# Alecensa

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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| II/0048 | To update sections 4.4 and 4.6 of the SmPC to update the safety information to amend the duration of the period for which female patients of child-bearing potential must use highly effective contraceptive methods following the last dose of Alecensa, and must be informed of potential harm to | 17/10/2024 | | SmPC and PL | SmPC new text:<br>Sections 4.4 and 4.6 of the SmPC were revised in order to reduce the duration to use highly effective contraceptive methods in female patients of child bearing-potential following the last dose of Alecensa from 3 months to 5 weeks and also to include a new recommendation regarding |

[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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| | the fetus in the event of pregnancy, from 3 months to 5 weeks and to also include a new recommendation for males with female partners of childbearing potential to use highly effective contraception during treatment and for at least 3 months after the last dose, based on the latest guidelines on contraception requirements for drugs with aneugenic potential. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | | | | contraception in male patients whereby male patients with female partners of child-bearing potential must use highly effective contraceptive methods during treatment and for at least 3 months following the last dose of Alecensa (see section 4.4).<br>Finally a new warning that male patients with female partners who become pregnant while the male patient is taking Alecensa, or during the 3 months following the last dose of Alecensa, must contact their doctor, and their female partner should seek medical advice due to the potential harm to the foetus based on its aneugenic potential was included in section 4.6 of the SmPC. |
| II/0047 | Extension of indication to include the use of Alecensa as monotherapy in adult patients with anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC) as adjuvant treatment following tumour resection, based on final results from study BO40336 (ALINA), a randomized, active controlled, multicenter, open-label, Phase III study designed to evaluate the efficacy and safety of alectinib compared with platinum-based chemotherapy in the adjuvant setting in patients with completely resected Stage IB (tumours 4 cm) to Stage IIIA ALKpositive NSCLC. 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. Version 4.2 of the RMP has also been agreed. In addition, the Marketing authorisation holder (MAH) took the opportunity to | 25/04/2024 | 06/06/2024 | SmPC, Annex II, Labelling and PL | Please refer to Scientific Discussion: Alecensa-H-C-4164-II-Var.No 0047. |

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| | update the list of local representatives in the Package Leaflet and to introduce editorial changes to the PI. As part of the application, the MAH is requesting a 1-year extension of the market protection.<br>Furthermore, the CHMP reviewed the data submitted by the marketing authorisation holder, taking into account the provisions of Article 14(11) of Regulation (EC) No 726/2004 and considers by consensus that the new therapeutic indication brings significant clinical benefit in comparison with existing therapies, as set out in Annex IV.<br><br>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one | | | | |
| N/0046 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 15/03/2023 | 06/06/2024 | PL | |
| IA/0045/G | This was an application for a group of variations.<br><br>A.7 - Administrative change - Deletion of manufacturing sites<br>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 | 01/03/2023 | n/a | | |
| PSUSA/10581 /202207 | Periodic Safety Update EU Single assessment - alectinib | 09/02/2023 | n/a | | PRAC Recommendation - maintenance |

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| II/0044 | Submission of an updated RMP version 3.3 in order to remove the important identified risks of Interstitial Lung Disease (ILD)/Pneumonitis, Hepatotoxicity, Photosensitivity, Bradycardia, Severe myalgia and Creatine Phosphokinase (CPK) elevations as well as the important potential risk of Embryo-fetal toxicity as safety concerns. Furthermore, template updates in line with the GVP Product or Population-Specific Considerations III: Pregnant and breastfeeding women are made.<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 | 12/01/2023 | n/a | | Not applicable. |
| II/0042 | Submission of the final report from study JO28928 (J-ALEX) a Randomized Phase III Open-Label Study Comparing the Efficacy and Safety of Crizotinib and CH5424802 in ALK-Positive Advanced or Recurrent Non-Small Cell Lung Cancer.<br><br>C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority | 27/10/2022 | n/a | | Not applicable. |
| II/0041 | B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant | 13/10/2022 | n/a | | |

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| | impact on the quality, safety or efficacy of the medicinal product | | | | |
| II/0037/G | This was an application for a group of variations.<br><br>Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add a new warning, dose modification advice and description of the known ADR haemolytic anaemia based on an updated Drug Safety Report; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce editorial updates in the English, Maltese, Romanian, French, Swedish and Italian product information. Moreover, the ATC code for alectinib is being updated from L01XE36 to L01ED03.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data<br>A.6 - Administrative change - Change in ATC Code/ATC Vet Code | 23/06/2022 | 02/08/2022 | SmPC and PL | SmPC new text:<br>Cases of haemolytic anaemia have been reported in the post-marketing period, with severity of anaemia ranging from Grade 1 to Grade 3. No Grade 4 or Grade 5 (fatal) cases of haemolytic anaemia were observed in the clinical trials or in the post-marketing setting.<br>If haemoglobin concentration is below 10 g/dL and haemolytic anaemia is suspected, Alecensa should be withheld and appropriate laboratory testing should be initiated. If haemolytic anaemia is confirmed, Alecensa should be resumed at a reduced dose upon resolution.<br>For more information, please refer to the Summary of Product Characteristics. |
| R/0039 | Renewal of the marketing authorisation. | 19/05/2022 | 15/07/2022 | SmPC, Annex II, Labelling and PL | Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Alecensa in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.<br>Pursuant to Article 23(3) of Regulation No (EU) 726/2004, Alecensa (alectinib) is removed from the additional monitoring list as a new active substance following five years of authorisation.<br>Therefore, the statement that this medicinal product is |

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| | | | | | subject to additional monitoring and that this will allow quick identification of new safety information, preceded by an inverted equilateral black triangle, is removed from the summary of product characteristics and the package leaflet. |
| IB/0040/G | This was an application for a group of variations.<br><br>B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)<br>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 | 15/06/2022 | 02/08/2022 | SmPC | |
| PSUSA/10581 /202107 | Periodic Safety Update EU Single assessment - alectinib | 10/02/2022 | n/a | | PRAC Recommendation - maintenance |
| IA/0038/G | This was an application for a group of variations.<br><br>A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)<br>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place | 20/01/2022 | n/a | | |
| II/0034 | C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance | 02/09/2021 | 15/07/2022 | SmPC, Annex II, Labelling | Haemolytic anaemia was added to the list of ADRs in section 4.8 of the SmPC with frequency uncommon. |

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| | data | | | and PL | For more information, please refer to the Summary of Product Characteristics. |
| II/0033 | Submission of an updated RMP version 3.1 in order to remove the safety concern of missing information - long term safety, based on a report of the cumulative safety data from the pivotal Phase III clinical trial ALEX (BO28984). The MAH has also taken the opportunity to update the RMP to remove study BO40643 from the pharmacovigilance plan, following assessment in procedure EMEA/H/C/004164/II/0030. In addition changes to section 4.8 of the SmPC and section 4 of the leaflet were made in order to update frequency and grades of adverse reactions taking into account the new safety data from ALEX study (BO28984).<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 | 02/09/2021 | 15/07/2022 | SmPC and PL | |
| IA/0035 | B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process | 03/05/2021 | n/a | | |
| IA/0032 | B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place | 15/02/2021 | n/a | | |

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| II/0030 | Submission of the final report from study (BO40643) listed as an additional pharmacovigilance activity in the RMP. This is a non-interventional post authorisation safety study (PASS) aimed at evaluating the effectiveness of the risk minimization measures (RMMs) for the important identified risks of ILD/pneumonitis, hepatotoxicity, bradycardia, photosensitivity, severe myalgia, and CPK elevations for Alecensa.<br><br>C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority | 11/02/2021 | n/a | | Following the assessment of a cat 3 PASS investigating the effectiveness of the risk minimization measures for the important identified risks of ILD/pneumonitis, hepatotoxicity, bradycardia, photosensitivity, severe myalgia, and CPK elevations, it was agreed that the routine risk minimisation measures as outlined in the approved SmPC of Alecensa are adequate for clinical practice. |
| PSUSA/10581 /202007 | Periodic Safety Update EU Single assessment - alectinib | 11/02/2021 | n/a | | PRAC Recommendation - maintenance |
| IA/0031/G | This was an application for a group of variations.<br><br>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place<br>A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) | 03/12/2020 | n/a | | |
| IA/0029/G | This was an application for a group of variations. | 17/11/2020 | n/a | | |

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| | B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process<br>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 | | | | |
| IB/0027/G | This was an application for a group of variations.<br><br>B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer<br>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place<br>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place<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.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size<br>B.I.a.4.b - Change to in-process tests or limits | 24/06/2020 | n/a | | |

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| | applied during the manufacture of the AS - Addition of a new in-process test and limits<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.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS<br>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS<br>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS<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 | | | | |
| IA/0026/G | This was an application for a group of variations.<br><br>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where | 11/05/2020 | n/a | | |

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| | batch control/testing takes place<br>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place | | | | |
| PSUSA/10581 /201907 | Periodic Safety Update EU Single assessment - alectinib | 30/01/2020 | 03/04/2020 | SmPC and PL | Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10581/201907. |
| IB/0024/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.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation<br>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure<br>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS<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 | 25/09/2019 | n/a | | |

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| | 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 | | | | |
| PSUSA/10581 /201901 | Periodic Safety Update EU Single assessment - alectinib | 11/07/2019 | n/a | | PRAC Recommendation - maintenance |
| IB/0023/G | This was an application for a group of variations.<br><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.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation<br>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<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<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 | 05/06/2019 | n/a | | |

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| PSUSA/10581 /201807 | Periodic Safety Update EU Single assessment - alectinib | 17/01/2019 | n/a | | PRAC Recommendation - maintenance |
| IB/0021/G | This was an application for a group of variations.<br><br>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place<br>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place<br>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place<br>B.I.a.1.i - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new site of micronisation<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.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation<br>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 | 14/12/2018 | n/a | | |

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| | B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation<br>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)<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.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation<br>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS<br>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS<br>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS<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 | | | | |

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| | or addition) for the AS or a starting material/intermediate<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<br>B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation | | | | |
| IB/0020/G | This was an application for a group of variations.<br><br>A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)<br>B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products<br>B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place<br>B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place<br>B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process | 04/12/2018 | n/a | | |

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| | 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<br>B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation<br>A.7 - Administrative change - Deletion of manufacturing sites | | | | |
| IB/0018/G | This was an application for a group of variations.<br><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.I.a.1.i - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new site of micronisation<br>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place<br>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place<br>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place | 11/10/2018 | n/a | | |

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| | 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.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation<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.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure<br>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS<br>B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS<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<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 | | | | |

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| | B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition<br>B.I.c.3.b - Change in test procedure for the immediate packaging of the AS - Other changes to a test procedure (including replacement or addition) | | | | |
| II/0016 | C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority | 13/09/2018 | n/a | | |
| N/0017 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 09/08/2018 | 03/04/2020 | PL | |
| PSUSA/10581 /201801 | Periodic Safety Update EU Single assessment - alectinib | 12/07/2018 | n/a | | PRAC Recommendation - maintenance |
| II/0010 | Update of sections 4.2 and 5.2 of the SmPC in order to update information on the effect of hepatic impairment on the pharmacokinetics of alectinib based on final results from study NP29783. The Package Leaflet is updated accordingly. The RMP has also been updated to version 3.0. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest EC guidance regarding warning statements on sodium.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | 26/04/2018 | 31/05/2018 | SmPC and PL | No starting dose adjustment is required in patients with underlying mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment. Patients with underlying severe hepatic impairment (Child-Pugh C) should receive a starting dose of 450 mg taken twice daily with food (total dose of 900 mg).<br>For all patients with hepatic impairment, appropriate monitoring (e.g. markers of liver function) is advised.<br>For more information, please refer to the Summary of Product Characteristics. |
| IB/0015/G | This was an application for a group of variations. | 17/04/2018 | n/a | | |

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| | B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site<br>B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site<br>B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place<br>B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products | | | | |
| T/0013 | Transfer of Marketing Authorisation | 20/02/2018 | 15/03/2018 | SmPC, Labelling and PL | |
| IG/0887 | A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) | 29/01/2018 | n/a | | |
| PSUSA/10581 /201707 | Periodic Safety Update EU Single assessment - alectinib | 11/01/2018 | n/a | | PRAC Recommendation - maintenance |
| IB/0011/G | This was an application for a group of variations.<br><br>B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process<br>B.II.b.4.a - Change in the batch size (including batch | 04/01/2018 | n/a | | |

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| | size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size<br>B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation | | | | |
| II/0001 | Extension of Indication for Alecensa (alectinib) to first line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) including final data report of study BO28984 object of the SOB in the annex II; as a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC and Annex II are updated. The Package Leaflet and the RMP are updated in accordance.<br>In addition, the CHMP, having considered the application as set out in the appended assessment report and on the basis of the evidence of compliance with the specific obligations submitted by the marketing authorisation holder, is of the opinion that the risk-benefit balance of the above mentioned medicinal product remains favourable. As all specific obligations laid down in Annex II have been fulfilled, pursuant to Article 7 of Regulation (EC) No 507/2006, the CHMP recommends by consensus the granting of a Marketing Authorisation in accordance with Article 14(1) of Regulation (EC) No 726/2004 for the above mentioned medicinal product.<br><br>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one | 12/10/2017 | 18/12/2017 | SmPC, Annex II and PL | Please refer to the Scientific Discussion Alecensa H-4164-II-01. |

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| R/0007 | Renewal of the marketing authorisation. | 12/10/2017 | 01/12/2017 | | The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations through variation II/01 and having confirmed the positive benefit risk-balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated.<br>Furthermore, in the framework of the variation II/01, the CHMP concludes that the remaining specific obligation for the Conditional Marketing Authorisation is fulfilled and recommends granting a Marketing Authorisation no longer subject to specific obligations. |
| IB/0008/G | This was an application for a group of variations.<br><br>B.II.e.1.b.1 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Solid, semi-solid and non-sterile liquid pharmaceutical forms<br>B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product | 25/09/2017 | 01/12/2017 | SmPC, Labelling and PL | |
| N/0006 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 27/06/2017 | 01/12/2017 | PL | |
| IB/0005 | B.I.b.1.h - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition or replacement (excl. Biol. or immunol. substance) of a specification parameter as a result of a safety or quality issue | 21/06/2017 | n/a | | |

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| II/0003 | Update of section 4.8 of the SmPC in order to add "Increased blood alkaline phosphatase" as new Adverse Drug Reaction with a common frequency identified during routine signal detection. The package leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some formatting changes in the Product Information.<br><br>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | 09/06/2017 | 01/12/2017 | SmPC and PL | |
| IA/0004/G | This was an application for a group of variations.<br><br>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<br>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<br>A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)<br>A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites | 04/05/2017 | n/a | | |

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| | (excluding manufacturer for batch release) | | | | |
| IB/0002 | B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data) | 18/04/2017 | 01/12/2017 | SmPC | |