Lynparza

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/0022	B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation	26/07/2018		SmPC, Labelling and PL	The instructions on how to store Lynparza have been updated to recommend storage in a refrigerator (2°C – 8°C). If preferred, Lynparza capsules can be kept out of the refrigerator (below 30°C) for up to 3 months. After this period, any capsules that have not been used must be thrown away. Lynparza should not be frozen. The shelf-life has also been extended from 18 months to 2 years.
PSUSA/10322	Periodic Safety Update EU Single assessment -	12/07/2018	n/a		PRAC Recommendation - maintenance

[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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/201712	olaparib				
IB/0021/G	This was an application for a group of variations. B.I.b.1.h - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition or replacement (excl. Biol. or immunol. substance) of a specification parameter as a result of a safety or quality issue B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	16/05/2018	n/a		
X/0016/G	This was an application for a group of variations. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data Annex I_2.(a) Change of bioavailability Annex I_2.(b) Change of pharmacokinetics change in rate of release Annex I_2.(c) Change or addition of a new strength/potency Annex I_2.(d) Change or addition of a new pharmaceutical form	22/02/2018	08/05/2018	SmPC, Annex II, Labelling and PL	
PSUSA/10322 /201706	Periodic Safety Update EU Single assessment - olaparib	11/01/2018	n/a		PRAC Recommendation - maintenance
PSUSA/10322 /201612	Periodic Safety Update EU Single assessment - olaparib	20/07/2017	18/09/2017	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for

					PSUSA/10322/201612.
IB/0017/G	This was an application for a group of variations. B.II.d.1.g - Change in the specification parameters and/or limits of the finished product - Addition or replacement (excluding biological or immunological product) of a specification parameter wit its corresponding test method as a result of a safety or quality issue 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	12/06/2017	18/09/2017	SmPC	
IB/0012	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	12/04/2017	n/a		
IB/0015	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	07/04/2017	n/a		
IB/0014	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	07/04/2017	n/a		
PSUSA/10322 /201606	Periodic Safety Update EU Single assessment - olaparib	12/01/2017	n/a		PRAC Recommendation - maintenance
IA/0011	B.I.b.2.a - Change in test procedure for AS or starting	12/12/2016	n/a		

	material/reagent/intermediate - Minor changes to an approved test procedure				
II/0009/G	This was an application for a group of variations. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	10/11/2016	12/12/2016	SmPC and PL	
II/0008/G	This was an application for a group of variations. Update of section 4.2 and 5.2 of the SmPC with recommendations for patients with renal impairment based on the results of study D0816C00006 (MEA 006), that evaluated the influence of mild and moderate renal impairment on the pharmacokinetics of Olaparib. The Package Leaflet and RMP were updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update local representatives in the PL, to bring the PI in line with the latest QRD template version and introduce minor corrections in the PI. Furthermore, a grouping of two type IB variation is submitted to revise the study milestones dates for the category 3 study D0816C00005 and category 1 study D0816C00002 in the RMP. Annex II has been amended accordingly. The requested group of variations proposed	15/09/2016	21/10/2016	SmPC, Annex II, Labelling and PL	The MAH provided a PK study conducted in patients with renal insufficiency (study D0816C00006). In patients with mild renal impairment (creatinine clearance 51 to 80 ml/min), AUC increased by 24% and Cmax by 15% compared with patients with normal renal function. No Lynparza dose adjustment is required for patients with mild renal impairment. In patients with moderate renal impairment (creatinine clearance 31 to 50 ml/min), AUC increased by 44% and Cmax by 26% compared with patients with normal renal function. Lynparza dose adjustment is recommended for patients with moderate renal impairment. These findings have been reflected in section 4.2 as follows: For patients with moderate renal impairment (creatinine clearance 31 to 50 ml/min) the recommended dose of Lynparza is 300 mg twice daily (equivalent to a total daily dose of 600 mg). Lynparza can be administered in patients with mild renal impairment (creatinine clearance 51 to 80 ml/min) with no dose adjustment. Lynparza is not recommended for use in patients with severe

	amendments to the Summary of Product Characteristics, Annex II, Labelling, Package Leaflet and Annex A and to the Risk Management Plan (RMP) C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation				renal impairment or end-stage renal disease (creatinine clearance ≤ 30 ml/min) since there are no data in such patients.
PSUSA/10322 /201512	Periodic Safety Update EU Single assessment - olaparib	07/07/2016	n/a		PRAC Recommendation - maintenance
II/0001/G	This was an application for a group of variations. Update of sections 4.2, 4.4, 4.5, 4.6 and 5.2 of the SmPC in order to include further information related to pharmacokinetic interactions based on the in vivo interaction study D0816C00008, 3 in vitro interaction studies (ADME-AZS-Wave3-140714, ADME-AZS-Wave3-140725 and 140483) and data from previously submitted interaction studies. The provision of the final CSR for study D0816C00008 addresses the post-authorisation measure MEA 004. Further, the MAH provided the study report for in vitro study 8305083 as part of the application. In addition, the MAH took the opportunity to add the published ATC code in section 5.1 of the SmPC, and to	25/02/2016	31/03/2016	SmPC, Labelling and PL	Concomitant use of strong and moderate CYP3A inhibitors is not recommended and alternative agents should be considered. If a strong or moderate CYP3A inhibitor must be co-administered, the recommended olaparib dose reduction is to 150 mg taken twice daily (equivalent to a total daily dose of 300 mg) with a strong CYP3A inhibitor or 200 mg taken twice daily (equivalent to a total daily dose of 400 mg) with a moderate CYP3A inhibitor. Olaparib co administration with strong CYP3A inducers is not recommended. In the event that a patient already receiving olaparib requires treatment with a strong CYP3A inducer, the prescriber should be aware that the efficacy of olaparib may be substantially reduced. For further more detailed information, please consult section

	implement minor editorial changes in the SmPC, labelling and Package Leaflet. A revised RMP version 9 was agreed during the procedure, which includes consequential changes related to data on interactions. Further, the MAH took the opportunity to update the due dates for the provision of the final study reports of the category 3 studies D0816C00005 and D0816C00006, and to add the new category 3 study D0816C00010. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.13 - Other variations not specifically covered				4.5 of the SmPC.

	elsewhere in this Annex which involve the submission of studies to the competent authority				
PSUSA/10322 /201506	Periodic Safety Update EU Single assessment - olaparib	14/01/2016	n/a		PRAC Recommendation - maintenance
IA/0006/G	This was an application for a group of variations. B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process 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 B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	11/01/2016	n/a		
IB/0004	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	16/12/2015	n/a		
IG/0633	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	09/12/2015	n/a		

	location				
IB/0003	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	17/11/2015	n/a		