



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Afstyla

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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| N/0057 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 17/12/2024 | | PL | |
| IB/0058 | B.I.b.1.i - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Where there is no | 13/12/2024 | 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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| | monograph in the European/National Ph. for the AS, a change in specification from in-house to a non-official/third country Ph. | | | | |
| II/0055 | B.II.g.2 - Introduction of a post approval change management protocol related to the finished product | 11/07/2024 | n/a | | |
| PSUSA/10559 /202401 | Periodic Safety Update EU Single assessment - lonoctocog alfa | 11/07/2024 | n/a | | PRAC Recommendation - maintenance |
| IB/0056 | 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 | 13/06/2024 | n/a | | |
| IB/0053 | 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 | 02/04/2024 | n/a | | |
| IA/0052/G | <p>This was an application for a group of variations.</p> <p>B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits</p> <p>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits</p> <p>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting</p> | 15/03/2024 | n/a | | |

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| | <p>material/intermediate/reagent - Tightening of specification limits</p> <p>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</p> <p>B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits</p> | | | | |
| WS/2503/G | <p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.d.1.h - Change in the specification parameters and/or limits of the finished product - Update of the dossier to comply with the provisions of an updated general monograph of the Ph. Eur. for the finished product</p> <p>B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation</p> | 09/11/2023 | n/a | | |
| II/0050 | B.I.d.1.a.3 - Stability of AS - Change in the re-test period/storage period - Extension of storage period of a biological/immunological AS not in accordance with an approved stability protocol | 21/09/2023 | n/a | | |
| PSUSA/10559 /202301 | Periodic Safety Update EU Single assessment - lonoctocog alfa | 31/08/2023 | n/a | | PRAC Recommendation - maintenance |

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| IA/0049/G | <p>This was an application for a group of variations.</p> <p>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits</p> <p>B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure</p> | 26/04/2023 | n/a | | |
| II/0046/G | <p>This was an application for a group of variations.</p> <p>B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS</p> <p>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)</p> <p>B.I.a.4.d - Change to in-process tests or limits applied during the manufacture of the AS - Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the AS</p> | 16/03/2023 | n/a | | |
| IA/0047 | B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure | 08/03/2023 | n/a | | |
| IAIN/0045/G | <p>This was an application for a group of variations.</p> <p>B.IV.1.a.1 - Change of a measuring or administration</p> | 26/10/2022 | n/a | | |

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| | <p>device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking</p> <p>B.IV.1.b - Change of a measuring or administration device - Deletion of a device</p> | | | | |
| PSUSA/10559 /202201 | Periodic Safety Update EU Single assessment - lonoctocog alfa | 01/09/2022 | n/a | | PRAC Recommendation - maintenance |
| II/0042 | <p>Update of section 5.1 of the SmPC in order to update efficacy and safety information based on final results from study 3001 listed as a category 3 study in the RMP; this is an open label, multicenter extension study to assess the Safety and Efficacy of Afstyla in subjects with severe Hemophilia A. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. The RMP version 6.0 has also been submitted.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p> | 10/06/2022 | 29/06/2023 | SmPC, Labelling and PL | <p>Submission of study results of Study 3001 which aimed at investigating the safety and efficacy of Afstyla in previously treated (PTPs) and previously untreated patients (PUPs) with severe haemophilia A.</p> <p>For more information, please refer to the Summary of Product Characteristics.</p> |
| IB/0044/G | <p>This was an application for a group of variations.</p> <p>B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation</p> <p>B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process</p> <p>B.I.a.4.b - Change to in-process tests or limits</p> | 03/06/2022 | n/a | | |

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| | <p>applied during the manufacture of the AS - Addition of a new in-process test and limits</p> <p>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS</p> <p>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS</p> | | | | |
| PSUSA/10559 /202107 | Periodic Safety Update EU Single assessment - lonoctocog alfa | 10/02/2022 | n/a | | PRAC Recommendation - maintenance |
| IB/0041/G | <p>This was an application for a group of variations.</p> <p>B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation</p> <p>B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure</p> | 04/02/2022 | n/a | | |
| IB/0039 | 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 | 09/09/2021 | n/a | | |
| PSUSA/10559 /202101 | Periodic Safety Update EU Single assessment - lonoctocog alfa | 02/09/2021 | n/a | | PRAC Recommendation - maintenance |
| R/0037 | Renewal of the marketing authorisation. | 24/06/2021 | 20/08/2021 | SmPC, Annex II, Labelling | Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of |

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| | | | | and PL | Afstyla in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity. |
| PSUSA/10559 /202007 | Periodic Safety Update EU Single assessment - lonoctocog alfa | 11/02/2021 | n/a | | PRAC Recommendation - maintenance |
| IA/0036 | B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier | 01/12/2020 | n/a | | |
| PSUSA/10559 /202001 | Periodic Safety Update EU Single assessment - lonoctocog alfa | 03/09/2020 | n/a | | PRAC Recommendation - maintenance |
| II/0033 | 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 | 18/06/2020 | n/a | | |
| IA/0034 | B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure | 29/05/2020 | n/a | | |
| II/0029/G | This was an application for a group of variations. B.I.b.1.e - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP B.I.b.1.g - Change in the specification parameters and/or limits of an AS, starting | 14/05/2020 | n/a | | |

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| | 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 B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits | | | | |
| IB/0031 | B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS | 13/03/2020 | n/a | | |
| II/0030 | 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 | 12/03/2020 | n/a | | |
| PSUSA/10559/201907 | Periodic Safety Update EU Single assessment - lonoctocog alfa | 16/01/2020 | n/a | | PRAC Recommendation - maintenance |
| IB/0027 | B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS | 25/11/2019 | n/a | | |
| IG/1160/G | This was an application for a group of variations. B.II.e.5.b - Change in pack size of the finished product - Deletion of a pack size(s) B.II.e.5.b - Change in pack size of the finished | 24/10/2019 | 03/04/2020 | SmPC, Labelling and PL | |

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| | product - Deletion of a pack size(s) | | | | |
| IB/0025/G | <p>This was an application for a group of variations.</p> <p>B.I.z - Quality change - Active substance - Other variation</p> <p>B.II.z - Quality change - Finished product - Other variation</p> | 19/09/2019 | n/a | | |
| II/0023/G | <p>This was an application for a group of variations.</p> <p>B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation</p> <p>B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS</p> <p>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</p> <p>B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range</p> <p>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)</p> | 12/09/2019 | n/a | | |
| PSUSA/10559 /201901 | Periodic Safety Update EU Single assessment - lonoctocog alfa | 11/07/2019 | n/a | | PRAC Recommendation - maintenance |

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| IB/0021/G | <p>This was an application for a group of variations.</p> <p>B.II.e.6.a - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that affects the product information</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> <p>B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes</p> | 29/06/2019 | 03/04/2020 | SmPC, Labelling and PL | |
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| IA/0022/G | <p>This was an application for a group of variations.</p> <p>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</p> <p>A.7 - Administrative change - Deletion of manufacturing sites</p> <p>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier</p> <p>B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation</p> | 29/05/2019 | n/a | | |
| IB/0018 | B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure | 22/05/2019 | n/a | | |
| IB/0017 | C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation | 12/05/2019 | 03/04/2020 | SmPC, Labelling and PL | |
| IAIN/0020 | B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking | 04/04/2019 | n/a | | |
| IB/0016 | C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation | 30/01/2019 | n/a | | |

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| PSUSA/10559 /201807 | Periodic Safety Update EU Single assessment - lonoctocog alfa | 17/01/2019 | n/a | | PRAC Recommendation - maintenance |
| IB/0014 | B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation | 10/01/2019 | n/a | | |
| IA/0015 | B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits | 18/12/2018 | n/a | | |
| N/0013 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 28/11/2018 | 25/02/2019 | PL | |
| PSUSA/10559 /201801 | Periodic Safety Update EU Single assessment - lonoctocog alfa | 12/07/2018 | n/a | | PRAC Recommendation - maintenance |
| IA/0011 | B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter | 31/05/2018 | n/a | | |
| IB/0008 | B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product | 01/03/2018 | n/a | | |
| II/0007 | C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data | 22/02/2018 | 25/02/2019 | SmPC, Labelling and PL | |
| PSUSA/10559 /201707 | Periodic Safety Update EU Single assessment - lonoctocog alfa | 11/01/2018 | n/a | | PRAC Recommendation - maintenance |

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| IB/0009 | B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process | 05/01/2018 | n/a | | |
| II/0001 | B.I.e.2 - Introduction of a post approval change management protocol related to the AS | 12/10/2017 | n/a | | |
| IB/0006 | B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation | 11/10/2017 | n/a | | |
| IB/0003 | B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation | 13/07/2017 | n/a | | |
| IA/0004/G | This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process | 29/05/2017 | n/a | | |
| N/0002 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 21/04/2017 | 25/02/2019 | PL | |