Frequently Asked Questions for Veklury (remdesivir)

Q. Is Veklury (remdesivir) approved by the FDA to treat COVID-19?
A. On October 22, 2020, FDA approved Veklury (remdesivir) for use in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) for the treatment of COVID-19 requiring hospitalization. Veklury should only be administered in a hospital or in a healthcare setting capable of providing acute care comparable to inpatient hospital care.

Q. Is Veklury approved for use in pediatric patients?
A. Veklury is approved for certain pediatric patients, specifically for use in pediatric patients (12 years of age and older and weighing at least 40 kg) for the treatment of COVID-19 requiring hospitalization. Veklury should only be administered in a hospital or in a healthcare setting capable of providing acute care comparable to inpatient hospital care. For additional information on the approved uses for Veklury, refer to the Prescribing Information.

While not FDA-approved, the Emergency Use Authorization (EUA) for Veklury continues to authorize Veklury for emergency use by licensed healthcare providers for the treatment of suspected or laboratory-confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg ***or*** hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg. For additional information on the authorized use of Veklury under the EUA, refer to the Fact Sheet for Healthcare Providers.

Clinical trials assessing the safe and effective use of Veklury in pediatric populations remain ongoing.

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 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. EUAs do not remain in effect indefinitely and FDA will consider whether a sponsor is working towards seeking FDA approval when evaluating the continued appropriateness of the EUA.

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[1] 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.

[1] Biologics are approved upon submission and review of a biologic license application (BLA).

Q. What does the EUA for Veklury allow?
A. The EUA continues to authorize Veklury for injection (lyophilized powder), manufactured by Gilead, for emergency use by licensed healthcare providers to treat suspected or laboratory-confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg ***or*** hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg.

Q. How is the revised EUA for Veklury different than the EUA initially granted on May 1, 2020 and the revision on August 28, 2020?
A. On May 1, 2020, FDA granted Gilead's EUA request authorizing Veklury for emergency use by licensed healthcare providers to treat suspected or laboratory-confirmed COVID-19 in hospitalized adult and pediatric patients with severe disease. When initially granted, the EUA limited the authorization of Veklury to hospitalized adult and pediatric patients with severe disease, which was defined as patients with low blood oxygen levels or needing oxygen therapy or more intensive breathing support such as a mechanical ventilator.

On August 28, 2020, FDA revised the EUA for Veklury to broaden the scope of its authorized uses. Under the revised EUA, Veklury was authorized for emergency use by licensed healthcare providers for the treatment of suspected or laboratory-confirmed COVID-19 in all hospitalized adult and pediatric patients, irrespective of their severity of disease.

On October 22, 2020, FDA approved Gilead's New Drug Application (NDA) for Veklury for use in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) for the treatment of COVID-19 requiring hospitalization. Veklury should only be administered in a hospital or in a healthcare setting capable of providing acute care comparable to inpatient hospital care. This approval does not include pediatric patients weighing 3.5 kg to less than 40 kg ***or*** pediatric patients less than 12 years of age. Clinical trials assessing the safety and efficacy of Veklury in the pediatric patient population remain ongoing.

On October 22, 2020, FDA revised the EUA for Veklury to remove those uses that are now approved under Gilead's NDA. The EUA for Veklury continues to authorize Veklury for emergency use by licensed healthcare providers for the treatment of suspected or laboratory-confirmed COVID-19 in hospitalized pediatric patients weighing 3.5 kg to less than 40 kg ***or*** hospitalized pediatric patients less than 12 years of age weighing at least 3.5 kg.

Q. What data supports FDA's determination that Veklury is safe and effective for use in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) for the treatment of COVID-19 requiring hospitalization?
A. Full information regarding the data and evidence used to approve Veklury can be found in the "Combined Cross-Discipline Team Leader, Division Director, and ODE Director Summary Review."

Based on FDA's analysis of the scientific data included in Gilead's NDA, including data from three randomized, controlled clinical trials, FDA approved Veklury for use in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) for the treatment of COVID-19 requiring hospitalization. Veklury should only be administered in a hospital or in a healthcare setting capable of providing acute care comparable to inpatient hospital care. The agency concluded that the data met all

applicable scientific and legal standards and demonstrated that Veklury is safe and effective for the approved use.

Q. What did FDA do to facilitate the development and expedite the review of Veklury?
A. On March 26, 2020, FDA granted Fast Track designation to Gilead for Veklury, which among other things, maximizes the opportunities for Gilead to engage with the Agency on its development of Veklury, for the treatment of COVID-19.

Based on this designation, on April 6, 2020, FDA granted Gilead's request and accepted its proposal to allow for a rolling review of its development program for Veklury. Under this process, Gilead could submit and FDA reviewed sections of Gilead's New Drug Application (NDA) for Veklury as they arrived. Under traditional processes, FDA's review of an NDA does not begin until the sponsor has submitted the entire application to the Agency.

In August 2020, Gilead announced publicly the submission of their New Drug Application (NDA) for Veklury for the treatment of COVID-19. See https://www.gilead.com/news-and-press/press-room/press-releases/2020/8/gilead-submits-new-drug-application-to-us-food-and-drug-administration-for-veklury-remdesivir-for-the-treatment-of-covid19

On October 22, 2020, 76 days after receiving Gilead's NDA for Veklury, FDA approved the drug Veklury for use in adults and pediatric patients (12 years of age and older and weighing at least 40 kg) for the treatment of COVID-19 requiring hospitalization. Veklury should only be administered in a hospital or in a healthcare setting capable of providing acute care comparable to inpatient hospital care.

Q. Are there side effects of Veklury?
A. Possible side effects of Veklury are:

- Hypersensitivity reactions, including infusion-related and anaphylactic reactions. Hypersensitivity reactions, including infusion-related and anaphylactic reactions, have been seen during a Veklury infusion or around the time Veklury was given. Signs and symptoms may include: changes in blood pressure and heart rate, low blood oxygen level, fever, shortness of breath, wheezing, swelling (e.g. lips, around the eyes, under the skin), rash, nausea, sweating, and shivering.
- Increases in levels of liver enzymes, seen in liver blood tests. Increases in levels of liver enzymes have been seen in people who have received Veklury, which may be a sign of liver injury.

These are not all the possible side effects of Veklury. Because all possible side effects of a drug can't be anticipated based on preapproval studies, FDA maintains a system of postmarketing surveillance and risk assessment programs to identify adverse events that did not appear during the drug approval process.

Q. How can Veklury be obtained for use?
A. As of October 1, 2020, the United States Government no longer directs the allocation of Veklury. Gilead and its authorized distributors distribute Veklury to hospitals and healthcare facilities for use. Licensed healthcare providers interested in administering Veklury should contact Gilead.

Q. Is a supply of Veklury available immediately for the approved use?
A. FDA does not intend to object to the continuing distribution of Veklury 100 mg injection lyophilized powder and Veklury 100 mg/20 mL injection solution that are labeled with the statement *"For use under*

Emergency Use Authorization" after FDA approval of Gilead's NDA. However, FDA's discretion is limited to a six-month period starting from the date of the Veklury approval.

FDA's regulatory discretion is contingent on a Dear Healthcare Provider accompanying distribution of Veklury to ensure patient safety. Please see Gilead's Dear Healthcare Provider Letter for more information.

Q. Can Veklury be used outside the hospital (i.e., for non-hospitalized patients)?
A. Veklury should only be administered in a hospital or in a healthcare setting capable of providing acute care comparable to inpatient hospital care.

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 Veklury to report all medication errors and serious adverse events considered to be potentially related to 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 Gilead.

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 serious adverse events considered to be potentially related to Veklury occurring during Veklury treatment is required.

Q. Can Veklury be used to prevent COVID-19?
A. The safety and efficacy of Veklury for the prevention of COVID-19 have not been established and it is not FDA-approved for this use.

Q. Why is there a warning about drug interactions between hydroxychloroquine sulfate/chloroquine phosphate and Veklury in the healthcare provider Fact Sheet and Veklury's prescribing information?
A. Laboratory testing was conducted that raised serious concerns about a risk of reduced antiviral activity for Veklury when Veklury is co-administered with chloroquine phosphate (CQ) or hydroxychloroquine sulfate (HCQ). This means there is the potential for Veklury to not work as well to treat COVID-19 when it is taken with CQ/HCQ. Although further testing needs to be done, FDA has determined that the data are sufficient to warn health care providers, and FDA recommends against administering the drugs together.

Q. What if I take hydroxychloroquine sulfate for a chronic condition? Does this mean I should not take Veklury?
A. There is the potential for Veklury to not work as well to treat COVID-19 when it is taken with hydroxychloroquine sulfate (HCQ) or chloroquine phosphate (CQ). FDA recommends against taking the drugs together. If you are taking HCQ or CQ, discuss your options and specific situation with your health care provider.

Q. How is the SOLIDARITY clinical trial different than the clinical trials supporting FDA's approval of Veklury (remdesivir)?

A. The approval of Veklury was supported by the agency's independent, in-depth analysis of data from three randomized, controlled clinical trials that included patients hospitalized with mild-to-severe COVID-19. This included the ACTT-1 trial sponsored by National Institute of Allergy and Infectious Disease (NIAID) and the "SIMPLE" trials sponsored by Gilead Sciences Inc. The most compelling evidence of effectiveness was provided by the NIAID-sponored ACTT-1 trial, with its rigorous trial design.

The ACTT-1 trial was a randomized, placebo-controlled, double-blinded trial in hospitalized subjects with mild, moderate and severe COVID-19 who received Veklury or placebo, plus standard of care. The primary goal of the ACTT-1 trial was to look at the time to recovery of hospitalized patients. Recovery was defined as either being discharged from the hospital or being hospitalized but not requiring supplemental oxygen and no longer requiring ongoing medical care. The median time to recovery from COVID-19 was 10 days for the Veklury group compared to 15 days for the placebo group, a strongly statistically significant difference. The odds of clinical improvement at Day 15 were also statistically significantly higher in the Veklury group when compared to the placebo group. The overall 29-day mortality was 11% for the Veklury group vs 15% for the placebo group; this difference was not statistically significant.

FDA's review of the scientific evidence from the ACTT-1 trial, combined with its review of the "SIMPLE" trials sponsored by Gilead Sciences Inc., supported the Agency's determination that the standard for substantial evidence of effectiveness and demonstration of safety as required for new drug approval was met.

The SOLIDARITY trial was a World Health Organization-sponsored, open-label, randomized trial comparing different investigational interventions plus standard-of-care to standard-of-care alone in hospitalized patients with COVID-19. One of the drugs studied in SOLIDARITY was Veklury. The SOLIDARITY trial's primary goal was to assess for effects of treatment interventions on in-hospital mortality. The SOLIDARITY trial did not find a statistically significant difference in mortality between the Veklury arm and the standard-of-care arm.

While both the SOLIDARITY trial and the ACTT-1 trial contribute to our understanding of interventions to help treat COVID-19, the two clinical trials had different trial designs and primary goals. The design of ACTT-1 (i.e., randomized, placebo-controlled, double-blinded) was better suited to rigorously assess a time to recovery endpoint compared to a trial with an open-label design, such as the SOLIDARITY trial. Based on the findings of the ACTT-1 trial, benefit to patients for Veklury was demonstrated including a shorter time to recovery and better odds of clinical improvement. The SOLIDARITY results do not refute these findings of benefit to patients.

Q. Can health care providers share the patient/caregiver Fact Sheet electronically?

A. The letter of authorization for 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 it electronically, the Fact Sheet is delivered as a PDF (not a URL), and the patient is able to obtain access to the electronic version prior to receiving the medicine. Additionally, health care providers should confirm receipt of the fact sheet with the patient. Paper copies must be available for patients who request them.

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