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National Institutes of Health Treatment Guidelines: Recommendations for VEKLURY®

The selected information presented on the following pages was developed based on the final COVID-19 treatment guidelines published **February 29, 2024**. This update is the result of the Panel's final review of the clinical data, providing NIH treatment recommendations for clinicians who are caring for patients with COVID-19.[1]

Strength of Recommendations: A=Strong recommendation for the statement; **B**=Moderate recommendation for the statement; **C**=Weak recommendation for the statement.

Evidence for Recommendation: I: *High quality of evidence:* 1 or more randomized trials without major limitations,[a] well-powered subgroup analyses of such trials, or meta-analyses without major limitations; **IIa:** *Moderate quality of evidence:* Randomized trials and subgroup analyses of randomized trials that do not meet the criteria for a **I** rating; **IIb:** *Moderate quality of evidence:* Observational studies without major limitations[b]; **III:** Expert opinion.

[a]The rating may be lower than **I** in cases where trials have produced conflicting results.
[b]This category also includes meta-analyses of observational studies.

INDICATION

VEKLURY is indicated for the treatment of COVID-19 in adults and pediatric patients (birth to <18 years of age weighing ≥1.5 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 additional Important Safety Information within and full Prescribing Information.

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NIH Recommendations for VEKLURY Use in Nonhospitalized Adult Patients[1]

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-e]

NIH lists therapies in the following order of preference: ritonavir-boosted nirmatrelvir (AIIa),[e] start as soon as possible and within 5 days of symptom onset, **VEKLURY**,[b,e] start as soon as possible and within 7 days of symptom onset; see footnote on drug interactions for ritonavir-boosted nirmatrelvir.[f] For patients who cannot take ritonavir-boosted nirmatrelvir because of significant drug-drug interactions, the Panel recommends **VEKLURY**.

Advanced planning may be needed to increase access to IV **VEKLURY**, which can be administered in skilled nursing facilities, home health care settings, and outpatient facilities such as infusion centers.

[a]For a list of risk factors, see the CDC webpage Underlying Medical Conditions Associated With Higher Risk for Severe COVID-19 (or see page 6). 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 affects the level of risk.

[b]Administration of **VEKLURY** requires an IV infusion once daily for 3 days.

[c]For a discussion of potential treatment options for patients who are immunocompromised and have prolonged COVID-19 symptoms and evidence of ongoing viral replication, please see *Special Considerations in People Who Are Immunocompromised* in the NIH COVID-19 Treatment Guidelines.

[d]Concerns about a viral rebound or the recurrence of symptoms should not be a reason to avoid using antiviral therapies when their use is indicated. See the NIH Guidelines for viral rebound and symptom recurrence details.

[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* in the NIH COVID-19 Treatment Guidelines or more information.

Please visit the NIH Coronavirus Disease 2019 (COVID-19) Treatment Guidelines for more information.

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).

Please see additional Important Safety Information within and full Prescribing Information.

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NIH Recommendations for VEKLURY Use in Hospitalized Adult Patients[1]

No supplemental oxygen required — hospitalized for reasons other than COVID-19

For patients with mild-to-moderate COVID-19 who are at high risk of progressing to severe COVID-19,[a,b] see NIH Recommendations for **VEKLURY** Use in Nonhospitalized Adult Patients on the previous page.

No supplemental oxygen required — hospitalized for COVID-19

For patients who are at high risk of progressing to severe COVID-19,[a] **VEKLURY** is the only recommended therapy for patients who are immunocompromised **(BIIb)** and for other high-risk patients **(BIII)**.

Evidence suggests that the benefit of VEKLURY is greatest when the drug is given early in the course of COVID-19 (eg, within 10 days of symptom onset).

For all patients, the Panel **recommends against** the use of **dexamethasone (AIIa)** or **other systemic corticosteroids (AIII)** for the treatment of COVID-19.[c]

[a]For a list of risk factors, see the CDC webpage Underlying Medical Conditions Associated With Higher Risk for Severe COVID-19.
[b]If the patient is hospitalized for reasons other than COVID-19, the treatment duration for **VEKLURY** is 3 days.
[c]Corticosteroids that are prescribed for an underlying condition should be continued.

Please visit the NIH Coronavirus Disease 2019 (COVID-19) Treatment Guidelines for more information.

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.
- **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.

Please see additional Important Safety Information within and full Prescribing Information.

NIH Recommendations for VEKLURY Use in Hospitalized Adult Patients[1] (cont'd)

Requires conventional oxygen[a]

VEKLURY is recommended for patients who require minimal conventional oxygen **(BIIa)**.[b]

For most patients, use **VEKLURY** plus **dexamethasone (BIIa)**. If **VEKLURY** cannot be obtained, use **dexamethasone (BI)**.

For patients who are receiving VEKLURY and who progress to high-flow nasal cannula (HFNC) oxygen, NIV, MV, or ECMO, the full course of VEKLURY should still be completed.

For patients who are receiving **dexamethasone** and who have rapidly increasing oxygen needs and systemic inflammation, add **PO baricitinib**[c] **(BIIa)** or **IV tocilizumab**[c] **(BIIa)** to 1 of the options above. Alternatives (listed in alphabetical order) include IV abatacept (CIIa) or IV infliximab (CIIa).

Requires high-flow nasal cannula oxygen or noninvasive ventilation

Dexamethasone should be administered to all patients **(AI)**. If the patient has not already received a second immunomodulator, promptly add 1 of the following[c,d]:

- Preferred, **PO baricitinib (AI)**
- Preferred alternative, **IV tocilizumab (BIIa)**
- Additional alternative, **IV abatacept (CIIa)**
- Additional alternative, **IV infliximab (CIIa)**

Add **VEKLURY** to 1 of the options above in certain patients.

Examples of patients who may benefit most from adding VEKLURY include patients who:

- Are immunocompromised **(BIIb)**
- Have evidence of ongoing viral replication (eg, those with a low Ct value, as measured by an RT-PCR result or with a positive rapid antigen test result) **(BIII)**
- Are within 10 days of symptom onset **(CIIa)**[e]

[a]Conventional oxygen refers to oxygen supplementation that is not HFNC oxygen, NIV, MV, or ECMO.

[b]Evidence suggests that the benefit of **VEKLURY** is greatest when the drug is given early in the course of COVID-19 (eg, within 10 days of symptom onset).

[c]If none of the preferred or alternative options are available or feasible to use, the JAK inhibitor **PO tofacitinib (CIIa)** or the IL-6 inhibitor **IV sarilumab (CIIa)** can be used in combination with dexamethasone.

[d]Dexamethasone should be initiated immediately, without waiting until the second immunomodulator can be acquired. If other immunomodulators cannot be obtained or are contraindicated, use dexamethasone alone **(AI)**.

[e]For more information on immunocompromising conditions, please see *Special Considerations in People Who Are Immunocompromised* in the NIH COVID-19 Treatment Guidelines.

Please visit the NIH Coronavirus Disease 2019 (COVID-19) Treatment Guidelines for more information.

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.

Please see additional Important Safety Information within and full Prescribing Information.

Ct=cycle threshold; ECMO=extracorporeal membrane oxygenation; IL-6=interleukin-6; JAK=Janus kinase; MV=mechanical ventilation; NIV=noninvasive ventilation; PO=oral; RT-PCR=reverse transcription–polymerase chain reaction.

NIH Recommendations for VEKLURY Use in Hospitalized Adult Patients[1] (cont'd)

Requires mechanical ventilation or ECMO

Dexamethasone should be administered to all patients **(AI)**. If the patient has not already received a second immunomodulator, promptly add 1 of the following (listed in alphabetical order)[a]:

- **PO baricitinib[b] (BIIa)**
- **IV tocilizumab[b] (BIIa)**

There is insufficient evidence for the Panel to recommend either for or against the use of **VEKLURY** in hospitalized patients with COVID-19 who require MV or ECMO. Some Panel members would add **VEKLURY** to immunomodulator therapy in patients who:

- Have recently been placed on MV or ECMO
- Are immunocompromised
- Have evidence of ongoing viral replication
- Are within 10 days of symptom onset

[a]Dexamethasone should be initiated immediately, without waiting until the second immunomodulator can be acquired. If other immunomodulators cannot be obtained or are contraindicated, use dexamethasone alone **(AI)**.

[b]If PO baricitinib and IV tocilizumab are not available or feasible to use, **PO tofacitinib** can be used instead of PO baricitinib **(CIIa)**, and **IV sarilumab** can be used instead of IV tocilizumab **(CIIa)**.

Please visit the NIH Coronavirus Disease 2019 (COVID-19) Treatment Guidelines for more information.

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.
  - 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.
  - For patients who are hospitalized and require invasive mechanical ventilation and/or ECMO, the recommended total treatment duration is 10 days.

Please see additional Important Safety Information within and full Prescribing Information.

ECMO=extracorporeal membrane oxygenation; MV=mechanical ventilation; PO=oral.

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Centers for Disease Control and Prevention (CDC): Underlying Medical Conditions Associated With Higher Risk for Severe COVID-19[2]

Based on evidence from published reports, scientific articles in press, unreviewed preprints, and internal data, the CDC has compiled the following list of underlying medical conditions that place adults of any age at increased risk for severe COVID-19 illness.

This list was developed based on information available to the CDC as of July 30, 2024. As the science evolves, the CDC may update the list. Please visit the CDC website for more information.

- Alpha-1 antitrypsin deficiency
- Asthma
- Bronchopulmonary dysplasia
- Cancer, including hematologic malignancies
- Cerebrovascular disease
- Children with certain underlying conditions
- Chronic kidney disease,* including people receiving dialysis†
- Chronic liver diseases limited to: cirrhosis; nonalcoholic fatty liver disease; alcoholic liver disease; autoimmune hepatitis
- Chronic lung diseases limited to: bronchiectasis; COPD (chronic obstructive pulmonary disease); interstitial lung disease; pulmonary embolism; pulmonary hypertension
- Cystic fibrosis
- Diabetes mellitus, type 1; and diabetes mellitus, type 2*
- Disabilities,‡ including Down syndrome
- Heart conditions (such as heart failure, coronary artery disease, or cardiomyopathies)
- Hepatitis B
- Hepatitis C
- HIV (human immunodeficiency virus)
- Hypertension*
- Mental health conditions limited to: mood disorders, including depression; schizophrenia spectrum disorders
- Neurologic conditions limited to dementia‡
- Obesity (BMI ≥30 kg/m^2 or ≥95th percentile in children)
- Overweight (BMI ≥25 kg/m^2 but <30 kg/m^2)
- Physical inactivity
- Pregnancy and recent pregnancy
- Primary immunodeficiencies
- Sickle cell disease
- Smoking, current and former
- Solid organ or blood stem cell transplantation
- Substance abuse disorders
- Thalassemia
- Tuberculosis
- Use of corticosteroids or other immunosuppressive medications

*Indicates presence of evidence for pregnant and nonpregnant people.
†Risk may be further increased for people receiving dialysis.
‡Underlying conditions for which there is evidence in pediatric patients.

IMPORTANT SAFETY INFORMATION (cont'd)

Dosage and administration (cont'd)

- **Treatment duration** (cont'd)**:**
  - 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.

Please see additional Important Safety Information within and full Prescribing Information.

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VEKLURY Is Included in Multiple COVID-19 Treatment Guidelines[1,3-5]

- **NIH** National Institutes of Health
- **WHO** World Health Organization
- **IDSA** Infectious Diseases Society of America
- **SCCM** Society of Critical Care Medicine

IMPORTANT SAFETY INFORMATION (cont'd)

Dosage and administration (cont'd)

- **Testing prior to and during treatment:** Perform hepatic laboratory and prothrombin time testing prior to initiating VEKLURY and during use as clinically appropriate.
- **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.

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.

Please see additional Important Safety Information within and full Prescribing Information.

References: 1. National Institutes of Health. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Updated February 29, 2024. Accessed October 17, 2024. https://www.ncbi.nlm.nih.gov/books/NBK570371/pdf/Bookshelf_NBK570371.pdf **2.** Centers for Disease Control and Prevention. Underlying conditions and the higher risk for severe COVID-19. Updated July 30, 2024. Accessed September 13, 2024. https://www.cdc.gov/covid/hcp/clinical-care/underlyingconditions.html?CDC_AAref_Val=https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinicalcare/underlyingconditions.html **3.** World Health Organization. Therapeutics and COVID-19: living guideline, 10 November 2023. Updated November 10, 2023. Accessed September 17, 2024. https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2023.2 **4.** Infectious Diseases Society of America. IDSA guidelines on the treatment and management of patients with COVID-19. Updated June 26, 2023. Accessed September 17, 2024. https://www.idsociety.org/COVID19guidelines **5.** Society of Critical Care Medicine. COVID-19 guidelines. Updated January 29, 2021. Accessed September 17, 2024. https://www.sccm.org/SurvivingSepsisCampaign/Guidelines/COVID-19

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INDICATION

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