# Yescarta

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 |
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| WS/2771 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>Submission of an updated RMP version 5.1 for Tecartus and version 11.2 for Yescarta following the PRAC recommendation for the Secondary malignancy of T-cell origin signal (EPITT no: 20040), and of a | 18/09/2025 | 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).

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| | PASS protocol for a framework for the sampling and testing of secondary malignancies of T-cell origin.<br><br>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 | | | | |
| PSUSA/10703 /202410 | Periodic Safety Update EU Single assessment - axicabtagene ciloleucel | 22/05/2025 | 17/07/2025 | SmPC and PL | Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10703/202410. |
| II/0085 | C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority | 22/05/2025 | n/a | | |
| WS/2821/G | This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>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<br>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 | 27/03/2025 | n/a | | |

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| WS/2736 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>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 | 27/02/2025 | n/a | | |
| WS/2813/G | This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>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<br>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 | 16/01/2025 | n/a | | |
| IB/0082/G | This was an application for a group of variations.<br><br>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS<br>B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation<br>B.II.b.3.a - Change in the manufacturing process of | 14/01/2025 | n/a | | |

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| | the finished or intermediate product - Minor change in the manufacturing process | | | | |
| II/0077 | B.II.g.2 - Introduction of a post approval change management protocol related to the finished product | 12/12/2024 | n/a | | |
| WS/2500 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>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 | 12/12/2024 | n/a | | |
| II/0075/G | This was an application for a group of variations.<br><br>Grouped application comprising two type II variations as follows:<br>C.I.13 - Submission of the final report from study KTE-C19-101 (ZUMA-1) listed as a category 3 study in the RMP. This is a Phase 1/2 Multicenter Study Evaluating The Safety And Efficacy Of Kte-C19 In Subjects With Refractory Aggressive Non-Hodgkin Lymphoma.<br>C.I.13 - Submission of the final report from study KTE-C19-106 (ZUMA-6) listed as a category 3 study in the RMP. This is a Phase 1-2 Multi-Center Study Evaluating The Safety And Efficacy Of Kte-C19 In Combination With Atezolizumab In Subjects With | 17/10/2024 | n/a | | The presented end-of-study efficacy results are consistent with results presented in prior reports currently described in the SmPC. No new safety aspects were identified, and the safety profile of Yescarta remains unchanged.<br>For more information, please refer to the Summary of Product Characteristics. |

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| | Refractory Diffuse Large B-Cell Lymphoma (Dlbcl). The RMP version 11.0 has also been submitted.<br><br>C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority<br>C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority | | | | |
| WS/2689 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>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 | 19/09/2024 | n/a | | |
| IG/1781 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 14/08/2024 | 14/11/2024 | SmPC, Annex II and PL | |
| WS/2613 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) | 04/07/2024 | n/a | | |

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| IB/0079 | B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product | 02/07/2024 | n/a | | |
| PSUSA/10703 /202310 | Periodic Safety Update EU Single assessment - axicabtagene ciloleucel | 16/05/2024 | n/a | | PRAC Recommendation - maintenance |
| WS/2632 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>Update of section 4.2 of the SmPC in order to update the safety monitoring timelines based on data from clinical studies, postmarketing studies, and literature. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes to other sections of the SmPC to align the language across both products.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | 25/04/2024 | 14/11/2024 | SmPC and PL | Based on accumulated data for Tecartus and Yescarta, the SmPCs for both products are updated to indicate that the daily monitoring for signs and symptoms of potential CRS, neurologic events, and other toxicities can be reduced from 10 to 7 days following CAR T cell infusion.<br><br>For more information, please refer to the Summary of Product Characteristics. |
| WS/2607 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>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 | 25/04/2024 | n/a | | |

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| | method or a method using a biological reagent for a biological AS | | | | |
| WS/2646 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>B.II.z - Quality change - Finished product - Other variation | 04/04/2024 | n/a | | |
| IB/0069 | B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product | 26/02/2024 | n/a | | |
| IAIN/0071 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 22/02/2024 | 14/11/2024 | SmPC and PL | |
| II/0065 | Update of section 4.8 of the SmPC in order to add Infusion Related Reactions to the list of adverse drug reactions (ADRs) with frequency Common, based on a cumulative review of the MAH safety database, clinical trials and postmarketing data. The Package Leaflet is updated accordingly.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | 14/12/2023 | 14/11/2024 | SmPC and PL | Not applicable<br>For more information, please refer to the Summary of Product Characteristics. |
| II/0063 | Update of section 5.1 of the SmPC in order to include new clinical data based on Overall Survival (OS) Primary Analysis from study KTE-C19-107 (ZUMA-7); this is a phase 3, randomized, open-label study | 09/11/2023 | 14/11/2024 | SmPC | SmPC new text<br>The median study duration was 24.9 months at the time of the primary EFS analysis and 47.2 months at the time of the primary OS analysis. The primary analysis of OS was |

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| | evaluating the efficacy of axicabtagene ciloleucel versus standard of care therapy in subjects with relapsed/refractory diffuse large B cell lymphoma (DLBCL) in the 2nd line setting. In addition, the MAH took the opportunity to include the date of the latest renewal in section 9 and to submit a consolidated Environmental Risk Assessment (ERA) document.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | | | | performed at the protocol-specified timepoint of 5 years from the first subject enrolled. A statistically significant improvement in OS in favour of Yescarta was demonstrated. The estimated 48-month OS rates were 54.6% in the Yescarta arm and 46.0% in the SOCT arm. Fifty-seven percent of patients received cellular immunotherapy after no response to or relapse after randomisation to SOCT. The OS HR for Yescarta versus SOCT was 0.735 [95% CI: 0.338, 1.600] for patients with HGBL per central laboratory.<br>For more information, please refer to the Summary of Product Characteristics. |
| IB/0066 | B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process | 03/11/2023 | n/a | | |
| WS/2558/G | This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation<br>B.I.b.1.i - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Where there is no monograph in the European/National Ph. for the AS, a change in specification from in-house to a non-official/third country Ph. | 05/10/2023 | n/a | | |

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| IB/0062 | B.I.b.z - Change in control of the AS - Other variation | 28/09/2023 | n/a | | |
| R/0056 | Renewal of the marketing authorisation. | 25/05/2023 | 24/07/2023 | 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 Yescarta in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity, the final solution of the supplementary information in response to Day 90 RfSI provided. |
| WS/2389/G | This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>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<br>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 | 25/05/2023 | n/a | | |
| II/0057 | B.II.g.2 - Introduction of a post approval change management protocol related to the finished product | 25/05/2023 | n/a | | |
| PSUSA/10703 /202210 | Periodic Safety Update EU Single assessment - axicabtagene ciloleucel | 12/05/2023 | n/a | | PRAC Recommendation - maintenance |

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| WS/2426 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>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 | 30/03/2023 | n/a | | |
| N/0058 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 17/01/2023 | 24/07/2023 | Labelling | |
| PSUSA/10703 /202204 | Periodic Safety Update EU Single assessment - axicabtagene ciloleucel | 01/12/2022 | n/a | | PRAC Recommendation - maintenance |
| II/0046 | Extension of indication to include treatment of adult patients with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) for Yescarta; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the product information with minor editorial changes.<br><br>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one | 15/09/2022 | 14/10/2022 | SmPC, Labelling and PL | Please refer to Scientific Discussion 'Yescarta-II-46' |

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| IB/0055 | B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation | 10/10/2022 | n/a | | |
| WS/2247 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>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 | 15/09/2022 | n/a | | |
| PSUSA/10703 /202110 | Periodic Safety Update EU Single assessment - axicabtagene ciloleucel | 23/06/2022 | 17/08/2022 | SmPC and PL | Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10703/202110. |
| IB/0054 | B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation | 09/08/2022 | n/a | | |
| IB/0053 | B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS | 08/08/2022 | n/a | | |
| WS/2269 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>B.II.b.3.z - Change in the manufacturing process of | 23/06/2022 | n/a | | |

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| | the finished or intermediate product - Other variation | | | | |
| II/0042 | Extension of indication to include the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after three or more lines of systemic therapy. Consequently, sections 4.1, 4.8, 5.1 and 5.2 of the SmPC and Package Leaflet are proposed to be updated. As a consequence, the RMP (version 7.0) has been updated to align with the indication extension.<br>In addition, the applicant has taken the opportunity to make minor editorial corrections throughout the SmPC and package leaflet.<br><br>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one | 22/04/2022 | 21/06/2022 | SmPC, Annex II, Labelling and PL | Please refer to Scientific Discussion 'Yescarta-H-C-004480/II/0042" |
| WS/2194 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) | 22/04/2022 | n/a | | |
| WS/2197 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the | 24/02/2022 | n/a | | |

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| | manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol | | | | |
| II/0040 | C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority | 24/02/2022 | n/a | | |
| WS/2181 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) | 27/01/2022 | n/a | | |
| PSUSA/10703 /202104 | Periodic Safety Update EU Single assessment - axicabtagene ciloleucel | 02/12/2021 | n/a | | PRAC Recommendation - maintenance |
| IB/0043/G | This was an application for a group of variations.<br><br>A.7 - Administrative change - Deletion of manufacturing sites<br>B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation | 16/11/2021 | n/a | | |
| WS/2071 | This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.<br><br>B.I.b.2.d - Change in test procedure for AS or | 16/09/2021 | n/a | | |

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| | 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 | | | | |
| PSUSA/10703 /202010 | Periodic Safety Update EU Single assessment - axicabtagene ciloleucel | 10/06/2021 | n/a | | PRAC Recommendation - maintenance |
| IB/0038 | 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 | 30/04/2021 | n/a | | |
| IB/0036 | B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation | 23/04/2021 | n/a | | |
| II/0035 | 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 | 22/04/2021 | n/a | | |
| II/0028 | Update of section 4.8 of the SmPC on cytokine release syndrome (CRS) and neurologic adverse reaction grading and management and update of section 5.1 of the SmPC to include data from 36-month and 48-month analyses from ZUMA-1 study Cohorts 1 and 2. The Package leaflet is updated accordingly. In addition, other minor updates are included in the product information. | 22/04/2021 | | SmPC, Labelling and PL | For more information, please refer to the Summary of Product Characteristics. |

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| | The RMP (version 3.5) has been updated accordingly.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | | | | |
| IB/0037 | 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 | 31/03/2021 | n/a | | |
| II/0031 | 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 | 25/03/2021 | n/a | | |
| II/0030 | 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 | 25/03/2021 | n/a | | |
| II/0033 | B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation | 28/01/2021 | n/a | | |
| IA/0032 | B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits | 02/12/2020 | n/a | | |

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| PSUSA/10703 /202004 | Periodic Safety Update EU Single assessment - axicabtagene ciloleucel | 26/11/2020 | n/a | | PRAC Recommendation - maintenance |
| IB/0029 | B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation | 29/10/2020 | n/a | | |
| IA/0027 | 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 | 07/08/2020 | n/a | | |
| IA/0025 | B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS | 15/07/2020 | n/a | | |
| IA/0024 | 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 | 07/07/2020 | n/a | | |
| II/0015 | Changes to the manufacturing process of the biological active substance, axicabtagene ciloleucel, to extend the storage time for which the apheresis starting material used to isolate the PBMC Intermediate can be held. The apheresis material shipping temperature range can be extended from, between 2 and 10°C for a maximum time of 48 hours, to between 2°C and 16°C with a maximum shipping duration 72 hours.<br>The requested variation proposed no amendments to | 25/06/2020 | n/a | | |

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| | the Product Information.<br><br>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 | | | | |
| IAIN/0023 | A.1 - Administrative change - Change in the name and/or address of the MAH | 22/06/2020 | 25/11/2020 | SmPC, Labelling and PL | |
| IB/0020 | B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product | 11/06/2020 | 25/11/2020 | Annex II | |
| II/0021 | Update of the SmPC, Annex II, package leaflet and RMP to change the dose of tocilizumab to one dose instead of four doses in order to manage the Cytokine Release Syndrome. In addition, treatment centres should have access to an additional dose within 8 hours of each previous dose. Additional changes to the SmPC have been made with regards to the wording on GMO requirements.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | 28/05/2020 | 25/11/2020 | SmPC, Labelling and PL | Update of the SmPC, Annex II, package leaflet and RMP to change the dose of tocilizumab to one dose instead of four doses in order to manage the Cytokine Release Syndrome. In addition, treatment centres should have access to an additional dose within 8 hours of each previous dose. Additional changes to the SmPC have been made with regards to the wording on GMO requirements. |
| PSUSA/10703 /201910 | Periodic Safety Update EU Single assessment - axicabtagene ciloleucel | 14/05/2020 | n/a | | PRAC Recommendation - maintenance |

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| IA/0022 | A.7 - Administrative change - Deletion of manufacturing sites | 11/05/2020 | 25/11/2020 | Annex II and PL | |
| II/0019 | 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 | 26/03/2020 | n/a | | |
| II/0018 | 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 | 26/03/2020 | n/a | | |
| IB/0016 | B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation | 29/01/2020 | n/a | | |
| PSUSA/10703 /201904 | Periodic Safety Update EU Single assessment - axicabtagene ciloleucel | 14/11/2019 | 13/01/2020 | SmPC and Labelling | Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10703/201904. |
| IB/0013 | B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product | 10/12/2019 | 25/11/2020 | SmPC, Annex II, Labelling and PL | |
| II/0011 | B.II.e.1.b.2 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Sterile medicinal products and biological/immunological medicinal products | 17/10/2019 | n/a | | |
| II/0012 | B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial | 19/09/2019 | n/a | | |

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| | change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS | | | | |
| II/0008 | 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 | 19/09/2019 | n/a | | |
| II/0007 | 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 | 25/07/2019 | n/a | | |
| II/0006 | B.II.g.2 - Introduction of a post approval change management protocol related to the finished product | 27/06/2019 | n/a | | |
| IB/0009 | C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation | 13/06/2019 | n/a | | |
| PSUSA/10703 /201810 | Periodic Safety Update EU Single assessment - axicabtagene ciloleucel | 16/05/2019 | n/a | | PRAC Recommendation - maintenance |
| II/0003 | C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | 26/04/2019 | 21/10/2019 | SmPC, Annex II, Labelling and PL | In the 24-month follow-up analysis of study ZUMA-1 and based on the mITT population (results from an independent review committee), the Objective Response Rate and the Complete Response rate were 74% and 54%, respectively. The median time to response was 1.0 months (range: 0.8 to 12.2 months). The Duration of Response was longer in |

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| | | | | | patients who achieved Complete Response compared to patients with a best response of Partial Response. Of the 55 patients who achieved CR, 7 patients had SD and 10 had PR at their initial tumour assessment and converted to CR as late as 12 months after YESCARTA infusion. Median duration of response and median overall survival have not been reached.<br>Due to the on-target, off-tumour effect of YESCARTA, a period of B-cell aplasia is expected following treatment. Among 73 patients with evaluable samples at baseline, 40% had detectable B cells; the B cell aplasia observed in the majority of patients at baseline was attributed to prior therapies. Following YESCARTA treatment, the proportion of patients with detectable B cells decreased: 20% had detectable B cells at Month 3, and 22% had detectable B cells at Month 6. The initiation of B cell recovery was first noted at Month 9, when 56% of patients had detectable B-cells. This trend of B- cell recovery continued over time, as 64% of patients had detectable B- cells at Month 18, and 77% of patients had detectable B- cells at Month 24. It is important to note that patients were not required to be followed after they progressed; thus, the majority of patients with evaluable samples were responders.<br>For more information please refer to the Summary of Product Characteristics. |
| IB/0002 | C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation | 14/01/2019 | 21/10/2019 | Annex II | |
| IB/0004 | B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation | 09/01/2019 | n/a | | |

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| IAIN/0001 | 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 | 19/10/2018 | 21/10/2019 | Annex II and PL | |