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IMPORTANT PRESCRIBING INFORMATION

Subject: **Updated Emergency Use Authorization (EUA) for treatment of coronavirus disease 2019 (COVID-19) in pediatric patients weighing 3.5 kg to less than 40 kg or pediatric patients less than 12 years of age weighing at least 3.5 kg with positive results of direct severe acute respiratory syndrome coronavirus 2 (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, and variations in carton and vial labeling of VEKLURY® (remdesivir)**

Dear Healthcare Provider:

Gilead Sciences, Inc., would like to clarify the appropriate use and the variable packaging and labeling of the antiviral **VEKLURY® (remdesivir)**.

Gilead's remdesivir (brand name VEKLURY) was approved by the US Food and Drug Administration (FDA) on January 21, 2022 for adults and pediatric patients (12 years of age and older and weighing at least 40 kg) for the treatment of coronavirus disease 2019 (COVID-19) with positive results of direct severe acute respiratory syndrome coronavirus 2 (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.

Healthcare providers should administer VEKLURY in these patients per the current US Prescribing Information available at www.gilead.com/science-and-medicine/medicines; please also see Important Safety Information at the end of this letter.

Emergency use of Gilead's remdesivir (brand name VEKLURY) for treatment of COVID-19 in pediatric patients weighing 3.5 kg to less than 40 kg or pediatric patients less than 12 years of age weighing at least 3.5 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.

On January 21, 2022, FDA revised the Emergency Use Authorization (EUA) for VEKLURY, which now authorizes VEKLURY for use by healthcare providers to treat COVID-19 in pediatric patients weighing 3.5 kg to less than 40 kg or pediatric patients less than 12 years of age weighing at least 3.5 kg with positive results of direct SARS-CoV-2 viral testing, who are: hospitalized, or not hospitalized and have mild-to-

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moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death. Only Gilead's VEKLURY (remdesivir) for injection (supplied as 100 mg lyophilized powder in vial) is authorized for emergency use under the terms and conditions set forth in the Letter of Authorization for the EUA.

The safety and efficacy of VEKLURY to treat COVID-19 in pediatric patients weighing 3.5 kg to less than 40 kg or pediatric patients less than 12 years of age weighing at least 3.5 kg with positive results of direct SARS-CoV-2 viral testing has not been established, and VEKLURY is not FDA approved for this use. For information about the authorized use of VEKLURY in pediatric patients weighing 3.5 kg to less than 40 kg or pediatric patients less than 12 years of age weighing at least 3.5 kg, including dosing, administration, and preparation instructions, please review the EUA Fact Sheet for Healthcare Providers and FDA Letter of Authorization available at www.gilead.com/remdesivir.

Variations in packaging and labeling of Gilead's remdesivir (brand name VEKLURY)

Gilead's VEKLURY (remdesivir) has been manufactured for use under an EUA, and for commercial use. As such, VEKLURY has different packaging, labeling, and expiration dates depending on the date of manufacture. Packaging and labeling for Gilead's remdesivir EUA use may not necessarily include the brand name, VEKLURY.

To help avoid potential drug shortage, hospitals should continue to use all unexpired, unopened vials of Gilead's remdesivir – whether or not the vial includes the brand name VEKLURY or is labeled for use under EUA. Refer to the attached chart at the end of this letter that outlines what hospitals should do with unexpired, unopened vials of Gilead's remdesivir.

Authentic VEKLURY or remdesivir, manufactured by Gilead Sciences, Inc., will include the GILEAD name and logo on the carton and vial label. All packaging includes the drug name remdesivir. Current packaging variations for the two formulations are described below. Both formulations are for intravenous infusion only.

- **VEKLURY® (remdesivir) for injection (supplied as 100 mg lyophilized powder in vial).** The lyophilized powder formulation is always supplied with a red cap and the package and labeling may be marked "for use under Emergency Use Authorization (EUA)".

- **VEKLURY® (remdesivir) injection (supplied as 100 mg/20 mL [5 mg/mL], solution in vial).** The solution formulation is supplied with a blue cap and the package and labeling may be marked "for use under Emergency Use Authorization (EUA)". **The solution should only be used in adults and pediatric patients 12 years of age and older and weighing at least 40 kg**.

Veklury (remdesivir) injection (solution; left) and Veklury (remdesivir) for injection (lyophilized powder; right) now approved by FDA for use in accordance with the prescribing information (PI).

Veklury (remdesivir) injection (solution; left) and Veklury (remdesivir) for injection (lyophilized powder; right) previously authorized for emergency use.

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Reporting Adverse Events and Medication Errors

Healthcare providers should direct questions on VEKLURY packaging or use to Gilead Sciences at 1-866-633-4474 or www.askgileadmedical.com.

Under the Emergency Use Authorization, the prescribing healthcare provider and/or the provider's designee are/is responsible for mandatory reporting of all serious adverse events and medication errors potentially related to VEKLURY treatment within 7 calendar days from the healthcare provider's awareness of the event using FDA Form 3500. Healthcare providers must report all serious adverse events and medication errors to FDA when utilizing VEKLURY under the EUA in accordance with the Healthcare Provider Fact Sheet.

For additional information about VEKLURY, including the full Prescribing Information, please visit www.vekluryhcp.com.

Information and reports of suspicious, counterfeit, or unregistered remdesivir can be submitted to Gilead anticounterfeiting@gilead.com and/or www.fraud.org/fakerx.

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Appropriate use of Gilead's remdesivir (brand name VEKLURY), including vials labeled for Emergency Use Authorization (EUA) use		
Product	**Remdesivir for injection, 100 mg, lyophilized powder**	**Remdesivir injection, 100 mg/20 mL (5 mg/mL), solution**
Labeled "For use under Emergency Use Authorization (EUA)" (vials and cartons do not include the brand name, VEKLURY)	Continue use in: • Adults and pediatric patients (12 years of age and older and weighing at least 40 kg) requiring hospitalization or non-hospitalized patients with mild-to-moderate COVID-19 who are at high risk for progression to severe COVID-19, including hospitalization or death. • 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 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 **under the provisions of the Emergency Use Authorization (EUA) – Please review the EUA Fact Sheet for Healthcare Providers and FDA Letter of Authorization**, available at gilead.com/remdesivir.	Continue use in: • Adults and pediatric patients (12 years of age and older and weighing at least 40 kg) requiring hospitalization or non-hospitalized patients with mild-to-moderate COVID-19 who are at high risk for progression to severe COVID-19, including hospitalization or death.
FDA-approved VEKLURY (carton and vials will include the brand name, VEKLURY)	Use in: • Adults and pediatric patients (12 years of age and older and weighing at least 40 kg) requiring hospitalization or non-hospitalized patients with mild-to-moderate COVID-19 who are at high risk for progression to severe COVID-19, including hospitalization or death. • 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 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 **under the provisions of the Emergency Use Authorization (EUA) – Please review the EUA Fact Sheet for Healthcare Providers and FDA Letter of Authorization**, available at gilead.com/remdesivir.	Use in: • Adults and pediatric patients (12 years of age and older and weighing at least 40 kg) requiring hospitalization or non-hospitalized patients with mild-to-moderate COVID-19 who are at high risk for progression to severe COVID-19, including hospitalization or death.

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U.S. Indication and Important Safety Information for VEKLURY® (remdesivir)

Indication

VEKLURY is indicated for the treatment of COVID-19 in adults and pediatric patients ≥12 years old and weighing ≥40 kg with positive results of 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.

Important Safety Information

Contraindication

- VEKLURY is contraindicated in patients with a history of clinically significant hypersensitivity reactions to VEKLURY or any of its components.

Warnings and precautions

- **Hypersensitivity, including infusion-related and anaphylactic reactions:** Hypersensitivity, including infusion-related and anaphylactic reactions, has been observed during and following administration of VEKLURY; most occurred within 1 hour. Monitor patients during infusion and observe for at least 1 hour after infusion is complete for signs and symptoms of hypersensitivity as clinically appropriate. Symptoms may include hypotension, hypertension, tachycardia, bradycardia, hypoxia, fever, dyspnea, wheezing, angioedema, rash, nausea, diaphoresis, and shivering. Slower infusion rates (maximum infusion time of up to120 minutes) can potentially prevent these reactions. If a severe infusion-related hypersensitivity reaction occurs, immediately discontinue VEKLURY and initiate appropriate treatment (see Contraindications).
- **Increased risk of transaminase elevations:** Transaminase elevations have been observed in healthy volunteers and in patients with COVID-19 who received VEKLURY; these elevations have also been reported as a clinical feature of COVID-19. Perform hepatic laboratory testing in all patients (see Dosage and administration). Consider discontinuing VEKLURY if ALT levels increase to >10x ULN. Discontinue VEKLURY if ALT elevation is accompanied by signs or symptoms of liver inflammation.
- **Risk of reduced antiviral activity when coadministered with chloroquine or hydroxychloroquine:** Coadministration of VEKLURY with chloroquine phosphate or hydroxychloroquine sulfate is not recommended based on data from cell culture experiments, demonstrating potential antagonism, which may lead to a decrease in the antiviral activity of VEKLURY.

Adverse reactions

- The most common adverse reaction (≥5% all grades) was nausea.
- The most common lab abnormalities (≥5% all grades) were increases in ALT and AST.

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Drug interactions

- Drug interaction trials of VEKLURY and other concomitant medications have not been conducted in humans.

Dosage and administration

- **Dosage:** For adults and pediatric patients ≥12 years old and weighing ≥40 kg: 200 mg on Day 1, followed by once-daily maintenance doses of 100 mg from Day 2 administered only via intravenous infusion. VEKLURY should be initiated as soon as possible after diagnosis of symptomatic COVID-19.
- **Treatment duration:**
  - For hospitalized patients requiring invasive mechanical ventilation and/or ECMO, the recommended total treatment duration is 10 days.
  - For hospitalized patients not requiring invasive mechanical ventilation and/or ECMO, the recommended treatment duration is 5 days. If a patient does not demonstrate clinical improvement, treatment may be extended for up to 5 additional days, for a total treatment duration of up to 10 days.
  - For non-hospitalized patients diagnosed with mild-to-moderate COVID-19 who are at high risk for progression to severe COVID-19, including hospitalization or death, the recommended total treatment duration is 3 days.
- **Testing prior to and during treatment:** Perform eGFR, hepatic laboratory, and prothrombin time testing prior to initiating VEKLURY and during use as clinically appropriate.
- **Renal impairment:** VEKLURY is not recommended in individuals with eGFR <30 mL/min.
- **Dose preparation and administration:** See full Prescribing Information.

Pregnancy and lactation

- **Pregnancy:** A pregnancy registry has been established. There are insufficient human data on the use of VEKLURY during pregnancy. COVID-19 is associated with adverse maternal and fetal outcomes, including preeclampsia, eclampsia, preterm birth, premature rupture of membranes, venous thromboembolic disease, and fetal death.
- **Lactation:** It is not known whether VEKLURY can pass into breast milk. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

Please see full Prescribing Information for VEKLURY, available at www.gilead.com.