Fasturtec

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification[1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
IA/0070	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	13/05/2024		Annex II	

[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).

II/0069	B.II.b.3.b - Change in the manufacturing process of the finished or intermediate product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product	22/02/2024	n/a		
IB/0068/G	This was an application for a group of variations. B.I.z - Quality change - Active substance - Other variation B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	30/10/2023	n/a		
PSUSA/2613/ 202302	Periodic Safety Update EU Single assessment - rasburicase	28/09/2023	n/a		PRAC Recommendation - maintenance
N/0067	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/06/2023	07/12/2023	Labelling and PL	
II/0064/G	This was an application for a group of variations. B.II.e.4.c - Change in shape or dimensions of the container or closure (immediate packaging) - Sterile medicinal products B.II.b.3.b - Change in the manufacturing process of the finished or intermediate product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product	08/12/2022	07/12/2023	SmPC and PL	

T/0065	Transfer of Marketing Authorisation	28/10/2022	18/11/2022	SmPC, Labelling and PL	
II/0063/G	This was an application for a group of variations. B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised 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 B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	28/04/2022	n/a		
IB/0061	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	19/11/2021	n/a		
N/0062	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/11/2021	18/11/2022	PL	
IAIN/0060	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer	20/11/2020	15/11/2021	Annex II and PL	

	responsible for batch release				
WS/1829	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	12/11/2020	15/11/2021	SmPC, Annex II and PL	
PSUSA/2613/ 202002	Periodic Safety Update EU Single assessment - rasburicase	01/10/2020	n/a		PRAC Recommendation - maintenance
N/0057	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/02/2020	15/11/2021	PL	
IB/0056	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	29/01/2020	n/a		
IB/0055/G	This was an application for a group of variations. 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 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	25/10/2019	n/a		
N/0054	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/11/2017	15/11/2021	Labelling and PL	

PSUSA/2613/201702	Periodic Safety Update EU Single assessment - rasburicase	28/09/2017	n/a		PRAC Recommendation - maintenance
IAIN/0052/G	This was an application for a group of variations. A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	17/01/2017	24/05/2017	Annex II and PL	
IA/0051	B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information	07/10/2016	n/a		
II/0049	Update of sections 4.4 and 4.8 of the SmPC concerning cases of anaphylaxis and/or anaphylactic shock with potential fatal outcome reported in the post-marketing setting. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives for Italy and Latvia in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	07/07/2016	24/05/2017	SmPC and PL	N/A

IB/0050	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	14/06/2016	n/a		
N/0048	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	14/07/2015	22/02/2016	PL	
IB/0047/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.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure 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 specification limits B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State B.I.b.z - Change in control of the AS - Other	28/05/2015	n/a		

	variation				
IB/0046/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.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.z - Quality change - Active substance - Other variation	05/05/2015	n/a		
II/0044	Update of section 4.8 of the SmPC to list all ADRs in a single table and to reflect the results of the re-categorisation of the frequency for nausea, vomiting, headache, fever and diarrhea to “very common” following a PRAC request in conclusion of PSUV/0041). 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	26/03/2015	22/02/2016	SmPC and PL	The Tabulated list of adverse reactions in section 4.8 of the SmPC has been updated to include all adverse reactions and to reflect that nausea, vomiting, headache, fever and diarrhea have been re-clasified to a frequency of "very common".
IAIN/0045	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	19/02/2015	22/02/2016	Annex II and PL	
IB/0043/G	This was an application for a group of variations. B.I.b.2.e - Change in test procedure for AS or	02/01/2015	n/a		

	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.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
PSUV/0041	Periodic Safety Update	23/10/2014	16/12/2014	SmPC and PL	Please refer to Fasturtec PSUV 0041 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
IG/0454	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	17/07/2014	n/a		
N/0040	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/04/2014	27/10/2014	PL	
IAIN/0039	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	15/11/2013	27/10/2014	SmPC and PL	
IG/0313	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	24/06/2013	n/a		
IA/0037	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	05/06/2013	n/a		
IAIN/0036	A.5.a - Administrative change - Change in the name and/or address of a manufacturer responsible for	07/11/2012	20/11/2013	Annex II and PL	

	batch release				
II/0034	Update of section 4.1 and 5.1 of the SmPC in order to clarify the age range of paediatric patients following CHMP request made further to the assessment of a study submitted in accordance with Article 46 of Regulation (EC) No1901/2006 (P46-042). The Package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. C.I.3.z - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Other variation	20/09/2012	25/10/2012	SmPC and PL	Please refer to EPAR – Assessment Report Fasturtec-H-C-331-II-0034.
II/0035	Change to the manufacture of the finished product B.II.b.3.c - Change in the manufacturing process of the finished product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability	20/09/2012	n/a		
T/0033	Transfer of Marketing Authorisation	25/04/2012	25/05/2012	SmPC, Labelling and PL	
IAIN/0032	A.1 - Administrative change - Change in the name and/or address of the MAH	23/03/2012	25/05/2012	SmPC, Labelling and PL	

II/0031	Update of SmPC section 5.2 based on pharmacokinetic data obtained from healthy adult subjects as well as adult patients. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	16/02/2012	19/03/2012	SmPC	The pharmacokinetics of rasburicase were evaluated in both paediatric and adult patients with leukemia, lymphoma or other haematological malignancies. Clearance of rasburicase was ca. 3.5 ml/h/kg. The mean terminal half-life was similar between paediatric and adult patients and ranged from 15.7 to 22.5 hours. In adults (≥ the age of 18 years), age, gender, baseline liver enzymes and creatinine clearance did not impact the pharmacokinetics of rasburicase. A cross-study comparison revealed that after administration of rasburicase at 0.15 or 0.20 mg/kg, the geometric mean values of body-weight normalized clearance were approximately 40% lower in Japanese (n=20) than that in Caucasians (n=26).
II/0030	Update of SmPC sections 4.4 and 5.1 based on the results of a Phase 3 study in adult patients with hyperuricemia or at high risk for tumour lysis syndrome (EFC4978). The MAH also took the opportunity to introduce changes to the PI in line with QRD template version 8, revision 1 as well as an update of the List of local Representatives. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	16/02/2012	19/03/2012	SmPC, Annex II, Labelling and PL	In a randomized (1:1:1), multi-center, open-label study, 275 adult patients with leukemia and lymphoma at risk for hyperuricemia and tumour lysis syndrome (TLS) were treated with either rasburicase at a dose of 0.2 mg/kg/day, intravenously, for 5 days (arm A: n=92), rasburicase at a dose of 0.2 mg/kg/day, intravenously, from day 1 through day 3 followed by oral allopurinol at a dose of 300 mg once a day from day 3 through day 5 (overlap on day 3: rasburicase and allopurinol administered approximately 12 hours apart) (arm B: n=92), or oral allopurinol at a dose of 300 mg once a day for 5 days (arm C: n=91). The uric acid response rate (proportion of patients with plasma uric acid levels ≤7.5 mg/dl from day 3 to day 7 after initiation of antihyperuricemic treatment) was 87% in arm A, 78% in arm B, and 66% in arm C. The response rate in arm A was significantly greater than in arm C (p=0.0009); the response rate was higher for arm B compared to arm C although this difference was not statistically significant. Uric

					acid levels were <2 mg/dl in 96% of patients in the two arms containing rasburicase and 5% of patients in the allopurinol arm at 4 hours of the day 1 dose. The safety results of patients treated with Fasturtec in Study EFC4978 were consistent with the adverse events profile observed in previous clinical studies with predominantly paediatric patients.
N/0029	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/04/2009	n/a	Labelling and PL	
II/0028	Update of SPC section 4.8 and PL section 4 with the adverse event "urticaria" as requested by the CHMP following the assessment of the PSUR 9-13. Update of Summary of Product Characteristics, Labelling and Package Leaflet	22/01/2009	26/02/2009	SmPC, Labelling and PL	With the assessment of the PSUR the CHMP noted that since all the safety information listed in the CCSI should be included in the SPC, the adverse event "urticaria" should be added to the sentence "common allergic reactions, mainly rash and urticaria". Consequently, the PL section 4 has also been amended.
II/0027	Additional manufacturing and EU batch release site for the drug product with consequential changes to the manufacturing process and control of the drug product. Additional vial supplier for the drug product. Change(s) to the manufacturing process for the finished product	18/12/2008	26/01/2009	Annex II and PL	
II/0024	Change(s) to the manufacturing process for the active substance	24/01/2008	28/02/2008	Annex II	
N/0026	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/02/2008	n/a	PL	

II/0022	Change(s) to the manufacturing process for the finished product	18/10/2007	24/10/2007		
II/0023	Update of section 4.9 "Overdose" of the SPC in order to reflect the fact that cases of overdose have been reported with rasburicase. Update of Summary of Product Characteristics	20/09/2007	19/10/2007	SmPC	To update further the source for the change proposed, the sentence "No case of overdose has been reported" has been deleted from section 4.9 of the SPC.
II/0021	Update of Summary of Product Characteristics and Package Leaflet	21/06/2007	10/08/2007	SmPC and PL	The MAH has applied to modify sections 4.2 and 5.1 with additional paediatric data available. This variation was requested by the CHMP in June 2006 following assessments of the data submitted by the MAH in March 2006.
IA/0020	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	01/03/2007	n/a	Annex II and PL	
II/0019	Update of Summary of Product Characteristics	27/07/2006	01/09/2006	SmPC	The MAH has applied to update section 4.6 of the SPC in order to update non-clinical information.
II/0018	Update of Summary of Product Characteristics and Package Leaflet	28/06/2006	07/08/2006	SmPC and PL	The MAH has applied to update section 4.2 of the SPC to modify treatment duration. In addition, the MAH also takes this opportunity to include modifications in sections 3 and 6 of the Package Leaflet to update the list of Local Representatives and to update one sentence in the section "information intended for healthcare professionals" in order to bring it in line with section 6.6 of the SPC.
II/0017	Change(s) to the manufacturing process for the active substance	27/04/2006	05/05/2006		

II/0016	Update of Summary of Product Characteristics and Package Leaflet	23/03/2006	27/04/2006	SmPC and PL	The MAH has applied to update section 4.8 of the SPC and section 4 of the Package Leaflet, accordingly. This variation application is submitted following the assessment of 7th and 8th PSURs. The MAH has also taken the opportunity to update the list of local representatives in the Package Leaflet.
R/0015	Renewal of the marketing authorisation.	14/12/2005	09/02/2006	SmPC, Annex II, Labelling and PL	
II/0012	Change(s) to the manufacturing process for the active substance	27/07/2005	08/08/2005		
II/0011	Change(s) to the test method(s) and/or specifications for the active substance	27/07/2005	08/08/2005		
IA/0014	IA_05_Change in the name and/or address of a manufacturer of the finished product	03/08/2005	n/a		
N/0013	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/07/2005	n/a	PL	
IA/0010	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	29/03/2005	n/a	Annex II	
IA/0009	IA_01_Change in the name and/or address of the marketing authorisation holder	10/12/2004	n/a	SmPC, Labelling and PL	
IA/0008	IA_05_Change in the name and/or address of a manufacturer of the finished product	10/12/2004	n/a	Annex II and PL	

IB/0007	IB_37_a_Change in the specification of the finished product - tightening of specification limits	11/11/2004	n/a		
N/0006	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	31/08/2004	n/a	PL	
IB/0005	IB_37_a_Change in the specification of the finished product - tightening of specification limits	24/06/2004	n/a		
I/0004	17_Change in specification of the medicinal product	10/10/2003	16/10/2003		
II/0002	Update of Summary of Product Characteristics and Package Leaflet	19/03/2003	30/06/2003	SmPC and PL	
I/0003	20_Extension of shelf-life as foreseen at time of authorisation	18/04/2003	04/06/2003	SmPC	
II/0001	New presentation(s)	17/01/2002	18/04/2002	SmPC, Labelling and PL	