Phesgo

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
IA/0010/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	08/02/2022	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).

	corresponding test method 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.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				
PSUSA/10906 /202106	Periodic Safety Update EU Single assessment - pertuzumab / trastuzumab	13/01/2022	n/a		PRAC Recommendation - maintenance
II/0004	Update in Section 4.8, Undesirable Effects, to present the pooled data from Perjeta and Phesgo studies. In addition to this, the MAH has taken the opportunity to introduce minor updates in the SmPC and the Package leaflet: • Update in Section 9 of the SmPC to reflect the date of first authorisation • Editorial update in Section 4 of the the Package leaflet to add a space • Update in Section 6 of the the Package leaflet to adapt to the revised QRD Template v10.2 C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/01/2022		SmPC and PL	
WS/2131	This was an application for a variation following a	25/11/2021	n/a		

	worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation				
II/0007	Update of the immunogenicity information in the section 4.8 of the SmPC based on the analysis of the Federica study (Phase III clinical trial in patients with HER2 overexpressing early breast cancer). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/09/2021		SmPC	In the FEDERICA study, the incidence of treatment-emergent anti-pertuzumab and anti-trastuzumab antibodies was 6.1 % (15/245) and 0.4 % (1/245), respectively, in patients treated with intravenous pertuzumab and trastuzumab. Among patients that tested positive to anti-pertuzumab antibodies, neutralizing anti-pertuzumab antibodies were detected in two patients. The incidence of anti-pertuzumab and anti-trastuzumab antibodies detected at any time point (including baseline) was 10.3 % (26/252) and 1.2 % (3/252), respectively, in patients treated with intravenous pertuzumab and trastuzumab. Among these patients, neutralizing anti-pertuzumab antibodies were detected in three patients. The incidence of treatment-emergent anti-pertuzumab, anti-trastuzumab, and anti-vorhyaluronidase alfa antibodies was 8.3 % (20/241), 1.7 % (4/241), and 3.8 % (9/238), respectively, in patients treated with Phesgo. Among these patients, neutralizing anti-pertuzumab antibodies were detected in two patients, and neutralizing anti-trastuzumab antibodies were detected in one patient. The incidence of anti-pertuzumab, anti-trastuzumab, and anti-vorhyaluronidase alfa antibodies detected at any time point (including baseline) was 12.1 % (30/248), 3.2 % (8/248), and 9 % (22/245), respectively, in patients treated with Phesgo. Among these patients, neutralizing

					anti-pertuzumab antibodies were detected in three patients, neutralizing anti-trastuzumab antibodies were detected in one patient, and neutralizing anti-vorhyaluronidase alfa antibodies were detected in one patient. For more information, please refer to the Summary of Product Characteristics.
WS/2093	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	02/09/2021	n/a		
PSUSA/10906 /202012	Periodic Safety Update EU Single assessment - pertuzumab / trastuzumab	08/07/2021	n/a		PRAC Recommendation - maintenance
II/0002	Update of sections 4.2, and 4.8, and 5.1 of the SmPC in order to support the safety of switching from intravenous to subcutaneous route of administration or vice versa, based on results from study MO40628; this is a Phase II, randomised, open-label, cross-over study to assess preference for intravenous or subcutaneous route of administration in patients with HER2-positive early breast cancer. Minor editorial changes have been introduced in the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to	24/06/2021		SmPC	SmPC new text This variation introduced information on switching from intravenous pertuzumab and trastuzumab to Phesgo. Study MO40628 investigated the safety of switching between intravenous pertuzumab and trastuzumab and Phesgo subcutaneous and vice versa with a primary objective to evaluate patient preference for either the intravenous or the subcutaneous route of administration: 85 % of patients preferred the subcutaneous route, whereas 13.8 % preferred the IV administration, and 1.2 %

	new quality, preclinical, clinical or pharmacovigilance data				had no preference. A total of 160 patients were included in this 2-arm, cross-over study: 80 patients were randomized to Arm A (3 cycles of intravenous pertuzumab and trastuzumab followed by 3 cycles of Phesgo) and 80 patients were randomized to Arm B (3 cycles of Phesgo followed by 3 cycles intravenous pertuzumab and trastuzumab). At primary analysis, the median exposure to adjuvant pertuzumab and trastuzumab (both IV and SC administration) was 11 cycles (range: 6 to 15). Among the patients in Arm A, the incidence of AEs during Cycles 1-3 (intravenous treatment) was 77.5 % (62/80 patients) compared to Cycles 4-6 (subcutaneous treatment) which was 72.5 % (58/80 patients). Among the patients in Arm B, the incidence of AEs during Cycles 1-3 (subcutaneous treatment) was 77.5 % (62/80 patients) compared to Cycles 4-6 (intravenous treatment) which was 63.8 % (51/80 patients), mainly due to higher incidence of local injection site reactions (all grade 1 or 2) during Phesgo administration. Pre-switching rates (Cycles 1-3) for serious adverse events, grade 3 adverse events and treatment discontinuations due to adverse events were low (<106 %) and similar to post-switching rates (Cycles 4-6). No grade 4 or grade 5 adverse events were reported. For more information, please refer to the Summary of Product Characteristics.
IB/0005	B.II.b.4.z - Change in the batch size (including batch size ranges) of the finished product - Other variation	14/06/2021	n/a		