Tecentriq

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/0087	Update of sections 4.2 in order to include information regarding switching treatment between Tecentriq intravenous and subcutaneous (and vice versa), based on primary results from study MO43576 (IMscin002); this is a phase II, randomised, multicenter, open-label cross-over study to evaluate participants and healthcare professional reported	12/12/2024		SmPC and PL	SmPC new text In the method of administration part of section 4.2 of the SmPC, it has been added that patients currently receiving intravenous Tecentriq can switch to atezolizumab solution for injection or vice versa. For more information, please refer to the Summary of Product Characteristics.

[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).

	reference for subcutaneous atezolizumab compared with intravenous atezolizumab formulation in participants with non-small cell lung cancer. The package leaflet has been revised accordingly. The RMP version 31.2 is agreed. In addition, the MAH took the opportunity to introduce minor formatting changes to the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
II/0088	Update of Sections 4.8 and 5.1 of the SmPC in order to add "Xerosis" and "blood creatine phosphokinase increased" to the list of adverse drug reactions (ADRs) with frequency "common" and "uncommon" respectively and update the efficacy information based on the final disease-free survival (DFS) results and second interim overall survival (OS) results from study GO29527 (IMpower010); this is a phase III, open-label, randomized study to investigate the efficacy and safety of atezolizumab (Anti-PD-L1 Antibody) compared with best supportive care following adjuvant cisplatin-based chemotherapy in patients with completely resected stage IB-IIIA Non-Small Cell Lung Cancer (NSCLC); the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the SmPC. The MAH also took the opportunity to align the wording in the Package Leaflet with the statement in Section 4.4 of the SmPC related to patient card and to bring the Package leaflet in line	19/09/2024		SmPC and PL	SmPC new text Inclusion of xerosis and blood creatine phosphokinase increased as new adverse reactions in section 4.8 with frequencies common and uncommon respectively. Section 5.1 has also been updated with regards to the adjuvant treatment of early-stage NSCLC in order to reflect the updated efficacy results for DFS and OS which are consistent with the previous results. For more information, please refer to the Summary of Product Characteristics.

	with the EMA guidance on polysorbates used as excipients. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
II/0082	Extension of indication to include first-line treatment of adult patients with advanced non-small cell lung cancer (NSCLC) who are ineligible for platinum-based therapy (see section 5.1 for selection criteria), for TECENTRIQ, based on final results from study MO29872 (IPSOS); this is a phase 3, open-label, multicenter, randomised study to investigate the efficacy and safety of atezolizumab compared with chemotherapy in patients with treatment naive advanced or recurrent (stage IIIB not amenable for multimodality treatment) or metastatic (stage IV) NSCLC who are deemed unsuitable for platinum-containing therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The new indication has been reflected in the SmPC for the IV and the SC formulations. Version 29.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. The variation leads to amendments to the Summary of Product Characteristics and to the Risk Management Plan (RMP). C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or	25/07/2024	26/08/2024	SmPC	Please refer to Scientific Discussion 'Tecentriq-H-C-004143-II-0082'.

	modification of an approved one				
IB/0085/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 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.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test A.7 - Administrative change - Deletion of manufacturing sites	04/07/2024	26/08/2024	Annex II	
IAIN/0086/G	This was an application for a group of variations. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	28/06/2024	26/08/2024	SmPC and PL	

II/0084	Update of section 4.8 of the SmPC in order to add 'hypophysitis' to the list of adverse drug reactions (ADRs) with frequency 'uncommon' based on interim results from study WO39391 (IMpassion030). This is a Phase III, randomized, open label study comparing atezolizumab in combination with adjuvant anthracycline/taxane-based chemotherapy versus chemotherapy alone in patients with operable triple-negative breast cancer; the package leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes to the SmPC, labelling and package leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	11/04/2024	26/08/2024	SmPC, Labelling and PL	SmPC new text Update of section 4.8 to upgrade hypophysitis from a "rare" to an "uncommon" adverse reaction for atezolizumab monotherapy and to include hypophysitis as a new uncommon adverse reaction for atezolizumab in combination therapy. In addition, footnote m clarifies the term hypophysitis according to MedDRA (Medical Dictionary for Regulatory Activities) version 26.1. Further information has been added to the paragraph on "Immune mediated endocrinopathies", section on "Hypophysitis", particularly regarding atezolizumab in combination. Hypophysitis occurred in 1.4% (15/1 093) of patients who received atezolizumab in combination with paclitaxel followed by atezolizumab, dose-dense doxorubicin or epirubicin, and cyclophosphamide. The median time to onset was 3.8 months (range: 2.4 to 10.7 months). Eleven patients (1.0%) required the use of corticosteroids. Treatment with atezolizumab was discontinued in 7 (0.6%) patients. The paragraph on atezolizumab monotherapy has also been revised with the new updated clinical data. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10644 /202305	Periodic Safety Update EU Single assessment - atezolizumab	14/12/2023	22/02/2024	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10644/202305.
II/0083/G	This was an application for a group of variations. C.I.4: Update of section 5.1 of the SmPC in order to update efficacy information based on final results from study IMvigor210 (GO29293) listed as a PAES	08/02/2024	26/08/2024	SmPC, Annex II and Labelling	SmPC new text Section 5.1 of the SmPC was updated to reflect efficacy information based on final results from study IMvigor210 (GO29293), a Phase II, multicenter, single-arm study of atezolizumab in patients with locally advanced or

	in the Annex II; this is a Phase II, multicenter, single-arm study of atezolizumab in patients with locally advanced or metastatic urothelial bladder cancer. The Annex II is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and to update section 3 of the SmPC with information on pH and osmolality to bring it in line with the latest QRD template and SmPC guideline. C.I.13: Submission of the final report from study SAUL (MO29983) listed as a category 3 study in the RMP. This is an open-label, single arm, multicenter, safety study of atezolizumab in locally advanced or metastatic urothelial or non-urothelial carcinoma of the urinary tract. The RMP version 30.1 has been agreed. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				metastatic urothelial bladder cancer: At the time of the final analysis for Cohort 1, patients had a median survival follow-up time of 96.4 months. Median OS was 12.3 months (95% CI: 6.0, 49.8) in patients with PD L1 expression ≥ 5% (patients who are included in the therapeutic indication). At the time of the final analysis for Cohort 2, patients had a median survival follow-up time of 46.2 months. Median OS was 11.9 months (95% CI: 9.0, 22.8) in patients with PD L1 expression ≥ 5%, 9.0 months (95% CI: 7.1, 11.1) in patients with PD L1 expression ≥ 1%, and 7.9 months (95% CI: 6.7, 9.3) in all comers. For more information, please refer to the Summary of Product Characteristics.
X/0076	Annex I_2.(c) Change or addition of a new strength/potency Annex I_2.(d) Change or addition of a new pharmaceutical form Annex I_2.(e) Change or addition of a new route of administration	09/11/2023	11/01/2024	SmPC, Labelling and PL	Please refer to Scientific Discussion: EMEA/H/C/004143/X/0076.

II/0078	Update of section 5.1 of the SmPC in order to include the final overall survival (OS) analysis results based on final results from study WO30070 listed as a PAES in the Annex II; this is a Phase III, multicenter, randomized, placebo-controlled study of atezolizumab as monotherapy and in combination with platinum-based chemotherapy in patients with untreated locally advanced or metastatic urothelial carcinoma. Annex II of the SmPC has also been updated to remove the PAES as it has now been fulfilled. The RMP version 27.1 is agreed. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	31/08/2023	11/01/2024	SmPC and Annex II	SmPC new text Sub-section Urothelial carcinoma in section 5.1 of the SmPC was updated to present the final results of IMvigor130 a phase III study of atezolizumab monotherapy and in combination with platinum-based chemotherapy in patients with untreated locally advanced or metastatic urothelial carcinoma. Out of 719 patients enrolled in the atezolizumab monotherapy (n=360) and chemotherapy alone (n=359) arms, 50 and 43 patients, respectively, were cisplatin-ineligible by Galsky criteria and had tumours with high PD-L1 expression (☐ 5% of immune cells staining positive for PD-L1 by immunohistochemistry using VENTANA PD-L1 [SP142] assay). In an exploratory analysis in this subgroup of patients, the unstratified HR for OS was 0.56 (95% CI: 0.34, 0.91). The median OS was 18.6 months (95% CI: 14.0, 49.4) in the atezolizumab monotherapy arm vs. 10.0 months (95% CI: 7.4, 18.1) in the chemotherapy alone arm. For more information, please refer to the Summary of Product Characteristics.
IB/0079	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	15/08/2023	n/a		
II/0077/G	This was an application for a group of variations. Grouped application comprising two type II variations as follows: - Update of sections 4.2, 4.4. and 4.8 of the SmPC in	26/04/2023	26/05/2023	SmPC, Annex II and PL	SmPC new text Three new adverse reactions were included: Facial paresis (frequency rare), myelitis (frequency rare) and dry mouth (frequency common). Myelitis and dry mouth have been observed for Tecentriq monotherapy only, while facial

	order to add dose modification advice and new warning for two new important identified risks of immune-mediated myelitis and immune-mediated facial paresis and to add facial paresis and myelitis to the list of adverse drug reactions (ADRs) with frequency Rare following a safety signal based on the cumulative review of the MAH safety database and literature search. - Update of section 4.8 of the SmPC in order to add dry mouth to the list of adverse drug reactions (ADRs) with frequency Common, based on the results from study WO39210 (IMmotion010), a multicenter, randomized, placebo-controlled, double-blind study evaluating the efficacy and safety of atezolizumab versus placebo in patients with renal cell carcinoma (RCC) who are at high risk of disease recurrence following resection. In addition, minor frequencies update of existing adverse reactions were made to reflect the updated pool of patients for atezolizumab monotherapy. The Annex II and Package Leaflet are updated accordingly. The RMP version 26.1 has also been approved. In addition, the MAH took the opportunity to introduce editorial changes to the SmPC and to update the list of local representatives in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				paresis has been observed for both Tecentriq monotherapy and in combination therapy. For facial paresis and myelitis, dose modification advice were included as well as warning to closely monitor for signs and symptoms suggestive of facial paresis and myelitis. Minor frequencies update of existing adverse reactions were made to reflect the updated pool of patients for atezolizumab monotherapy. For more information, please refer to the Summary of Product Characteristics.

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
II/0074	Submission of the final report from study MO39171 listed as a category 3 study in the RMP in order to fulfil MEA/008. This is a Phase III/IV, Single Arm, multicenter, interventional study of Atezolizumab to Investigate Long-term Safety and Efficacy in previously treated Patients with Locally Advanced or Metastatic Non-small Cell Lung Cancer. The RMP version 25.1 has also been agreed. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	09/02/2023	n/a		Not applicable
PSUSA/10644 /202205	Periodic Safety Update EU Single assessment - atezolizumab	15/12/2022	09/02/2023	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10644/202205.
II/0075	Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add 'pericardial disorders' to the list of adverse drug reactions (ADRs) with frequency common in monotherapy and uncommon in combination therapy based on the final results from Drug Safety Report (DSR 1115896) including review of available clinical trial data, post-marketing data, and literature. In addition, the MAH took the opportunity to update Annex II section D of the SmPC to refer to immune-mediated adverse reactions and to implement editorial changes in the	26/01/2023	27/02/2023	SmPC, Annex II and PL	Pericardial disorders, including pericarditis, pericardial effusion and cardiac tamponade, some leading to fatal outcomes, have been observed with atezolizumab. Pericardial disorders occurred in 1.1% (47/4 349) of patients who received Tecentriq monotherapy. The median time to onset was 1.4 months (range: 6 days to 17.5 months). The median duration was 1.4 months (range: 0 to 19.3+ months; + denotes a censored value). Pericardial disorders led to discontinuation of Tecentriq in 3 (< 0.1%) patients. Pericardial disorders requiring the use of corticosteroids occurred in 0.2% (7/4 349) of patients.

	SmPC. The Package Leaflet was updated accordingly. The RMP version 23.1 has also been agreed. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				Patients should be monitored for clinical signs and symptoms of pericardial disorders. For suspected Grade 1 pericarditis, treatment with atezolizumab should be withheld and prompt cardiology consultation with diagnostic workup according to current clinical guidelines should be initiated. For suspected Grade ≥ 2 pericardial disorders, treatment with atezolizumab should be withheld, prompt treatment with systemic corticosteroids at a dose of 1 to 2 mg/kg bw/day of prednisone or equivalent should be started and prompt cardiology consultation with diagnostic workup according to current clinical guidelines should be initiated. Once a diagnosis of a pericardial disorder event is established, treatment with atezolizumab must be permanently discontinued for Grade ≥ 2 pericardial disorders. For more information, please refer to the Summary of Product Characteristics.
IB/0073/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	02/11/2022	n/a		
II/0070/G	This was an application for a group of variations. B.II.d.2.z - Change in test procedure for the finished product - Other variation B.II.d.2.z - Change in test procedure for the finished product - Other variation	01/09/2022	n/a		

	B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation 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 an obsolete parameter) B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation 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 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.a - Change in test procedure for the finished product - Minor changes to an approved test procedure 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 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 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.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test A.7 - Administrative change - Deletion of manufacturing sites				
IB/0071	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	25/07/2022	09/02/2023	Annex II	Annex II has been revised to amend the due date for the provision of a final study report.
II/0064	C.I.6 (Extension of indication) Extension of indication to include adjuvant treatment of non-small cell lung cancer (NSCLC) following resection and platinum-based chemotherapy for adult patients whose tumours have PD-L1 expression on ≥ 50% of tumour cells (TC) for Tecentriq as	22/04/2022	07/06/2022	SmPC and PL	Please refer to Scientific Discussion 'EMEA/H/C/004143/II/0064'

	monotherapy based on the results from the pivotal phase III Study GO29527 (IMpower010); as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. Minor editorial changes have been made throughout the SmPC. The Package Leaflet is updated in accordance. Version 21.2 of the RMP has also been submitted. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
R/0069	Renewal of the marketing authorisation.	24/02/2022	25/04/2022	SmPC, Annex II and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Tecentriq in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10644 /202105	Periodic Safety Update EU Single assessment - atezolizumab	16/12/2021	23/02/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10644/202105.
II/0067	Update of section 4.8 of the SmPC in order to include the new ADR of rhinorrhoea for atezolizumab in combination therapy, as part of the grouped term of nasopharyngitis identified in the IMpassion031 study and reviewed in the context of a drug safety report. The package leaflet is proposed to be updated accordingly. Additional amendments are proposed to the footnotes of ADRs in the SmPC, the removal of the term 'lung infection', the inclusion of the term 'orthostatic hypertension' and the inclusion of a new footnote listing the preferred terms covered for the	02/12/2021	23/02/2022	SmPC and PL	The section 4.8 of the SmPC has been updated to reflect data from study IMpassion031. The new ADR of "rhinorrhoea" has been added as part of the grouped term of "nasopharyngitis" for atezolizumab in combination therapy, the new ADR of "orthostatic hypertension" has been added to the grouped term of "hypertension" and the frequencies of the most common ADRs have been updated to reflect the pooled combination therapy clinical trial data of 4,535 patients including 164 patients from IMpassion031. The posology of atezolizumab in combination therapy has been further clarified in section

	ADR of psoriasis. In addition, the MAH took the opportunity of this variation to further clarify the posology in section 4.2 of the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				4.2 of the SmPC.
II/0066	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	02/12/2021	n/a		
IAIN/0068	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	29/09/2021	23/02/2022	SmPC and PL	
II/0060	Update of section 4.2 of the SmPC in order to harmonise the atezolizumab posology regimen of 840 mg every 2 weeks, 1200 mg every 3 weeks and 1680 mg every 4 weeks administered as an IV infusion across the currently authorised indications of NSCLC, ES-SCLC, TNBC and HCC, based on PK modelling and simulation data. As a consequence of the harmonized dose schedules, the MAH is applying for a combined SmPC and PL. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to include minor editorial changes to the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/07/2021	20/08/2021	SmPC and PL	The interchangeable use of 840 mg q2w, 1200 mg q3w, and 1680 mg q4w IV atezolizumab dose regimens across all registered indications when atezolizumab is used in combination therapy with other agents and in the maintenance phase is supported by (1) similar clinical pharmacokinetics of atezolizumab observed between indications and between monotherapy and combination settings (i.e., no apparent PK DDI) (2) comparable predicted exposure for 840-mg q2w, 1200-mg q3w, 1680-mg q4w IV dosing regimens that fall within the flat part of the ER curve for both exposure-efficacy and exposure-safety in both monotherapy and combination therapy studies, and (3) the observed safety profile for atezolizumab in combination therapy is similar to that observed in monotherapy studies of atezolizumab with no new safety signals other than the known toxicities from the

					combination partners.
N/0063	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/08/2021	23/02/2022	PL	
II/0061	Submission of an updated RMP version 20.0 in order to add severe cutaneous adverse reactions (SCARs) as an important identified risk and its associated risk minimisation measures, a DHPC, following the addition of SCARS to the Tecentriq PI with procedure EMEA/H/C/004143/II/0054. In addition the MAH has also taken the opportunity to update the due dates of final CSR of two Post-authorisation efficacy studies. 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	08/07/2021	20/08/2021	Annex II	n/a
IA/0062	B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test	26/05/2021	n/a		
II/0059	Submission of the final report from study MO39196 (IMpassion131), a phase III, multicenter, randomized, placebo-controlled study of Tecentriq in combination with paclitaxel in 1L metastatic triple negative breast cancer as recommended by the CHMP during procedure EMEA/H/C/004143/X/0017.	20/05/2021	n/a		

	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
II/0058	Update of section 5.1 of the SmPC in order to include the updated efficacy results from study YO40245 (IMbrave150) with a data cut-off of 31 August 2020 as recommended by the CHMP in the context of variation EMEA/H/C/004143/II/0039; IMbrave 150 is a Phase III, open-label, multicenter, randomized, two-arm pivotal study designed to evaluate the efficacy and safety of atezolizumab + bevacizumab versus sorafenib in patients with locally advanced or metastatic hepatocellular carcinoma who had not received prior systemic treatment. In addition, the MAH took the opportunity to clarify in section 4.4 of the SmPC that the exclusion of patients with hepatitis B or hepatitis C infection only applies to non-HCC patients). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	06/05/2021	20/08/2021	SmPC	A descriptive updated efficacy analysis was performed with a median survival follow up time of 15.6 months. The median OS was 19.2 months (95% CI: 17.0, 23.7) in the atezolizumab + bevacizumab arm versus 13.4 months (95% CI: 11.4, 16.9) in the sorafenib arm with a HR of 0.66 (95% CI: 0.52, 0.85). The median PFS by independent review facility (IRF)-assessment per RECIST v1.1 was 6.9 months (95% CI: 5.8, 8.6) in the atezolizumab + bevacizumab arm versus 4.3 months (95% CI: 4.0, 5.6) in the sorafenib arm with a HR of 0.65 (95% CI: 0.53, 0.81). The IRF-assessed ORR per RECIST v1.1 was 29.8% (95% CI: 24.8, 35.0) in the atezolizumab + bevacizumab arm and 11.3% (95% CI: 6.9, 17.3) in the sorafenib arm. The median duration of response (DOR) by IRF-assessment per RECIST v1.1 in confirmed responders was 18.1 months (95% CI: 14.6, NE) in the atezolizumab + bevacizumab arm compared to 14.9 months (95% CI: 4.9, 17.0) in the sorafenib arm. For more information, please refer to the Summary of Product Characteristics.
II/0033	Extension of indication to include the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumours express PD-L1 for Tecentriq based on the results of the pivotal study GO29431 (IMpower110), comparing atezolizumab monotherapy to platinum-based	25/03/2021	30/04/2021	SmPC and PL	See Assessment Report for Tecentriq II-33

	chemotherapy. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. The RMP version 12.0 has also been submitted. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
II/0057/G	This was an application for a group of variations. 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 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.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.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 forms manufactured by complex manufacturing	22/04/2021	n/a		

	processes				
II/0054	Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add severe cutaneous adverse reactions (SCARs) to the list of adverse drug reactions (ADRs) with frequency uncommon, based on the review of safety data presented in a drug safety report (DSR 1105724); the Package Leaflet is updated accordingly. A direct health care professional communication (DHPC) is also proposed to communicate on this risk. In addition, the MAH took the opportunity to add the term pemphigoid to the description of rash in Section 4.8 of the SmPC. The MAH also took the opportunity to update minor typographical errors in the SmPC and PL. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/02/2021	31/03/2021	SmPC and PL	Severe cutaneous adverse reactions (SCARs) including cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) occurred in 0.7% (24/3,568) of patients who received atezolizumab monotherapy. The median time to onset was 5.9 months (range: 0.1 to 15.5 months). The median duration was 1.6 months (range: 0 to 22.1+ months; + denotes a censored value). SCARs led to discontinuation of atezolizumab in 3 (<0.1%) patients. SCARs requiring the use of systemic corticosteroids occurred in 0.2% (7/3,568) of patients receiving atezolizumab monotherapy. Patients should therefore be monitored for suspected severe skin reactions and other causes should be excluded. For suspected SCARs, patients should be referred to a specialist for further diagnosis and management. Based on the severity of the adverse reaction, atezolizumab should be withheld for Grade 3 skin reactions and treatment with systemic corticosteroids at a dose of 1-2 mg/kg/day of prednisone or equivalent should be started. Treatment with atezolizumab may be resumed if the event improves to ≤ Grade 1 within 12 weeks, and corticosteroids have been reduced to ≤ 10 mg prednisone or equivalent per day. Treatment with atezolizumab should be permanently discontinued for Grade 4 skin reactions, and corticosteroids should be administered. Atezolizumab should be withheld for patients with suspected SJS or TEN. For confirmed SJS or TEN, atezolizumab should be permanently discontinued. Caution should be used when considering the use of atezolizumab in a patient who has previously experienced a

					severe or life-threatening skin adverse reaction on prior treatment with other immune-stimulatory anticancer agents. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10644 /202005	Periodic Safety Update EU Single assessment - atezolizumab	28/01/2021	26/03/2021	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10644/202005.
II/0030	Update of section 4.8 of the SmPC to reflect the outcome of anti-drug antibody (ADA) analyses conducted across studies POPLAR, OAK, IMpower 150, IMpower 130, IMPower 131, IMpower 132, IMvigor 211, IMmotion 151, IMpower 133 and IMpassion 130, further to the CHMP recommendation. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	18/03/2021	30/04/2021	SmPC	Across multiple phase II and III studies, 13.1% to 54.1% of patients developed treatment-emergent anti-drug antibodies (ADAs). Patients who developed treatment-emergent ADAs tended to have overall poorer health and disease characteristics at baseline. Those imbalances in health and disease characteristics at baseline can confound the interpretation of pharmacokinetic (PK), efficacy and safety analyses. Exploratory analyses adjusting for imbalances in baseline health and disease characteristics were conducted to assess the effect of ADA on efficacy. These analyses did not exclude possible attenuation of efficacy benefit in patients who developed ADA compared to patients who did not develop ADA. The median time to ADA onset ranged from 3 weeks to 5 weeks.
IB/0056	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/02/2021	31/03/2021	SmPC	
II/0053	Submission of the final report from study GO29322 listed as a category 3 study in the RMP. This is a Phase Ib study investigating the safety and pharmacology of atezolizumab administered with ipilimumab, interferon-alpha, or other	11/02/2021	n/a		

	immunomodulating therapies in patients with locally advanced or metastatic solid tumours. The RMP version 19.1 has also been submitted to remove this category 3 study along with the related safety concern of concomitant use with other immuno-modulatory drugs. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				
II/0051	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	14/01/2021	26/03/2021	Annex II	
II/0048	Submission of the results of study WO41486 evaluating the effectiveness of the HCP brochure designed to mitigate important immune-related risks in patients receiving atezolizumab in the European Union. As a consequence, the MAH is updating section 4.4 of the SmPC, Annex II.D and the RMP. In addition, the MAH is proposing a delay in the due date for the submission of the CSR for IMvigor210 to 31 August 2021. 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	14/01/2021	26/03/2021	SmPC and Annex II	Following the assessment of a cat 3 PASS investigating the effectiveness of the educational materials for both Heath care professional and patients, it was agreed that the health care professional brochure for Tecentriq was no longer needed and could be removed from the conditions of the marketing authorisation.

	where significant assessment is required				
II/0037	Submission of a review of the effect of atezolizumab neutralising antibodies on the pharmacokinetics and efficacy endpoints including OS, PFS and ORR from the NSCLC studies POPLAR, OAK, IMpower 150, IMpower 130, IMPower 131 and IMpower 132 as well as on studies IMvigor 211 (UC), IMmotion 151 (RCC), IMpower 133 (SCLC) and IMpassion 130 (TNBC), as recommended by the CHMP. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/01/2021	n/a		An integrated overview of available data on the potential impact of atezolizumab neutralising antibodies (NAbs) on the pharmacokinetics and efficacy endpoints including OS, PFS and ORR was submitted. Given the exploratory nature of the analyses, a firm conclusion regarding a potential effect of anti-drug antibody and NAbs on PFS and OS is difficult to establish based on the current evidence.
IB/0055	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	06/01/2021	n/a		
II/0050	Update of section 5.1 of the SmPC in order to reflect efficacy results based on the final OS analysis from study WO29522 (IMpassion130) comparing atezolizumab in combination with nab-paclitaxel with placebo with nab-paclitaxel for patients with previously untreated metastatic triple-negative breast cancer. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	10/12/2020	26/03/2021	SmPC	The final OS analysis from study WO29522 (IMpassion130), a phase III randomised trial comparing atezolizumab in combination with nab-paclitaxel (atezo+nP) with placebo with nab-paclitaxel (pl+nP) for patients with previously untreated metastatic triple-negative breast cancer, was submitted. In patients with PD-L1 expression ≥ 1%, the median follow up was 19.12 months. The median OS was 25.4 months in patients treated with atezo+nP compared to 17.9 months in patients treated with pl+nP, HR (95% CI) of 0.67 (0.53, 0.86). Patients with PD-L1 expression <1% did not show improved OS when atezolizumab was added to nab-paclitaxel (HR of 1.02, 95% CI 0.84, 1.24). Exploratory subgroup analyses were performed in patients

					with PD-L1 expression ≥ 1%, exploring prior (neo)adjuvant treatment, BRCA1/2 mutation and asymptomatic brain metastases at baseline. In patients who had received prior (neo) adjuvant treatment (n=242), the hazard ratio for final OS was 0.77 while in patients who had not received prior (neo)adjuvant treatment (n=127), the hazard ratio was 0.54.
II/0039	Extension of Indication to include, in combination with with bevacizumab, the treatment of patients with unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy, based on the results of the pivotal study YO40245 (IMbrave150) as well as data from Arms A and F of the supportive Phase Ib study GO30140. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the Tecentriq 1200mg concentrate for solution for infusion SmPC are updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1 C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	17/09/2020	27/10/2020	SmPC and PL	Please refer to Scientific Discussion Tecentriq EMEA/H/C/004143/II/0039.
II/0047	Update of section 4.8 of the SmPC in order to add headache, dry skin and blood creatinine increased to the list of adverse drug reactions (ADRs) for atezolizumab given as monotherapy identified in study WO29636. The MAH has taken this opportunity to update the frequencies of existing ADRs in section	03/09/2020	27/10/2020	SmPC and PL	Headache, dry skin and blood creatinine increased have been identified as ADRs in study WO29636 (IMvigor 010). The frequency calculated on the basis of the pooled monotherapy data is very common (≥ 1/10) for headache and common (≥ 1/100 to < 1/10) for dry skin and blood creatinine increased. The frequencies of ADRs in subsection

	4.8 subsections 'Summary of the safety profile' and 'Description of selected adverse reactions' to reflect the updated pool of patients for atezolizumab monotherapy. Other minor corrections and editorial changes are being proposed. 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				"description of selected adverse reactions" have been revised to reflect the updated pool of patients for atezolizumab monotherapy.
PSUSA/10644 /201911	Periodic Safety Update EU Single assessment - atezolizumab	25/06/2020	19/08/2020	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10644/201911.
II/0036	Submission of the final report from study GO28915 (OAK) listed as a category 3 study in the RMP. This is a Phase III, open-label multicentre, randomized study to investigate the efficacy and safety of atezolizumab (anti−PD-L1 antibody) compared with docetaxel in patients with NSCLC after failure with platinum-containing chemotherapy. In addition, section 4.8 of the SmPC is updated to reflect available information regarding the potential relationship of ADA and safety based on an integrated analyses of studies IMvigor210, IMvigor211, OAK, POPLAR, IMpower150, IMpower130, IMpower131, IMpower132, IMpower133 and IMpassion130. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission	23/07/2020	27/10/2020	SmPC	Across pooled datasets of patients treated with atezolizumab monotherapy (N=2705) and with combination therapies (N=1811), the following rates of adverse events (AEs) have been observed for the ADA-positive population compared to the ADA-negative population, respectively: Grade 3-4 AEs 49.1% vs. 44.3%, Serious Adverse Events (SAEs) 42.4% vs. 37.6%, AEs leading to treatment withdrawal 6.1% vs 6.7% (for monotherapy); Grade 3-4 AEs 65.3% vs. 63.6%, SAEs 42.1% vs. 36.6%, AEs leading to treatment withdrawal 24.3% vs 19.5% (for combination therapy). However, available data do not allow firm conclusions to be drawn on possible patterns of adverse drug reactions. For more information, please refer to the Summary of Product Characteristics.

	of studies to the competent authority				
IAIN/0046	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/06/2020	19/08/2020	SmPC and PL	
IA/0045/G	This was an application for a group of variations. B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and 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.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	22/05/2020	n/a		
IB/0043	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	21/04/2020	n/a		
II/0040	Update of section 4.8 of the SmPC to include the adverse drug reactions (ADRs) hyperthyroidism with a "common" frequency and hypertension with a "very common" frequency for atezolizumab used in combination with chemotherapy, as identified in study IMvigor130. The MAH took the opportunity of this variation to add preferred terms (PTs) to the footnotes to the ADR table in section 4.8 of the	17/04/2020	19/08/2020	SmPC and PL	

	SmPC. The package leaflet is proposed to be updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IAIN/0044	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	10/04/2020	n/a		
IB/0041	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	24/03/2020	n/a		
II/0035	Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to reflect the results of study GO29664 (iMATRIX) evaluating the safety and pharmacokinetics of Tecentriq in paediatric (<18, n=69) and young adult patients (18-30 years, n=18) with relapsed or progressive solid tumours as well as with Hodgkin's and non-Hodgkin's lymphoma. This study was agreed under the Paediatric Investigational Plan EMEA-001638-PIP01-14-M02 (EMA decision: P/0207/2019). 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	13/02/2020	19/08/2020	SmPC and PL	In study GO29664 (iMATRIX), the clearance and volume of distribution of atezolizumab were comparable between paediatric patients receiving 15 mg/kg and young adult patients receiving 1,200 mg of atezolizumab every 3 weeks when normalized by body weight. Data for children <2 years is limited thus no definitive conclusions can be made. The safety of atezolizumab in children and adolescents has not been established. For more information please refer to the Summary of Product Characteristics.

II/0034	Update of section 5.1 of the SmPC in order to include updated overall survival data from study IMvigor 211 (GO29294), a phase III study to investigate the efficacy and safety of atezolizumab compared with chemotherapy in patients with locally advanced or metastatic urothelial bladder cancer after failure of platinum-containing chemotherapy. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/02/2020	19/08/2020	SmPC	An exploratory updated survival analysis was performed with a median duration of survival follow up of 34 months in the ITT population of study IMvigor 211 (GO29294). The median OS was 8.6 months (95% CI: 7.8, 9.6) in the atezolizumab arm and 8.0 months (95% CI: 7.2, 8.6) in the chemotherapy arm with a hazard ratio of 0.82 (95% CI: 0.71, 0.94). Consistent with the trend observed at primary analysis for 12-month OS rates, numerically higher 24-month and 30-month OS rates were observed for patients in the atezolizumab arm compared with the chemotherapy arm in the ITT population.
IB/0031	B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation	10/02/2020	19/08/2020	SmPC and PL	
II/0032	Update of section 4.8 of the SmPC in order to include blood alkaline phosphatase increased and blood creatinine increased as common and alopecia as very common adverse drug reactions for atezolizumab given in combination with other medicinal products based on the review of safety data from a pooled population. In addition, the instruction for treatment interruption due to neutropenia and peripheral neuropathies, when atezolizumab is used in combination with nab-paclitaxel in metastatic triple negative breast cancer, is being revised to only recommend interruption of nab-paclitaxel in section 4.4 of the SmPC. The MAH also took the opportunity of this variation to introduce minor editorial comments. The Package Leaflet is updated accordingly.	16/01/2020	19/08/2020	SmPC and PL	

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/10644 /201905	Periodic Safety Update EU Single assessment - atezolizumab	28/11/2019	n/a		PRAC Recommendation - maintenance
II/0019	Extension of Indication to include Tecentriq, in combination with nab-paclitaxel and carboplatin, indicated for the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC) who do not have EGFR mutant or ALK-positive NSCLC; as a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. RMP version 9.1 has been accepted. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	25/07/2019	03/09/2019	SmPC and PL	Please refer to the Scientific Discussion Tecentriq-H-C-4143-II-19.
II/0018	Extension of Indication to include, in combination with carboplatin and etoposide, first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC) for tecentriq; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 9.1 has been agreed. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or	25/07/2019	03/09/2019	SmPC and PL	Please refer to the Scientific Discussion Tecentriq-H-C-4143-II-0018.

	modification of an approved one				
II/0022	Update of sections 4.2 and 5.2 of the SmPC in order to add 2 dosing regimens, 840 mg every 2 weeks and 1680 mg every 4 weeks administered as an IV infusion for the approved indications, based on results of population pharmacokinetics modelling and simulation analyses (report No. 1085557) and supported by exposure-response analyses (report No. 1087176). Consequential changes are made to sections 4.1, 4.2 and 5.1 of the 840 mg strength SmPC in line with the existing urothelial cancer and lung cancer indications. The package leaflet is updated accordingly. An updated RMP (version 7.1) is also agreed in order to reflect the proposed new dosing regimens, and to align the indication statement for metastatic urothelial carcinoma with the SmPC. Moreover, the due date for submission of RMP commitments and an Annex II condition are updated. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	27/06/2019	26/08/2019	SmPC, Annex II and PL	Overall, modelling and simulation based analyses have demonstrated that exposure, safety and efficacy of the proposed two dosing regimens 840 mg q2w and 1680 mg q4w is comparable to the approved fixed dose regimen of 1200 mg q3w.
PSUSA/10644 /201811	Periodic Safety Update EU Single assessment - atezolizumab	27/06/2019	26/08/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10644/201811.
X/0017	Annex I_2.(c) Change or addition of a new strength/potency	27/06/2019	26/08/2019	SmPC, Labelling and PL	Please refer to the Scientific Discussion Tecentriq-H-C-4143-X-17.

II/0028	Update of section 4.8 of the SmPC with new ADRs identified in IMpower132 study. This change is supported by safety data as presented in a drug safety report referring to the IMpower132 safety report (report 1089805) previously submitted to the Agency. 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	11/07/2019	03/09/2019	SmPC and PL	he analysis of safety data from IMpower132 comparing atezolizumab + cisplatin to carboplatin + pemetrexed (n=291) identified vomiting, asthenia (very common), lymphocyte count decreased, ALT increased, and AST increased (common) as new ADRs for atezolizumab administered in combination with chemotherapy. The frequency of hypomagnesaemia has been updated from very common to common and stomatitis has been updated from common to very common.
II/0024	Update of sections 4.2, 4.4, and 4.8 of the SmPC regarding the risk of immune-related myositis identified during a comprehensive analysis of patients treated with Tecentriq. The additional risk minimisations in Annex 2D, the Package Leaflet and the RMP (final version v11.1) are updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	29/05/2019	08/07/2019	SmPC, Annex II and PL	Cases of myositis, including fatal cases, have been observed in clinical trials with Tecentriq. Patients should be monitored for signs and symptoms of myositis. Treatment with atezolizumab should be withheld for Grade 2 or 3 myositis and corticosteroid therapy (1-2 mg/kg/day prednisone or equivalent) should be initiated. If symptoms improve to ≤Grade 1, taper corticosteroids as clinically indicated. Treatment with Tecentriq may be resumed if the event improves to ≤Grade 1 within 12 weeks, and corticosteroids have been reduced to ≤10 mg oral prednisone or equivalent per day. Treatment with Tecentriq should be permanently discontinued for Grade 4 or grade 3 recurrent myositis, or when unable to reduce the corticosteroid dose to the equivalent of ≤10 mg prednisone per day within 12 weeks after onset.
IB/0027/G	This was an application for a group of variations. B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits	27/05/2019	n/a		

	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation				
IB/0026	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)	25/05/2019	08/07/2019	SmPC and PL	
IB/0025/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.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	21/05/2019	n/a		
II/0023	Update of section 4.8 of the SmPC in order to include new ADRs identified in IMmotion150 and IMmotion151 studies. The revision of the list of ADRs is supported by a drug safety report reflecting the ADRs in the updated pool of patients for monotherapy (n=3178) and combination therapy (n=1345). The Package Leaflet is updated accordingly.	02/05/2019	08/07/2019	SmPC and PL	The following new ADRs have been included in the monotherapy pool: hyperglycaemia (common), nasopharyngitis (common), oropharyngeal pain (common); and in the combination pool: dysphonia (common), proteinuria (very common), headache (very common).

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
II/0007/G	This was an application for a group of variations. Extension of indication to include in combination with bevacizumab, paclitaxel and carboplatin the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC), based on the interim results of study GO29436 (IMpower 150). As a consequence sections 4.1, 4.2, 4.4, 4.8, 5.1, 6.2 and 6.6 of the SmPC are updated. In addition update of section 4.8 of the SmPC in order to update the monotherapy safety data and reflect the largest pooled monotherapy population available (now including also data from IMvigor211 and PCD4989g studies). The Package Leaflet and the RMP (version 4.2) are updated in accordance. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to make small corrections and formatting changes throughout the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	31/01/2019	05/03/2019	SmPC and PL	Please refer to Scientific Discussion Tecentriq-H-C-4143-II-0007-G.

PSUSA/10644 /201805	Periodic Safety Update EU Single assessment - atezolizumab	13/12/2018	25/02/2019	SmPC, Labelling and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10644/201805.
IB/0020	B.I.e.4.b - Changes to an approved change management protocol - Minor changes that do not change the strategy defined in the protocol	18/12/2018	n/a		
N/0015	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/08/2018	25/02/2019	PL	
IA/0011/G	This was an application for a group of variations. 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.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits 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.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and 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.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of	13/07/2018	n/a		

	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				
II/0010	Update of sections 4.1, 4.2 and 5.1 of the SmPC in order to restrict the 'treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC) who are considered cipsplatin ineligible' indication by including 'and whose tumours have a PDL-1 expression ≥ 5%', based on the review of interim analysis data by the independent data monitoring committee (IDMC) from study IMvigor 130 (WO30070) listed as a PAES in the Annex II; this is a Phase III, multicentre, randomized, placebo-controlled study of atezolizumab administered as monotherapy or in combination with platinum-based chemotherapy compared with platinum-based chemotherapy in patients with untreated locally advanced or metastatic urothelial carcinoma enrolling patients in the first line setting who are both cisplatin eligible and cisplatin ineligible. The Package Leaflet is updated accordingly. A DHPC was considered necessary to communicate on the restricted indication. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	31/05/2018	02/07/2018	SmPC	Please refer to Scientific Discussion 'Tecentriq-H-C-4143-II-0010'

PSUSA/10644 /201711	Periodic Safety Update EU Single assessment - atezolizumab	14/06/2018	n/a		PRAC Recommendation - maintenance
II/0004	Update of section 4.8 of the SmPC in order to update the safety information based on the primary results from study IMvigor211 in order to fulfil ANX 002. This is a phase III, open-label, multicentre, randomized study to investigate the efficacy and safety of atezolizumab (anti- PD-L1 antibody) compared with chemotherapy in patients with locally advanced or metastatic urothelial bladder cancer after failure with platinum-containing chemotherapy. The annex II.D, the Package Leaflet and the RMP (version 3.2, according to GVP module V revision 2) are updated accordingly. Some editorial changes throughout the Product Information are also made. In addition the MAH took the opportunity of including the ATC code in section 5.1 of the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/06/2018	25/02/2019	SmPC, Annex II and PL	Following the submission of the primary clinical study report for study GO29294 (IMvigor 211), a phase III, open label, multi-centre, international, randomised study, to evaluate the efficacy and safety of atezolizumab compared with chemotherapy (investigator's choice of vinflunine, docetaxel, or paclitaxel) in patients with locally advanced or metastatic UC who progressed during or following a platinum containing regimen, the safety information in section 4.8 of the SmPC was updated. In the summary of safety profile and description of selected adverse events, figures from the top line results of study GO29294 initially available at time of the initial Marketing Authorisation were updated to reflect the updated pooled data. 'Cough', 'urinary tract infections' and 'back pain' were added as new adverse drug reactions and the frequency of the adverse drug reactions 'amylase increased and 'hepatitis' were also updated respectively to uncommon and common. In the description of selected adverse reactions, the figures have also been updated accordingly.
IB/0009	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	09/04/2018	n/a		
IB/0008	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	05/04/2018	n/a		

II/0002/G	This was an application for a group of variations. Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add myocarditis as a new adverse reaction, based on the results of a cumulative review of cases of suspected myocarditis provided in the drug safety report number 1080476. Consequently, the information regarding posology and special warnings have been updated. The Annex II and the Package Leaflet have been updated accordingly. The RMP version 2.1 has also been updated. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data 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	22/02/2018	04/04/2018	SmPC, Annex II and PL	Myocarditis occurred in < 0.1% (2/8,000) of patients across all atezolizumab clinical trials in multiple tumour types. The time to onset was 18 and 33 days. Both patients required corticosteroids and discontinued atezolizumab. Patients should be monitored for signs and symptoms of myocarditis. In addition treatment with atezolizumab should be withheld for Grade 2 myocarditis, and treatment with systemic corticosteroids at a dose of 1 to 2mg/kg/day of prednisone or equivalent should be started. Treatment with atezolizumab may be resumed if the event improves to ≤ Grade 1 within 12 weeks, and corticosteroids have been reduced to ≤ 10 mg prednisone or equivalent per day Treatment with atezolizumab must be permanently discontinued for Grade 3 or 4 myocarditis. In addition myocarditis has been added as a new adverse drug reaction under the SOC 'Cardiac disorders' with a rare frequency and 'immune-related myocarditis' has also been included in the guide for healthcare professionals and patient alert card in annex II.D and as a new important identified risk in the RMP.
T/0006	Transfer of Marketing Authorisation	20/02/2018	07/03/2018	SmPC, Labelling and PL	
II/0001	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	14/12/2017	n/a		
IB/0003/G	This was an application for a group of variations. B.I.d.1.a.4 - Stability of AS - Change in the re-test	10/11/2017	07/03/2018	SmPC, Labelling and PL	

	period/storage period - Extension or introduction of a re-test period/storage period supported by real time data B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol				