Veklury® remdesivir 100 MG FOR INJECTION

GUIDE FOR HEALTHCARE PROFESSIONALS

VEKLURY initiation in the outpatient setting

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 not hospitalized, 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.

Please see full Prescribing Information for VEKLURY.

Contents

IMPORTANT SAFETY INFORMATION (cont'd)

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 to 120 minutes) can potentially prevent these reactions. If a severe infusion-related hypersensitivity reaction occurs, immediately discontinue VEKLURY and initiate appropriate treatment (see Contraindications).

HCPCS=Healthcare Common Procedure Coding System.

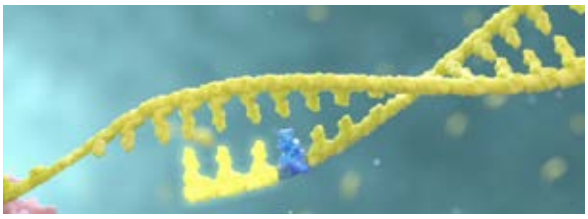
About VEKLURY

What is VEKLURY?

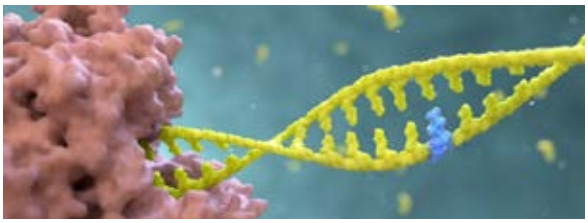
VEKLURY is an antiviral medication that directly inhibits viral replication of SARS-CoV-2. As a SARS-CoV-2 nucleotide analog, VEKLURY acts inside the cell to inhibit the viral RNA-dependent RNA polymerase (RdRp), which is essential for viral replication.[1,2]

Mechanism of action

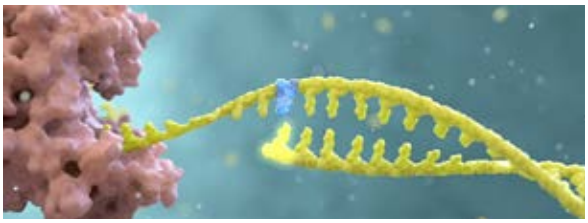
1. VEKLURY is a prodrug that distributes into cells where it is metabolized into the pharmacologically active remdesivir triphosphate (RDV-TP).[1,2]



2. RDV-TP acts as an analog of ATP and competes with it for incorporation into nascent SARS-CoV-2 viral RNA. This results in delayed chain termination (position i+3) and disruption of viral replication.[1,2]



3. At higher nucleotide concentrations, RDV-TP can also inhibit SARS-CoV-2 RNA synthesis after it has been incorporated into the viral RNA template as a result of read-through by the viral polymerase.[1,2]



4. The presence of the remdesivir nucleotide in the viral RNA template compromises the ability of the complementary natural nucleotide to be incorporated, thereby inhibiting viral RNA synthesis.[1,2]

Take a closer look at the mechanism of action video for VEKLURY.

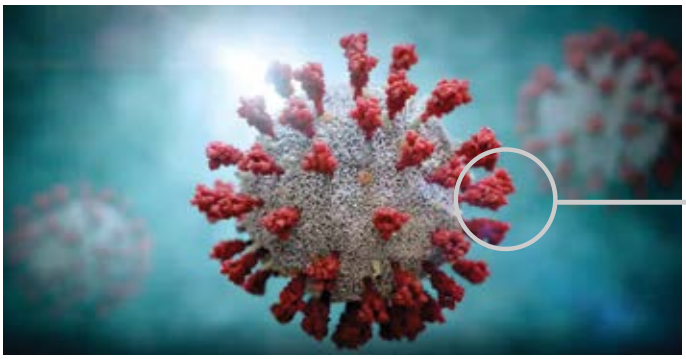
IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and precautions (cont'd)

- **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.

ATP=adenosine triphosphate.

Does VEKLURY retain antiviral activity against SARS-CoV-2 variants?



To date, known novel virus variants show mutations at different locations in the SARS-CoV-2 spike protein, which is on the outer surface of the virus and can cause decreased affinity of the anti–SARS-CoV-2 antibodies.[3-5]

No known SARS-CoV-2 variants have significantly altered the viral RNA polymerase.[6,7]

The antiviral activity of VEKLURY has been tested in vitro against clinical isolates of SARS-CoV-2 variants, including Alpha, Beta, Gamma, Delta, Epsilon, and Omicron. These laboratory findings demonstrated that the antiviral activity of VEKLURY against these variants is not reduced.[1,6]

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and precautions (cont'd)

- **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.

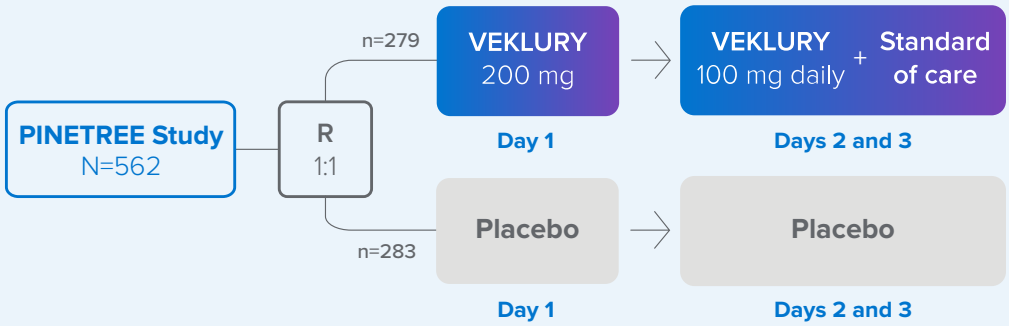
What study supports the use of VEKLURY in the outpatient setting?

PINETREE phase 3 trial (GS-US-540-9012)[1,8]

PINETREE was a randomized, double-blind, placebo-controlled clinical trial involving patients who were not hospitalized, had confirmed positive results for SARS-CoV-2 infection, showed symptoms of mild-to-moderate COVID-19 for ≤7 days, and had at least 1 risk factor for progression to hospitalization.

Risk factors for progression to hospitalization included age ≥60 years, obesity (BMI ≥30 kg/m^2), chronic lung disease, hypertension, cardiovascular or cerebrovascular disease, diabetes mellitus, immunocompromised state, chronic mild or moderate kidney disease, chronic liver disease, current cancer, and sickle cell disease.

Patients who received, required, or were expected to require supplemental oxygen were excluded from the trial.



Primary endpoints

The primary efficacy endpoint was a composite of COVID-19–related hospitalization (defined as ≥24 hours of acute care) or death from any cause by Day 28.

The primary safety endpoint was any adverse event.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

R=randomization.

What study supports the use of VEKLURY in the outpatient setting? (cont'd)

Baseline characteristics[8]

Demographic and baseline clinical characteristics were balanced between the two groups.

Characteristic	VEKLURY (n=279)	Placebo (n=283)
Median age ± SD	50±15	51±15
Age category, n (%)		
≥60 y	83 (29.7)	87 (30.7)
<18 y	3 (1.1)	5 (1.8)
Female sex, n (%)	131 (47.0)	138 (48.8)
Residence in the United States, n (%)	264 (94.6)	267 (94.3)
Race or ethnic group, n (%)*		
White	228 (81.7)	224 (79.2)
Black	20 (7.2)	22 (7.8)
American Indian or Alaska Native	15 (5.4)	21 (7.4)
Asian, Native Hawaiian, or Pacific Islander	7 (2.5)	7 (2.5)
Hispanic or Latinx	123 (44.1)	112 (39.6)
Other	3 (1.1)	2 (0.7)
Body mass index	31.2±6.7	30.8±5.8
Coexisting conditions, n (%)		
Diabetes mellitus	173 (62.0)	173 (61.1)
Obesity	154 (55.2)	156 (55.1)
Hypertension	138 (49.5)	130 (45.9)
Chronic lung disease	67 (24.0)	68 (24.0)
Current cancer	12 (4.3)	18 (6.4)
Cardiovascular or cerebrovascular disease	20 (7.2)	24 (8.5)
Immune compromise	14 (5.0)	9 (3.2)
Chronic kidney disease, mild or moderate	7 (2.5)	11 (3.9)
Chronic liver disease	1 (0.4)	1 (0.4)
Residence in skilled nursing facility, n (%)	8 (2.9)	7 (2.5)
Median duration of symptoms before first infusion (IQR), days	5 (3-6)	5 (4-6)
Median time since RT-PCR confirmation of SARS-CoV-2 (IQR), days	2 (1-3)	3 (1-4)

*Race and ethnic group were reported by the patients. Patients could have had more than 1 race or ethnic group.

IQR=interquartile range; RT-PCR=reverse transcription–polymerase chain reaction.

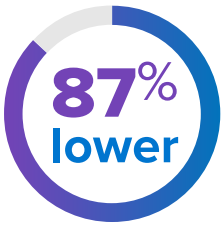
IMPORTANT SAFETY INFORMATION (cont'd)

Drug interactions

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

What study supports the use of VEKLURY in the outpatient setting? (cont'd)

VEKLURY reduced risk of progression to severe COVID-19[1,8]



risk of COVID-19–related hospitalization or death from any cause by Day 28 compared with placebo

- 0.7% of patients treated with VEKLURY compared to 5.3% of patients treated with placebo had a COVID-19–related hospitalization or death from any cause by Day 28; hazard ratio: 0.13, p=0.008
- No deaths were reported in either group by Day 28

The safety profiles of VEKLURY and placebo were comparable[1,8]

- The most common adverse reaction (≥5%) in patients taking VEKLURY was nausea

"Remdesivir is another important option for outpatients with COVID-19."[8]

— Gottlieb RL, et al. *N Engl J Med.* 2022;386(4):305-315.

Based on the PINETREE Study, the National Institutes of Health (NIH) added VEKLURY to the COVID-19 Treatment Guidelines as a therapeutic option for patients with mild-to-moderate COVID-19 who are not hospitalized but are at risk of disease progression, including hospitalization or death.[9]

Please see the NIH Guidelines for more information on Therapeutic Management of Nonhospitalized Adults With COVID-19.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

Considerations for treatment with VEKLURY

Who is considered at high risk of disease progression?

In the PINETREE Study, high risk was defined as being 12 years of age or older and having at least 1 risk factor associated with progression to hospitalization or death, as follows[8]:

Hypertension

Chronic lung disease

Cardiovascular or cerebrovascular disease

Diabetes mellitus

Obesity (BMI ≥30 kg/m²)

Immunocompromised state

Chronic mild or moderate kidney disease

Chronic liver disease

Current cancer

Sickle cell disease

All patients 60 years of age or older were considered at high risk

IMPORTANT SAFETY INFORMATION (cont'd)

Dosage and administration (cont'd)

- **Treatment duration:**
  - For patients who are not hospitalized, diagnosed with mild-to-moderate COVID-19, and are at high risk for progression to severe COVID-19, including hospitalization or death, the recommended total treatment duration is 3 days.

What should be considered before prescribing VEKLURY?

A center planning to administer VEKLURY in the outpatient setting should consider multiple factors before prescribing VEKLURY, including[1]:

For prescribing: Clinicians should be familiar with the contents of the VEKLURY Prescribing Information.
Please see full Prescribing Information for VEKLURY.

Requirements for ordering: Qualified nonhospital, outpatient facilities are those that have previously administered monoclonal antibodies or completed a certification through AmerisourceBergen Specialty Division.

Laboratory testing: Perform eGFR, hepatic laboratory, and prothrombin time testing prior to initiating VEKLURY and during use as clinically appropriate.

IV infusion: The center should have the ability to administer VEKLURY IV infusion for 3 consecutive days, have a designated location for infusion and postinfusion patient monitoring, and appropriate clinical staffing.

Adverse events management: The center should be able to manage any adverse events or reactions and provide additional medical care during or after the infusion, as needed.

IMPORTANT SAFETY INFORMATION (cont'd)

Dosage and administration (cont'd)

- **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.

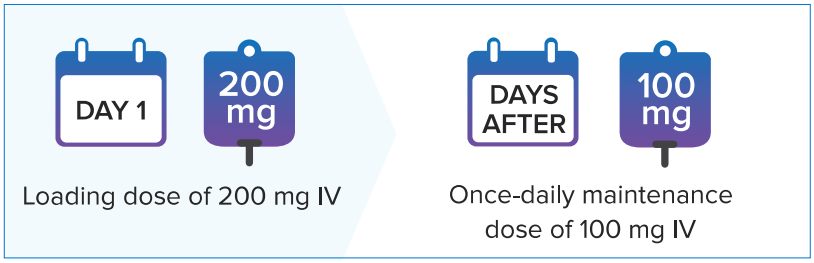
eGFR=estimated glomerular filtration rate.

Administration in the outpatient setting

What is the recommended dosage and total treatment duration?

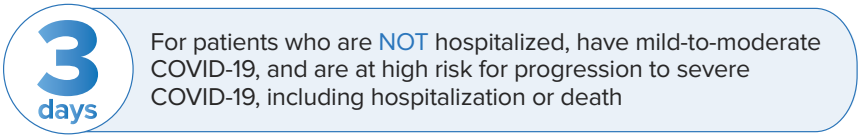
Recommended dosage[1]

The recommended dosage for adults and pediatric patients 12 years of age and older and weighing at least 40 kg is a single loading dose of **VEKLURY® (remdesivir) 200 mg on Day 1** followed by once-daily maintenance doses of **VEKLURY 100 mg on Days 2 and 3**. VEKLURY is administered via IV infusion.*



For nonhospitalized patients with COVID-19 who are at risk for disease progression, initiate VEKLURY as soon as possible.

Recommended total treatment duration[1]



*For dosing information for emergency use in nonhospitalized 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, please refer to the Emergency Use Authorization Fact Sheet for Healthcare Providers available at **gilead.com/remdesivir**.

IMPORTANT SAFETY INFORMATION (cont'd)

Dosage and administration (cont'd)

- **Dose preparation and administration:** See full **Prescribing Information**.

How long should infusions take, and for how long should patients be monitored?

The standard infusion time is 30–120 minutes.[1]

Monitor patients during infusion and observe patients for at least 1 hour after infusion is complete for signs and symptoms of hypersensitivity as clinically appropriate.[1]

If signs and symptoms of a clinically significant hypersensitivity reaction occur, immediately discontinue administration of VEKLURY® (remdesivir) and initiate appropriate treatment.[1]

The use of VEKLURY is contraindicated in patients with known hypersensitivity to VEKLURY or any components of the product.[1]

How do I administer VEKLURY?

VEKLURY may be administered only in settings in which healthcare providers have immediate access to medications to treat a severe infusion or hypersensitivity reaction, such as anaphylaxis, and the ability to activate the emergency medical system, as necessary.[1]

Administer VEKLURY for the treatment of COVID-19 in adults and pediatric patients who are 12 years of age and older and weighing at least 40 kg by IV infusion only. Do not administer by any other route.[1]

VEKLURY for injection, 100 mg lyophilized powder (red cap), must be reconstituted with 19 mL Sterile Water for Injection prior to diluting in a 100 mL or 250 mL 0.9% sodium chloride infusion bag.

Carefully follow the product-specific preparation instructions in the Prescribing Information for VEKLURY or visit vekluryhcp.com.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

Ordering and access information

How can I order VEKLURY?

Hospital ordering process

Hospitals can place orders with any of the following distributors by calling directly:

- AmerisourceBergen Specialty Distribution, 1-800-746-6273
- Cardinal Specialty, 1-855-855-0708
- McKesson Plasma, 1-877-625-2566

Nonhospital ordering process

Nonhospitals can contact AmerisourceBergen Specialty Distribution by calling 1-800-746-6273 or emailing C19therapies@AmerisourceBergen.com for more information.

What is the HCPCS code for VEKLURY in the outpatient setting?

On January 7, 2022, the Centers for Medicare & Medicaid Services assigned a permanent HCPCS code, **J0248**, for VEKLURY in the outpatient setting to help facilitate payment and simplify claims documentation and processing. This code is effective for dates of service on or after December 23, 2021.[10]

For more information, please see Coding and Reimbursement Information.

IMPORTANT SAFETY INFORMATION (cont'd)

Pregnancy and lactation (cont'd)

- **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.

HCPCS=Healthcare Common Procedure Coding System.

Does VEKLURY have a co-pay coupon program for commercially insured patients?

Beginning March 7, 2022, commercially insured patients may be eligible for the Gilead Advancing Access® co-pay program for VEKLURY. Restrictions apply. To enroll, patients should call the Advancing Access program at 1-800-226-2056. Phone lines are open M–F, 9 AM–8 PM ET. Voicemails may be left, and a program associate will return calls within the next business day.

Whom do I contact if I have additional questions?

Clinical inquiries may be directed to Gilead Medical Information at 1-866-633-4474.

For inquiries about access and coverage, please call the Advancing Access program at 1-800-226-2056 (Option 4), M–F, 9 AM–8 PM ET.

An Advancing Access program specialist is available for further assistance; you can also leave a confidential message any time and day of the week.

INDICATION

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IMPORTANT SAFETY INFORMATION

Contraindication

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

References

1. Veklury. Prescribing Information. Gilead Sciences, Inc.; 2022.
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10. Special edition. COVID-19: new HCPCS code for remdesivir antiviral medication. News release. Centers for Medicare & Medicaid Services. January 7, 2022. Accessed January 24, 2022. https://www.cms.gov/outreach-and-educationoutreachffsprovpartprogprovider-partnership-email-archive/2022-01-07-mlnc-se

Please see Important Safety Information within and full Prescribing Information.
For more information, visit vekluryhcp.com.