Ozempic

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
R/0030	Renewal of the marketing authorisation.	21/07/2022	21/09/2022	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Ozempic in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.

[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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IB/0034	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	08/09/2022	n/a		
IB/0031	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	15/07/2022	n/a		
PSUSA/10671 /202111	Periodic Safety Update EU Single assessment - semaglutide	07/07/2022	n/a		PRAC Recommendation - maintenance
IB/0029/G	This was an application for a group of variations. B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation 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	24/06/2022	21/09/2022	Annex II and PL	
WS/2141	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of section 5.1 of the Ozempic SmPC in order to include information on the use of semaglutide s.c. once weekly vs insulin aspart three times daily, both as add-on to metformin and optimised insulin glargine U100 treatment in subjects with inadequately controlled T2DM; based on the final report from study NN9535-4386 (SUSTAIN-11), listed as a category 3 study in the RMP. This is a 52-week, multi-centre, multinational, open-label, active controlled, two armed,	07/04/2022	21/09/2022	SmPC	In a 52-week open-label trial, 1748 subjects with inadequately controlled T2D after a 12-week run-in period on insulin glargine and metformin were randomised to 1:1 to receive either semaglutide once-weekly (0.5 mg or 1.0 mg) or insulin aspart three times daily. The included population had a mean diabetes duration of 13.4 years and a mean HbA1c of 8.6%, with a target HbA1c of 6.5-7.5%. Treatment with semaglutide resulted in reduction in HbA1c at week 52 (-1.5% for semaglutide vs. -1.2% for insulin aspart). The number of severe hypoglycaemic

	parallel, randomised trial undertaken to investigate the effect on glycaemic control, body weight, safety and health-related quality of life. The SmPC of Rybelsus (semaglutide p.o.) is not impacted. The RMP common for both products has also been updated to version 7.1. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				episodes in both treatment arms was low (4 episodes with semaglutide vs. 7 episodes with insulin aspart). Mean baseline body weight decreased with semaglutide (-4.1 kg) and increased with insulin aspart (+2.8 kg) and the estimated treatment difference was -6.99 kg (95%CI -7.41 to -6.57) at week 52.
IA/0028	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	14/03/2022	n/a		
PSUSA/10671 /202105	Periodic Safety Update EU Single assessment - semaglutide	13/01/2022	n/a		PRAC Recommendation - maintenance
X/0021	Annex I_2.(c) Change or addition of a new strength/potency	11/11/2021	11/01/2022	SmPC, Labelling and PL	
IB/0026/G	This was an application for a group of variations. B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	22/11/2021	n/a		
IB/0025	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the	17/11/2021	n/a		

	manufacturing process				
PSUSA/10671 /202011	Periodic Safety Update EU Single assessment - semaglutide	08/07/2021	n/a		PRAC Recommendation - maintenance
PSUSA/10671 /202005	Periodic Safety Update EU Single assessment - semaglutide	28/01/2021	22/03/2021	SmPC and PL	Please refer to Ozempic PSUSA-10671-202005 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
II/0019	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	14/01/2021	n/a		
IB/0020/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process 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.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	09/12/2020	n/a		
II/0014	Update of sections 4.2 and 5.1 of the SmPC in order to include information on the use of semaglutide once weekly in combination with a SGLT-2 inhibitor, based on the final results from the SUSTAIN 9 study (study NN9535-4269); a 30-weeks, randomised, double-blind, placebo-controlled	03/12/2020	22/03/2021	SmPC and PL	n/a

	phase 3 trial investigating the efficacy and safety of semaglutide as add-on to treatment with an SGLT-2 inhibitor ± metformin or sulphonylurea in subjects with T2DM. 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				
IB/0018	B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS	15/10/2020	n/a		
PSUSA/10671 /201911	Periodic Safety Update EU Single assessment - semaglutide	23/07/2020	30/09/2020	SmPC and PL	Please refer to OZEMPIC PSUSA-10671-201911 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
IA/0016	B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits	29/05/2020	n/a		
II/0011	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	14/05/2020	n/a		
IB/0015	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	30/04/2020	n/a		
N/0012	Minor change in labelling or package leaflet not connected	09/04/2020	30/09/2020	PL	

	with the SPC (Art. 61.3 Notification)				
PSUSA/10671 /201905	Periodic Safety Update EU Single assessment - semaglutide	30/01/2020	27/03/2020	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10671/201905.
IG/1092	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	12/07/2019	n/a		
PSUSA/10671 /201811	Periodic Safety Update EU Single assessment - semaglutide	14/06/2019	n/a		PRAC Recommendation - maintenance
IB/0008	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	11/04/2019	n/a		
II/0006	Submission of an updated RMP version 3.1 in order to reflect that final protocols for Studies NN9535-4447 and NN9535-4352 have been provided (included as milestones under 'additional pharmacovigilance activities' in the RMP). Further the RMP is updated in line with the new template in accordance with Guideline on GVP Module V – Risk management systems (Rev 2). C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	11/04/2019	n/a		n/a
PSUSA/10671 /201805	Periodic Safety Update EU Single assessment - semaglutide	17/01/2019	n/a		PRAC Recommendation - maintenance
II/0001	Update of sections 4.8 and 5.1 of the SmPC in order to reflect the final results from the SUSTAIN 7 trial (NN9535-4216), a	18/10/2018	13/05/2019	SmPC	The MAH submitted the final results from the SUSTAIN 7 trial (NN9535-4216), a 40-week

	40-week open-label trial comparing the safety and efficacy of 0.5 mg of Ozempic to 0.75 mg of dulaglutide and 1 mg of Ozempic to 1.5 mg of dulaglutide in patients on metformin with type-2 diabetes. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				open-label trial conducted in 1,201 patients and comparing the safety and efficacy of 0.5 mg of Ozempic to 0.75 mg of dulaglutide and of 1 mg of Ozempic to 1.5 mg of dulaglutide in patients on metformin with type-2 diabetes. Superiority of semaglutide treatment in reducing HbA1c levels from baseline to week 40 was demonstrated for semaglutide 0.5 mg versus dulaglutide 0.75 mg as well as for semaglutide 1.0 mg versus dulaglutide 1.5 mg. A weight loss of ≥5% and ≥10% was achieved for more subjects with Ozempic 0.5 mg compared with dulaglutide 0.75 mg and with Ozempic 1 mg compared with dulaglutide 1.5 mg. Section 5.1 of the SmPC has been updated accordingly. Sections 4.8 and 5.1 have also been updated to reflect an observed increase in heart rate in Ozempic-treated subjects with cardiovascular risk factors in the long-term trial, compared to data from the phase 3a trials. Section 5.1 was also updated to reflect data on the comparison against dulaglutide, Gastrointestinal disorders were the most frequently observed adverse events, occurring in similar proportions of patients receiving Ozempic 0.5 mg, Ozempic 1 mg or dulaglutide 1.5 mg; although fewer patients had gastrointestinal disorders with dulaglutide 0.75 mg.
IA/0004	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	30/08/2018	n/a		

II/0002/G	This was an application for a group of variations. B.IV.1.c - Change of a measuring or administration device - Addition or replacement of a device which is an integrated part of the primary packaging B.IV.1.z - Change of a measuring or administration device - Other variation B.IV.1.z - Change of a measuring or administration device - Other variation 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 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	31/05/2018	13/05/2019	SmPC, Labelling and PL	