Trajenta

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/0032	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/06/2018		PL	
WS/1201/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.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an	14/09/2017	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).

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	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 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 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				
IB/0030	C.I.11.a - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of wording agreed by the competent authority	12/07/2017	n/a		
WS/1162	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	01/06/2017	12/03/2018	SmPC	
IG/0798/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	05/05/2017	n/a		

	manufacturer of a novel excipient 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.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.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites				
WS/1140	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/03/2017	12/03/2018	SmPC and PL	
WS/0915	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Extension of indication to include the use of Trajenta and Jentadueto in combination with other diabetes medicines; as a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated based on studies 1245.30, 1275.10 and 1275.1. The Package Leaflet is	15/12/2016	27/01/2017	SmPC and PL	Please refer to the Scientific Discussion for Trajenta /Jentadueto H/C/WS0915.

	updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to make minor editorial changes in the PI. Moreover, the RMP version 10 (for Trajenta) and version 12 (for Jentadueto) have been updated. Furthermore, the PI is brought in line with the latest QRD template version 10.0. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IA/0026	B.I.a.1.i - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new site of micronisation	14/09/2016	n/a		
IB/0025	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	28/06/2016	n/a		
IA/0024	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)	09/06/2016	n/a		
II/0023	Update of section 4.8 of the SmPC in order to update ADR frequency categories based on the pooled safety analysis of the placebo-controlled trials undertaken. 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	28/04/2016	27/01/2017	SmPC and PL	Compared with the previous ADR frequency update, 'hypersensitivity' has changed frequency category from 'not known' to 'uncommon' for linagliptin monotherapy, linagliptin+metformin+sulphonylurea, and linagliptin+insulin combinations, and from 'rare' to 'uncommon' for the linagliptin+metformin combination. Compared with the previous ADR frequency update,

	data				'amylase increased' has changed frequency category from 'uncommon' to 'rare' for linagliptin monotherapy, and from 'not known' to 'uncommon' for the linagliptin+metformin+sulphonylurea combination.
R/0021	Renewal of the marketing authorisation.	28/01/2016	22/03/2016	SmPC, Labelling and PL	
PSUSA/1886/201505	Periodic Safety Update EU Single assessment - linagliptin	17/12/2015	18/02/2016	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1886/201505.
N/0019	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/07/2015	23/09/2015	PL	
II/0018	Submission of a revised RMP in order to add cardiac failure as important potential risk. 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		
PSUV/0016	Periodic Safety Update	04/12/2014	n/a		PRAC Recommendation - maintenance
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/11/2014	23/09/2015	PL	
WS/0524	This was an application for a variation following a worksharing procedure according to Article 20 of	25/09/2014	23/09/2015	SmPC and PL	

	Commission Regulation (EC) No 1234/2008. 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				
IG/0432	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	16/04/2014	n/a		
IB/0013	B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)	20/12/2013	n/a		
IAIN/0012	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	22/11/2013	n/a		
IG/0350	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	30/08/2013	18/09/2014	SmPC and PL	
N/0010	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/08/2013	18/09/2014	PL	
WS/0356	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	21/03/2013	22/04/2013	SmPC	In this variation the MAH has provided an update of the prospective CV meta-analysis. A first analysis of this study was submitted with the MAA. Additionally an updated

	Update of section 5.1 of the SmPC in order to update the information with the current data from the cardiovascular risk meta-analysis. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				summary was performed in 2011 to support the types II variation for the add-on to insulin indication (EMEA/H/C/002110/II/0004/G). Compared to earlier analyses no significant changes have been observed. In total there were 60 primary events on linagliptin and 62 on comparators. The overall CV risk ratio was not significantly reduced for linagliptin versus combined comparators. No difference in CV risk for linagliptin was observed versus placebo in the placebo-controlled trials only. The secondary and tertiary composite CV endpoints also do not show an increased risk for linagliptin as compared with combined comparators. Section 5.1 of the SmPC has been updated to reflect this new data.
WS/0351	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 4.8 of the SmPC in order to include the new adverse reaction “rash” following a CHMP request after the evaluation of the latest PSUR. The Package Leaflet was updated accordingly. In addition, the MAH took the opportunity to implement minor typographical corrections in the SmPC. Furthermore, Annex II was updated to reflect the latest version of the QRD template. C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a	21/03/2013	22/04/2013	SmPC, Annex II and PL	Following the assessment of the latest PSUR for linagliptin, the CHMP requested that, considering the reported de- and re-challenge cases, “rash” should be clearly included as a new adverse reaction in the product information. The MAH has complied with the mentioned CHMP request. Based on the incidence of “rash” in clinical trials (0.4%), frequency uncommon was proposed to be assigned, and the CHMP considered it to be acceptable. Furthermore, the MAH proposals to: - change of the frequency of “hypersensitivity” from uncommon to rare and - addition of “urticaria” and “angioedema” to the SOC “Skin and subcutaneous tissue disorders” with the frequency rare. For these ADRs an asterix is used to indicate that these events were derived from post-marketing experience;

	PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH				were in line with the conclusions of PSUR-2 and therefore were considered acceptable by the CHMP. The other proposed changes and corrections to the SmPC and PL were accepted. Based on the information presented by the MAH to support this variation, there is no impact on the overall benefit/risk balance.
II/0004/G	This was an application for a group of variations. This was an application for a group of variations. Update of sections 4.1, 4.2, 4.4, 4.7, 4.8 and 5.1 of the SmPC: extension of indication for the treatment of type 2 diabetes in combination with insulin (with or without metformin) when this regimen alone, with diet and exercise, does not provide adequate glycaemic control. Sections 1, 2 and 4 of the Package Leaflet are updated accordingly. Update of sections 4.2, 4.8 and 5.1 of the SmPC to include the results of study 1218.63, a study conducted in elderly patients. In addition, the MAH took the opportunity to include the Marketing Authorisation numbers in the SmPC and Labelling and to make linguistic corrections in the Spanish Annexes. Furthermore, the PI is being brought in line with the latest QRD template version 8. The requested group of variations proposed amendments to the Update of Summary of Product Characteristics, Annex II, Labelling and Package Leaflet.	20/09/2012	24/10/2012	SmPC, Annex II, Labelling and PL	For further information please refer to the scientific conclusion: Trajenta H-2110-II-04-G-AR.

	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				
IB/0007/G	This was an application for a group of variations. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	02/10/2012	n/a		
IG/0211	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	05/09/2012	n/a		
IA/0006	A.7 - Administrative change - Deletion of manufacturing sites	28/08/2012	n/a		
WS/0255/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. Update of the Description of Pharmacovigilance System (DDPS). C.I.9.z - Changes to an existing pharmacovigilance system as described in the DDPS - Other variation C.I.9.z - Changes to an existing pharmacovigilance	24/05/2012	24/05/2012		Changes to an existing pharmacovigilance system as described in the DDPS. The MAH update the Detailed Description of the Pharmacovigilance System (DDPS) for Aptivus, MicardisPlus, Mirapexin, Onduarp, Pradaxa, Sifrol, Trajenta, Twynsta and Viramune.

	system as described in the DDPS - Other variation C.I.9.f - Changes to an existing pharmacovigilance system as described in the DDPS - Deletion of topics covered by written procedure(s) describing pharmacovigilance activities C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system				
IA/0002	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	15/03/2012	n/a		
N/0001	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/03/2012	24/10/2012	PL	