Frequently Asked Questions on the Emergency Use Authorization for Olumiant (baricitinib) in Combination with Veklury (remdesivir) for Treatment of Mild to Moderate COVID-19

Q. What is the difference between an Emergency Use Authorization (EUA) and an FDA approval?
A. Under section 564 of the Federal Food, Drug & Cosmetic Act (FD&C Act), the FDA may, pursuant to a determination and declaration by the HHS Secretary, authorize an unapproved product or unapproved uses of an approved product for emergency use. In issuing an EUA, the FDA must determine, among other things, that the product may be effective in diagnosing, treating, or preventing a serious or life-threatening disease or condition caused by a chemical, biological, radiological, or nuclear agent; that the known and potential benefits of the product, when used to diagnose, treat, or prevent such diseases or conditions, outweigh the known and potential risks for the product; and that there are no adequate, approved, and available alternatives. Emergency use authorization is NOT the same as FDA approval or licensure.

FDA approves New Drug Applications (NDAs) under section 505(c) of the FD&C Act. The NDA is the vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical that is not a biologic for sale and marketing in the U.S. In approving an NDA, FDA reviewers must determine, among other things, that the drug is safe and effective for its labeled use(s), and that the benefits of the drug outweigh the risks; that the drug's labeling (package insert) is appropriate; and that the methods used in manufacturing the drug and the controls used to maintain the drug's quality are adequate to preserve the drug's identity, strength, quality, and purity. The statutory standard for an NDA approval requires substantial evidence of effectiveness, which is a higher level of evidence of effectiveness than required for an EUA.

Q. What does this EUA authorize?
A. The EUA authorizes Olumiant (baricitinib), manufactured by Eli Lilly and Company (Lilly), for emergency use by healthcare providers, in combination with Veklury (remdesivir), for the treatment of suspected or laboratory-confirmed COVID-19 in hospitalized adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

Q. Is Olumiant approved by the FDA to treat COVID-19?
A. No. Olumiant is not FDA-approved for the treatment of COVID-19.

Olumiant is currently FDA-approved for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more tumor necrosis factor (TNF) antagonist therapies. FDA has determined Olumiant is safe and effective for this use when used in accordance with the FDA-approved labeling.

Q. Can Olumiant be used outside the hospital (i.e., for non-hospitalized patients)?
A. Under the EUA, Olumiant is authorized for emergency use, in combination with Veklury to treat certain hospitalized adults and pediatric patients with suspected or laboratory-confirmed COVID-19. The Letter of Authorization clarifies that individuals determined as being appropriate for acute inpatient hospitalization and who are admitted or transferred to an alternate care site (ACS) that is capable of providing acute care that is comparable to general inpatient hospital care are within the terms and

conditions of the EUA. An ACS is intended to provide additional hospital surge capacity and capability for communities overwhelmed by patients with COVID-19.

Q. Are there data showing Olumiant in combination with Veklury might benefit patients with COVID-19?

A. The data supporting this EUA are based primarily on analysis from the Adaptive COVID-19 Treatment Trial 2 (ACTT-2) study in hospitalized adults diagnosed with COVID-19. ACTT-2 was a randomized, double-blind, placebo-controlled clinical trial in hospitalized patients with mild, moderate and severe COVID-19 who received Olumiant plus Veklury or a placebo plus Veklury. Patients treated with the Olumiant plus Veklury combination received the following regimen:

- Olumiant 4 mg once daily (orally) for 14 days or until hospital discharge
- Veklury 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

The primary endpoint was time to recovery within 29 days. 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.

The study met its primary endpoint. The median time to recovery from COVID-19 was 7 days for Olumiant plus Veklury and 8 days for placebo plus Veklury. The hazard ratio of 1.15 and 95% confidence interval of (1.00, 1.31) indicated a statistically significant effect. The odds of clinical improvement at Day 15 was also higher in the Olumiant plus Veklury group versus the placebo plus Veklury group. The effects were statistically significant.

The odds of patient progression to death or ventilation at Day 29 was lower in the Olumiant plus Veklury group versus the placebo plus Veklury group. The proportion of patients who died or progressed to noninvasive ventilation/high-flow oxygen or invasive mechanical ventilation by Day 29 was lower in the Olumiant plus Veklury group (23%) compared to the placebo plus Veklury group (28%). The effects were statistically significant. The overall 29-day mortality was 4.7% for the Olumiant plus Veklury group vs. 7.1% for placebo plus Veklury group.

Based on the totality of the scientific evidence available, FDA determined that it is reasonable to believe that Olumiant in combination with Veklury may be effective for the treatment of mild to moderate COVID-19 in adults and pediatric patients 2 years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or ECMO.

Q. Are there clinical trials underway evaluating Olumiant for COVID-19?

A. Yes. Clinical trials remain ongoing to study Olumiant for investigational uses.

Q. Are side effects possible with Olumiant?

A. Yes. Possible side effects of Olumiant are:

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

Olumiant. Olumiant is not recommended for patients with known active tuberculosis infections, who are on dialysis, have end-stage renal disease, or have acute kidney injury.
- See Warnings and Precautions in the FDA-approved full prescribing information for additional information on risks associated with longer-term treatment with Olumiant.

Q. How can Olumiant for use under the EUA and Veklury be obtained?
A. Lilly and its authorized distributors distribute Olumiant to hospitals and healthcare facilities for its authorized use under the EUA. Licensed healthcare providers interested in administering Olumiant should contact Lilly.

Licensed healthcare providers interested in administering Veklury should contact Gilead. Veklury is an FDA-approved intravenous antiviral drug for use in adult and pediatric patients 12 years of age and older and weighing at least 40 kilograms (about 88 pounds) for the treatment of COVID-19 requiring hospitalization. Veklury also remains authorized for emergency use for the treatment of suspected or laboratory-confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg (about 7.7 pounds) to less than 40 kg or hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg.

Q. Is there a requirement for providers to report side effects as part of the EUA?
A. Yes. As part of the EUA, FDA is requiring health care providers who prescribe Olumiant in combination with Veklury to treat COVID-19 to report all medication errors and serious adverse events considered to be potentially related to Olumiant and Veklury through FDA's MedWatch Adverse Event Reporting program. Providers can complete and submit the report online; or download and complete the form, then submit it via fax at 1-800-FDA-0178. This requirement is outlined in the EUA's health care provider fact sheet. FDA MedWatch forms should also be provided to Lilly.

Q. Do patient outcomes need to be reported under the EUA?
A. No, reporting of patient outcomes is not required under the EUA. However, reporting of all medication errors and adverse events considered to be potentially related to the emergency use of Olumiant occurring during treatment is required.

Q. Does the EUA authorize Olumiant in combination with Veklury to be used to prevent COVID-19?
A. No. The EUA for Olumiant does not authorize the emergency use of Olumiant, either alone or in combination with Veklury, for the prevention of COVID-19.

Q. Can health care providers share the patient/caregiver Fact Sheet electronically?
A. The letter of authorization for Olumiant in combination with Veklury requires that Fact Sheets be made available to healthcare providers and to patients/caregivers, "through appropriate means." Electronic delivery of the Fact Sheet is an appropriate means. For example, when the patient requests the Fact Sheet electronically, it can be delivered as a PDF prior to medication administration. Health care providers should confirm receipt of the Fact Sheet with the patient.