Jyseleca

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
IAIN/0036	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	23/10/2024		Annex II and PL	

[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).

T/0035	Transfer of Marketing Authorisation	02/08/2024	22/08/2024	SmPC, Labelling and PL	
IB/0034/G	This was an application for a group of variations. B.II.e.1.z - Change in immediate packaging of the finished product - Other variation B.II.e.1.z - Change in immediate packaging of the finished product - Other variation B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products 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 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	05/07/2024	22/08/2024	SmPC	
II/0031/G	This was an application for a group of variations. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data A.6 - Administrative change - Change in ATC Code/ATC Vet Code	11/04/2024	22/08/2024	SmPC	
PSUSA/10879 /202309	Periodic Safety Update EU Single assessment - filgotinib	11/04/2024	n/a		PRAC Recommendation - maintenance

IB/0030/G	This was an application for a group of variations. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation 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	01/03/2024	n/a		
IA/0032	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	30/01/2024	n/a		
IB/0029	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	05/01/2024	n/a		
PSUSA/10879 /202303	Periodic Safety Update EU Single assessment - filgotinib	09/11/2023	05/01/2024		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10879/202303.
IA/0027/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor	04/07/2023	n/a		

	changes to an approved test procedure 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				
IAIN/0025	B.II.a.1.a - Change or addition of imprints, bossing or other markings including replacement, or addition of inks used for product marking - Changes in imprints, bossing or other markings	29/05/2023	05/01/2024	SmPC and PL	
IB/0024/G	This was an application for a group of variations. B.I.z - Quality change - Active substance - Other variation B.II.z - Quality change - Finished product - Other variation	19/04/2023	n/a		
PSUSA/10879 /202209	Periodic Safety Update EU Single assessment - filgotinib	14/04/2023	n/a		PRAC Recommendation - maintenance
A20/0014	Pursuant to Article 20 of Regulation (EC) No 726/2004, the European Commission requested on 28 January 2022 the opinion of the European Medicines Agency further to the safety issues on MACE, VTE, serious infections, malignancy and mortality for all JAK inhibitors used in the treatment of inflammatory disorders. The CHMP was requested to assess the impact thereof on the benefit-risk balance of Cibinqo, Jyseleca, Olumiant, Rinvoq and Xeljanz and to give its recommendation whether the	23/01/2023	10/03/2023	SmPC, Annex II and PL	Please refer to the assessment report: Jyseleca (filgotinib) EMEA/H-A20/1517/C/005113/0014

	marketing authorisation of this product should be maintained, varied, suspended or revoked. As the request results from the evaluation of data resulting from pharmacovigilance activities, the CHMP opinion was adopted on the basis of a recommendation of the Pharmacovigilance Risk Assessment Committee.				
IA/0023/G	This was an application for a group of variations. 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) 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) 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 A.7 - Administrative change - Deletion of manufacturing sites B.II.c.2.b - Change in test procedure for an excipient - Deletion of a test procedure if an alternative test procedure is already authorised 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	13/02/2023	n/a		

	the AS -replacement or addition of a site where batch control/testing takes place				
PSUSA/10879 /202203	Periodic Safety Update EU Single assessment - filgotinib	27/10/2022	n/a		PRAC Recommendation - maintenance
IAIN/0021	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	12/10/2022	n/a		
IB/0020	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	05/10/2022	n/a		
II/0018	Update of sections 4.4 and 4.6 of the SmPC in order to update information on fertility based on interim results from studies GLPG0634-CL-227 (MANTA Ray) and GS-US-418-4279 (MANTA) listed as a category 3 study in the RMP. Additionally, minor editorial changes have been proposed. The Package Leaflet and Annex II are updated accordingly. The RMP version 4.1 has also been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	29/09/2022	10/03/2023	SmPC, Annex II and PL	In animal studies, decreased fertility, impaired spermatogenesis, and histopathological effects on male reproductive organs were observed (see section 5.3). The data from two dedicated Phase 2 clinical studies (MANTA and MANTA RAay, n=240) to evaluate the human testicular safety in men with inflammatory arthritis diseases and inflammatory bowel diseases did not reveal a difference between treatment groups in the proportion of patients who had a 50% or more decrease from baseline in semen parameters at week 13 (pooled primary endpoint: filgotinib 6.7%, placebo 8.3%) and at week 26. Further, the data did not show any relevant changes in sex hormone levels or change from baseline in semen parameters across treatment groups. Overall, these clinical data were not suggestive of filgotinib-related effects on testicular function. For more information, please refer to the Summary of Product Characteristics.

					Animal studies did not indicate effects with respect to fertility in females.
IB/0019	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)	13/09/2022	10/03/2023	SmPC	
II/0008	C.I.4 - Update of section 4.8 of the SmPC in order to add Lymphopenia to the list of adverse drug reactions (ADRs) with frequency common and update the information on serum phosphate and the experience from the long-term extension studies based on interim results from study GS-US-417-0304 (FINCH 4); this is a Multicenter, Double-Blind, Long Term Extension Study to Assess the Safety and Efficacy of Filgotinib in Subjects with Rheumatoid Arthritis; the Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	30/06/2022	10/03/2023	SmPC and PL	Long-term efficacy and safety data from the ongoing long-term extension (LTE) study, GS US 417 0304 (FINCH 4) were submitted. Across all filgotinib Phase 2 and 3 clinical studies, the overall exposure adjusted incidence rate (EAIR) of herpes zoster was numerically higher in the 200 mg group (1.6) compared to the 100 mg group (1.1). In rheumatoid arthritis clinical studies, the risk of herpes zoster appeared to be higher in female patients, Asian patients, patients ≥ 50 years of age, patients with a medical history of herpes zoster, patients with a medical history of chronic lung disease and patients treated with filgotinib 200 mg once daily. Accordingly, recommendation of immunisations prior to initiation of filgotinib treatment was updated to include prophylactic zoster vaccination. Based on the data from 12-week placebo-controlled period for patients with rheumatoid arthritis who received filgotinib 200 mg, the frequency of lymphopenia (1.0%) was added in the overall description of the most commonly reported adverse reactions and table of adverse reactions in Section 4.8 of the SmPC. Dose dependent decreases in serum phosphate levels occurred during treatment with filgotinib up to week 24. These were generally mild, transient or intermittent, and resolved without discontinuation of treatment.

					For more information, please refer to the Summary of Product Characteristics.
IAIN/0016/G	This was an application for a group of variations. 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 B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	02/05/2022	10/03/2023	Annex II and PL	
IB/0015	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	19/04/2022	n/a		
PSUSA/10879 /202109	Periodic Safety Update EU Single assessment - filgotinib	07/04/2022	n/a		PRAC Recommendation - maintenance
T/0012	Transfer of Marketing Authorisation	23/11/2021	16/12/2021	SmPC, Labelling and PL	
II/0001	Extension of indication to include the treatment of active ulcerative colitis in adults patients for Jyseleca. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC and the Package Leaflet are updated accordingly. The RMP is updated to Version 4.0. In addition, the Marketing authorisation holder (MAH) took the opportunity to do minor updates to the Annex II and to implement	16/09/2021	12/11/2021	SmPC, Annex II and PL	Please refer to Scientific Discussion Jyseleca EMEA/H/C/5113/II/0001.

	minor editorial changes in the SmPC and Package Leaflet. The variation leads to amendments to the Summary of Product Characteristics, Annex II and Package Leaflet and to the Risk Management Plan (RMP). C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
PSUSA/10879 /202103	Periodic Safety Update EU Single assessment - filgotinib	28/10/2021	n/a		PRAC Recommendation - maintenance
II/0006	C.I.4 - Update of sections 4.5 and 5.2 of the SmPC in order to reflect new pharmacokinetic information on the effect of filgotinib on OATP/CYP3A, OATP/BCRP, and OATP substrates based on final results from study GS-US-417-5937; this is a Phase 1, randomized, two-way crossover, open-label, single and multiple dose, single center study to evaluate the effect of filgotinib on a mixed OATP/CYP3A, OATP/BCRP, and OATP substrates using phenotypic probes; the Package Leaflet is updated accordingly. The RMP version 2.1 is accepted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	16/09/2021	12/11/2021	SmPC and PL	based on data obtained from the drug-drug interaction study GS US 417 5937, designed to investigate the effect of multiple doses of filgotinib on OATPs using three OATP1 substrates - atorvastatin, rosuvastatin, and pravastatin. Data demonstrated a low potential of drug drug interactions for filgotinib through inhibition of OATPs. The modest increase in rosuvastatin exposure (AUC and Cmax of 42% and 68%, respectively) when co-administered with filgotinig was not considered clinically relevant. Therefore, filgotinib co-administration with OATP substrates does not warrant dose adjustment. Consequently, sections 4.5. and 5.2 have been updated by removing the statements "In vitro studies indicate that filgotinib and its primary metabolite GS 829845 are inhibitors of OATP1B1 and OATP1B3. No clinical studies have been performed to investigate interactions with OATP1B1 and OATP1B3 substrates. Therefore, it cannot be excluded that co administration of filgotinib with OATP1B1 or OATP1B3 substrates may increase their exposure and

					the risk of adverse events. Co administration with sensitive OATP1B1 or OATP1B3 substrates (e.g., valsartan, statins) is therefore not recommended." and "In vitro data indicate that filgotinib and GS 829845 have the potential to inhibit OATP1B1, OATP1B3, OCT2, MATE1 (filgotinib only), and MATE 2K.", respectively.
IB/0009	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)	23/08/2021	12/11/2021	SmPC	
IB/0010	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	20/08/2021	n/a		
IA/0011	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	05/08/2021	n/a		
IB/0007/G	This was an application for a group of variations. B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)	01/07/2021	n/a		
II/0003	Update to Sections 4.5 and 5.2 of the SmPC to update the wording on the inhibition of P-gp and BCRP by the primary metabolite of filgotinib (GS-829845) based upon results from an in vitro study	22/04/2021	12/11/2021	SmPC and PL	Based on the results from study AD 417 2028 "An in vitro assessment of GS 829845, a metabolite of filgotinib with human P gp and BCRP" it is concluded that filgotinib and GS 829845 are not inhibitors of P-gp, BCRP at clinically

	(AD-417-2028) which assessed in vitro inhibition of human P-gp and BCRP by GS-829845. The Package Leaflet has been updated accordingly. The MAH took this opportunity to update the details of the local representatives in Germany and United Kingdom (Northern Ireland). The RMP has been updated accordingly (version 2.0). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				relevant concentrations. For more information, please refer to the Summary of Product Characteristics.
IG/1381	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	06/04/2021	n/a		
IA/0002/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient B.I.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	18/11/2020	n/a		

	corresponding test method 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 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 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				