Gardasil 9

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/10389 /201706	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine (recombinant, adsorbed)	11/01/2018	n/a		PRAC Recommendation - maintenance
IB/0022	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	05/01/2018	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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N/0021	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/11/2017		Labelling and PL	
II/0019/G	This was an application for a group of variations. B.II.b.1.c: To add MSD International GmbH T/A MSD Ireland (Carlow), Dublin Road, Carlow, Co. Carlow, Ireland as an alternative site responsible for final formulated bulk pooling and primary packaging of Gardasil 9 suspension for injection in pre-filled syringes. B.II.b.2.a: To add MSD International GmbH T/A MSD Ireland (Carlow), Dublin Road, Carlow, Co. Carlow, Ireland as an alternative site responsible for batch/control testing for bacterial endotoxin and sterility tests for Gardasil 9 suspension for injection in pre-filled syringes. 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 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	13/07/2017	n/a		

PSUSA/10389 /201612	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine (recombinant, adsorbed)	06/07/2017	n/a		PRAC Recommendation - maintenance
N/0018	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/03/2017		PL	
IG/0777	A.1 - Administrative change - Change in the name and/or address of the MAH	23/02/2017		SmPC, Labelling and PL	
II/0013	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	19/01/2017	n/a		
PSUSA/10389 /201606	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine (recombinant, adsorbed)	12/01/2017	n/a		PRAC Recommendation - maintenance
IG/0758	A.1 - Administrative change - Change in the name and/or address of the MAH	11/01/2017	03/03/2017	SmPC, Labelling and PL	
N/0014	Update of the package leaflet with revised contact details of the local representatives. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/12/2016	03/03/2017	PL	
PSUSA/10389 /201512	Periodic Safety Update EU Single assessment - human papillomavirus 9-valent vaccine	07/07/2016	n/a		PRAC Recommendation - maintenance

	(recombinant, adsorbed)				
II/0010	Update of section 5.1 of the SmPC in order to include clinical data based on the final clinical study report for the paediatric study V503-020 (GDS07C), provided as per the requirements of article 46 of the paediatric regulation. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	12/05/2016	03/03/2017	SmPC	Study GDS07C compared immune responses to 9vHPV vaccine with immune responses to 4vHPV vaccine in 16-26 years old boys and men. The responses to the 4 common HPV types (6, 11, 16 and 18) were shown to be non-inferior in the 9vHPV group compared to the 4vHPV group. The responses to the 5 new HPV types were greater in the 9vHPV group compared to the 4 vHPV group. The results were overall in agreement with the results previously shown in women 16-26 years of age. The safety results confirm the safety profile of the 9vHPV vaccine, and non new safety signal was detected.
IB/0011	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	26/04/2016	n/a		
II/0004	Update of sections 4.2 and 5.1 of the SmPC in order to add an alternative 2-dose vaccination schedule for children from 9 to 14 years of age based on study results of Protocol V503-010 and section 4.8 of the SmPC in order to add bronchospasm and urticaria. The Package Leaflet is updated accordingly. For clarity, minor amendments have been included in Sections 4.4, and 4.6 and 5.1 of the SmPC. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet, to bring the PI in line with the latest QRD template version 10 and to combine the SmPCs of the suspension for injection and the suspension for injection in a pre	25/02/2016	04/04/2016	SmPC, Annex II, Labelling and PL	The MAH provided the results of a study V503-010 to investigate an alternative 2-dose vaccination schedule for children from 9 to 14 years of age. Results showed comparable immune responses in 2-dose recipients compared to the 3-dose recipients and support the proposed addition of a 2-dose schedule. For completeness and to align with the SmPC of Gardasil section 4.8 of the SmPC was updated to add bronchospasm and urticaria.

	filled syringe. Furthermore, the MAH implemented minor linguistic revisions in the Portuguese, Czeck and Slovak texts. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
II/0007	Update of section 5.1 of SmPC with the results of 4 long term follow-up studies (final study P018-11 and interim reports for Studies P015-21, P019-21 and P020-21). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	01/04/2016	03/03/2017	SmPC	Section 5.1 of SmPC was updated with the results of 4 long term follow-up studies in adolescents (final study P018-11 and interim reports for long term follow-up studies in young/mid-adult women and young men (Studies P015-21, P019-21 and P020-21). In the long-term extension registry study for 16-23 year old women vaccinated with qHPV vaccine, a durable protection was statistically demonstrated to approximately 8 years.
IB/0008	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	26/01/2016	n/a		
A20/0001	Pursuant to Article 20 of Regulation (EC) No 726/2004, the European Commission requested on 09 July 2015 the opinion of the European Medicines Agency on whether there is evidence of a causal association between HPV vaccination and CRPS and/or POTS, and if available information may require updates to the advice to healthcare professionals and patients, including changes to product information or other regulatory measures on	19/11/2015	12/01/2016		Please refer to the assessment report: Cervarix: EMEA/H/A20/1421/C/0721/0071 Gardasil: EMEA/H/A20/1421/C/0703/0060 Gardasil 9: EMEA/H/A20/1421/C/3852/0001 Silgard: EMEA/H/A20/1421/C/0732/0054

	the marketing authorisations concerned. As the request results from the evaluation of data resulting from pharmacovigilance activities, the CHMP opinion should be adopted on the basis of a recommendation of the Pharmacovigilance Risk Assessment Committee.				
N/0006	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/12/2015	04/04/2016	PL	
IG/0625	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	16/11/2015	n/a		
II/0003	B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product	15/10/2015	n/a		
II/0002	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	17/09/2015	n/a		