25 June 2026
EMADOC-1700519818-3329933
Human Medicines Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Olumiant

Baricitinib

Procedure no: EMA/PAM/0000338022

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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Status of this report and steps taken for the assessment			
Current step[1]	**Description**	**Planned date**	**Actual Date**
☐	CHMP Rapporteur AR	1 June 2026	1 June 2026
☐	CHMP comments	15 June 2026	15 June 2026
☐	Updated CHMP Rapporteur AR	18 June 2026	23 June 2026
☒	CHMP outcome	25 June 2026	25 June 2026

[1] Tick the box corresponding to the applicable step – do not delete any of the steps. If not applicable, add n/a instead of the date.

[2] Criteria for CHMP plenary discussion: substantial disagreement between the Rapporteur and other CHMP members and/or at the request of the Rapporteur or the Chair

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1. Introduction

On 16 March 2026, the MAH submitted a completed paediatric study for Olumiant, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that Study I4V-MC-KHAB is a stand-alone study.

2.2. Information on the pharmaceutical formulation used in the study

Study KHAB involved open-label QD oral administration of baricitinib as shown in Table 1.

Table 1: Planned Dose and Mode of Administration for Baricitinib Participants in Study KHAB

Treatment Name	Baricitinib Oral Suspension (2 mg/mL)	
Dose Levels by Age Group	Dose	Volume
10 to <18 years	4 mg	2 mL
2 to <10 years	2 mg[a]	1 mL[a]
1 to <2 years	1.5 mg[a]	0.75 mL[a]

[a] Planned dosing regimen: pending a data review after at least 8 participants aged 10 to <18 years complete the PK and safety assessments, the actual dose may be adjusted, if necessary, for participants aged 1 to <10 years.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

- Study I4V-MC-KHAB, a Multicenter, Open-Label, Pharmacokinetic and Safety Study of Baricitinib in Pediatric Patients from 1 Year to Less Than 18 Years Old Hospitalized with COVID-19.

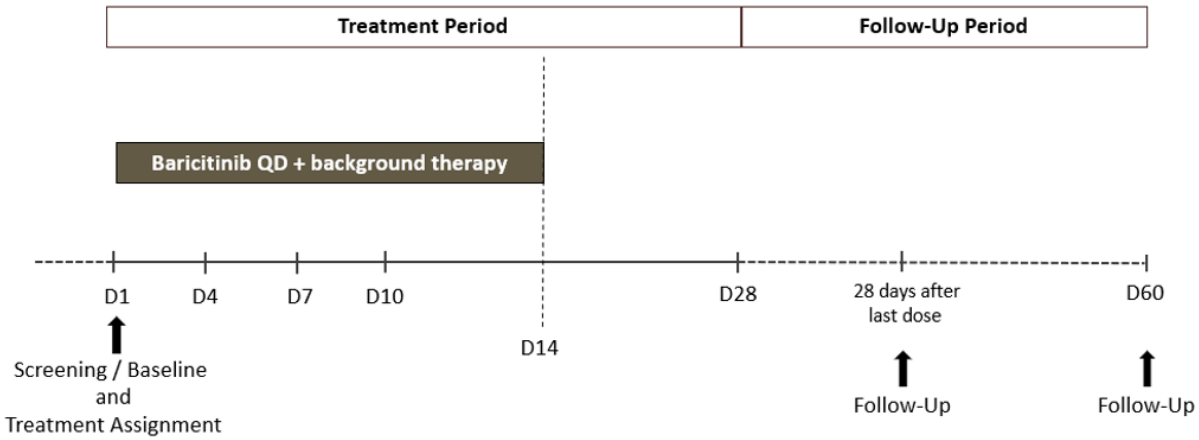
2.3.2. Clinical study I4V-MC-KHAB

Study I4V-MC-KHAB, a Multicenter, Open-Label, Pharmacokinetic and Safety Study of Baricitinib in Pediatric Patients from 1 Year to Less Than 18 Years Old Hospitalized with COVID-19

Description

Study KHAB was a multicentre, open-label, single-group Phase 3 study designed to characterise the PK and safety profile of baricitinib in paediatric patients (1 to <18 years of age) who are hospitalised with confirmed COVID-19. All participants received a daily dose of baricitinib that produced exposure equivalent to that produced by baricitinib 4 mg once daily (QD) in adults.

Figure 1 illustrates the design for Study KHAB.



Notes: Baricitinib dose levels are assigned according to the participant's age. To allow for optimization of the dose for younger participants (<10 years), enrollment will be conducted in age-based cohorts, beginning with older participants (10 to <18 years). For all cohorts, dosing will occur from the day of treatment assignment up to Day 14, or until hospital discharge, whichever comes first. Baricitinib is given with background therapy in keeping with local clinical practice for management of COVID-19, as defined in the protocol.

Abbreviations: D = study day; QD = once daily.

Figure 1: Scheme of Study I4V-MC-KHAB.

Methods

Study participants

The study population was to include male and female paediatric patients who

- were aged from 1 to <18 years of age (inclusive) at the time of enrolment,
- were hospitalised with coronavirus (SARS-CoV-2) infection, confirmed by NAAT such as rt-PCR tests or immunodiagnostic tests detecting viral structural protein antigens such as nucleocapsid protein antigen spike (S) or other structural protein antigens,
- required supplemental oxygen, or noninvasive or invasive mechanical ventilation (including ECMO), and have chest imaging findings to confirm respiratory disease due to COVID-19 within 72 hours of study entry and enrolment.

Participants were excluded if they

- were receiving
    - biologic treatments (such as TNF inhibitors, interleukin inhibitors, T-cell- or B-cell-targeted therapies, interferons, or JAK inhibitors) for any indication at study entry; or were receiving other immunosuppressants such that, in the opinion of the investigator, participating in the study would put the participant at an unacceptable risk of immunosuppression, or
    - strong inhibitors of OAT3 (such as probenecid) that cannot be discontinued at study entry,
- had a diagnosis of current active TB or, if known, latent TB treated for <4 weeks with appropriate anti-TB therapy per local guidelines,
- had a suspected serious, active bacterial, fungal, viral, or other infection (besides COVID-19) that in the opinion of the investigator could constitute a risk when taking investigational product.

Treatments

Study KHAB involved open-label QD oral administration of baricitinib as shown in Table 1.

For all participants, dosing occurred from the day of treatment assignment up to Day 14, or until hospital discharge, whichever came first.

Objective(s), Outcomes/endpoints

Table 2 summarizes the objectives and endpoints for Study KHAB.

Table 2: Objectives and Endpoints of Study KHAB

Objectives	**Endpoints**
Primary	
To characterise the PK of baricitinib* in paediatric patients with COVID-19	Pharmacokinetic (PK) parameters, including AUC and C_{max} of baricitinib, in paediatric patients with COVID-19
Secondary	
To describe the safety of baricitinib* in paediatric patients with COVID-19	Safety assessments, including AEs and laboratory abnormalities
To describe the effect of baricitinib* on COVID-19 progression in paediatric patients	• Proportion of patients who require noninvasive ventilation/high-flow oxygen or invasive mechanical ventilation (including ECMO) by Day 28 • Proportion of patients who die or require noninvasive ventilation/high-flow oxygen or invasive mechanical ventilation (including ECMO) by Day 28
To describe clinical outcomes in paediatric patients with COVID-19 treated with baricitinib	• Proportion of patients with at least 1-point improvement on NIAID-OS or live discharge from hospital at Day 4, Day 7, Day 10, Day 14, and Day 28 • Number of ventilator-free days (Day 1 to Day 28) • Time to recovery on the NIAID-OS (Day 1 to Day 28) • Overall improvement on the NIAID-OS evaluated at Day 4, Day 7, Day 10, Day 14, and Day 28 • Duration of hospitalisation (Day 1 to Day 28) • All-cause mortality (Day 1 to Day 28 and Day 60) • Duration of stay in the intensive care unit (ICU) in days (Day 1 to Day 28)
Exploratory	
Exploratory objectives and endpoints include cytokines and other inflammatory markers implicated in COVID-19 such as interleukins and chemokines.	
Notes: *Baricitinib dose that produces an exposure equivalent to that produced by baricitinib 4 mg QD in adults. Recovery is defined as the first day or time from study start on which the participant satisfies 1 of the following 3 categories from the ordinal scale: Hospitalised, not requiring supplemental oxygen – no longer requires ongoing medical care; Not hospitalised, limitation on activities and/or requiring home oxygen; Not hospitalised, no limitations on activities (applies to live discharge from hospital to home as well). Abbreviations: ECMO = extracorporeal membrane oxygenation; NIAID-OS = National Institute of Allergy and Infectious Diseases ordinal scale.	

Primary estimand/coprimary estimands

The primary endpoint of interest was PK parameters, including area under the concentration versus time curve (AUC) and maximum observed drug concentration (C_{max}) of baricitinib. The population of interest was pediatric participants 1 year to <18 years of age with COVID-19 who required supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

Secondary estimands

A treatment policy strategy estimand was implemented for the secondary estimands. All of the listed secondary efficacy endpoints were endpoints of interest for this study. Pediatric participants from 1 year to <18 years of age who were hospitalized with COVID-19 were the population of interest. The summary measure for binary variables was the proportion, and the summary measure for continuous variables was the average. As this was expected to be a short study, intercurrent events such as treatment discontinuation were considered irrelevant in defining the treatment effect. The value for the variable of interest was used, regardless of whether or not the intercurrent event occurred. Additionally, as death was an endpoint for this study, it will not be considered as an intercurrent event.

Sample size

The sample size for Study KHAB was estimated based on the method proposed by Wang et al. (Wang et al. 2012). It estimated that a total of 8 participants in the age group of 10 to <18 years will achieve at least 80% power to be able to estimate the 95% CI within 60% and 140% of the geometric mean estimates of the PK parameters of interest, using the variability estimates of 34.3% for AUC. Given possible uncertainty in the PK in participants with COVID-19 (that is, possibly augmented renal clearance and/or different absorption and bioavailability), this estimated number was increased to at least 12 participants, which represents a 50% increase in the sample size in the 10 to <18 years of age group. In addition, to ensure adequate coverage of the low end of the age range, it is further specified that at least 3 participants aged 10 to <12 years should be included.

Because severe respiratory disease in patients with COVID-19 is rare in children <10 years of age, enrollment is likely to be challenging in this age group. Therefore, the plan is to include

- at least 6 participants from 6 to <10 years of age
- at least 3 participants from 4 to <6 years of age, and
- at least 3 participants from 1 to <4 years of age.

Randomisation and blinding (masking)

N/a, this is a single-group treatment study without blinding (open-label).

Pharmacokinetic analysis

PK samples were to be drawn on Day 1, 15 and 30 minutes postdose and any time between 2 to 4 hours postdose. On Day 4, a predose PK sample was to be collected, as well as PK samples 1 hour postdose and any time between 6 to 10 hours postdose.

Limited data available prevented full model development and evaluation. Therefore, an existing pediatric population model was utilized to evaluate exposures to compare them with other pediatric and adult populations. Comparisons are presented for typical PK assessments.

Statistical Methods

The primary objective of this study was to characterize the PK of baricitinib in pediatric participants with COVID-19, as assessed by PK parameters, such as AUC and C_{max} of baricitinib in pediatric participants with COVID-19.

The original intent of this study design was to compare summary data between pediatric participants and adult participants (from Study I4V-MC-KHAA [KHAA]) with COVID-19 who have been treated with baricitinib (Marconi et al. 2021). It was intended that hypothesis testing would be performed to

compare selected comparable endpoints for pediatric patients treated with baricitinib and the adult placebo population.

However, due to the limited enrollment of only 6 participants in this study, the sample size was insufficient to conduct the formal statistical analyses outlined in the statistical analysis plan. Given this constraint, individual patient data has been presented for all required endpoints to provide a comprehensive view of the observed responses.

Results

Participant flow and recruitment

In summary, 8 participants were screened, 6 participants were enrolled, and 5 participants completed the study.

First participant first visit was 21 December 2021

Last participant last visit was 04 November 2024

Study enrollment closed early, on 17 September 2025. The analyses presented in this report are based on a database lock date of 10 December 2025. A short (44 pages) clinical study report was submitted, this report was signed by the principle investigator on 17 Febr 2026.

Baseline data

Participants ranged from 1 to 14 years of age and included 4 males and 2 females. All enrolled participants fell within the <25 kg/m² BMI category, indicating that no overweight or obese individuals were represented in the study population. At baseline, every participant met the criteria for 'Not Impaired' renal function, with eGFR ≥60 mL/min/1.73 m². Most participants had pre-existing comorbid conditions.

Number analysed

Planned: approximately 24 participants

Enrolled: 6 participants

Completed: 5 participants

One participant did not complete the study and had relevant pre-existing comorbid conditions. The participant received baricitinib for a short duration (4 days) and improvement in National Institute of Allergy and Infectious Diseases ordinal scale was observed.

Pharmacokinetic results

Whole blood and plasma samples were collected from the 6 participants enrolled in Study KHAB. Of the 22 samples available, 5 samples from 1 participant were inadvertently frozen during transfer from the site to the bioanalytical laboratory, and the resultant concentrations were deemed invalid and were not included in any summary evaluation. The resultant 17 samples from 5 participants were not sufficient to fully develop or inform a paediatric COVID-19 PK model.

To provide exposure estimates and allow for comparison to other paediatric populations, the existing paediatric population PK model for baricitinib, along with parameter settings established in the paediatric atopic dermatitis population (Study I4V-MC-JAIP [JAIP]), was used to estimate baricitinib exposure for each patient utilising the actual dosing administered.

The structural model utilized was a 2-compartment model with zero-order absorption, including lag time and a semi-mechanistic partitioning of CL/F into an eGFR-dependent renal component and a non-renal component. An allometric relationship was used for the effect of weight on clearance-related parameters with the allometric exponent fixed to 0.75, and for the effect of weight on central and peripheral volume of distribution with the exponent fixed to 1. To allow for better individual estimates, the model was allowed to predict the non-renal and renal CL terms.

The model predictions fit reasonably well with the actual data collected, allowing comparison of estimated exposure for each participant in Study KHAB. Figures showing the model-estimated concentration with actual sample data, individual exposure estimates and the model file used to estimate exposures have been provided in the clinical study report. A summary of the estimated exposures is provided in Table 3.

Table 3: Baricitinib Post Hoc Exposure in Participants in Study KHAB

Dose level	**All doses** [a]	**4 mg QD**
N	6	3
$AUC_{T,ss}$ (ng*hr/mL)	222 (152) [b,c]	523 (81) [c]
$C_{max,ss}$ (ng/mL)	55.1 (41) [b,c]	56.7 (42) [c]

Abbreviations: $AUC_{T,SS}$ = area under the plasma concentration versus time curve during the dosing interval at steady state; $C_{max,SS}$ = maximum observed drug concentration during a dosing interval at steady state; N = number of patients.

a Dosing in Study KHAB was based on age: 4 mg (10 to <18 years), 2 mg (2 to <10 years), and 1.5 mg (1 to <2 years).

b Post hoc exposure for all patients regardless of dose.

c Geometric mean and CV%.

Comparison of exposure estimates of baricitinib from Study KHAB with other paediatric populations shows exposure (AUC) to be within the range for participants given 4 mg QD (334 ng*hr/mL, Study I4V-MC-JAIO in alopecia areata and 529 ng*hr/mL, Study JAIP in atopic dermatitis; KHAB CSR Table 2.3) and slightly lower for participants receiving 2 mg QD or less with similar weights and ages. Exposures (AUC) in Study KHAB are also estimated to be within the range of adult exposures from 4 mg QD across indications, with healthy adult exposure on the low end at 245 ng*hr/mL and the higher end from participants with atopic dermatitis at an average of 415 ng*hr/mL (KHAB CSR Table 2.4).

Observed AUCs from the 2-mg and 1.5-mg doses for the youngest patients aged appear to be lower than other corresponding adult and paediatric exposure ranges for similar dosing. Small sample size makes any definitive conclusions difficult; however, the dosing targets selected do appear to achieve reasonable exposures without exceeding the original 4-mg QD adult equivalent exposure target.

Efficacy results

No deaths occurred and overall disease progression was limited in this study (see Table *4* below, prepared by the CHMP). None of the participants progressed to a greater level of respiratory support than at baseline, and 5 of the 6 participants had recovered by the end of the treatment period. However, based on the limited data no efficacy conclusions can be drawn.

Table 4: Summary of Efficacy endpoints ITT population

Outcome Measure	Time frame	Statistic	Result (N = 6)
Percentage of participants who require Non-Invasive Ventilation/High Flow Oxygen or Invasive Mechanical Ventilation (including ECMO)	Day 1 to Day 28	n (%)	0 (0.0%)
Percentage of participants who Die or require Non-Invasive Ventilation/High Flow Oxygen or Invasive Mechanical Ventilation (including ECMO)	Day 1 to Day 28	n (%)	0 (0.0%)
Percentage of participants with at least 1-point improvement on NIAID-OS	Day 4	n (%)	1 (16.7%)
	Day 7	n (%)	4 (66.7%)
	Day 10	n (%)	5 (83.3%)
	Day 14	n (%)	6 (100.0%)
	Day 28	n (%)	5 (83.3%)
Number of Ventilator -Free Days (Days)	Day 1 to Day 28	Median (Min,Max)	28 (3,28)
Time to Recovery	Day 1 to Day 28	Median (Min,Max)	8 (5,28)
Duration of Hospitalization (Days)	Day 1 to Day 28	Median (Min,Max)	6.5 (4,28)
Duration of stay in the ICU (Days)	Day 1 to Day 28	Median (Min,Max)	0 (0,28)
All-Cause Mortality	Day 1 to Day 28 and Day 60	n (%)	0 (0.0%)
Overall Improvement on the NIAID-OS	Day 28		
	0 point improvement	n (%)	1 (16.7%)
	1 point improvement	n (%)	0 (0.0%)
	2 point improvement	n (%)	0 (0.0%)
	3 point improvement	n (%)	1 (16.7%)
	4 point improvement	n (%)	4 (66.7%)

Abbreviations: ECMO = Extracorporeal Membrane Oxygenation ICU = Intensive Care Unit; NIAID-OS = National Institute of Allergy and Infectious Diseases ordinal scale.

Safety results

Given the small sample size and the severity of underlying COVID 19 illness in the enrolled paediatric population, safety findings are summarised descriptively, with a clear distinction between observed AEs and those assessed as treatment emergent. Overall, no new or unexpected safety signals were identified.

Overview of adverse events

A total of 5 participants completed the study. A limited number of AEs were observed, most of which were mild or moderate. These AEs are listed below by preferred term.

- Notable events included cases of Pneumonia,.
- Moderate events were reported across several system organ classes, including
    - Diarrhea
    - Hypocalcemia
    - Hypokalemia
    - Dermatitis contact
    - Tracheostomy, and
    - Sinus bradycardia.
- All remaining events were mild with no apparent clustering, including
    - Headache
    - Asthma

- Contusion
- Insomnia
- Dermatitis diaper
- Pustule
- Lip edema
- Pain in extremity, and
- Alanine aminotransferase increased.

There were no events of venous thromboembolism, malignancy, or major adverse cardiovascular events reported in this study.

Treatment-Emergent Adverse Events

Treatment-emergent adverse events, excluding Pneumonia, Respiration abnormal, and Insomnia (which were not TEAEs), were consistent with the expected safety profile for the study population and investigational treatment. Most events were mild to moderate, self-resolving, and did not require permanent discontinuation of study drug. No new or unexpected safety signals were identified.

Serious Adverse Events

One participant reported a serious adverse event, which occurred after completion of study treatment. The investigator considered the event not related to study drug.

Adverse Events of Special Interest

Adverse events of special interest for this trial included VTE and infection.

No events of VTE were reported. Pneumonia events and pustule were reported within the Infections and infestations system organ class. No other adverse events of special interest were observed.

Clinical Laboratory Evaluation

Laboratory values were generally unremarkable, with only transient, non clinically significant abnormalities noted.

2.3.3. Discussion on clinical aspects

The present submission includes the Clinical Study Report for study I4V-MC-KHAB, a multicentre, open-label, single-group Phase 3 study designed to characterise the PK and safety profile of baricitinib in paediatric patients (1 to <18 years of age) who are hospitalised with confirmed COVID-19. Participants were planned to be divided into 2 age cohorts: 1 to <10 years and 10 to <18 years. It was initially planned that analyses of the PK and safety profile from at least 8 participants in the older cohort would confirm or, if necessary, adjust the planned dose for the younger cohort.

Due to enrolment challenges, only 6 participants were eventually enrolled (out of 8 screened), of which 5 completed the study. Three participants were in the age range of 10-14 years and the other three participants were young children (<5 years). The reason why one of the participants did not complete the study was provided upon request. of the study drug intervention and was therefore considered not to have completed the study. The sample size was insufficient to conduct any formal statistical analyses.

Although individual PK data were collected, the small sample size precludes meaningful interpretation of dose exposure relationships or variability in this paediatric population. Consequently, the PK findings from Study KHAB, while similar to exposures in adults administered 4 mg QD, are descriptive in nature and do not alter the existing understanding of baricitinib PK derived from adult studies or other paediatric development programs.

Observed AUCs from the 2-mg and 1.5-mg doses for the youngest patients aged appear to be distinctly lower than other corresponding adult and paediatric exposure ranges for similar dosing. Small sample size makes any definitive conclusions difficult; but it cannot be excluded that these doses are too low.

None of the participants progressed to a greater level of respiratory support than at baseline, and 5 of the 6 participants had recovered by the end of the treatment period. However, based on the limited data no efficacy conclusions can be drawn.

Given the small sample size and the severity of underlying COVID 19 illness in the enrolled paediatric population, safety findings are summarised descriptively. It was unclear why the safety assessment was only done on the 5 participants who completed the study. Safety information on the participant who did not complete the study were provided upon request.

Overall, no new safety risks were identified, and the findings remain broadly aligned with the established safety profile of baricitinib in other paediatric and adult clinical programs.

The Applicant concludes that the totality of evidence does not indicate any need for changes to the SmPC based on safety outcomes from Study KHAB and there is no added value in including the results of the study in the SmPC. This is agreed, provided the requested additional information does not raise concerns.

3. CHMP updated overall conclusion and recommendation

☒ **Fulfilled:**

Based on the data submitted, the MAH should provide information on the participant who did not complete the study as part of this procedure. (see section "Request for supplementary information")

4. Request for supplementary information

Based on the data submitted, the MAH should address the following questions as part of this procedure:

1. The Applicant should detail the reason one of the enrolled participants did not complete the study.
2. The Applicant should provide available safety information for the participant who did not complete the study.

The timetable is a 30 day response timetable without clock stop.

MAH responses to Request for supplementary information

1. The Applicant should detail the reason one of the enrolled participants did not complete the study.

Applicant's response

One enrolled participant was discontinued from the study intervention early, at the investigator's discretion, following clinical recovery from COVID-19, and was subsequently discharged from the hospital. This participant did not attend the protocol-required follow-up visits after discontinuation of the study and was therefore considered not to have completed the study.

CHMP assessment of applicant's response:

The applicant clarified that one participant did not complete the study. The issue is herewith considered solved.

Conclusion:

Issue considered resolved

Additional resulting questions:

None

Updated documentation:

☒ Overview/CHMP AR; ☐ B/R conclusions; ☐ SmPC; ☐ RMP.

2. The Applicant should provide available safety information for the participant who did not complete the study.

Applicant's response

The participant who did not complete the study had relevant pre-existing comorbid conditions and received baricitinib for a short duration (4 days). No adverse events were reported for this participant during the study.

CHMP assessment of applicant's response:

The applicant provided the requested safety information

Conclusion:

Issue considered resolved

Additional resulting questions:

None

Updated documentation:

☒ Overview/CHMP AR; ☐ B/R conclusions; ☐ SmPC; ☐ RMP.