Mylotarg

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/0030	Update of sections 4.8, 5.1, and 5.2 of the SmPC in order to update efficacy, pharmacokinetic and safety information based on interim results from study WI203680 - MyeChild 01-International Randomised Phase III Clinical Trial in Children With Acute Myeloid Leukaemia – Incorporating an Embedded Dose	12/10/2023		SmPC	SmPC new text (extracted and summarized): The major dose finding part of the paediatric study MyeChild 01 Investigated the number of doses of MYLOTARG 3 mg/m2 (up to a maximum of 3 doses; each dose was capped at one 5 mg vial/dose) which can be combined safely with cytarabine plus either mitoxantrone

[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).

	Finding Study for Gemtuzumab Ozogamicin in Combination With Induction Chemotherapy. This is a dose finding sub-study aimed to identify the optimum tolerated number of doses of GO 3 mg/m2 (up to a maximum of 3 doses) which can be combined safely with AraC plus mitoxantrone or liposomal DAUNO in induction therapy. The company took also the occasion to update the date of the latest renewal in section 9 of the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				or liposomal daunorubicin in induction therapy. There were 3 cohorts: Cohort 1 (n=15): Patients received a single dose of MYLOTARG (3 mg/m2) on day 4 of Course 1 of induction chemotherapy. Cohort 2 (n=20): Patients received a single dose of MYLOTARG (3 mg/m2) on days 4 and 7 of Course 1 of induction chemotherapy. Cohort 3 (n=19): Patients received a single dose of MYLOTARG (3 mg/m2) on days 4, 7 and 10 of Course 1 of induction chemotherapy. The MyeChild 01 study is ongoing. The optimal dose of gemtuzumab ozogamicin for paediatric patients is not yet established. In the dose finding part of the paediatric study MyeChild 01 the safety profile was similar with that observed in the other studies of gemtuzumab ozogamicin combined with intensive chemotherapy in adult and paediatric patients with de novo AML. For more information, please refer to the Summary of Product Characteristics.
II/0029/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS 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	31/08/2023	n/a		

IB/0028/G	This was an application for a group of variations. B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification 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.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification 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	03/07/2023	n/a		
IA/0027	B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	03/02/2023	n/a		
R/0025	Renewal of the marketing authorisation.	15/09/2022	15/11/2022	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 Mylotarg in the approved indication remains favourable and

					therefore recommended the renewal of the marketing authorisation with unlimited validity.
IA/0026	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	11/07/2022	15/11/2022	SmPC	
II/0024	Update of sections 4.8, 5.1, and 5.2 of the SmPC based on the final results from study B176103; this is a single-arm, open-label, phase 4 study evaluating the QT interval, pharmacokinetics, and safety of gemtuzumab ozogamicin as a single-agent regimen in patients with relapsed or refractory CD33-positive Acute Myeloid Leukemia. The RMP version 2.2 has also been submitted. In addition, the MAH took the opportunity to introduce some editorial changes in the product information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/06/2022	15/11/2022	SmPC and PL	SmPC new text For more information, please refer to the Summary of Product Characteristics.
II/0023/G	This was an application for a group of variations. B.I.e.3 - Deletion of an approved change management protocol related to the AS B.I.e.2 - Introduction of a post approval change management protocol related to the 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 method at the site is a biol/immunol method	10/03/2022	15/11/2022	Annex II and PL	

	A.7 - Administrative change - Deletion of manufacturing sites B.I.e.4.a - Changes to an approved change management protocol - Major changes 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 B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits A.7 - Administrative change - Deletion of manufacturing sites B.I.e.2 - Introduction of a post approval change management protocol related to the AS B.I.c.1.b - Change in immediate packaging of the AS - Qualitative and/or quantitative composition for sterile and non-frozen biological/immunological ASs B.I.b.1.g - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Widening of the approved specs for starting mat./intermediates, which may have a significant effect on the quality of the AS and/or the FP A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release 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 B.II.h.1.b.2 - Update to the Adventitious Agents Safety Evaluation information - Replacement of obsolete studies related to manufacturing steps and adventitious agents already reported in the dossier - without modifications of risk assessment 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.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 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.3.c - Change in batch size (including batch size ranges) of AS or intermediate - The change requires assessment of the comparability of a biological/immunological AS 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.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.e.3 - Deletion of an approved change management protocol related to the AS				

	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				
PSUSA/10688 /202105	Periodic Safety Update EU Single assessment - gemtuzumab ozogamicin	02/12/2021	n/a		PRAC Recommendation - maintenance
N/0022	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	01/10/2021	15/11/2022	PL	
PSUSA/10688 /202005	Periodic Safety Update EU Single assessment - gemtuzumab ozogamicin	14/01/2021	n/a		PRAC Recommendation - maintenance
N/0020	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/11/2020	30/04/2021	PL	
IB/0019/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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) B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	11/11/2020	30/04/2021	SmPC, Annex II and PL	
IB/0018	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	10/11/2020	30/04/2021	SmPC	

IB/0016/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites 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	11/06/2020	n/a		
PSUSA/10688 /201911	Periodic Safety Update EU Single assessment - gemtuzumab ozogamicin	11/06/2020	n/a		PRAC Recommendation - maintenance
IB/0015	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	19/05/2020	n/a		
IAIN/0014/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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	18/05/2020	30/04/2021	Annex II and PL	
IB/0013	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process	15/04/2020	n/a		

	of the AS				
II/0010/G	This was an application for a group of variations. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	16/01/2020	n/a		
IB/0011	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	28/11/2019	n/a		
PSUSA/10688 /201905	Periodic Safety Update EU Single assessment - gemtuzumab ozogamicin	28/11/2019	n/a		PRAC Recommendation - maintenance
II/0008	Update of sections 4.2 and 4.4 of the SmPC in relation to posology and administration and with information regarding traceability, respectively. Following the re-analysis of data from the paediatric study AAML0531 sections 4.8 and 5.1 of the SmPC are also updated with information on safety and efficacy of Mylotarg in previously untreated AML patients. In addition, the Marketing authorisation holder (MAH) took the opportunity to include minor editorial changes in sections 4.2, 4.4, 4.8 and 5.2 of the SmPC and to make minor updates to bring the PI in line with the latest QRD template version.	19/09/2019	21/10/2019	SmPC and PL	

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
II/0007	Update of sections 4.8 and 5.1 of the SmPC based on safety and efficacy data for paediatric patients with relapsed or refractory AML from a systematic literature review, as requested by the gemtuzumab ozogamicin Paediatric Investigation Plan (PIP) EMEA-001733-PIP02-15-M01 (measure 4). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	19/09/2019	21/10/2019	SmPC	Please refer to Scientific Discussion 'Mylotarg-H-C-4204-II-07'
PSUSA/10688 /201810	Periodic Safety Update EU Single assessment - gemtuzumab ozogamicin	16/05/2019	n/a		PRAC Recommendation - maintenance
IB/0006	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	04/03/2019	n/a		
IB/0004/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.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites	10/12/2018	21/10/2019	Annex II and PL	

	(excluding manufacturer for batch release) B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation 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)				
IB/0003	B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	18/10/2018	n/a		
T/0001	Transfer of Marketing Authorisation	11/07/2018	30/07/2018	SmPC, Labelling and PL	
IB/0002/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.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of	23/07/2018	n/a		

	an obsolete parameter)				