FACT SHEET FOR HEALTHCARE PROVIDERS
EMERGENCY USE AUTHORIZATION (EUA) OF BARICITINIB

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of baricitinib for treatment of coronavirus disease 2019 (COVID-19) in 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).

Baricitinib has been authorized by FDA for the emergency uses described above. Baricitinib is not FDA-approved for these uses.

Baricitinib is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of baricitinib under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization revoked sooner.

This EUA is for the unapproved use of baricitinib 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.

Baricitinib is administered orally.

To request baricitinib under Emergency Use Authorization (EUA): In-patient pharmacies may order directly from an Authorized Distributor of Record. A current list of Lilly's Authorized Distributors of Record is available at www.lillytrade.com or visit www.baricitinibemergencyuse.com for additional access information.

The prescribing healthcare provider and/or the provider's designee is/are responsible for mandatory reporting of all serious adverse events and medication errors potentially related to baricitinib within 7 calendar days from the healthcare provider's awareness of the event.
See specific reporting instructions below.

The recommended dosage of baricitinib under the EUA is:

- Pediatric patients 9 years of age and older: 4 mg once daily
- Pediatric patients 2 years to less than 9 years of age: 2 mg once daily

Dosage modifications are recommended for laboratory abnormalities, including renal impairment (see **Table 1**).

The optimal duration of treatment is unknown.

The recommended total treatment duration of baricitinib is 14 days or until hospital discharge, whichever comes first.

For information on clinical trials that are testing the use of baricitinib in COVID-19, please see www.clinicaltrials.gov.

This Fact Sheet may be updated as new data become available. The most recent version of this Fact Sheet is available at www.baricitinibemergencyuse.com for download.

INSTRUCTIONS FOR ADMINISTRATION

This section provides essential information on the unapproved use of baricitinib 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 under this EUA.

For more information, including pharmacokinetics and safety information of baricitinib, tradename Olumiant®, see the FDA-approved package insert at http://pi.lilly.com/us/olumiant-uspi.pdf.

Contraindications

There are no known contraindications for baricitinib.

Dosing

Patient Selection

- Evaluate baseline eGFR, liver enzymes, and complete blood count to determine treatment suitability and dose. Monitor closely patients with abnormal baseline and post-baseline laboratory values. See **Table 1** for dosage modifications for patients with laboratory abnormalities.
- Baricitinib is not recommended for:
    - Patients who are on dialysis, have end-stage renal disease (ESRD, EGFR <15 mL/min/1.73 m^2), or have acute kidney injury
    - Patients with known active tuberculosis

Recommended Dosage for Pediatric Patients

Limited data informing baricitinib dosing in pediatric patients comes from ongoing clinical trials for other uses. Based on the available information, treatment for COVID-19 for pediatric patients under this EUA is as follows:

- The recommended dosage for patients 9 years of age and older is 4 mg once daily, with or without food, for 14 days of total treatment or until hospital discharge, whichever is first.
- The recommended dosage for patients ages 2 years through less than 9 years of age is 2 mg once daily, with or without food, for 14 days of total treatment or until hospital discharge, whichever is first.
- Baricitinib is not authorized for patients younger than 2 years of age.
- Dosage modifications in patients with renal or hepatic impairment are recommended (*see* Renal Impairment, Hepatic Impairment).

Table 1: Dosage Modifications

Dosage Modifications for Patients with Abnormal Laboratory Values[a, b]		
Laboratory Analyte	**Laboratory Analyte Value**	**Recommendation**
eGFR	60 - <90 mL/min/1.73 m^2	• Pediatric patients 9 years of age and older: 4 mg once daily • Pediatric patients 2 years to less than 9 years of age: 2 mg once daily
	30 - <60 mL/min/1.73 m^2	• Pediatric patients 9 years of age and older: 2 mg once daily • Pediatric patients 2 years to less than 9 years of age: 1 mg[c] once daily
	15 - <30 mL/min/1.73 m^2	• Pediatric patients 9 years of age and older: 1 mg[c] once daily • Pediatric patients 2 years to less than 9 years of age: Not recommended
	<15 mL/min/1.73 m^2	Not recommended
Absolute Lymphocyte Count (ALC)	≥200 cells/μL	Maintain dose
	<200 cells/μL	Consider interruption until ALC is ≥200 cells/μL
Absolute Neutrophil Count (ANC)	≥500 cells/μL	Maintain dose
	<500 cells/μL	Consider interruption until ANC is ≥500 cells/μL
Aminotransferases	If increases in ALT or AST are observed and drug-induced liver injury (DILI) is suspected	Interrupt baricitinib until the diagnosis of DILI is excluded
Dosage Modifications when Coadministered with Other Medications		
Concomitant Medication		**Recommendation**
Strong OAT3 Inhibitors (e.g., probenecid)		• If the recommended baricitinib dose is 4 mg once daily, reduce dose to 2 mg once daily. • If the recommended baricitinib dose is 2 mg once daily, reduce dose to 1 mg[c] once daily. • If the recommended baricitinib dose is 1 mg once daily, consider discontinuing probenecid.

[a] Abbreviations: ALC = absolute lymphocyte count, ALT = alanine transaminase, ANC = absolute neutrophil count, AST = aspartate transaminase, DILI = drug induced liver injury, eGFR = estimated glomerular filtration rate.

[b] If a laboratory abnormality is likely due to the underlying disease state, consider the risks and benefits of continuing baricitinib at the same or a reduced dose.

[c] Only if a 1 mg tablet is not available, a 2 mg tablet can be split using a tablet splitter that has a razor blade to administer half a 2 mg tablet once daily. The tablet should be split along the longest diameter. If the portions of the tablet are determined to be visually unequal they should be discarded. Take care in storing the second tablet half to avoid breakage prior to next dose.

Pregnancy

Baricitinib should be used during pregnancy only if the potential benefit justifies the potential risk for the mother and the fetus. Consistent with the mechanism of action,

embryo-fetal toxicities including skeletal anomalies and reduced fertility have been observed in animals dosed in excess of the maximum human exposure. The limited human data on use of baricitinib in pregnant women are not sufficient to inform a drug-associated risk for major birth defects or miscarriage.

See also Section 8.1 Pregnancy in the FDA approved full prescribing information for more information.

Renal Impairment

There are limited data for baricitinib in patients with severe renal impairment:

- Baricitinib is not recommended for patients who are on dialysis, have ESRD, or have acute kidney injury.
- See **Table 1** for treatment modifications for patients with laboratory abnormalities:
    - Baricitinib should only be used in pediatric patients 9 years of age and older with eGFR 15 to <30 mL/min/1.73 m^2 if the potential benefit outweighs the potential risk.
    - Baricitinib is not recommended for pediatric patients ages 2 years through less than 9 years of age with eGFR <30 mL/min/1.73 m^2.

Hepatic Impairment

Baricitinib has not been studied in patients with severe hepatic impairment. Baricitinib should only be used in patients with severe hepatic impairment if the potential benefit outweighs the potential risk. It is not known if dosage modification is needed in patients with severe hepatic impairment.

See **Table 1** for dosage modifications for patients with abnormal laboratory values.

Administration

Baricitinib tablets are given orally once daily; with or without food.

Alternative Administration for Patients Unable to Swallow Tablets

For patients who are unable to swallow whole tablets, an alternative mode of administration may be considered:

- Oral dispersion
- Gastrostomy tube (G tube)
- Nasogastric tube (NG tube) or orogastric tube (OG tube)

Intact tablets are not hazardous. Tablets may be crushed to facilitate dispersion. It is not known if powder from the crushed tablets may constitute a reproductive hazard to the preparer. Use proper control measures (e.g., ventilated enclosure) or personal protective equipment (i.e., N95 respirator).

Dispersed tablets are stable in water for up to 4 hours.

Preparation Instructions for Alternative Administration

- *Oral administration of dispersed tablets in water:*
  For patients who are unable to swallow whole tablets, 1-mg, 2-mg, or 4-mg baricitinib tablet(s), or any combination of tablets necessary to achieve the desired dose up to 4-mg may be placed in a container with approximately 10 mL (5 mL minimum) of

room temperature water, dispersed by gently swirling the tablet(s) and immediately taken orally. The container should be rinsed with an additional 10 mL (5 mL minimum) of room temperature water and the entire contents swallowed by the patient (**Table 2**).

- *Administration via G tube:*
  For patients with a G tube, 1-mg, 2-mg, or 4-mg baricitinib tablet(s), or any combination of tablets necessary to achieve the desired dose up to 4-mg may be placed in a container with approximately 15 mL (10 mL minimum) of room temperature water and dispersed with gentle swirling. Ensure the tablet(s) are sufficiently dispersed to allow free passage through the tip of the syringe. Withdraw entire contents from the container into an appropriate syringe and immediately administer through the gastric feeding tube. Rinse container with approximately 15 mL (10 mL minimum) of room temperature water, withdraw the contents into the syringe, and administer through the tube (**Table 2**).

- *Administration via NG or OG tube:*
  For patients with an NG or OG tube, 1-mg, 2-mg, or 4-mg baricitinib tablet(s), or a combination of tablets necessary to achieve the desired dose up to 4-mg may be placed into a container with approximately 30 mL of room temperature water and dispersed with gentle swirling. Ensure the tablet(s) are sufficiently dispersed to allow free passage through the tip of the syringe. Withdraw the entire contents from the container into an appropriate syringe and immediately administer through the enteral feeding tube. To avoid clogging of small diameter tubes (smaller than 12 Fr), the syringe can be held horizontally and shaken during administration. Rinse container with a sufficient amount (minimum of 15 mL) of room temperature water, withdraw the contents into the syringe, and administer through the tube (**Table 2**).

Table 2: Dispersion and Rinse Volume for Alternative Administration

Administration via	Dispersion Volume	Container Rinse Volume
Oral dispersion	10 mL	10 mL
G tube	15 mL	15 mL
NG or OG tube	30 mL	15 mL

Drug Interactions

Strong OAT3 Inhibitors: Baricitinib exposure is increased when baricitinib is co-administered with strong OAT3 inhibitors (such as probenecid). See **Table 1** for dosage modifications for patients taking strong OAT3 inhibitors, such as probenecid.

Other JAK Inhibitors or biologic disease modifying anti-rheumatic drugs (DMARDs): Baricitinib has not been studied in combination with other JAK inhibitors or with biologic DMARDs (biologic treatments targeting cytokines, B-cells, or T-cells) and is not recommended.

Pharmacology

Pharmacokinetics: The pharmacokinetics (PK) in adult patients with COVID-19 who are intubated and have baricitinib administered via NG tube is similar to that in healthy adult subjects. The half-life of baricitinib in healthy subjects is approximately 10 hours.

The PK of baricitinib in pediatric patients with COVID-19 has not been evaluated.

Based on an analysis of interim PK data from ongoing clinicals of baricitinib in other pediatric chronic autoimmune disorders, the recommended dosing regimen is expected to result in comparable steady-state plasma exposures of baricitinib in pediatric patients 2 to less than 18 years of age as observed in healthy adults.

Warnings

There are limited clinical data available for baricitinib in pediatric patients 2 to less than 18 years of age hospitalized with COVID-19 requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO.

Serious Infections

There is limited information regarding use of baricitinib in patients with COVID-19 and concomitant active serious infections.

Serious infections, including viral reactivation, have occurred in patients with COVID-19 receiving baricitinib:

- Avoid the use of baricitinib with known active tuberculosis.
- Consider if the potential benefits outweigh the potential risks of baricitinib treatment in patients with active serious infections other than COVID-19 or chronic / recurrent infections.

Thrombosis

Serious venous thrombosis, including pulmonary embolism have been observed in COVID-19 patients treated with baricitinib and are known adverse drug reactions of baricitinib. If clinical features of deep vein thrombosis/pulmonary embolism occur, patients should be evaluated promptly and treated appropriately.

Abnormal Laboratory Values

There is limited information regarding use of baricitinib in patients with COVID-19 and any of the following clinical findings:

- ANC <1000 cells/mm^3
- ALC <200 cells/mm^3
- Hemoglobin <8 g/dL

Evaluate at baseline and thereafter according to local patient management practice. Monitor closely when treating patients with abnormal baseline and post-baseline laboratory values.

See **Table 1** for dosage modifications for patients with abnormal renal, hematological and hepatic laboratory values. Manage patients according to routine clinical guidelines.

Vaccinations

Avoid use of live vaccines with baricitinib.

Hypersensitivity

If a serious hypersensitivity occurs, discontinue baricitinib while evaluating the potential causes of the reaction.

See **Warnings and Precautions** in the FDA approved full prescribing information for additional information on risks associated with baricitinib treatment.

Serious Side Effects

Serious venous thrombosis, including pulmonary embolism, and serious infections have been observed in COVID-19 patients treated with baricitinib and are known adverse drug reactions of baricitinib.

Scientific Evidence Supporting This EUA

Baricitinib is being studied in an ongoing clinical trial in pediatric patients hospitalized with COVID-19 requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or ECMO. Use in this age group is based on extrapolation of pediatric efficacy from the adequate and well-controlled studies in adults, ACTT-2 and COV-BARRIER, and safety data from ongoing clinical trials of baricitinib in other pediatric conditions.

The efficacy and safety of baricitinib were assessed in 2 Phase 3, randomized, double-blind, placebo-controlled clinical trials:

- COVID I (ACTT-2, NCT04401579) which evaluated the combination of baricitinib 4 mg + remdesivir compared to placebo + remdesivir.
- COVID II (COV-BARRIER, NCT04421027), which evaluated baricitinib 4 mg compared to placebo. Patients could remain on background therapy, as defined per local guidelines. An additional exploratory sub-study in patients requiring invasive mechanical ventilation or ECMO at baseline was also conducted under this protocol and analyzed separately.

<u>Efficacy</u>

COVID I

A randomized, double-blind, placebo-controlled clinical trial (NCT04401579) of hospitalized adults with confirmed SARS-CoV-2 infection compared treatment with baricitinib plus remdesivir (n=515) with placebo plus remdesivir (n=518). Patients had to have laboratory-confirmed SARS-CoV-2 infection as well as at least one of the following to be enrolled in the trial: radiographic infiltrates by imaging, SpO_2 ≤94% on room air, a requirement for supplemental oxygen, or a requirement for mechanical ventilation or ECMO. Patients treated with the combination received the following regimen:

- Baricitinib 4 mg once daily (orally) for up to 14 days or until hospital discharge, whichever came first
- Remdesivir 200 mg on Day 1 and 100 mg once daily (via intravenous infusion) on subsequent days for a total treatment duration of 10 days or until hospital discharge

In this study prophylaxis for venous thromboembolic event (VTEs) was recommended for all patients unless a major contraindication was noted.

For the overall population (N=1033 patients) at randomization, mean age was 55 years (with 30% of patients aged 65 or older); 63% of patients were male, 51% were Hispanic or Latino, 48% were White, 15% were Black or African American, and 10% were Asian;

14% did not require supplemental oxygen, 55% required supplemental oxygen, 21% required non-invasive ventilation or high-flow oxygen, and 11% required invasive mechanical ventilation or ECMO. The most common comorbidities were obesity (56%), hypertension (52%), and type 2 diabetes (37%). Demographics and disease characteristics were balanced across the combination group and the placebo group.

The primary endpoint, for the intent to treat population, was time to recovery within 29 days after randomization. Recovery was defined as being discharged from the hospital without limitations on activities, being discharged from the hospital with limitations on activities and/or requiring home oxygen or hospitalized but not requiring supplemental oxygen and no longer requiring medical care. The key secondary endpoint was clinical status on Day 15 assessed on an 8-point ordinal scale (OS) consisting of the following categories:

1. Not hospitalized, no limitations on activities [OS-1];
2. Not hospitalized, limitation on activities and/or requiring home oxygen [OS-2];
3. Hospitalized, not requiring supplemental oxygen - no longer requires ongoing medical care [OS-3];
4. Hospitalized, not requiring supplemental oxygen - requiring ongoing medical care (COVID-19 related or otherwise) [OS 4];
5. Hospitalized, requiring supplemental oxygen [OS 5];
6. Hospitalized, on non-invasive ventilation or high-flow oxygen devices [OS 6];
7. Hospitalized, on invasive mechanical ventilation or ECMO [OS 7]; and
8. Death [OS 8]

For the overall population, the median time to recovery (defined as discharged from hospital or hospitalized but not requiring supplemental oxygen or ongoing medical care) was 7 days for baricitinib + remdesivir compared to 8 days for placebo + remdesivir [hazard ratio: 1.16 (95% CI 1.01, 1.33); p=0.035].

Patients assigned to baricitinib + remdesivir were more likely to have a better clinical status (according to an 8-point ordinal scale) at Day 15 compared to patients assigned to placebo + remdesivir [odds ratio: 1.26 (95% CI 1.01, 1.57); p=0.044].

The proportion of patients who died or progressed to non-invasive ventilation/high-flow oxygen or invasive mechanical ventilation by Day 29 was lower in baricitinib + remdesivir (23%) compared to placebo + remdesivir (28%) [odds ratio: 0.74 (95% CI 0.56, 0.99); p=0.039]. Patients who required non-invasive ventilation/high-flow oxygen or invasive mechanical ventilation (including ECMO) at baseline needed to worsen by at least 1 point on an 8-point ordinal scale to progress.

The proportion of patients who died by Day 29 was 4.7% (24/515) for baricitinib + remdesivir compared to 7.1% (37/518) for placebo + remdesivir [Kaplan Meier estimated difference in Day 29 probability of mortality: -2.6% (95% CI -5.8%, 0.5%); hazard ratio = 0.65 (95% CI: 0.39, 1.09)].

COVID II

A randomized, double-blind, placebo-controlled clinical trial (NCT04421027) of hospitalized adults with confirmed SARS-CoV-2 infection compared treatment with baricitinib 4mg once daily (n=764) with placebo (n=761) for 14 days or hospital

discharge, whichever came first. Patients could remain on background standard of care, as defined per local guidelines, including antimalarials, antivirals, corticosteroids, and/or azithromycin. In this study prophylaxis for venous thromboembolic event (VTE) prophylaxis was required for all patients unless contraindicated.

The most frequently used therapies at baseline were:

- corticosteroids (79% of patients, mostly dexamethasone)
- remdesivir (19% of patients)

Patients had to have laboratory-confirmed SARS-CoV-2 infection, at least one instance of elevation in at least one inflammatory marker above the upper limit of normal according to local laboratory ranges (CRP, D-dimer, LDH, ferritin), and at least one of the following to be enrolled in the trial: radiographic infiltrates by imaging, SpO_2 <94% on room air, evidence of active COVID infection (with clinical symptoms including any of the following: fever, vomiting, diarrhea, dry cough, tachypnea defined as respiratory rate >24 breaths/min) or requirement for supplemental oxygen.

For the overall population (N=1525 patients) at randomization, mean age was 58 years (with 33% of patients aged 65 or older); 63% of patients were male, 60% were White, 5% were Black or African American,11% were Asian; 12% did not require supplemental oxygen (OS 4), 63% required supplemental oxygen (OS 5), 24% required non-invasive ventilation or high-flow oxygen (OS 6). The most common comorbidities were hypertension (48%), obesity (33%), and type 2 diabetes (29%). Demographics and disease characteristics were balanced across the baricitinib and placebo groups.

The primary endpoint was the proportion of patients who died or progressed to non-invasive ventilation/high-flow oxygen or invasive mechanical ventilation within the first 28-days of the study. Patients who required non-invasive ventilation/high-flow oxygen at baseline needed to worsen by at least 1 point on an 8-point OS to progress (refer to the description of COVID I for the definition of the 8-point OS). A key secondary endpoint was all-cause mortality by Day 28.

The estimated proportion of patients who died or progressed to non-invasive ventilation/high-flow oxygen or invasive mechanical ventilation was lower in patients treated with baricitinib (27.8%) compared to placebo (30.5%), but this effect was not statistically significant [odds ratio: 0.85 (95% CI 0.67, 1.08); p=0.180].

The proportion of patients who died by Day 28 was 8.1% (62/764) for baricitinib compared to 13.3% (101/761) for placebo [estimated difference in Day 28 probability of mortality = -4.9% (95% CI: -8.0%, -1.9%); hazard ratio = 0.56 (95% CI: 0.41, 0.77)].

COVID II Exploratory Sub-Study

In a separate group of patients requiring invasive mechanical ventilation or ECMO at baseline and enrolled in an addendum to COVID II, a pre-specified exploratory analysis showed that the proportion who died by Day 28 was 39.2% (20/51) for baricitinib compared to 58.0% (29/50) for placebo [estimated difference in Day 28 risk of mortality = -18.8% (95% CI: -36.3%, 0.6%); hazard ratio = 0.54 (95% CI: 0.31, 0.96)].

Safety

The safety of baricitinib was evaluated in two randomized, placebo-controlled clinical trials of hospitalized adults with COVID-19 for up to 29 days, in which 1307 patients received at least one dose of baricitinib 4 mg once daily, and 1310 patients received placebo, for up to 14 days or hospital discharge, whichever occurred first. In these studies, prophylaxis for venous thromboembolic event (VTEs) was recommended or required for all patients unless a major contraindication was noted.

Overall, the safety profile observed in patients with COVID-19 treated with baricitinib was consistent with the safety profile in patients with rheumatoid arthritis.

Overall Infections – During the first 29 days of the randomized clinical trials, infections were reported in 194 patients (14.8%) treated with baricitinib 4 mg and by 219 patients (16.7%) treated with placebo. The most commonly reported infection with baricitinib was pneumonia (3.1%).

Serious Infections – During the first 29 days of the randomized clinical trials, serious infections were reported in 98 patients (7.5%) treated with baricitinib 4 mg and 120 patients (9.2%) treated with placebo. The most commonly reported serious infections with baricitinib were COVID-19 pneumonia (2.1%) and septic shock (2.1%).

Opportunistic Infections – During the first 29 days of the randomized clinical trials, opportunistic infections were reported in 12 patients (0.9%) treated with baricitinib 4 mg and 14 patients (1.1%) treated with placebo. Tuberculosis was reported in 1 patient (0.1%) treated with baricitinib 4 mg and 0 patients treated with placebo.

Venous Thrombosis Events - During the first 29 days of the randomized clinical trials, pulmonary embolism was reported in 20 patients (1.5%) treated with baricitinib 4 mg and 11 patients (0.8%) treated with placebo. Deep Vein Thrombosis was reported in 20 patients (1.5%) treated with baricitinib 4 mg and 18 patients (1.4%) treated with placebo.

Of the known adverse drug reactions of baricitinib in clinical trials of other indications, Table 3 summarizes the observed frequencies of adverse reactions occurring in ≥ 1% of patients during the first 29 days of studies COVID I and COVID II.

Table 3: Adverse Reactions That Occurred in Greater Than or Equal to 1% of Patients Treated with Baricitinib 4 mg Treated Patients During the First 29 Days in Placebo-Controlled Trials for COVID-19

	Placebo **N = 1310** **n (%)**	**Baricitinib 4 mg** **N = 1307** **n (%)**
ALT ≥3 x ULN[a]	201(16.0)	230 (18.1)
AST ≥3 x ULN[a]	117 (9.4)	149 (11.8)
Thrombocytosis >600,000 cells/mm^3[a]	34 (4.6)	59 (7.9)
Creatine phosphokinase (CPK) >5 x ULN[a, b]	38 (4.7)	36 (4.5)
Neutropenia <1000 cells/mm^3[a]	22 (1.8)	26 (2.2)
Deep vein thrombosis	18 (1.4)	20 (1.5)
Pulmonary embolism	11 (0.8)	20 (1.5)
Urinary tract infection	13 (1.0)	19 (1.5)

[a] As assessed by measured values within the clinical trial database. Frequencies are based on shifts from pre-treatment to post-treatment (with number at risk as the denominator), except for ALT and AST for which frequencies are based on observed elevation during treatment.
[b] Creatine phosphokinase frequencies presented in the table were available for a single trial (COVID II) in patients with COVID-19 and do not represent integrated data.

How Supplied/Storage and Handling

How Supplied

Baricitinib for oral administration is available as debossed, film-coated, immediate-release tablets. Each tablet contains a recessed area on each face of the tablet surface.

Under this EUA, baricitinib is supplied in 30 count bottles as follows:

- OLUMIANT (baricitinib) tablet 1 mg (NDC 0002-4732-30)
- OLUMIANT (baricitinib) tablet 2 mg (NDC 0002-4182-30), and
- OLUMIANT (baricitinib) tablet 4 mg (NDC 0002-4479-30)

Storage and Handling

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F).

Keep out of reach of children.

Important Information for Patients, Parents and Caregivers

See Fact Sheets for Patients, Parents and Caregivers.

INSTRUCTIONS FOR HEALTHCARE PROVIDERS

As the healthcare provider, you must communicate to your patient or parent/caregiver, as age appropriate, information consistent with the “Fact Sheet for Patients, Parents and Caregivers” (and provide a copy of the Fact Sheet) prior to the patient receiving baricitinib, including:

- FDA has authorized the emergency use of baricitinib 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 extracorporeal membrane oxygenation (ECMO). This is not an FDA-approved use of baricitinib.
- The patient or parent/caregiver has the option to accept or refuse baricitinib.
- The significant known and potential risks and benefits of baricitinib, and the extent to which such potential risks and benefits are unknown.
- Information on available alternative treatments and the risks and benefits of those alternatives, including clinical trials.

If providing this information will delay the administration of baricitinib to a degree that would endanger the lives of patients, the information must be provided to the patients as soon as practicable after baricitinib is administered.

For information on clinical trials that are testing the use of baricitinib for COVID-19, please see www.clinicaltrials.gov.

MANDATORY REQUIREMENTS FOR BARICITINIB ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION

In order to mitigate the risks of using this approved product for an unapproved use under EUA and to optimize the potential benefit of baricitinib, the following items are required. Use of baricitinib under this EUA is limited to the following (all requirements **must** be met):

1. Treatment of coronavirus disease 2019 (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.
2. As the healthcare provider, communicate to your patient or parent/caregiver information consistent with the "Fact Sheet for Patients, Parents and Caregivers" prior to the patient receiving baricitinib. Healthcare providers (to the extent practicable given the circumstances of the emergency) must document in the patient's medical record that the patient/caregiver has been:
    a. Given the "Fact Sheet for Patients, Parents and Caregivers",
    b. Informed of alternatives to receiving authorized baricitinib, and
    c. Informed that baricitinib is an approved drug that is authorized for the unapproved use under this Emergency Use Authorization.
3. Patients must have an eGFR, aminotransferases, and CBC with differential determined prior to first administration of baricitinib.
4. The prescribing healthcare provider and/or the provider's designee is/are responsible for mandatory reporting of all serious adverse events* and medication errors potentially related to baricitinib within 7 calendar days from the healthcare provider's awareness of the event, using FDA Form 3500 (for information on how to access this form, see below). The FDA requires that such reports, using FDA Form 3500, include the following:

    - Patient demographics and baseline characteristics (e.g., patient identifier, age or date of birth, gender, weight, ethnicity, and race)
    - A statement "Baricitinib use for COVID-19 under Emergency Use Authorization (EUA)" under the "Describe Event, Problem, or Product Use/Medication Error" heading
    - Information about the serious adverse event or medication error (e.g., signs and symptoms, test/laboratory data, complications, timing of drug initiation in relation to the occurrence of the event, duration of the event, treatments required to mitigate the event, evidence of event improvement/disappearance after stopping or reducing the dosage, evidence of event reappearance after reintroduction, clinical outcomes).
    - Patient's preexisting medical conditions and use of concomitant products
    - Information about the product (e.g., dosage, route of administration, NDC #).

    Submit adverse event and medication error reports, using Form 3500, to FDA MedWatch using one of the following methods:
        - Complete and submit the report online: www.fda.gov/medwatch/report.htm
        - Complete and submit a postage-paid Form FDA 3500 (https://www.fda.gov/media/76299/download) and return by:

        - Mail to MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787, or
        - Fax (1-800-FDA-0178), or
    - Call 1-800-FDA-1088 to request a reporting form.

In addition, please provide a copy of all FDA MedWatch forms to:
Eli Lilly and Company, Global Patient Safety
Fax: 1-317-277-0853
E-mail: mailindata_gsmtindy@lilly.com
Or call Eli Lilly and Company at 1-855-LillyC19 (1-855-545-5921) to report adverse events.

The prescribing healthcare provider and/or the provider's designee is/are responsible for mandatory responses to requests from FDA for information about adverse events and medication errors following receipt of baricitinib.

*Serious Adverse Events are defined as:

- Death;
- A life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- A congenital anomaly/birth defect;
- Other important medical event, which may require a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly.

APPROVED AVAILABLE ALTERNATIVES

Veklury (remdesivir) is FDA-approved for the treatment of COVID-19 in adults and 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. Veklury is administered via intravenous infusion for a total treatment duration of 3-5 days. 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.

Additional information on COVID-19 treatments can be found at https://www.cdc.gov/coronavirus/2019-ncov/index.html. The healthcare provider should visit https://clinicaltrials.gov/ to determine whether the patient may be eligible for enrollment in a clinical trial.

JUSTIFICATION FOR EMERGENCY USE OF DRUGS DURING THE COVID-19 PANDEMIC

There is currently an outbreak of Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV2, a novel coronavirus. The Secretary of HHS has declared that:

- A public health emergency related to COVID-19 has existed since January 27, 2020.
- Circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic (March 27, 2020 declaration).

An EUA is a FDA authorization for the emergency use of an unapproved product or unapproved use of an approved product (i.e., drug, biological product, or device) in the United States under certain circumstances including, but not limited to, when the Secretary of HHS declares that there is a public health emergency that affects the national security or the health and security of United States citizens living abroad, and that involves biological agent(s) or a disease or condition that may be attributable to such agent(s). Criteria for issuing an EUA include:

- The biological agent(s) can cause a serious or life-threatening disease or condition;
- Based on the totality of the available scientific evidence (including data from adequate and well-controlled clinical trials, if available), it is reasonable to believe that
    - the product may be effective in diagnosing, treating, or preventing the serious or life-threatening disease or condition; and
    - the known and potential benefits of the product - when used to diagnose, prevent, or treat such disease or condition - outweigh the known and potential risks of the product, taking into consideration the material threat posed by the biological agent(s);
- There is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating the serious or life-threatening disease or condition.

CONTACT INFORMATION

If you have questions, please contact:
1-855-LillyC19 (1-855-545-5921)
For additional information visit:
www.baricitinibemergencyuse.com

END FACT SHEET

Revised May 2022

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A3.0-BAR-NL0004-EUA HCP-YYYYMMDD