Rybelsus

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/10671 /202305	Periodic Safety Update EU Single assessment - semaglutide	25/01/2024	27/03/2024	SmPC, Annex II and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10671/202305.
II/0036	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	14/09/2023	27/03/2024	SmPC and PL	

[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).

	data				
WS/2541	This was an application for a variation following a worksharing procedure according to Article 20 of 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	31/08/2023	n/a		
IB/0034	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	27/07/2023	n/a		
II/0033/G	This was an application for a group of variations. 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	20/07/2023	n/a		
PSUSA/10671 /202205	Periodic Safety Update EU Single assessment - semaglutide	26/01/2023	04/04/2023	SmPC and PL	Please refer to semaglutide PSUSA/10671/202205 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
IB/0032/G	This was an application for a group of variations. B.I.b.1.b - Change in the specification parameters	31/01/2023	n/a		

	and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits				
II/0030	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	12/01/2023	n/a		
IB/0031	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	13/12/2022	n/a		
WS/2343	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	20/10/2022	n/a		
IB/0029	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	12/09/2022	n/a		
IB/0026	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)	26/07/2022	n/a		

PSUSA/10671 /202111	Periodic Safety Update EU Single assessment - semaglutide	07/07/2022	n/a		PRAC Recommendation - maintenance
II/0025	Update of section 4.8 of the SmPC in order to add 'Hypersensitivity' to the list of adverse drug reactions with frequency uncommon; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/06/2022	16/12/2022	SmPC and PL	Hypersensitivity with frequency uncommon has been added to the list of adverse drug reactions. The detection of hypersensitivity is the outcome of a signal of hypersensitivity including rash and urticaria identified via routine signal detection activities examining post-marketing data for oral semaglutide. For more information, please refer to the Summary of Product Characteristics.
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, parallel, randomised trial undertaken to investigate the effect on glycaemic control, body weight, safety and health-related	07/04/2022	16/12/2022	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 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.

	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				
IA/0024	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	07/03/2022	n/a		
IB/0022	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 originally approved batch size	10/02/2022	n/a		
II/0020	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	27/01/2022	n/a		
PSUSA/10671 /202105	Periodic Safety Update EU Single assessment - semaglutide	13/01/2022	n/a		PRAC Recommendation - maintenance
IB/0019/G	This was an application for a group of variations. 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	09/12/2021	16/12/2022	SmPC, Labelling and PL	

	the range of the currently approved pack sizes				
IA/0021	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	06/12/2021	n/a		
PSUSA/10671 /202011	Periodic Safety Update EU Single assessment - semaglutide	08/07/2021	n/a		PRAC Recommendation - maintenance
IA/0016	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	21/06/2021	n/a		
IB/0015	B.I.e.4.b - Changes to an approved change management protocol - Minor changes that do not change the strategy defined in the protocol	17/05/2021	n/a		
IB/0014/G	This was an application for a group of variations. 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	22/04/2021	n/a		
II/0012	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	22/04/2021	n/a		

	forms manufactured by complex manufacturing processes				
PSUSA/10671 /202005	Periodic Safety Update EU Single assessment - semaglutide	28/01/2021	28/01/2021	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/0007	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	14/01/2021	n/a		
IB/0010/G	This was an application for a group of variations. 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 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	13/11/2020	18/08/2021	SmPC, Labelling and PL	
II/0006	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	12/11/2020	n/a		

IB/0009	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	15/10/2020	n/a		
IA/0008	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	23/09/2020	n/a		
IB/0005	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	22/09/2020	n/a		
IB/0004	B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition	22/09/2020	n/a		
IB/0002	B.II.c.z - Change in control of excipients in the Finished Product - Other variation	30/06/2020	n/a		
IAIN/0001/G	This was an application for a group of variations. B.II.f.1.a.1 - Stability of FP - Reduction of the shelf life of the finished product - As packaged for sale B.II.f.1.e - Stability of FP - Change to an approved stability protocol	19/05/2020	18/08/2021	SmPC	