency common. For more information, please refer to the Summary of Product Characteristics.

[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).

	new quality, preclinical, clinical or pharmacovigilance data				
WS/2353	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	09/02/2023	n/a		
II/0034	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	01/12/2022	n/a		
WS/2303/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.4.e - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of an in-process test which may have a significant effect on the overall quality of the AS B.I.a.4.e - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of an in-process test which may have a significant effect on the overall quality of the AS	24/11/2022	n/a		
IB/0031/G	This was an application for a group of variations.	07/07/2022	n/a		

	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation				
II/0030	Update in the SmPC section 5.1 based on results from phase 3a clinical trial NN8022-4179, listed as part of PIP, to evaluate efficacy/safety of liraglutide in obese children with Prader-Willi Syndrome from 6 up to 18 years. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	16/12/2021	16/12/2022	SmPC	A 16-week double-blind, 36 week open-label study was conducted to evaluate the efficacy and safety of Saxenda in paediatric patients with Prader-Willi Syndrome and obesity. The study included 32 patients between 12 to <18 years of age (part A) and 24 patients between 6 to <12 years of age (part B). Patients were randomized 2:1 to receive Saxenda or placebo. Patients with a body weight less than 45 kg started dose escalation at a lower dose; 0.3 mg instead of 0.6 mg and were escalated to a maximum dose of 2.4 mg. The estimated treatment difference in mean BMI SDS at 16 weeks (part A: -0.20 vs -0.13, part B: -0.50 vs -0.44) and 52 weeks (part A: -0.31 vs -0.17, part B: -0.73 vs -0.67) were similar with Saxenda and placebo. No additional safety concerns were seen in the trial.
PSUSA/1892/202012	Periodic Safety Update EU Single assessment - liraglutide	16/09/2021	22/11/2021	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1892/202012.
II/0026	Extension of Indication to include treatment as an adjunct to a healthy nutrition and increased physical activity for weight management in adolescent patients from the age of 12 years and above with obesity (BMI corresponding to ≥30 kg/m2 for adults) and body weight above 60 kg, based on Study NN8022-4180 that evaluated the efficacy of	25/03/2021	26/04/2021	SmPC and PL	Please refer to Scientific Discussion 'Saxenda-H-C-3780-II-26'

	liraglutide 3.0 mg in adolescents aged 12 to less than 18 years with obesity. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are being updated and the Package Leaflet is updated in accordance. The application relates to paediatric studies submitted according to Article 46 of the paediatric regulation. The application included an updated RMP version 32.0. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
WS/1997	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	11/03/2021	n/a		
PSUSA/1892/ 201912	Periodic Safety Update EU Single assessment - liraglutide	23/07/2020	24/09/2020	SmPC and PL	Please refer to (SAXENDA, VICTOZA) PSUSA-1892-201912 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
II/0025	Submission of the final report from study NN8022-4241, a retrospective drug utilisation study (DUS) undertaken to investigate patterns of use of liraglutide containing drugs in routine clinical practice, listed as a category 3 study in the RMP. An	13/02/2020	n/a		n/a

	updated RMP version 31 was agreed during the procedure. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
R/0024	Renewal of the marketing authorisation.	17/10/2019	09/12/2019	SmPC, Annex II and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Saxenda in the approved indications remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/1892/ 201812	Periodic Safety Update EU Single assessment - liraglutide	25/07/2019	23/09/2019	SmPC and PL	Please refer to PSUSA/00001892/201812 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
II/0023	Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information regarding hypoglycaemia in patients with type 2 diabetes mellitus treated with insulin based on the final results from the Phase 3b clinical trial NN8022-4272 (SCALE Insulin), undertaken to investigate the effect and safety of liraglutide 3.0 mg in subjects with overweight or obesity and type 2 diabetes mellitus treated with basal insulin. 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	14/06/2019	23/09/2019	SmPC and PL	In a clinical trial in overweight or obese patients with type 2 diabetes mellitus treated with insulin and liraglutide 3.0 mg/day in combination with diet and exercise and up to 2 OADs, severe hypoglycaemia (requiring third party assistance) was reported by 1.5% of patients treated with liraglutide 3.0 mg/day. In this trial, documented symptomatic hypoglycaemia (defined as plasma glucose ≤3.9 mmol/L accompanied by symptoms) was reported by 47.2% of patients treated with liraglutide 3.0 mg/day and by 51.8% of patients treated with placebo. Among patients concomitantly treated with sulfonylurea, 60.9% of patients treated with liraglutide 3.0 mg/day and 60.0% of patients treated with placebo reported documented symptomatic hypoglycaemic events.

IAIN/0022	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	05/04/2019	20/06/2019	SmPC	
WS/1478	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.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	14/02/2019	n/a		
PSUSA/1892/ 201712	Periodic Safety Update EU Single assessment - liraglutide	12/07/2018	n/a		PRAC Recommendation - maintenance
II/0018	Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update the safety information based on the conclusions of the assessment of two PK Clinical trial reports (NN8022-3967 and NN8022-4181), previously submitted in accordance with Article 46 of Regulation (EC) No1901/2006, as amended, and assessed by the CHMP (P46 016). C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH	28/06/2018	20/06/2019	SmPC	The primary objective of trials 4181 and 3967 was to investigate the safety and tolerability of liraglutide for weight management in the paediatric population with obesity. Pharmacokinetic properties were assessed in clinical pharmacology studies in the paediatric population with obesity aged 12 to 17 years (14 patients, body weight 80-122 kg) and 7 to 11 years (16 patients, body weight 45-87 kg) respectively. The data from these trials showed that the liraglutide exposure in adolescents (age 12-17 years), was similar to that in adults with obesity. Exposure associated with 3.0 mg liraglutide was found to be comparable between children aged 7 to 11, adolescents and adult subjects, after correction for body weight. In addition, in children aged 7 to 11 years and in adolescents, no unexpected safety and

					tolerability issues were found. However, currently available PD and PK results are too limited to draw conclusions on the efficacy of Saxenda in children. Therefore the benefit risk in children cannot yet be established.
II/0016	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	08/03/2018	n/a		
IG/0872	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)	30/11/2017	n/a		
IA/0014	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	05/09/2017	n/a		
PSUSA/1892/ 201612	Periodic Safety Update EU Single assessment - liraglutide	06/07/2017	n/a		PRAC Recommendation - maintenance
II/0011	Update of section 4.4 and 5.1 of the SmPC based on the results of the LEADER (EX2211-3748: liraglutide effect on and action in diabetes, evaluation of cardiovascular outcome results) study. This was a category 3 study in the RMP to address the important potential risk of cardiovascular disorders in patients with Type 2 Diabetes Mellitus. The Package Leaflet and Labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement minor editorial changes throughout the product information. An	22/06/2017	15/11/2017	SmPC, Labelling and PL	The LEADER clinical study was a large cardiovascular outcome trial that has shown a reduction in cardiovascular events (MACE-3, expanded MACE, CV mortality) in type 2 diabetes patients, most of whom had established cardiovascular disease. It is agreed that these results are also important for the population of obese patients that is targeted by Saxenda, but the extrapolation requires caution. The MAH fulfilled the requirement of submitting the results of the LEADER study and the two post-approval commitments in relation to the cardiovascular outcomes trial (MEA 002), as well as to provide additional information

	updated RMP (version 27) was also submitted in consequence (MEA 002), as well as to provide additional information on the breast cancer cases found in LEADER (MEA 005). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				on the breast cancer cases found in LEADER (MEA 005). The benefit-risk balance of Saxenda remains positive.
WS/0943	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of the final results from the Optum Database study (NN2211-3784, RMP category 3 study); this was a post-marketing safety surveillance study to observe the safety profile of liraglutide and to compare it with that of other antidiabetic medications when used in a real-life setting in the U.S. The study included a sub-study specifically addressing the safety concern of breast cancer. The updated RMP version 26 has been submitted. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	21/04/2017	n/a		
II/0010	Update of sections 4.2 and 5.1 of the SmPC in order to update the documented treatment effect previously limited to 1 year. The proposed update of the wording for long-term efficacy, safety and	01/12/2016	15/11/2017	SmPC, Annex II, Labelling and PL	Trial 1 (SCALE Obesity & Pre-Diabetes-1839): A total of 3,731 patients with obesity (BMI ≥30 kg/m²), or with overweight (BMI ≥27 kg/m²) with dyslipidaemia and/or hypertension were stratified according to pre-diabetes

	tolerable use in the management of obesity is based on 3-year data from trial 1839. In addition, the Marketing authorisation holder took the opportunity to bring the PI in line with the latest QRD template version 10 and implement minor linguistic updates. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				status at screening and BMI at baseline (≥30 kg/m² or <30 kg/m²). All 3,731 patients were randomised to 56 weeks of treatment and the 2,254 patients with pre-diabetes at screening were randomised to 160 weeks of treatment. Both treatment period were followed by a 12-week off drug/placebo observational follow-up period. Lifestyle intervention in the form of an energy-restricted diet and exercise counselling was background therapy for all patients. The 56 week part of trial 1 assessed body weight loss in all the 3,731 randomised patients (2,590 completers). In this part, 67.5% of randomised patients achieved ≥5% weight loss after 12 weeks. In the 160 weeks part of trial 1 the weight loss occurred mainly in the first year, and was sustained throughout 160 weeks. The 160 week part of trial 1 assessed time to onset of type 2 diabetes in the 2,254 randomised patients with pre-diabetes (1,128 completers). At week 160, while on treatment, 3% treated with Saxenda and 11% treated with placebo were diagnosed with type 2 diabetes mellitus. The estimated time to onset of type 2 diabetes mellitus for patients treated with liraglutide 3.0 mg was 2.7 times longer (with a 95% confidence interval of [1.9, 3.9]), and the hazard ratio for risk of developing type 2 diabetes mellitus was 0.2 for liraglutide versus placebo.
PSUSA/1892/ 201512	Periodic Safety Update EU Single assessment - liraglutide	21/07/2016	22/09/2016	SmPC, Labelling and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1892/201512.
WS/0892	This was an application for a variation following a worksharing procedure according to Article 20 of	25/02/2016	n/a		

	Commission Regulation (EC) No 1234/2008. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation				
PSUSA/1892/ 201506	Periodic Safety Update EU Single assessment - liraglutide	14/01/2016	n/a		PRAC Recommendation - maintenance
II/0006	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	19/11/2015	n/a		
WS/0784	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	24/09/2015	n/a		
IB/0002	B.I.a.z - Change in manufacture of the AS - Other variation	08/07/2015	n/a		
IA/0003	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)	06/07/2015	n/a		
WS/0746	This was an application for a variation following a worksharing procedure according to Article 20 of	25/06/2015	n/a		

	Commission Regulation (EC) No 1234/2008. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation				