Trodelvy

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/0037	Update of sections 4.2 and 4.4 the SmPC in order to add information on the timing of fatal infections as well as recommendations on the use of primary prophylaxis with G-CSF in patients who are at high risk for neutropenia, based on clinical trials data, post-marketing data and the literature. The Package	25/04/2025	05/06/2025	SmPC and PL	4.2 Posology and method of administration […] Prophylaxis for Neutropenia Primary prophylaxis with granulocyte colony-stimulating factor (G-CSF) should be considered starting in the first cycle in patients at increased risk of febrile neutropenia

[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).

	Leaflet is updated accordingly. In addition, the MAH took the opportunity to update section 6.6 of the SmPC to remove the requirement to calculate the required dose at the beginning of each treatment cycle or more frequently if the patient's body weight changed by more than 10% since the previous administration as well as the requirement to warm the vials to room temperature. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				(see section 4.4). Dose modifications for adverse reactions Management of adverse reactions may require temporary interruption, dose reduction, or treatment discontinuation of sacituzumab govitecan. The recommended dosage reduction schedule is presented in Table 1 and the recommended dosage modifications for adverse reactions are provided in Table 2. The sacituzumab govitecan dose should not be re-escalated after a dose reduction for adverse reactions has been made. 4.4 Special warnings and precautions for use […] Neutropenia Sacituzumab govitecan can cause severe or life-threatening neutropenia (see section 4.8). Fatal infections in the setting of neutropenia have been observed in clinical studies with sacituzumab govitecan, primarily in the first two cycles of treatment. Primary prophylaxis with G-CSF should be considered starting in the first cycle of treatment in patients at increased risk of febrile neutropenia, e.g., older patients (in particular aged 65 years and older), patients with previous neutropenia, poor performance status, organ dysfunction (including renal, liver or cardiovascular dysfunction), or multiple comorbid conditions. Monitor absolute neutrophil count (ANC) during treatment. Sacituzumab govitecan should not be administered if the ANC is below 1500/mm3 on Day 1 of any cycle or if the neutrophil count is below 1000/mm3 on Day 8 of any cycle. Sacituzumab govitecan should not be administered in case of neutropenic fever. Dose modifications may be required due to neutropenia or febrile neutropenia. Treat

					neutropenia with G-CSF and consider prophylaxis in subsequent cycles as clinically indicated (see sections 4.2 and 4.8). For more information, please refer to the Summary of Product Characteristics.
IA/0039/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.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol 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	13/01/2025	n/a		
IB/0038	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	19/12/2024	n/a		

II/0035/G	This was an application for a group of variations. B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method	19/12/2024	n/a		
PSUSA/10959 /202404	Periodic Safety Update EU Single assessment - sacituzumab govitecan	28/11/2024	n/a		PRAC Recommendation - maintenance
IB/0036/G	This was an application for a group of variations. B.II.d.z - Change in control of the Finished Product - Other variation B.II.d.z - Change in control of the Finished Product - Other variation	13/11/2024	n/a		
II/0033	B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS	11/07/2024	n/a		

II/0030/G	This was an application for a group of variations. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation 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 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.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test	20/06/2024	n/a		

	method at the site is a biol/immunol method B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation 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 A.7 - Administrative change - Deletion of manufacturing sites B.I.b.1.e - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP 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.1.f - Change in the specification parameters and/or limits of the finished product - Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS				

	B.II.f.1.e - Stability of FP - Change to an approved stability protocol A.7 - Administrative change - Deletion of manufacturing sites 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.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation				
II/0031	Submission of an updated RMP version 3.2 in order to remove the important identified risks 'Severe diarrhoea' and 'Hypersensitivity, and the important potential risk 'Embryo-foetal toxicity' from the list of safety concerns, and in addition to extend the due date for the final CSR for the category 3 study IMMU-132-15 from December 2023 to June 2027 in the Pharmacovigilance plan. 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	16/05/2024	n/a		

II/0032	B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability	25/04/2024	n/a		
II/0029	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	11/01/2024	n/a		
PSUSA/10959 /202304	Periodic Safety Update EU Single assessment - sacituzumab govitecan	30/11/2023	n/a		PRAC Recommendation - maintenance
IB/0027/G	This was an application for a group of variations. 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) B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	04/09/2023	n/a		
IB/0028	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	01/09/2023	n/a		
II/0024/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.4.d - Change to in-process tests or limits applied during the manufacture of the AS - Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the	31/08/2023	n/a		

	AS B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation 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				
II/0023/G	This was an application for a group of variations. B.I.c.1.z - Change in immediate packaging of the AS - Other variation B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier 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.c.2.z - Change in the specification parameters and/or limits of the immediate packaging of the AS - Other variation	31/08/2023	n/a		
IB/0025	B.II.z - Quality change - Finished product - Other variation	26/07/2023	n/a		

II/0020	Extension of indication to include treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced setting based on final results from study IMMU-132-09 (TROPiCS-02); this is an open-label, randomized, multicenter phase 3 study of sacituzumab govitecan (IMMU-132) versus treatment of physician's choice (TPC) in subjects with hormonal receptor-positive (HR+) human epidermal growth factor receptor 2 (HER2) negative metastatic breast cancer (mBC) who have failed at least two prior chemotherapy regimens. 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 (PL) is updated accordingly. Version 3.0 of the RMP is approved. The MAH has also taken the opportunity to introduce minor modifications to the product information related to the QRD Template and SmPC guideline. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	22/06/2023	26/07/2023	SmPC and PL	Please refer to Scientific Discussion 'Trodelvy-H-C-5182-II-20'
PSUSA/10959 /202210	Periodic Safety Update EU Single assessment - sacituzumab govitecan	12/05/2023	n/a		
PSUSA/10959 /202204	Periodic Safety Update EU Single assessment - sacituzumab govitecan	15/12/2022	15/02/2023	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10959/202204.

IB/0021/G	This was an application for a group of variations. 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 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 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.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.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	31/01/2023	n/a		

	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				
II/0018/G	This was an application for a group of variations. Grouped application comprising two type II variations as follows: - To update section 4.8 of the SmPC based on an integrated summary of immunogenicity. - To update sections 4.5 and 5.2 of the SmPC based on data on the impact of concomitant medications including UGT1A1 inhibitors/inducers on SN-38 pharmacokinetic (PK) based on the PopPK model refinement. 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	12/01/2023	26/07/2023	SmPC	Based on the limited data available from patients who received UGT1A1 inhibitors (N=16) or inducers (N=5) while being treated with sacituzumab govitecan, free SN-38 exposures in these patients were comparable to those in patients who did not receive UGT1A1 inhibitor or inducer. Across clinical studies in patients treated with sacituzumab govitecan, 9 (1.1%) of 785 patients developed antibodies to sacituzumab govitecan; 6 of these patients (0.8% of all patients treated with sacituzumab govitecan) had neutralizing antibodies against sacituzumab govitecan. For more information, please refer to the Summary of Product Characteristics.
II/0017	B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS -	08/12/2022	n/a		

	Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method				
IA/0019	B.I.c.2.b - Change in the specification parameters and/or limits of the immediate packaging of the AS - Addition of a new specification parameter to the specification with its corresponding test method	31/10/2022	n/a		
II/0016/G	This was an application for a group of variations. B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol 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 B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	27/10/2022	n/a		
IB/0015	B.z - Quality Change - Other variation	08/08/2022	n/a		

IB/0012/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.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.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	12/07/2022	n/a		
IB/0011	B.II.f.1.b.3 - Stability of FP - Extension of the shelf life of the finished product - After dilution or reconstitution (supported by real time data)	12/07/2022	15/02/2023	SmPC and PL	
IB/0014/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	11/07/2022	n/a		
IB/0010/G	This was an application for a group of variations. B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	11/07/2022	n/a		

	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation				
II/0008	Submission of the final report from the repeat-dose toxicity study (3277-001) with the novel excipient 2-(N-morpholino) ethane sulfonic acid (MES). This is a non-clinical toxicology study titled "A 1-Month Study of MES by Intravenous Injection in Sprague Dawley Rats with a 1- and a 7-Day Post Dose Observation Periods". C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	16/06/2022	n/a		
IB/0009	B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB	17/05/2022	n/a		
II/0003	B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol	17/03/2022	n/a		
II/0002/G	This was an application for a group of variations. B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS	17/03/2022	n/a		

	B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.II.d.2.z - Change in test procedure for the finished product - Other variation				
IB/0007	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	04/03/2022	n/a		
IB/0006	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	02/03/2022	n/a		
IB/0005	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	25/01/2022	n/a		
IB/0004/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	24/01/2022	n/a		
IB/0001	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)	10/01/2022	n/a		