Emergency Use Authorization (EUA) for baricitinib, FOR THE UNAPPROVED USE OF AN APPROVED PRODUCT
Center for Drug Evaluation and Research (CDER) Review

Identifying Information

Application Type (EUA or Pre-EUA) If EUA, designate whether pre-event or intra-event EUA request.	EUA
EUA Application Number(s)[1]	92
Sponsor (entity requesting EUA or pre-EUA consideration), point of contact, address, phone number, fax number, email address	Eli Lilly and Company Lilly Corporate Center Indianapolis IN 46285 Attention: Jillian Fuhs, JD, PharmD Advisor, Global Regulatory Affairs-North America (b) (6) jillian_fuhs@lilly.com
Submission Date(s)	March 31, 2022
Receipt Date(s)	March 31, 2022
OND Division / Office	Division of Rheumatology and Transplant Medicine (DRTM)/Office of Immunology and Inflammation (OII)
Proprietary Name	Olumiant
Established Name/Other names used during development	Baricitinib
Dosage Forms/Strengths	Tablet, 1 mg, 2 mg, 4 mg
Therapeutic Class	Janus kinase inhibitor
Intended Use or Need for EUA	Treatment of coronavirus disease 2019 (COVID-19)
Intended Population(s)	Hospitalized pediatric patients 2 to less than 18 years with COVID-19 requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO)

I. Issue Summary

The December 20, 2021 Emergency Use Authorization (EUA) 092 authorized use of Olumiant (baricitinib) for the treatment of coronavirus disease 2019 (COVID-19) in

[1] If a Pre-EUA is in existence at the time of the EUA request submission and has been assigned an EUA number, the EUA request should use the same EUA number and electronic archive file.

hospitalized adults and pediatric patients 2 years of age or older who require supplemental oxygen, noninvasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). Baricitinib should only be administered in a hospital or healthcare setting capable of providing acute care comparable to inpatient hospital care.

Based on the review of the New Drug Application (NDA) 207924 Supplement 6, for baricitinib, the Agency has concluded that the data support approval of baricitinib for the treatment of COVID-19 in hospitalized adults patients requiring supplemental oxygen, non-invasive or invasive mechanical ventilation or ECMO. The NDA indication will not include pediatric patients less than 18 years of age at this time.

At the time of the NDA approval the Agency will issue a Pediatric Research Equity Act (PREA) post-marketing (PMR) for the conduct of a clinical trial in pediatric patients and the submission of the results from that trial to the Agency; the aforementioned pediatric trial is currently ongoing and once completed, the data may support revising the NDA indication to include use in pediatric patient population.

Upon approval of NDA 207924 Supplement 6, the Agency will revise the EUA for baricitinib to remove the authorized uses covered under the approved NDA. The Agency will continue to authorize baricitinib for emergency use to treat COVID-19 in hospitalized pediatric patients 2 to less than 18 years of age requiring supplemental oxygen, non-invasive or invasive mechanical ventilation or ECMO. The Agency has determined that retaining this authorized use is appropriate to protect public health or safety under section 564 of the Federal Food, Drug and Cosmetic Act.[2]

Maintaining the EUA for pediatric patients 2 to less than 18 years of age will ensure that important information about the recommended use (e.g., dosing recommendations) for pediatric patients not covered under the approved labeling for adult patients will continue to be available to health care providers. As noted above, the EUA will be reissued for pediatric patients 2 to less than 18 years of age concurrent with the approval of Olumiant for the treatment of COVID-19 in the adult patients.

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[2] On October 22, 2020, Veklury (remdesivir) was initially approved to treat COVID-19 in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) requiring hospitalization. On April 25, 2022, a supplement to NDA 214787 was approved to expand the indication for Veklury to also include the treatment of COVID-19 in pediatric patients (28 days of age and older and weighing at least 3 kg) with positive results of direct SARS-CoV-2 viral testing, who are hospitalized, or not hospitalized and have mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death. Although Veklury is an approved alternative treatment of COVID-19 in pediatric patients (28 days of age and older and weighing at least 3 kg) with positive results of direct SARS-CoV-2 viral testing, who are hospitalized, FDA does not consider Veklury to be an adequate alternative to baricitinib for this authorized use. Veklury is a nucleoside ribonucleic acid polymerase inhibitor that has demonstrated antiviral activity against SARS-COV-2. Baricitinib is a Janus kinase (JAK) inhibitor, a class of drugs that block extracellular signals from multiple cytokines that are involved in inflammatory diseases and thought to contribute to inflammation and worsening of COVID-19. This is distinct from Veklury, which acts as an antiviral agent.

II. Summary of Revision to EUA Facts Sheets

- Authorized Use:
  - Revised the scope of the authorized use to the treatment of hospitalized pediatric patients 2 to less than 18 years of age requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).
- Dosing:
  - Revised to describe dosing regimen for the pediatric population covered under the scope of this pediatric EUA.
- Pharmacology:
  - Revision including that the pharmacokinetics (PK) of baricitinib in pediatric patients with COVID-19 has not been evaluated. Provided information regarding analysis of interim PK from ongoing pediatric trials of baricitinib in other conditions.
- Warnings:
  - Added language regarding limited clinical data in pediatric patients and clarification for warnings related to thrombosis and serious infections, to provide consistency with Prescribing Information.
- Scientific Evidence Supporting This EUA:
  - Revised section to clarify that the safety and efficacy assessed in the phase 3 trials was conducted in adults.
  - Added information regarding the ongoing clinical trial in pediatric patients with COVID-19 and clinical trials in other pediatric conditions.
- Efficacy Summary:
  - Added efficacy information for KHAA substudy in patients requiring mechanical ventilation at baseline and updates to provide consistency with Prescribing Information upon approval of sNDA.
- Safety Summary:
  - Added integrated safety information from ACTT-2, KHAA and KHAA substudy to provide consistency with Prescribing Information upon approval of sNDA.
- Other:
  - Editorial revision for clarity, readability, and consistency.
  - Editorial revision to Mandatory Requirements for Baricitinib Administration Under Emergency Use Authorization.
  - Added section for Justification for Emergency Use of Drugs During the COVID-19 Pandemic.

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/s/

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