Onivyde pegylated liposomal

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/0034	Extension of indication to include first-line treatment of adult patients with metastatic adenocarcinoma of the pancreas for Onivyde in combination with oxaliplatin, 5 fluorouracil (5 FU) and leucovorin (LV) based on final results from phase 3 study NAPOLI 3 (D-US-60010-001); this is an interventional study	21/03/2024	25/04/2024	SmPC and PL	Please refer to Scientific Discussion 'Onivyde pegylated limosomal-H-C-004125-II-34'

[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).

	with a primary objective to evaluate the efficacy of the regimen of irinotecan liposome injection + oxaliplatin + 5-fluorouracil (5-FU)/leucovorin (LV) versus nab-paclitaxel + gemcitabine in improving overall survival (OS) in subjects who have not previously received chemotherapy for metastatic adenocarcinoma of the pancreas; As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. The updated RMP version 5.0 is also submitted. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
PSUSA/10534 /202210	Periodic Safety Update EU Single assessment - irinotecan (liposomal formulations)	12/05/2023	n/a		PRAC Recommendation - maintenance
PSUSA/10534 /202110	Periodic Safety Update EU Single assessment - irinotecan (liposomal formulations)	23/06/2022	22/08/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10534/202110.
II/0031	Update of section 4.6 of the SmPC in order to update the duration of effective contraception in women with childbearing potential in line with the CHMP Safety working party (SWP) recommendations on the duration of contraception following the end of treatment with a genotoxic drug and to add a statement about the preservation of gametes. In addition, the MAH took the opportunity to introduce minor changes to section 6.6 of the SmPC to provide	10/06/2022	22/08/2022	SmPC and PL	SmPC new text Women of childbearing potential should use effective contraception during ONIVYDE pegylated liposomal treatment and 7 months thereafter. Males should use condoms during ONIVYDE pegylated liposomal treatment and 4 months thereafter. There are no adequate data on the use of ONIVYDE pegylated liposomal in pregnant women. ONIVYDE

	clarification regarding the size of the needle to be used for the preparation of the infusion prior to administration. 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				pegylated liposomal can cause harm to the foetus when administered to the pregnant woman, as the main ingredient irinotecan has been shown to be embryotoxic and teratogenic in animals (see section 5.3). Therefore, based on results from animal studies and the mechanism of action of irinotecan, ONIVYDE pegylated liposomal should not be used during pregnancy unless clearly necessary. If ONIVYDE pegylated liposomal is used during pregnancy or if the patient becomes pregnant while receiving therapy, the patient should be informed about the potential hazard to the foetus. It is unknown whether ONIVYDE pegylated liposomal or its metabolites are excreted into human milk. Because of the potential for serious adverse reactions of ONIVYDE pegylated liposomal in breast feeding infants, ONIVYDE pegylated liposomal is contraindicated during breast feeding (see section 4.3). Patients should not breast-feed until one month after the last dose. There are no data on the impact of ONIVYDE pegylated liposomal on human fertility. Non liposomal irinotecan was shown to cause atrophy of male and female reproductive organs after multiple daily irinotecan doses in animals (see section 5.3). Prior to starting the administration of ONIVYDE pegylated liposomal consider advising patients on the preservation of gametes. For more information, please refer to the Summary of Product Characteristics.

II/0029/G	This was an application for a group of variations. B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) 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.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition) B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition) B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition) B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) 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	13/01/2022	n/a		

	forms manufactured by complex manufacturing processes B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.z - Change in control of excipients in the Finished Product - Other variation				
IA/0028	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	21/09/2021	22/08/2022	SmPC	
R/0025	Renewal of the marketing authorisation.	20/05/2021	16/07/2021	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 Onivyde pegylated liposomal in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IAIN/0027/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.III.1.a.1 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from an already approved manufacturer	05/07/2021	n/a		

PSUSA/10534 /202010	Periodic Safety Update EU Single assessment - irinotecan (liposomal formulations)	10/06/2021	n/a		PRAC Recommendation - maintenance
IB/0024/G	This was an application for a group of variations. B.II.c.4.z - Change in synthesis or recovery of a non-pharmacopoeial or novel excipient - Other variation B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.z - Change in control of excipients in the Finished Product - Other variation	06/01/2021	n/a		
PSUSA/10534 /202004	Periodic Safety Update EU Single assessment - irinotecan (liposomal formulations)	26/11/2020	n/a		PRAC Recommendation - maintenance
IA/0023	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/09/2020	16/07/2021	SmPC, Labelling and PL	
IB/0022/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are	19/08/2020	n/a		

	aseptically manufactured) excluding biological/ immunological medicinal products 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.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)				
PSUSA/10534 /201910	Periodic Safety Update EU Single assessment - irinotecan (liposomal formulations)	28/05/2020	10/08/2020	SmPC, Annex II, Labelling and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10534/201910.
IB/0020	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	18/06/2020	n/a		
IB/0018	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale	07/02/2020	23/04/2020	SmPC and PL	

	(supported by real time data)				
II/0015	Submission of an updated RMP version 3.0 in order to update the RMP further to the last PSUSA procedures (PSUSA/00010534/201804 and (PSUSA/00010534/201810) and in accordance with GVP Module V Rev.2 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	28/11/2019	n/a		
PSUSA/10534 /201904	Periodic Safety Update EU Single assessment - irinotecan (liposomal formulations)	31/10/2019	n/a		PRAC Recommendation - maintenance
IAIN/0017	A.2.a - Administrative change - Change in the (invented) name of the medicinal product for CAPs	25/10/2019	23/04/2020	SmPC, Labelling and PL	
PSUSA/10534 /201810	Periodic Safety Update EU Single assessment - irinotecan (liposomal formulations)	16/05/2019	n/a		PRAC Recommendation - maintenance
IAIN/0014	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	29/03/2019	23/04/2020	Annex II and PL	

II/0008	Update of sections 1, 2, 4.2, 4.8, 4.9, 5.1, 5.2, 5.3 and 6.6 of the SmPC in order to reflect the expression of strength based on irinotecan anhydrous free-base. The Labelling and Package Leaflet are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes. The updated RMP version 2.6 has also been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/12/2018	31/01/2019	SmPC, Labelling and PL	
PSUSA/10534 /201804	Periodic Safety Update EU Single assessment - irinotecan (liposomal formulations)	15/11/2018	14/01/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10534/201804.
T/0012	Transfer of Marketing Authorisation	19/10/2018	07/12/2018	SmPC, Labelling and PL	
IB/0011/G	This was an application for a group of variations. B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits 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	31/10/2018	n/a		
IA/0010/G	This was an application for a group of variations.	03/08/2018	n/a		

	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.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State				
PSUSA/10534 /201710	Periodic Safety Update EU Single assessment - irinotecan (liposomal formulations)	17/05/2018	n/a		PRAC Recommendation - maintenance
IA/0007/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 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 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	26/04/2018	n/a		

PSUSA/10534 /201704	Periodic Safety Update EU Single assessment - irinotecan (liposomal formulations)	26/10/2017	n/a		PRAC Recommendation - maintenance
IB/0005/G	This was an application for a group of variations. B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method 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	15/08/2017	n/a		
N/0003	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/05/2017	07/12/2018	Labelling and PL	
II/0002	B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a manufacturer of the AS supported by an ASMF	21/04/2017	n/a		
IA/0001	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	28/11/2016	n/a		