Olumiant

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
II/0043	Submission of an updated RMP version 22.1, dated 9 June 2023 in order to remove existing additional pharmacovigilance activities (category 3 studies): Study I4V-MC-JAJA (JAJA) and Study I4V-MC-JAJD (JAJD). The RMP version 22.2, dated 26 September 2023, is acceptable. C.I.11.b - Introduction of, or change(s) to, the	30/11/2023	n/a		The Article 20 referral for JAKi introduced significant restrictions presented in the SmPC on the use of baricitinib in patients' subpopulations with cardiovascular, oncological or thromboembolic risk factors. The warnings and precautions introduced complicate the imposed controlled baricitinib assessment in this risk groups. Consequently the studies are not expected to provide meaningful understanding of the risks. Therefore, it is accepted to

[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).

	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				remove the studies JAJA and JAJD as additional pharmacovigilance activities.
IA/0045	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	20/11/2023	n/a		
II/0037	Extension of indication to include the treatment of paediatric patients (from 2 years of age and older) with moderate to severe atopic dermatitis for OLUMIANT, based on the final results from study I4V-MC-JAIP; this is a Phase III, multicentre, randomised, double blind, placebo controlled, parallel-group, outpatient study evaluating the pharmacokinetics, efficacy, and safety of baricitinib in paediatric patients with moderate-to-severe atopic dermatitis. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet has been updated accordingly. The RMP Version 21.2 is acceptable. The variation leads to amendments to the Summary of Product Characteristics 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	14/09/2023	18/10/2023	SmPC and PL	Please refer to Scientific Discussion Olumiant-H-C-004085-II-0037.

PSUSA/10578 /202302	Periodic Safety Update EU Single assessment - baricitinib	28/09/2023	n/a		PRAC Recommendation - maintenance
X/0035/G	This was an application for a group of variations. Extension application to introduce a new strength (1 mg film-coated tablet), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment, as monotherapy or in combination with conventional synthetic disease modifying antirheumatic drugs (DMARDs), of active juvenile idiopathic arthritis (JIA) in patients 2 years of age and older who have had an inadequate response or intolerance to one or more prior conventional synthetic or biologic DMARDs, based on final results from the pivotal study JAHV (I4V-MC-JAHV); this is a multicentre, double-blind, randomised, placebo-controlled, medication-withdrawal Phase 3 study in children from 2 years to less than 18 years of age with JIA who have had an inadequate response or intolerance to treatment with at least 1 cDMARD or bDMARD. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. The guide for HCPs in the Annex II was updated to recommend paediatric patients are immunised prior to initiation of treatment. Version 20.2 of the RMP has also been approved. Annex I_2.(c) Change or addition of a new	20/07/2023	15/09/2023	SmPC, Annex II, Labelling and PL	Please refer to Scientific Discussion “Olumiant EMEA/H/C/004085/X/0035/G".

	strength/potency C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IG/1620	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	01/08/2023	n/a		
II/0038	Update of section 5.1 of the SmPC to update efficacy information following the CHMP assessment of procedure R/0025 based on final results from study I4V-MC-JADY (JADY; RA BEYOND); This is a long-term extension Study: a Phase 3, Multicenter Study to Evaluate the Long-Term Safety and Efficacy of Baricitinib in Patients with Rheumatoid Arthritis. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	20/07/2023	15/09/2023	SmPC	The results of Study I4V-MC-JADY (JADY; RA BEYOND) were submitted. This was a long-term extension Phase 3, Multicenter Study to Evaluate the Long-Term Safety and Efficacy of Baricitinib in Patients with Rheumatoid Arthritis with a follow-up of 84 months (7 years). The long-term data presented appear to be in line with the known efficacy and safety profile of baricitinib in patients with RA. The long-term efficacy data do support a claim on durable responses regarding low disease activity/remission over 6 years, and the long term safety data support that there are no apparent differences with the existing safety profile. For more information, please refer to the Summary of Product Characteristics.
II/0039/G	This was an application for a group of variations. Submission of the final reports from studies I4V-MC-B016 and I4V-MC-B011 (in terms of Objective 4 for RA cohort) listed as category 3 non-interventional PASS studies in the RMP. B016 is a drug utilisation study for the assessment of off-label use of	08/06/2023	n/a		At the time of the final report, study B016 identified 1527 unique patients in the Clinical Practice Research Datalink (CPRD) (adults and/or paediatrics) with at least 1 recorded baricitinib prescription. Twelve of these patients (0.79%; 95% CI 0.41% to 1.37%) were under 18 years of age at the time of first CRPD-recorded baricitinib prescription. Given the low proportion of CPRD patients prescribed

	baricitinib in the paediatric population in the United Kingdom. B011 is a retrospective cohort study to assess the safety of baricitinib compared with other therapies used in the treatment of rheumatoid arthritis in Nordic countries. The RMP version 19.1 has also been submitted. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				baricitinib who were <18 years of age (0.79%), the B016 study results cannot be the basis for determining the safety of the drug in the pediatric population and for introducing changes to the PI or RMP for Olumiant. This is being reviewed in parallel ongoing procedures. B011 study (objective 4) was able to describe the occurrence of events relevant to the baricitinib additional RMM within a cohort of incident baricitinib users, identified low occurrence of selected infections or pregnancies, identified 9.3% of patients had their lipids monitored, based on the proxy measure of changes in their statin medication. The current results from Study B011 suggest that prescribers adhered to recommendations within the additional RMM and communication of the additional risk minimisation key messages for baricitinib is effective. As part of this procedure, the RMP (v 19.1) has been updated to reflect completion of analysis for Objective 4 of Study B011, RA cohort, and completion of Study B016. Based on the current evaluation, no changes are warranted to the additional risk minimisation activities or the SmPC.
IB/0041	C.I.3.z - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation	23/05/2023	15/09/2023	SmPC	
PSUSA/10578 /202208	Periodic Safety Update EU Single assessment - baricitinib	16/03/2023	n/a		PRAC Recommendation - maintenance
A20/0032	Pursuant to Article 20 of Regulation (EC) No 726/2004, the European Commission requested on 28 January 2022 the opinion of the European	23/01/2023	10/03/2023	SmPC, Annex II and PL	Please refer to the assessment report: Olumiant (baricitinib) EMEA/H-A20/1517/C/004085/0032

	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 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.				
II/0031	Submission of the final study report from study I4V-MC-B023, a non-interventional PASS which provided a comparative assessment of VTE and other risks among patients with rheumatoid arthritis with baricitinib versus TNF inhibitors listed as category 3 in the RMP. An RMP (version 18.2) has also been updated. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/01/2023	n/a		In the observational study B023, meta-analysis of results from 14 data sources showed a significantly elevated incidence rate ratio for VTE in baricitinib compared with TNFi-treated cohorts. The incidence rate of VTE was greater among patients treated with baricitinib than with TNFi, with a difference of 0.26 (95% CI -0.04, 0.57) per 100 PY. Data analysed for this study was primarily from insurance claims records and also included the data from RA registries. Patients compared in these analyses were propensity score-matched based on risk factors for VTE, including age, sex, cancer history, cardiovascular disease, immune disorders, diabetes, prescription medication use, and health care resource utilisation. In addition, the study also showed a numerically greater

					incidence rate ratio (IRR) of incident serious infection and MACE in patients with RA treated with baricitinib compared with TNFi. The results of this study were assessed as part of the article 20 referral for the Janus kinase inhibitors. For further information, please refer to the outcome of the referral (Janus kinase inhibitors (JAKi) | European Medicines Agency (europa.eu)).
PSUSA/10578 /202202	Periodic Safety Update EU Single assessment - baricitinib	29/09/2022	n/a		PRAC Recommendation - maintenance
IA/0034	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	24/08/2022	n/a		
II/0029/G	This was an application for a group of variations. Grouping of the following variations: C.I.6 - Extension of indication to include treatment of severe alopecia areata in adult patients for Olumiant; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Changes were also made to the PI to bring it in line with the current Agency/QRD template. Version 12.3 of the RMP has been adopted. C.I.11.z - Update of RMP (version 12.1) to change the category 3 study PASS I4V-MC-B011 end of data collection for the Atopic Dermatitis cohort from 'December 2026' to 'December 2027' and the	19/05/2022	20/06/2022	SmPC and PL	Please refer to Scientific Discussion "Olumiant EMEA/H/C/004085/II/0029/G".

	subsequent final study report milestone from 'December 2027' to 'December 2028'. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
PSUSA/10578 /202108	Periodic Safety Update EU Single assessment - baricitinib	10/03/2022	n/a		PRAC Recommendation - maintenance
R/0025	Renewal of the marketing authorisation.	16/09/2021	12/11/2021	SmPC, Annex II and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Olumiant in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity. The information in Section 4.8 and 5.1 of the SmPC has been summarised as part of this application in line with the SmPC guideline.
PSUSA/10578 /202102	Periodic Safety Update EU Single assessment - baricitinib	30/09/2021	n/a		PRAC Recommendation - maintenance
IB/0024/G	This was an application for a group of variations. 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 B.z - Quality Change - Other variation	31/03/2021	n/a		

PSUSA/10578 /202008	Periodic Safety Update EU Single assessment - baricitinib	11/03/2021	n/a		PRAC Recommendation - maintenance
IA/0023	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	08/03/2021	n/a		
IA/0022	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	12/02/2021	n/a		
IB/0021	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	03/02/2021	n/a		
PSUSA/10578 /202002	Periodic Safety Update EU Single assessment - baricitinib	17/09/2020	20/11/2020	SmPC	Please refer to Olumiant EMEA/H/C/PSUSA/00010578/202002 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
II/0019	Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on diverticulitis following a signal assessment (EPITT: 19496; Procedure EMEA/H/C/4085/SDA/010); the Package Leaflet is updated accordingly. C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH	29/10/2020	12/11/2021	SmPC and PL	Events of diverticulitis and gastrointestinal perforation have been reported in clinical trials and from postmarketing sources. Baricitinib should be used with caution in patients with diverticular disease and especially in patients chronically treated with concomitant medications associated with an increased risk of diverticulitis: nonsteroidal anti-inflammatory drugs, corticosteroids, and opioids. Patients presenting with new onset abdominal signs and symptoms should be evaluated promptly for early identification of diverticulitis or gastrointestinal perforation. Diverticulitis is added as new undesirable effect with an uncommon

					frequency to the product information.
II/0017	Submission of the final report from Study I4V-MC-B010 "Rheumatologist Survey to Assess the Effectiveness of the Risk Minimisation Measures (RMM) for Olumiant" listed as a category 3 study in the RMP. This observational study was a multi-national cross-sectional survey. The RMP version 9.3 has been adopted. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	29/10/2020	n/a		The MAH conducted a survey to evaluate the effectiveness of Risk Minimisation Measures (RMM) associated with the use of baricitinib for the treatment of rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease modifying anti-rheumatic drugs. This survey was designed to assess rheumatologists' understanding of the important safety information detailed in the Health Care Professional (HCP) Educational Material. It also assessed the communication of the important safety information and distribution of the Patient Alert Card (PAC) to patients prescribed baricitinib for the first time. Based on the results of the survey, the RMM were considered effective.
II/0016	Extension of Indication to include a new indication in the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy for Olumiant; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The guide for HCPs and the patient alert card in the Annex II were updated to reflect the risk of deep venous thrombosis (DVT) and pulmonary embolism (PE). Minor editorial changes were brought to the Labelling. Furthermore, the Annex II is brought in line with the latest QRD template version 10.1. The RMP version 8.1 has also been submitted and adopted.	17/09/2020	19/10/2020	SmPC, Annex II, Labelling and PL	Please refer to the scientific discussion EMEA/H/C/004085/II/0016

	In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. The variation leads to amendments to the Summary of Product Characteristics, Annex II, Labelling 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/10578 /201908	Periodic Safety Update EU Single assessment - baricitinib	12/03/2020	n/a		PRAC Recommendation - maintenance
N/0014	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/12/2019	19/10/2020	PL	
PSUSA/10578 /201902	Periodic Safety Update EU Single assessment - baricitinib	19/09/2019	22/11/2019	SmPC and PL	Please refer to Olumiant EMEA/H/C/PSUSA/00010578/201902 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
IA/0013	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	14/08/2019	n/a		
IA/0011	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	12/04/2019	n/a		

PSUSA/10578 /201808	Periodic Safety Update EU Single assessment - baricitinib	14/03/2019	n/a		PRAC Recommendation - maintenance
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)	27/09/2018	16/09/2019	SmPC	
PSUSA/10578 /201802	Periodic Safety Update EU Single assessment - baricitinib	06/09/2018	n/a		PRAC Recommendation - maintenance
II/0006	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/07/2018	04/09/2018	SmPC and PL	
IA/0008	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	16/05/2018	n/a		
PSUSA/10578 /201708	Periodic Safety Update EU Single assessment - baricitinib	08/03/2018	n/a		PRAC Recommendation - maintenance
IG/0898	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	12/02/2018	29/06/2018	Annex II	
II/0003	Update of sections 4.4 and 5.1 of the SmPC in order to include results of a vaccination sub-study which was part of the long term extension study I4V-MC-JADY (‘A Phase 3, Multicenter Study to Evaluate the	25/01/2018	29/06/2018	SmPC	No data are available on the response to vaccination with live vaccines in patients receiving baricitinib. Use with live, attenuated vaccines during, or immediately prior to, Olumiant therapy is not recommended. Prior to initiating

	Long-Term Safety and Efficacy of Baricitinib in Patients with Rheumatoid Arthritis'). In addition, the updated, consolidated RMP version 5.0 has been agreed as part of this application. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				Olumiant, it is recommended that all patients be brought up to date with all immunisations in agreement with current immunisation guidelines. The influence of baricitinib on the humoral response to non-live vaccines was evaluated in 106 RA patients under stable treatment with baricitinib 2 or 4 mg, receiving inactivated pneumococcal or tetanus vaccination. The majority of these patients (n = 94) were co-treated with methotrexate. For the total population, pneumococcal vaccination resulted in a satisfactory IgG immune response in 68.0 % (95 % CI: 58.4 %, 76.2 %) of the patients. In 43.1 % (95 % CI: 34.0 %, 52.8 %) of the patients, a satisfactory IgG immune response to tetanus vaccination was achieved.
II/0002	Update of sections 4.5 and 5.2 of the SmPC based on the final study report of an in vitro study to investigate the inhibitory effect of baricitinib on the organic anion transporter 2 (OAT2) in fulfilment of post-authorisation measure MEA 001. In addition, the MAH took the opportunity to make minor editorial changes in the Package Leaflet (Patient Alert Card) to be aligned with Annex II. Furthermore, the updated RMP version 3.1 has been agreed as part of this application. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	09/11/2017	29/06/2018	SmPC and PL	In vitro, baricitinib is not an inhibitor of OAT1, OAT2, OAT3, organic cationic transporter (OCT) 2, OATP1B1, OATP1B3, BCRP, MATE1 and MATE2 K at clinically relevant concentrations. Baricitinib may be a clinically relevant inhibitor of OCT1, however there are currently no known selective OCT1 substrates for which clinically significant interactions might be predicted. In clinical pharmacology studies there were no clinically meaningful effects on exposure when baricitinib was coadministered with digoxin (Pgp substrate) or methotrexate (substrate of several transporters).
II/0001	Update of section 4.4 of the SmPC in order to add a warning on venous thromboembolism based on analyses of the occurrence of venous	20/07/2017	29/06/2018	SmPC and PL	Events of deep venous thrombosis (DVT) and pulmonary embolism (PE) have been reported in patients receiving baricitinib. Olumiant should be used with caution in patients

	thromboembolic events in clinical trials with baricitinib. The Package Leaflet is updated accordingly. The RMP version 2.0 has been submitted, as part of this application. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				with risk factors for DVT/PE, such as older age, obesity, a medical history of DVT/PE, or patients undergoing surgery and immobilisation. If clinical features of DVT/PE occur, Olumiant treatment should be temporarily interrupted and patients should be evaluated promptly, followed by appropriate treatment.