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 (≥28 days old and weighing ≥3 kg), who are:

- Hospitalized, or
- 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 reactions 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.

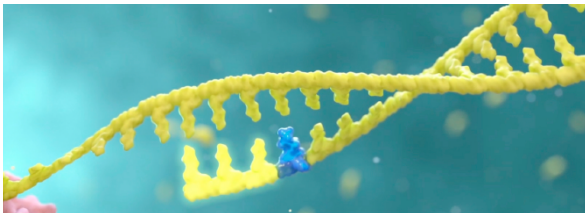
About VEKLURY

VEKLURY is an antiviral medication that directly inhibits viral replication of SARS-CoV-2

VEKLURY acts to inhibit the SARS-CoV-2 RNA-dependent RNA polymerase (RdRp), which is essential for viral replication – and thus creation of virions that circulate in the body.

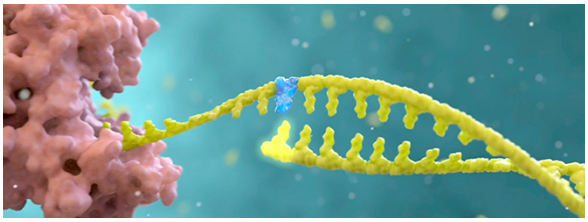
Mechanism of action

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]

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.

VEKLURY retained antiviral activity against the Omicron variant and all other known variants tested in vitro[3-8]

OMICRON	**DELTA**	**ALPHA**	**BETA**	**GAMMA**
(B.1.1.529/BA.1, BA.2, BA.2.12.1, BA.2.75, BA.4, BA.4.6, BA.5, BF.5, BF.7, BQ.1, BQ.1.1, CH.1.1, XBB, and XBB.1.5)	(B.1.617.2)	(B.1.1.7)	(B.1.351)	(P.1)
EPSILON	**ZETA**	**IOTA**	**KAPPA**	**LAMBDA**
(B.1.429)	(P.2)	(B.1.526)	(B.1.617.1)	(C.37)

The antiviral activity of VEKLURY has been tested in vitro against clinical isolates of SARS-CoV-2 variants. The resulting laboratory findings demonstrated that the **antiviral activity of VEKLURY is not reduced against these variants.**

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.

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.

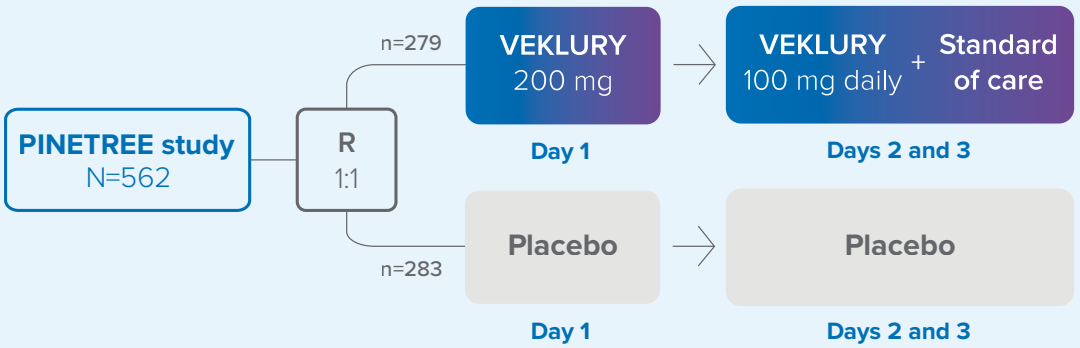
What study supports the use of VEKLURY in the outpatient setting?

PINETREE study (GS-US-540-9012)[1,9]

PINETREE was a phase 3, randomized, double-blind, placebo-controlled clinical trial in 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 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)

Dosage and administration

— Administration should take place under conditions where management of severe hypersensitivity reactions, such as anaphylaxis, is possible.

- **Treatment duration:**
  — For patients who **are hospitalized**, VEKLURY should be initiated as soon as possible after diagnosis of symptomatic COVID-19.

R=randomization.

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

Baseline characteristics[9]

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

Characteristic	VEKLURY (n=279)	Placebo (n=283)
Mean age ± SD, y	50±15	51±15
Age, 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 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 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, mean ± SD, kg/m^2	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)

*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.

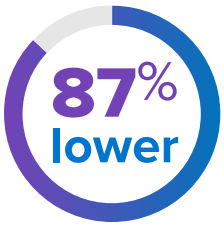
IMPORTANT SAFETY INFORMATION (cont'd)

Dosage and administration (cont'd)

- **Treatment duration** (cont'd)**:**
  - For patients who are hospitalized and do not require 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 up to 5 additional days, for a total treatment duration of up to 10 days.

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

VEKLURY reduced risk of progression to severe COVID-19[1,9]



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[1,9]

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

"Remdesivir is another important option for outpatients with COVID-19."[9]

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

NIH Recommendations for VEKLURY Use in Nonhospitalized Adult Patients[10]

VEKLURY is a preferred therapy for patients who do not require hospitalization or supplemental oxygen and who are at high risk of progressing to severe COVID-19 (BIIa)[a-c,d]

Ritonavir-boosted nirmatrelvir is also a preferred therapy for nonhospitalized patients[e] **(AIIa)**; see footnote on drug interactions.[f] For patients who cannot take ritonavir-boosted nirmatrelvir because of significant drug-drug interactions, the Panel recommends **VEKLURY**.

[a]For a list of risk factors, see the CDC webpage Underlying Medical Conditions Associated With Higher Risk for Severe COVID-19 (or see last page). When deciding whether to prescribe antiviral treatment to a patient who has been vaccinated, clinicians should be aware of the conditions associated with a high risk of disease progression. These conditions include older age, a prolonged amount of time since the most recent vaccine dose (eg, >6 months), and a decreased likelihood of an adequate immune response to vaccination due to a moderate to severe immunocompromising condition or the receipt of immunosuppressive medications. The number and severity of risk factors also affect the level of risk.

[b]Ritonavir-boosted nirmatrelvir has not been studied in hospitalized patients. The FDA EUA for ritonavir-boosted nirmatrelvir allows for its use in hospitalized patients with mild-to-moderate COVID-19 (ie, those who do not require supplemental oxygen) who are at high risk of progressing to severe COVID-19 and who are within 5 days of symptom onset.

[c]Administration of **VEKLURY** requires an IV infusion once daily for 3 consecutive days for nonhospitalized patients.

[d]Each recommendation in the NIH guidelines receives a rating for the strength of the recommendation (A, B, or C) and a rating for the evidence that supports it (I, IIa, IIb, or III).

[e]If a patient requires hospitalization after starting treatment, the full treatment course can be completed at the healthcare provider's discretion.

[f]Ritonavir-boosted nirmatrelvir has significant drug-drug interactions. Clinicians should carefully review a patient's concomitant medications and evaluate potential drug-drug interactions. See Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications for more information.

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

Considerations for treatment with VEKLURY

Who is considered at high risk for 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[9]:

Hypertension

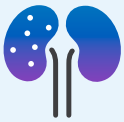
Chronic lung disease

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:** (cont'd)
  - For patients who are hospitalized and require invasive mechanical ventilation and/or ECMO, the recommended total treatment duration is 10 days.
  - 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. VEKLURY should be initiated as soon as possible after diagnosis of symptomatic COVID-19 and within 7 days of symptom onset for outpatient use.
- **Testing prior to and during treatment:** Perform hepatic laboratory and prothrombin time testing prior to initiating VEKLURY and during use as clinically appropriate.

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 prior to and during treatment: Perform 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 have 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.

Patients with COVID-19 and renal impairment

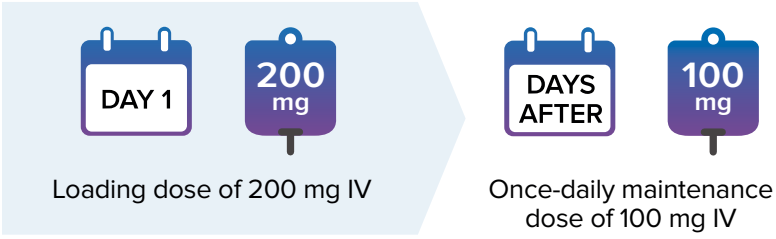
- Patients may receive VEKLURY regardless of renal impairment severity (eg, any eGFR), including those on dialysis.
- NO dosage adjustment of VEKLURY is recommended in patients with any degree of renal impairment.
- NO renal laboratory testing is required before or during treatment.

Administration in the outpatient setting

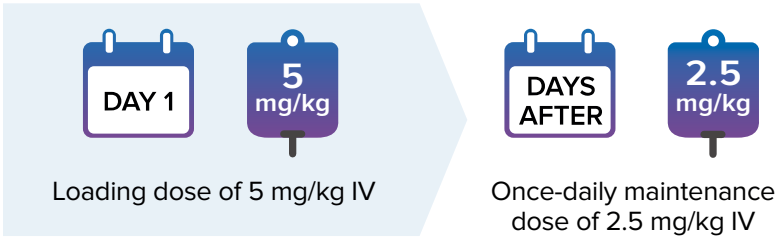
What is the recommended dosage and total treatment duration?

Recommended dosage[1]

The recommended dosage for adults and pediatric patients weighing at least 40 kg is a single loading dose of VEKLURY 200 mg on Day 1 followed by once-daily maintenance doses of VEKLURY 100 mg from Day 2.

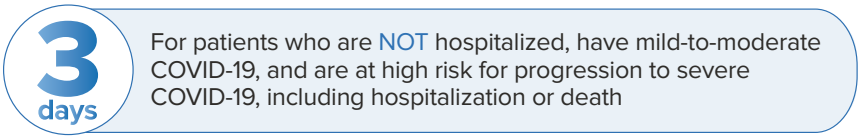


The recommended dosage for pediatric patients 28 days of age and older and weighing at least 3 kg to less than 40 kg is a single loading dose of VEKLURY 5 mg/kg on Day 1 followed by once-daily maintenance doses of VEKLURY 2.5 mg/kg from Day 2. VEKLURY is administered via IV infusion.



For patients with COVID-19 who are not hospitalized and are at high risk for disease progression, initiate VEKLURY as soon as possible after diagnosis of symptomatic COVID-19 and within 7 days of symptom onset.

Recommended total treatment duration[1]



IMPORTANT SAFETY INFORMATION (cont'd)

Dosage and administration (cont'd)

- **Renal impairment:** No dosage adjustment of VEKLURY is recommended in patients with any degree of renal impairment, including patients on dialysis. VEKLURY may be administered without regard to the timing of dialysis.

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 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 28 days of age and older and weigh at least 3 kg by IV infusion only. Do not administer by any other route.[1]

VEKLURY for injection, 100 mg lyophilized powder, must be reconstituted with 19 mL Sterile Water for Injection prior to diluting with 0.9% sodium chloride.[1]

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 for VEKLURY. Available clinical trial data for VEKLURY in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes following second- and third-trimester exposure. There are insufficient data to evaluate the risk of VEKLURY exposure during the first trimester. Maternal and fetal risks are associated with untreated COVID-19 in pregnancy.
- **Lactation:** VEKLURY can pass into breast milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for VEKLURY and any potential adverse effects on the breastfed child from VEKLURY or from an underlying maternal condition. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

Ordering and access information

How can I order VEKLURY?

Hospital ordering process

Hospitals can place orders with any of the 3 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

Nonhospital settings can contact one of these distributors for more information:

- AmerisourceBergen Specialty Distribution, 1-800-746-6273 or C19therapies@AmerisourceBergen.com;
- Cardinal Specialty, 1-855-855-0708 or GMB-SPD-CSORDERENTRY@cardinalhealth.com

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 has a 1 mg billing increment, is available for use by all payers, and is effective for dates of service on or after December 23, 2021.[11]

Effective April 1, 2022, the VEKLURY HCPCS code, J0248, was assigned a pass-through status indicator under the hospital Outpatient Prospective Payment System.[12]

For more information, please see Coding and Reimbursement Information.

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

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. Phone lines are open to speak to a live agent M–F, 5 AM–6 PM PT.

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.

Find VEKLURY at an outpatient location

THERAPEUTICS LOCATOR

This is a third-party website. Gilead is not responsible for the content of this website or its accuracy.

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References

1. VEKLURY. Prescribing Information. Gilead Sciences, Inc.; 2023.
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Please see Important Safety Information within and full Prescribing Information.
For more information, visit vekluryhcp.com.

GILEAD | Veklury® remdesivir 100 MG FOR INJECTION

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