



# Federal Response to COVID-19: Therapeutics Clinical Implementation Guide

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**Outpatient Administration Guide for Healthcare Providers  
February 2024**

*Unclassified*

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# Clinical Implementation Guide Objectives

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- Review available outpatient COVID-19 therapeutics used to treat eligible non-hospitalized patients who have mild to moderate symptoms of COVID-19.
- Summarize key information on COVID-19 therapeutics and support healthcare providers' understanding of these therapies and how to implement their administration.
- Describe process for obtaining and reporting COVID-19 therapeutics products purchased by HHS/ASPR, including collaboration with state and territorial health departments, as well as national healthcare and medical organizations and associations to ensure efficient and equitable distribution.

**IMPORTANT NOTE:** The *Clinical Implementation Guide* **will no longer be updated** after February 2024.

See the latest information on all [FDA authorized products under EUA](https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization) <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization>

# COVID-19 Therapeutics under Emergency Use Authorization (EUA)

- In certain types of emergencies, the FDA can issue an emergency use authorization (EUA), to provide more timely access to critical medical products (including medicines and tests) that may help during the emergency when there are no adequate, approved, and available alternative options.
- The EUA process is different than FDA approval, clearance, or licensing because the EUA standard may permit authorization based on significantly less data than would be required for approval, clearance, or licensing by the FDA. This enables the FDA to authorize the emergency use of medical products that meet the criteria within weeks rather than months to years. Since EUA products are not approved and, thus, do not have labeled indications, “off-label use” or *the use of the product outside of the EUA authorization is not permitted*.
- EUAs are in effect until the emergency declaration ends but can be revised or revoked. *The need will be evaluated during the emergency, availability of new data on the product’s safety and effectiveness, or as products meet the criteria to become approved, cleared, or licensed by the FDA.*
- ***Products packaged under the EUA must be prescribed/administered in accordance with the EUA even if the product receives FDA approval***

# COVID-19 Therapeutics: Resources for Health Care Professionals and Public Health Officials

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## **ASPR's Response to COVID-19 Therapeutics Website**

<https://aspr.hhs.gov/COVID-19/therapeutics/Pages/default.aspx>

## **New and Notable: COVID-19 Therapeutics Announcements**

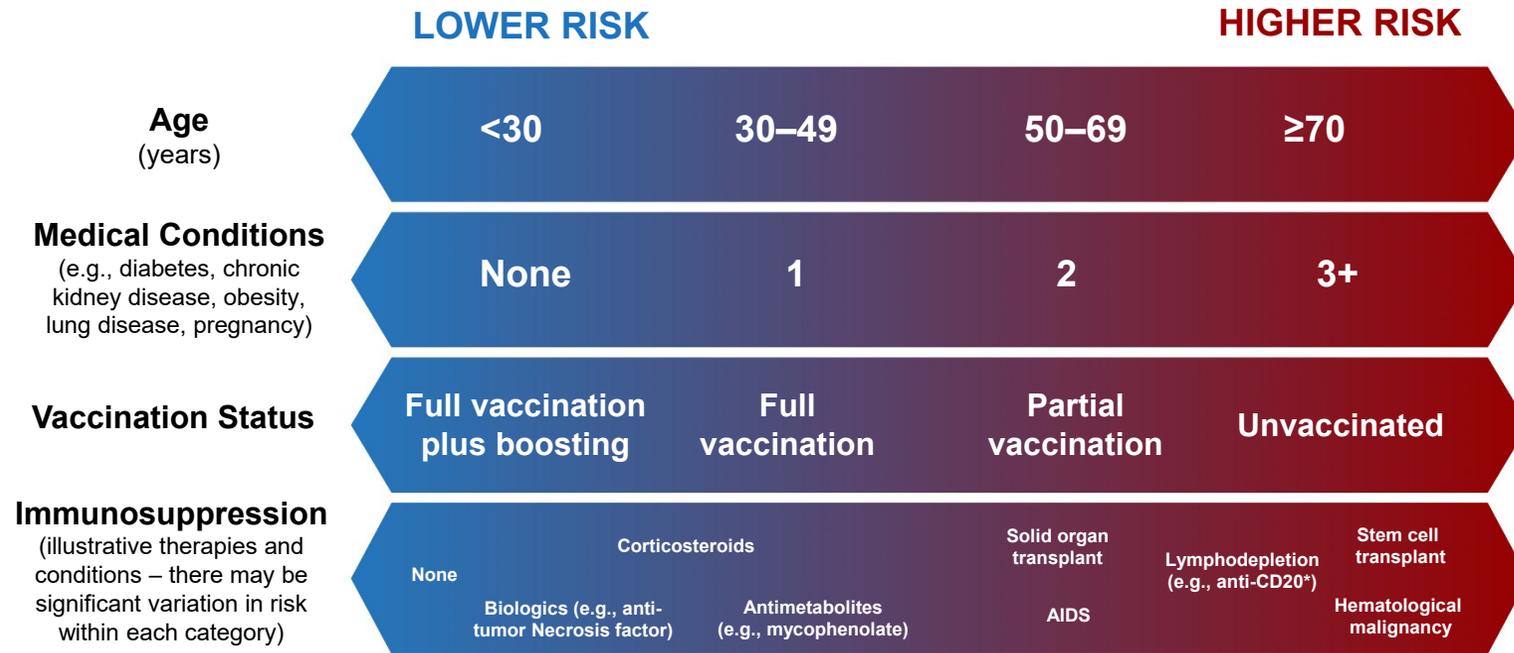
<https://aspr.hhs.gov/COVID-19/Therapeutics/updates/Pages/default.aspx>

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# **Module 1: COVID-19 Outpatient Therapeutics Overview**

# Who Is At Risk for Severe COVID-19?

## COVID-19 Risk Continuum

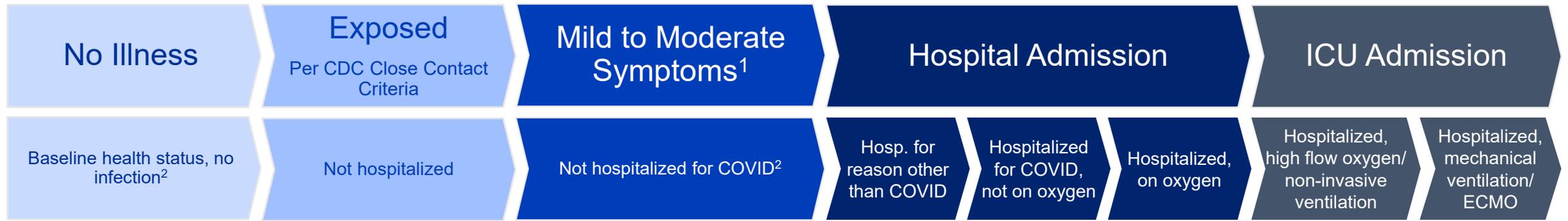


***Sociodemographic factors and non-pharmaceutical interventions affect exposure***

Original illustration by Dr. William Werbel, adapted for the COVID-19 Real-Time Learning Network

[CDC Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Professionals](https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html#anchor_1618433687270) [https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html#anchor\\_1618433687270](https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html#anchor_1618433687270)

# Summary of COVID-19 Preventative Agents & Treatments



**\*\*COVID19 Vaccines**

None currently authorized for use in any U.S. state or territory.

None currently authorized for use in any US state or territory.

**\*Oral Antivirals**  
• Paxlovid (nirmatrelvir + ritonavir, Pfizer)

**\*Oral Antivirals**  
• Lagevrio (molnupiravir Merck) – Alternative

**\*\*IV Antiviral**  
• Veklury® (remdesivir, Gilead)

Please see [NIH Current Inpatient Therapies#](https://www.covid19treatmentguidelines.nih.gov/therapies/)  
(<https://www.covid19treatmentguidelines.nih.gov/therapies/>)

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Patient assistance programs support continued access post commercialization

\*HHS distribution  
 \*\*Commercially available

<sup>1</sup> [Convalescent Plasma EUA](https://www.fda.gov/media/141478/download) <https://www.fda.gov/media/141478/download>  
*High titer convalescent plasma is authorized for specific immunocompromised patients.*  
<sup>2</sup> Refer to individual product Fact Sheets for authorization details

#Be sure to check latest updates on inpatient care  
[Therapeutic Management of Nonhospitalized Adults With COVID-19](https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/nonhospitalized-adults--therapeutic-management/)  
<https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/hospitalized-adults--therapeutic-management/>  
[Therapeutic Management of Hospitalized Adults With COVID-19](https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/hospitalized-adults--therapeutic-management/)  
<https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/hospitalized-adults--therapeutic-management/>

# NIH Guidelines For Treatment of Mild to Moderate COVID-19 in Non-hospitalized Adults Who Are at High Risk of Progressing to Severe COVID-19

- The COVID-19 Treatment Guidelines Panel (the Panel) recommends the following anti-SARS-CoV-2 therapies as preferred treatments for COVID-19.

These drugs are listed in order of preference:

- **Nirmatrelvir co-packaged with ritonavir (Paxlovid) (A1a)**
- **Remdesivir (Veklury) (B1a)**
- Alternative therapy. For use when the preferred therapies are not available, feasible to use, or clinically appropriate.
  - **Molnupiravir (Lagevrio) (C1a)**

# NIH: Patient Prioritization for Treatment<sup>1</sup>

- These guidelines<sup>1</sup> are for use only when logistical constraints limit the availability of therapies.
- Remdesivir is a recommended option if nirmatrelvir co-packaged with ritonavir cannot be used.
- Some treating facilities may not have the ability to provide a 3-day course of remdesivir intravenous infusions to all eligible patients. In these situations, prioritizing patients who will benefit the most from the therapy becomes necessary.
- Prioritization strategy includes 4 factors: age, vaccination status, immune status, and clinical risk factors.

<sup>1</sup>[NIH Prioritization Guidelines](https://www.covid19treatmentguidelines.nih.gov/overview/prioritization-of-therapeutics/) <https://www.covid19treatmentguidelines.nih.gov/overview/prioritization-of-therapeutics/>

# NIH: Patient Prioritization for Treatment<sup>1</sup> (continued)

Tier	Risk Group
1	<ul style="list-style-type: none"><li>• Immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccine status (see Immunocompromising Conditions below); or</li><li>• Unvaccinated individuals at the highest risk of severe disease (anyone aged <math>\geq 75</math> years or anyone aged <math>\geq 65</math> years with additional risk factors).</li></ul>
2	<ul style="list-style-type: none"><li>• Unvaccinated individuals not included in Tier 1 who are at risk of severe disease (anyone aged <math>\geq 65</math> years or anyone aged <math>&lt; 65</math> years with clinical risk factors)</li></ul>
3	<ul style="list-style-type: none"><li>• Vaccinated individuals at risk of severe disease (anyone aged <math>\geq 65</math> years or anyone aged <math>&lt; 65</math> years with clinical risk factors)</li></ul> <p><b>Note:</b> <i>Vaccinated individuals who are not up to date with their immunizations are likely at higher risk for severe disease; patients within this tier who are in this situation should be prioritized for treatment.</i></p>

<sup>1</sup>[NIH Prioritization Guidelines](https://www.covid19treatmentguidelines.nih.gov/overview/prioritization-of-therapeutics/) https://www.covid19treatmentguidelines.nih.gov/overview/prioritization-of-therapeutics/

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# **Recommendations for Special Populations: Immunocompromised & Pediatrics**

# NIH Guidelines for Patients Who are Immunocompromised

- All people who are moderately or severely immunocompromised should receive COVID-19 vaccination.
- All close contacts of people who are immunocompromised are strongly encouraged to be up to date on vaccination against COVID-19.
- There is insufficient evidence for recommendation for or against the use of SARS-CoV-2 serologic testing to assess for immunity or to guide clinical decision about using COVID-19 vaccines or PrEP for certain people.
- Management of COVID-19 in individuals who are moderately to severely immunocompromised:
  - Patients should be treated quickly with appropriate COVID-19 therapeutics
  - Decisions regarding stopping or reducing the doses of immunosuppressive drugs in patients with COVID-19 should be made in consultation with the appropriate specialists; When selecting treatments for COVID-19, clinicians should consider factors such as the underlying disease, the specific immunosuppressants being used, the potential for drug-drug interactions, and the severity of COVID-19

[Immunocompromised COVID-19 Treatment Guidelines](https://covid19treatmentguidelines.nih.gov/special-populations/immunocompromised/) <https://covid19treatmentguidelines.nih.gov/special-populations/immunocompromised/>

# Therapeutics for Pediatric Patients < 12 Years Old

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## Veklury (Remdesivir)

- Pediatric patients **28 Days of Age and Older and weighing 3 kg to less than 40 kg\***

\* Pediatric patients less than 12 years of age but weighing 40kg or greater receive Veklury at the adult dose

# NIH Guidelines For Therapeutic Management in Non-hospitalized Children With COVID-19

Risk of Severe COVID-19	Panel's Recommendations	
	Aged 12-17 years	Aged <12 years
<b>Symptomatic, Regardless of Risk Factors</b>	<ul style="list-style-type: none"> <li>Provide supportive care <b>(AIII)</b>.</li> </ul>	<ul style="list-style-type: none"> <li>Provide supportive care <b>(AIII)</b>.</li> </ul>
<b>High Risk<sup>a,b</sup></b>	<ul style="list-style-type: none"> <li>Use 1 of the following options (listed in order of preference):<sup>c</sup> <ul style="list-style-type: none"> <li><b>Nirmatrelvir co-packaged with ritonavir (Paxlovid)</b> within 5 days of symptom onset <b>(BIII)</b></li> <li><b>Remdesivir</b> within 7 days of symptom onset <b>(CIII)</b></li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Nirmatrelvir co-packaged with ritonavir is not authorized by the FDA for use in children aged &lt;12 years.</li> <li>There is insufficient evidence to recommend either for or against the routine use of remdesivir. Consider treatment based on age and other risk factors.</li> </ul>
<b>Intermediate Risk<sup>b,d</sup></b>	<ul style="list-style-type: none"> <li>There is insufficient evidence to recommend either for or against the use of any antiviral therapy. Consider treatment based on age and other risk factors.</li> </ul>	<ul style="list-style-type: none"> <li>There is insufficient evidence to recommend either for or against the routine use of remdesivir</li> </ul>
<b>Low Risk<sup>b,e</sup></b>	<ul style="list-style-type: none"> <li>Manage with supportive care alone <b>(BIII)</b>.</li> </ul>	<ul style="list-style-type: none"> <li>Manage with supportive care alone <b>(BIII)</b>.</li> </ul>

<sup>a</sup> Molnupiravir is not authorized by the FDA for use in children aged <18 years and should not be used.

<sup>b</sup> See Table 3b for the Panel's framework for assessing the risk of progression to severe COVID-19 based on patient conditions and COVID-19 vaccination status.

<sup>c</sup> Initiate treatment as soon as possible after symptom onset.

<sup>d</sup> The relative risk of severe COVID-19 for intermediate-risk patients is lower than the risk for high-risk patients but higher than the risk for low-risk patients.

<sup>e</sup> Low-risk patients include those with comorbid conditions that have a weak or unknown association with severe COVID-19. Patients with no comorbidities are included in this group.  
[Therapeutic Management of Nonhospitalized Children With COVID-19](https://www.covid19treatmentguidelines.nih.gov/tables/therapeutic-management-of-nonhospitalised-children/) <https://www.covid19treatmentguidelines.nih.gov/tables/therapeutic-management-of-nonhospitalised-children/>

# Additional Tools to Assist in COVID-19 Outpatient Therapeutic Selection

- [NIH's COVID-19 Treatment Guidelines - What's new](https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/)  
<https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/>
- [NIH Therapeutic Management of Nonhospitalized Children With COVID-19](https://www.covid19treatmentguidelines.nih.gov/management/clinical-management-of-children/nonhospitalized-children-therapeutic-Management)  
<https://www.covid19treatmentguidelines.nih.gov/management/clinical-management-of-children/nonhospitalized-children-therapeutic-Management>
- [CDC Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Professionals](https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html)  
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html>
- [CDC COVID Data Tracker](https://covid.cdc.gov/covid-data-tracker/#variant-proportions) <https://covid.cdc.gov/covid-data-tracker/#variant-proportions>  
The CDC monitors and publishes variant information
- [Clinical Decision Aid](https://aspr.hhs.gov/COVID-19-Therapeutics/Outpatient-Therapeutics-Clinical-Decision-Aide/Pages/default.aspx)  
<https://aspr.hhs.gov/COVID-19-Therapeutics/Outpatient-Therapeutics-Clinical-Decision-Aide/Pages/default.aspx>
- [Side-by-Side Overview of Outpatient Therapeutics](https://aspr.hhs.gov/COVID-19-Therapeutics/Side-by-Side-Overview/Pages/default.aspx)  
<https://aspr.hhs.gov/COVID-19-Therapeutics/Side-by-Side-Overview/Pages/default.aspx>
- [ASPR COVID-19 Therapeutics](https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/default.aspx)  
<https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/default.aspx>

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# Module 2: Product Information

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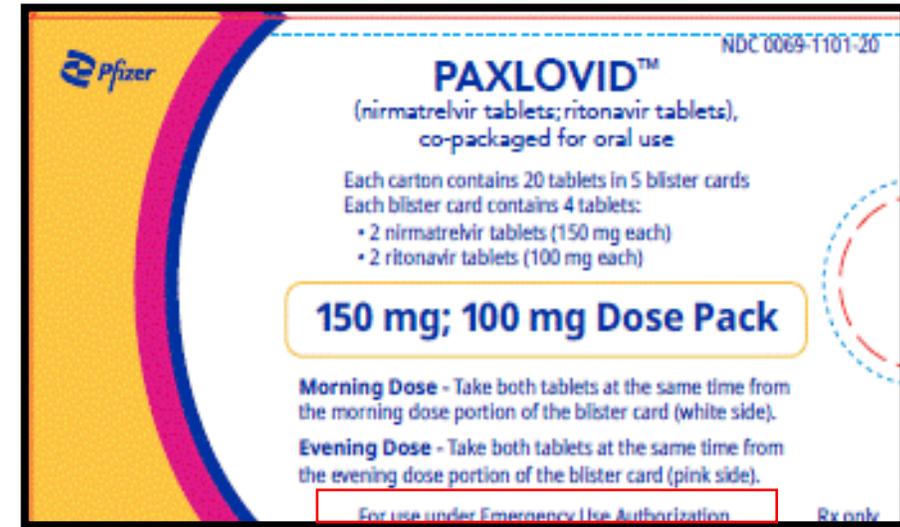
# **Products for Treatment of Mild-to-Moderate COVID-19: Preferred Therapies per NIH Guidelines**

# Paxlovid (nirmatrelvir co-packaged with ritonavir) – Pfizer Oral Antiviral (Preferred)\*

## Paxlovid Standard



## Paxlovid Reduced Dose (Renal)



\*Note both EUA (while supply remains) and NDA labeled Paxlovid is available

[Fact Sheet for Healthcare Providers for Paxlovid \(nirmatrelvir co-packaged with ritonavir\)](https://www.fda.gov/media/155050/download) <https://www.fda.gov/media/155050/download>  
[Paxlovid Prescribing Information](https://labeling.pfizer.com/ShowLabeling.aspx?id=19599) <https://labeling.pfizer.com/ShowLabeling.aspx?id=19599>

# Paxlovid (nirmatrelvir co-packaged with ritonavir)

## Product Information

- FDA Fact Sheets and Prescribing Information
  - [Paxlovid Prescribing Information](https://labeling.pfizer.com/ShowLabeling.aspx?id=19599) https://labeling.pfizer.com/ShowLabeling.aspx?id=19599
  - [Paxlovid provider fact sheet](https://www.fda.gov/media/155050/download) https://www.fda.gov/media/155050/download
  - [Fact Sheet for Patients, Parents and Caregivers](https://www.fda.gov/media/155051/download) https://www.fda.gov/media/155051/download
  - [Frequently Asked Questions on the Emergency Use Authorization for Paxlovid for Treatment of COVID-19 \(FDA\)](https://www.fda.gov/media/155052/download) https://www.fda.gov/media/155052/download
- Manufacturer's Resources:
  - [Pharmacist Instruction Sheet](https://www.covid19oralrx-hcp.com/files/Clean_EUA-105-mitigation-plan-for-moderate-renal-impairment-01-11-22.pdf) https://www.covid19oralrx-hcp.com/files/Clean\_EUA-105-mitigation-plan-for-moderate-renal-impairment-01-11-22.pdf
  - [Paxlovid Drug Interaction Checker](https://www.pfizermedicalinformation.com/en-us/drug-interaction-checker?product=PAXLOVID) https://www.pfizermedicalinformation.com/en-us/drug-interaction-checker?product=PAXLOVID
- Prescribing Resources:
  - [Paxlovid Patient Eligibility Screening Checklist Tool for Prescribers](https://www.fda.gov/media/158165/download) https://www.fda.gov/media/158165/download
  - [FDA Updates on Paxlovid for Health Care Providers](https://www.fda.gov/drugs/news-events-human-drugs/fda-updates-paxlovid-health-care-providers) https://www.fda.gov/drugs/news-events-human-drugs/fda-updates-paxlovid-health-care-providers
  - [Important Prescribing and Dispensing Information](https://www.fda.gov/media/155071/download) https://www.fda.gov/media/155071/download
  - [University of Liverpool COVID-19 Drug Interactions Checker](https://covid19-druginteractions.org) https://covid19-druginteractions.org
- Safety Reporting:
  - [FDA MedWatch](https://www.accessdata.fda.gov/scripts/medwatch/ind.cfm) https://www.accessdata.fda.gov/scripts/medwatch/ind.cfm
  - [Pfizer Safety Reporting](http://www.pfizersafetyreporting.com/) http://www.pfizersafetyreporting.com/

# Paxlovid (nirmatrelvir co-packaged with ritonavir) Emergency Use AUTHORIZATION

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- Paxlovid EUA authorized for the treatment of mild-to-moderate coronavirus disease (COVID-19) in adults and pediatric patients (12 years of age and older weighing *at least* 40 kg), who are at high risk for progression to severe COVID-19, including hospitalization or death
- Initiated as soon as possible after diagnosis of COVID-19 and **within 5 days** of symptom onset
- Paxlovid includes: nirmatrelvir (a SARS-CoV-2 main proteases inhibitor) co-packaged with ritonavir (a CYP34A inhibitor)
- PAXLOVID is not authorized for use as pre-exposure or post-exposure prophylaxis for prevention of COVID-19
- Paxlovid (nirmatrelvir co-packaged with ritonavir) may be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under state law to prescribe drugs in the therapeutic class to which Paxlovid (nirmatrelvir co-packaged ritonavir) belongs (i.e., anti-infectives). Pharmacists are also authorized under the EUA to prescribe Paxlovid under certain conditions

[Fact Sheet for Healthcare Providers for Paxlovid \(nirmatrelvir co-packaged with ritonavir\)](https://www.fda.gov/media/155050/download) <https://www.fda.gov/media/155050/download>

# Paxlovid (nirmatrelvir co-packaged with ritonavir)

## FDA APPROVAL

- On May 25, 2023, [FDA approved a New Drug Application \(NDA\) for Paxlovid](https://www.fda.gov/news-events/press-announcements/fda-approves-first-oral-antiviral-treatment-covid-19-adults) for the treatment of mild to moderate COVID-19 in adults who are at high risk for progression to severe COVID-19, including hospitalization or death <https://www.fda.gov/news-events/press-announcements/fda-approves-first-oral-antiviral-treatment-covid-19-adults>
  - [Paxlovid Prescribing Information](https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/217188s000lbl.pdf)  
[https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2023/217188s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/217188s000lbl.pdf)
- Paxlovid also remains authorized under EUA to ensure continued access for all eligible patients to the current supply of Paxlovid, including adult patients
  - [EUA fact sheet for health care providers](https://www.fda.gov/media/155050/download) <https://www.fda.gov/media/155050/download>
- The Emergency Use Authorization (EUA) continues to authorize Paxlovid to treat certain eligible pediatric patients, a patient population that is not covered under the approved NDA for Paxlovid at this time. Note: [EUA-labeled Paxlovid will no longer be authorized for emergency use after March 8, 2024](#), however the Paxlovid EUA will continue to authorize emergency use of NDA-labeled Paxlovid for pediatric patients (12 years of age and older weighing at least 40 kg). <https://www.fda.gov/drugs/drug-safety-and-availability/fda-revises-letter-authorization-emergency-use-authorization-paxlovid>
- NDA-labeled Paxlovid (nirmatrelvir tablets and ritonavir tablets) continues to be available from the federal government at no cost for federal Entities

# Paxlovid (nirmatrelvir co-packaged with ritonavir) – Pharmacist Prescribing Authorization under EUA

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As outlined in the EUA, Paxlovid may also be prescribed for an individual patient by a state-licensed pharmacist under the following conditions:

- Sufficient information is available, such as through access to health records less than 12 months old or consultation with a health care provider in an established provider-patient relationship with the individual patient, to assess renal and hepatic function; and
- Sufficient information is available, such as through access to health records, patient reporting of medical history, or consultation with a health care provider in an established provider-patient relationship with the individual patient, to obtain a comprehensive list of medications (prescribed and non-prescribed) that the patient is taking to assess for potential drug interaction.

# Paxlovid (nirmatrelvir co-packaged with ritonavir) – Pharmacist Prescribing Authorization under EUA (continued)

The state-licensed pharmacist should refer an individual patient for clinical evaluation (e.g., telehealth, in-person visit) with a physician, advanced practice registered nurse, or physician assistant licensed or authorized under state law to prescribe drugs, if any of the following apply:

- Sufficient information is not available to assess renal and hepatic function.
- Sufficient information is not available to assess for a potential drug interaction.
- Modification of other medications is recommended due to a potential drug interaction.
- Paxlovid is not an appropriate therapeutic option based on the authorized Fact Sheet for Healthcare Providers or due to potential drug interactions for which recommended monitoring would not be feasible.

# Paxlovid (nirmatrelvir co-packaged with ritonavir)

## Dosage and Administration

- **eGFR  $\geq$  60 mL/min:** 300 mg nirmatrelvir (two 150 mg tablets) co-packaged with 100 mg ritonavir (one 100 mg tablet) taken together twice daily for 5 days.
- **Dose reduction for moderate renal impairment eGFR  $\geq$  30 mL/min to  $<$  60 mL/min:** 150 mg nirmatrelvir (one 150 mg tablet) co-packaged with 100 mg ritonavir (one 100 mg tablet) taken together twice daily for 5 days.
- **eGFR  $<$ 30 mL/min:** currently not recommended
- **Severe hepatic impairment (Child-Pugh Class C):** currently not recommended

## Contraindications and Precautions

- History of clinically significant hypersensitivity reactions to the active ingredients or any other components.
- Co-administration with drugs highly dependent on CYP3A for clearance may result in life-threatening reactions<sup>1</sup>.
- Co-administration with potent CYP3A inducers may result in reduced nirmatrelvir plasma concentrations and potential loss of virologic response.
- The concomitant use of Paxlovid (nirmatrelvir co-packaged with ritonavir) and certain other drugs may result in potentially significant drug interactions.
- Hepatic transaminase elevations, hypersensitivity reactions, clinical hepatitis, and jaundice have occurred in patients receiving ritonavir.
- Paxlovid (nirmatrelvir co-packaged with ritonavir) use may lead to a risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection.

<sup>1</sup> [Liverpool Covid-19 interaction checker](https://covid19-druginteractions.org/) <https://covid19-druginteractions.org/>

[Fact Sheet for Healthcare Providers for Paxlovid \(nirmatrelvir co-packaged with ritonavir\)](https://www.fda.gov/media/155050/download) <https://www.fda.gov/media/155050/download>

[Paxlovid Prescribing Information](https://labeling.pfizer.com/ShowLabeling.aspx?id=19599) <https://labeling.pfizer.com/ShowLabeling.aspx?id=19599>

# Paxlovid (nirmatrelvir co-packaged with ritonavir) Patient Eligibility Screening Checklist Tool for Prescribers

## Medical History

- Mild to moderate COVID-19 with symptom onset within 5 days
- Age  $\geq$  12 years of age and weighing at least 40 kg (if utilizing product under EUA)
- Adult (if utilizing approved product)
- Has one or more [risk factors for progression to severe COVID-19](https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html)  
<https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html>
- Not requiring hospitalization due to severe or critical COVID-19 at treatment initiation
- No known or suspected severe renal impairment (eGFR < 30 mL/min)
  - Note that a dose reduction is required for patients with moderate renal impairment (eGFR  $\geq$ 30-<60 mL/min); see the Fact Sheet for Healthcare Providers.
- No known or suspected severe hepatic impairment
- No history of clinically significant hypersensitivity reactions to the active ingredients (nirmatrelvir or ritonavir) or other components of the product

[Paxlovid Prescribing Information](https://labeling.pfizer.com/ShowLabeling.aspx?id=19599) <https://labeling.pfizer.com/ShowLabeling.aspx?id=19599>

[Fact Sheet for Healthcare Providers for Paxlovid \(nirmatrelvir co-packaged with ritonavir\)](https://www.fda.gov/media/155050/download) <https://www.fda.gov/media/155050/download>

See table in [Paxlovid Patient Eligibility Screening Checklist Tool for Prescribers](https://www.fda.gov/media/158165/download) <https://www.fda.gov/media/158165/download>

[See list of risk factors for at least one severe COVID-19 outcome](https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html) <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html>

# Paxlovid (nirmatrelvir co-packaged with ritonavir) Patient Eligibility Screening Checklist Tool for Prescribers (continued)

## Concomitant Medications

- **Assess patient's home medication list for drug-drug interactions**
- See table in [Paxlovid Patient Eligibility Screening Checklist Tool for Prescribers](https://www.fda.gov/media/158165/download)  
<https://www.fda.gov/media/158165/download>
- **HMG-CoA reductase inhibitors (statins)**
  - Patient is taking lovastatin or simvastatin, which are contraindicated with Paxlovid coadministration: The statin can be held 12 hours prior to the first dose of Paxlovid treatment, held during the 5 days of treatment, and restarted 5 days after completing Paxlovid.
  - Patient is taking atorvastatin or rosuvastatin: Temporary discontinuation of atorvastatin and rosuvastatin during treatment with Paxlovid should be considered depending on statin dose. Atorvastatin and rosuvastatin do not need to be held prior to or after completing Paxlovid.
- **Hormonal contraceptives containing ethinyl estradiol:** Patient is taking a hormonal contraceptive containing ethinyl estradiol: The need for an additional non-hormonal method of contraception during the 5 days of Paxlovid treatment and until one menstrual cycle after stopping Paxlovid should be recommended.
- **Medications for HIV-1 Treatment:** Patient is taking medications for the treatment of HIV-1 infection: With the exception of maraviroc, HIV antiretroviral medications can be co-administered with Paxlovid without dose adjustment, but arranging follow-up by the HIV care provider to monitor for side effects is recommended.

## Other Drugs with Established and Other Potentially Significant Drug Interactions with Paxlovid

- See table in [Paxlovid Patient Eligibility Screening Checklist Tool for Prescribers](https://www.fda.gov/media/158165/download) <https://www.fda.gov/media/158165/download>

\*Prescriber is encouraged to include a note to the pharmacist in the prescription stating:

Please fill prescription by [insert date]. This prescription fill by date is within 5 days from symptom onset and complies with the patient eligibility criteria under the EUA.

# Paxlovid (nirmatrelvir co-packaged with ritonavir) Patient Eligibility Screening Checklist Tool for Prescribers (Table)

## PAXLOVID Patient Eligibility Screening Checklist Tool for Prescribers

Other Drugs with Established and Other Potentially Significant Drug Interactions with PAXLOVID (listed alphabetically by generic name)

### Interaction Codes:



Coadministration of this drug with PAXLOVID is CONTRAINDICATED. For further information, refer to the Fact Sheet for Healthcare Providers and the individual Prescribing Information for the drug.



Coadministration of this drug with PAXLOVID should be avoided and/or holding of this drug, dose adjustment of this drug, or special monitoring is necessary. Consultation with the prescriber of the potentially interacting drug is recommended. For further information, refer to the Health Care Provider Fact Sheet and the individual Prescribing Information for the drug.

Drug	Drug Class	Interaction Code
digoxin	Cardiac glycoside	***
dihydroergotamine	Ergot derivative	XXX
diltiazem	Calcium channel blocker	***
dronedarone	Antiarrhythmic	XXX

Drug	Drug Class	Interaction Code
abemaciclib	Anticancer drug	***
alfuzosin	Alpha 1-adrenoreceptor antagonist	XXX
amiodarone	Antiarrhythmic	XXX
amlodipine	Calcium channel blocker	***
apalutamide	Anticancer drug	XXX
bedaquiline	Antimycobacterial	***
bepridil	Antiarrhythmic	***
betamethasone	Systemic corticosteroid	***
bosentan	Endothelin receptor antagonist	***
budesonide	Systemic corticosteroid	***
bupropion	Antidepressant	***
carbamazepine	Anticonvulsant	***
ceritinib	Anticancer drug	***
ciclesonide	Systemic corticosteroid	***
clarithromycin	Anti-infective	***
clozapine	Antipsychotic	***
colchicine	Anti-gout	***
cyclosporine	Immunosuppressant	***
dabigatran	Anticoagulants	***
dasabuvir	Hepatitis C direct acting antiviral	***
dasatinib	Anticancer drug	***
dexamethasone	Systemic corticosteroid	***

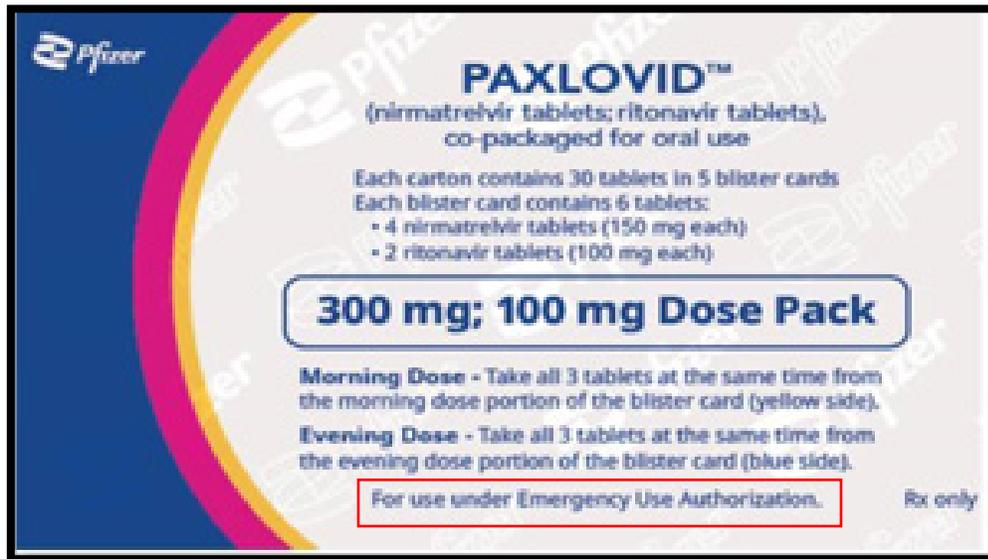
Drug	Drug Class	Interaction Code
rifabutin	Antimycobacterial	***
rifampin	Antimycobacterial	XXX
rivaroxaban	Anticoagulant	***
salmeterol	Long-acting beta-adrenoceptor agonist	***
sildenafil (Revatio®) when used for pulmonary arterial hypertension	PDE5 inhibitor	XXX
sirolimus	Immunosuppressant	***
sofosbuvir/velpatasvir/ voxilaprevir	Hepatitis C direct acting antiviral	***
St. John's Wort (hypericum perforatum)	Herbal product	XXX
tacrolimus	Immunosuppressant	***
trazodone	Antidepressant	***
triamcinolone	Systemic corticosteroid	***
triazolam	Sedative/hypnotic	XXX
venetoclax	Anticancer drug	***
vinblastine	Anticancer drug	***
vincristine	Anticancer drug	***
voriconazole	Antifungal	***
warfarin	Anticoagulant	***

See table in [Paxlovid Patient Eligibility Screening Checklist Tool for Prescribers](https://www.fda.gov/media/158165/download) https://www.fda.gov/media/158165/download

# Additional Paxlovid (nirmatrelvir co-packaged with ritonavir) Prescribing Resources

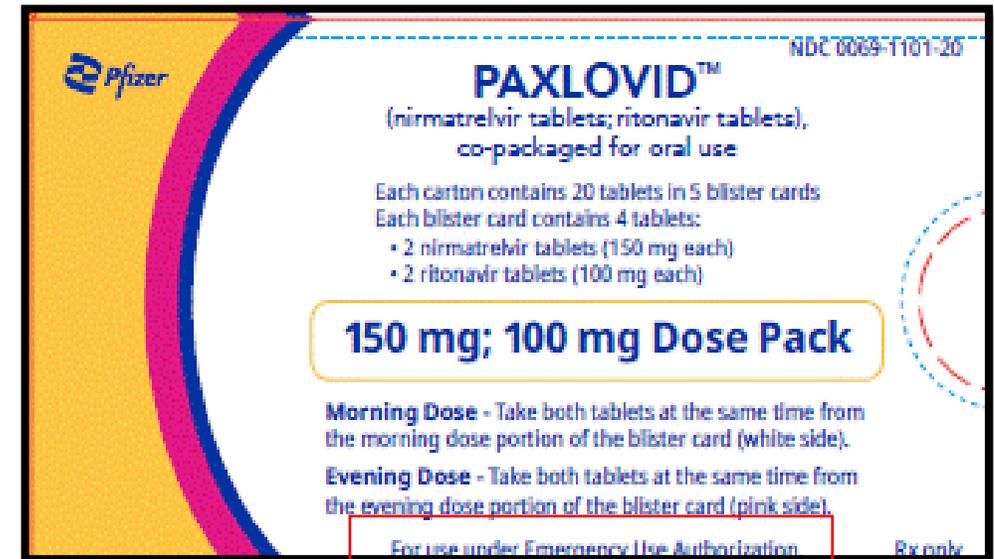
- [University of Liverpool COVID-19 Drug Interactions](https://covid19-druginteractions.org/checker)  
<https://covid19-druginteractions.org/checker>
- [FDA PAXLOVID Patient Eligibility Screening Checklist Tool for Prescribers](https://www.fda.gov/media/158165/download)  
<https://www.fda.gov/media/158165/download>
- [Pfizer Drug Interaction Checker](https://www.pfizermedicalinformation.com/drug-interaction-checker?product=PAXLOVID%E2%84%A2+%7C+nirmatrelvir+tablets%3B+ritonavir+tablets)  
<https://www.pfizermedicalinformation.com/drug-interaction-checker?product=PAXLOVID%E2%84%A2+%7C+nirmatrelvir+tablets%3B+ritonavir+tablets>
- [NIH COVID-19 Treatment Guidelines – Nirmatrelvir Co-Packaged with Ritonavir \(Paxlovid\)](https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ritonavir-boosted-nirmatrelvir--paxlovid/)  
<https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ritonavir-boosted-nirmatrelvir--paxlovid/>

# Paxlovid (nirmatrelvir co-packaged with ritonavir) Formulation and Packaging – EUA Product



## Standard Dose

300 mg nirmatrelvir; 100 mg ritonavir: Each carton contains 30 tablets divided in 5 daily dose blister cards. Each blister card contains 4 nirmatrelvir tablets (150 mg each) and 2 ritonavir tablets (100 mg each). Nirmatrelvir tablets and ritonavir tablets are supplied in separate blister cavities within the same child-resistant blister card.



## Reduced Dose (Renal)

150 mg nirmatrelvir; 100 mg ritonavir: Each carton contains 20 tablets divided in 5 daily dose blister cards. Each blister card contains 2 nirmatrelvir tablets (150 mg each) and 2 ritonavir tablets (100 mg each). Nirmatrelvir tablets and ritonavir tablets are supplied in separate blister cavities within the same child-resistant blister card.

**Note: EUA-labeled Paxlovid will no longer be authorized for emergency use after March 8, 2024**

[Paxlovid Prescribing Information](https://labeling.pfizer.com/ShowLabeling.aspx?id=19599) <https://labeling.pfizer.com/ShowLabeling.aspx?id=19599>

# Paxlovid (nirmatrelvir co-packaged with ritonavir) Formulation and Packaging – Commercial NDA-labeled



## Standard Dose

300 mg nirmatrelvir; 100 mg ritonavir: Each carton contains 30 tablets divided in 5 daily dose blister cards. Each blister card contains 4 nirmatrelvir tablets (150 mg each) and 2 ritonavir tablets (100 mg each). Nirmatrelvir tablets and ritonavir tablets are supplied in separate blister cavities within the same child-resistant blister card.



## Reduced Dose (Renal)

150 mg nirmatrelvir; 100 mg ritonavir: Each carton contains 20 tablets divided in 5 daily dose blister cards. Each blister card contains 2 nirmatrelvir tablets (150 mg each) and 2 ritonavir tablets (100 mg each). Nirmatrelvir tablets and ritonavir tablets are supplied in separate blister cavities within the same child-resistant blister card.

[Paxlovid Prescribing Information](https://labeling.pfizer.com/ShowLabeling.aspx?id=19599) <https://labeling.pfizer.com/ShowLabeling.aspx?id=19599>

# Viral RNA Rebound

- Post-treatment increases in SARS-CoV-2 RNA levels (i.e., viral RNA rebound) in nasopharyngeal samples were observed on Day 10 and/or Day 14 in a subset of Paxlovid and placebo recipients, irrespective of COVID-19 symptoms. The frequency of detection of post-treatment viral RNA rebound varied according to analysis parameters but was generally similar among Paxlovid and placebo recipients, regardless of the rebound definition used. A similar or smaller percentage of placebo recipients compared to Paxlovid recipients had nasopharyngeal viral RNA results < LLOQ (lower limit of quantitation) at all study timepoints in both the treatment and post-treatment periods.
- Post-treatment viral RNA rebound was not associated with the primary clinical outcome of COVID-19-related hospitalization or death from any cause through Day 28 following the single 5-day course of Paxlovid treatment. Post-treatment viral RNA rebound also was not associated with drug resistance as measured by Mpro sequencing. The clinical relevance or exact incidence of post-treatment increases in viral RNA following Paxlovid or placebo treatment is unknown at this time.
- Viral RNA rebound is not specific to Paxlovid or Lagevrio and has been seen in placebo recipients.

**\*\*\*Not exclusive to Paxlovid\*\*\***

See Microbiology (12.4): Viral RNA Rebound of [Fact Sheet for Healthcare Providers: EUA for Paxlovid](https://www.fda.gov/media/155050/download) <https://www.fda.gov/media/155050/download>  
[Paxlovid Prescribing Information](https://labeling.pfizer.com/ShowLabeling.aspx?id=19599) <https://labeling.pfizer.com/ShowLabeling.aspx?id=19599>

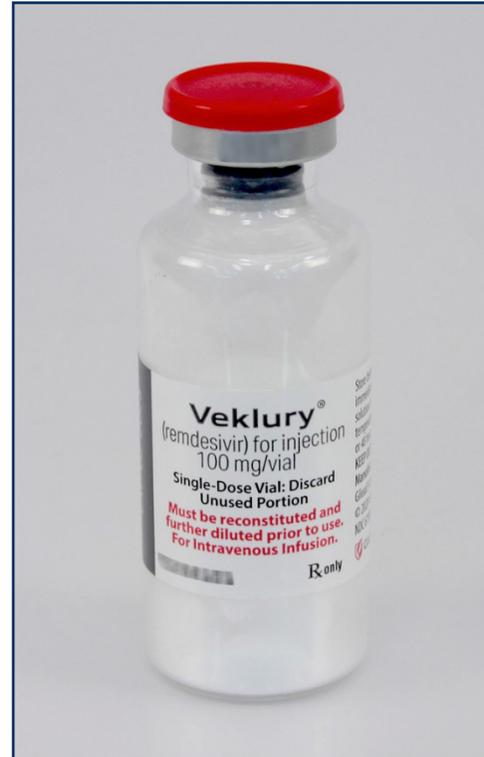
# Paxlovid (nirmatrelvir co-packaged with ritonavir)

## Product Information & Ordering Logistics

- **EUA Status:** EUA for pediatric patients (12 years of age and older weighing at least 40 kg) is active: NDA-labeled Paxlovid will be used –Active
- **Procurement:** USG purchased and commercially available.
- **Eligibility information for product labeled under EUA:**
  - [ASPR Paxlovid page](https://aspr.hhs.gov/COVID-19/Therapeutics/Products/Paxlovid/Pages/default.aspx) <https://aspr.hhs.gov/COVID-19/Therapeutics/Products/Paxlovid/Pages/default.aspx>
  - [Frequently Asked Questions: FDA EUA for Paxlovid \(FDA\)](https://www.fda.gov/media/155052/download) <https://www.fda.gov/media/155052/download>
  - [Letter of Authorization](https://www.fda.gov/media/155049/download?attachment): <https://www.fda.gov/media/155049/download?attachment>
- **Indications and usage for product labeled under FDA approval**
  - [Paxlovid Prescribing Information](https://labeling.pfizer.com/ShowLabeling.aspx?id=19599) <https://labeling.pfizer.com/ShowLabeling.aspx?id=19599>
- **To order:**
  - [Process for Ordering COVID-19 Therapeutics | HHS/ASPR](https://aspr.hhs.gov/HPOP/Pages/default.aspx)  
<https://aspr.hhs.gov/HPOP/Pages/default.aspx>
- **Where to find:**
  - [Treatments Locator \(hhs.gov\)](https://treatments.hhs.gov/) <https://treatments.hhs.gov/>

# Veklury (remdesivir) – Gilead Antiviral for IV Infusion (Preferred)

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[Veklury Product Information](https://www.vekluryhcp.com/)  
<https://www.vekluryhcp.com/>

# Veklury (remdesivir) Product Information

- Prescribing Information & FDA Fact Sheets
  - [Veklury \(remdesivir\) Prescribing Information](https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf) [https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury\\_pi.pdf](https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf)
  - [Veklury Patient Information](https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_patient_pi.pdf) [https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury\\_patient\\_pi.pdf](https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_patient_pi.pdf)
- Manufacturer's Resources:
  - [Website for Healthcare Providers](https://www.vekluryhcp.com/) <https://www.vekluryhcp.com/>
  - [Website for Patients](https://www.veklury.com/) <https://www.veklury.com/>
- Safety Reporting:
  - [FDA MedWatch](https://www.accessdata.fda.gov/scripts/medwatch/index.cfm) <https://www.accessdata.fda.gov/scripts/medwatch/index.cfm>
  - [Safety Reporting Email](mailto:Safety_fc@gilead.com) [Safety\\_fc@gilead.com](mailto:Safety_fc@gilead.com)
  - [Report a Pregnancy Exposure](https://covid-pr.pregistry.com) <https://covid-pr.pregistry.com>

# Veklury (remdesivir) – Outpatient Use

- FDA approved [Veklury \(remdesivir\)](#) for certain **non-hospitalized** adults and pediatric patients for treatment of mild-to-moderate COVID-19, including:
  - Adults and pediatric patients 28 days of age and older and weighing at least 3 kg, **AND**
  - Who are not hospitalized and have mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death
- The treatment course of Veklury (remdesivir) should be initiated as soon as possible after diagnosis of symptomatic COVID-19 has been made and **within 7 days** of symptom onset. The recommended total duration of treatment for non-hospitalized patients is 3 days.
- No dosage adjustment of Veklury is recommended in patients with any degree of renal impairment, including those on dialysis for adult and pediatric patients
  - Veklury may be administered without regard to the timing of dialysis in all patients
- No dosage adjustment of Veklury is recommended for patients with mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, or C)
  - The label still recommends:
    - Initial hepatic laboratory testing in all patients, before starting Veklury and during treatment as clinically appropriate
    - Discontinuation be considered if alanine transaminase (ALT) levels increase to 10 times the upper limit of normal or if ALT elevation is accompanied by signs or symptoms of liver inflammation.

# Veklury (remdesivir)

## Dosage and Administration

- Dosage:
  - For adults and pediatric patients who weight  $\geq$  40kg: **200 mg** on Day 1, followed by once-daily maintenance doses of **100 mg** from Day 2 administered only via intravenous infusion over 30 to 120 minutes
  - For pediatric patients 28 days of age and older and weighing 3 kg to less than 40 kg: **5 mg/kg** on Day 1 followed by **2.5 mg/kg** once daily from Day 2
- Dosage Forms:
  - For injection: **100 mg** of remdesivir as a lyophilized powder, in a single-dose vial
  - Injection: **100 mg/20 mL (5 mg/mL)** remdesivir, in a single-dose vial

## Contraindications and Precautions

- Contraindications
  - History of clinically significant hypersensitivity reactions to Veklury or any components of the product
  - Hypersensitivity including infusion-related and anaphylactic reactions
- Pre-administration testing
  - Perform hepatic laboratory testing in all patients before starting Veklury and during treatment as clinically appropriate
  - Assess prothrombin time before starting Veklury and monitor as clinically appropriate
- Increased risk of transaminase elevations with administration
- Risk of reduced antiviral activity when co-administered with chloroquine phosphate or hydroxychloroquine sulfate

# Veklury (remdesivir) Pediatric Eligibility Criteria

- Pediatric patients **28 Days of Age and Older** and weighing **3 kg to less than 40 kg\***
- Mild-to-moderate COVID-19 and at high risk for progression to severe disease
- Initiate within **7 days of symptom onset**

\* Pediatric patients less than 12 years of age but weighing 40kg or greater receive Veklury at the adult dose

# Veklury (remdesivir) Pediatric Dosing and Administration

Body weight	Recommended dosage form	Loading dose (on Day 1)	Maintenance dose (from Day 2)
3 kg to less than 40 kg	Veklury for injection, lyophilized powder <u>Only</u>	5 mg/kg	2.5 mg/kg

- Lyophilized powder: **100 mg** of Veklury (remdesivir) reconstituted with 19 mL of Sterile Water for Injection. The only approved dosage form of Veklury for pediatric patients weighing 3 kg to less than 40 kg is Veklury for injection (supplied as 100 mg lyophilized powder in vial).
- Further dilute to a concentration of 1.25 mg/mL using 0.9% sodium chloride
  - Small 0.9% sodium chloride infusion bags (e.g., 25, 50, or 100 mL) or an appropriately sized syringe should be used for pediatric dosing.

# Veklury (remdesivir)

## Recommended Rate of Infusion-Diluted Veklury for Injection Lyophilized Powder for Pediatric Patients Weighing 3 kg to Less than 40 kg

Infusion volume	Infusion time <sup>1</sup>	Rate of infusion
100 mL	30 min	3.33 mL/min
	60 min	1.67 mL/min
	120 min	0.83 mL/min
50 mL	30 min	1.67 mL/min
	60 min	0.83 mL/min
	120 min	0.42 mL/min
25 mL	30 min	0.83 mL/min
	60 min	0.42 mL/min
	120 min	0.21 mL/min
7 mL	30 min	0.23 mL/min
	60 min	0.12 mL/min
	120 min	0.06 mL/min

<sup>1</sup> See section 2.6 of [Veklury \(remdesivir\) Prescribing Information](https://www.gilead.com/-/media/files/pdfs/medicines/COVID-19/veklury/veklury_pi.pdf) [https://www.gilead.com/-/media/files/pdfs/medicines/COVID-19/veklury/veklury\\_pi.pdf](https://www.gilead.com/-/media/files/pdfs/medicines/COVID-19/veklury/veklury_pi.pdf)

# Operational Considerations for Outpatient Veklury Administration

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- Infusion schedule and hours of operation:
  - Infusion requires 3 consecutive days of administration
  - Infusion sites need to have appropriate hours of operation to accommodate complete infusion cycle
- Pediatric-specific infusion:
  - Providers credentialed in pediatrics
  - Staff trained in assessment and management of pediatric patients
- Capacity for lab testing, liver function, and prothrombin time as clinically appropriate

# Post-Veklury Administration Observation

- Per Veklury prescribing information, “Monitor patients during dose administration and observe for **at least 1 hour** after intravenous infusion or subcutaneous dosing is complete”.
- Provide education on follow-up, required isolation per CDC guidelines after COVID-19 exposure or diagnosis, red flags for seeking emergency care.
- Respond to severe adverse events/anaphylaxis.
- “Discharge” patient after one-hour post-administration observation if stable and without symptoms of severe adverse reaction, otherwise consider further observation or emergency department evaluation if clinical concern.
- To report SUSPECTED ADVERSE REACTIONS, contact Gilead Sciences, Inc. at 1-800-GILEAD-5 or FDA at 1-800-FDA-1088 or [MedWatch](#) (<https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program>)

[CDC Guidelines on Isolation and Precautions for People with COVID-19](https://www.cdc.gov/coronavirus/2019-ncov/your-health/isolation.html) <https://www.cdc.gov/coronavirus/2019-ncov/your-health/isolation.html>

[Possible Side Effects After Getting a COVID-19 Vaccine | CDC Archive](https://archive.cdc.gov/#/details?url=https://www.cdc.gov/coronavirus/2019-ncov/vaccines/expect/after.html) <https://archive.cdc.gov/#/details?url=https://www.cdc.gov/coronavirus/2019-ncov/vaccines/expect/after.html>

# Managing Adverse Reactions to Veklury

- **Veklury should only be administered** in settings in which health care providers have immediate access to medications (e.g., epinephrine) to treat a severe infusion or hypersensitivity reactions, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.
- Early identification of anaphylaxis. Symptoms may include:
  - Respiratory: hypoxia, dyspnea, wheezing, angioedema
  - Gastrointestinal: nausea, transaminase elevation
  - Cardiovascular: hypotension, hypertension, tachycardia, bradycardia
  - Skin/mucosal: rash
  - Neurologic: agitation, convulsions, altered mental status, sense of impending doom
  - Other: diaphoresis, shivering, fever

# Managing Adverse Reactions to Infused Outpatient COVID Therapeutics: Medications and Equipment

- **Should be available** at all sites:
  - Epinephrine (e.g., prefilled syringe or autoinjector)
  - H1 antihistamine (e.g., diphenhydramine, cetirizine)
  - Blood pressure monitor
- **If feasible**, include at sites (not required):
  - Pulse Oximeter
  - Oxygen
  - Bronchodilator (e.g., albuterol)
  - H2 antihistamine (e.g., famotidine, cimetidine)
  - Intravenous fluids
  - Intubation kit
  - Pocket mask with one-way valve (CPR mask) sized for adults and children

Adapted from [CDC Interim Considerations: Preparing for the Potential Management of Anaphylaxis at COVID-19 Vaccine Sites](https://www.cdc.gov/vaccines/covid-19/downloads/InterimConsiderations-for-the-Potential-Management-of-Anaphylaxis-at-COVID-19-Vaccine-Sites.pdf) <https://www.cdc.gov/vaccines/covid-19/downloads/InterimConsiderations-for-the-Potential-Management-of-Anaphylaxis-at-COVID-19-Vaccine-Sites.pdf>

# Veklury Storage and Preparation

## Administration preparation process:

- Prepare sterile infusions in a manner consistent with local laws, regulations, guidelines and policies
- Obtain new vial(s) and/or IV bags if the drug product contains any visible particulate matter
- See [Prescribing Information](#) for reconstitution instructions  
[https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury\\_pi.pdf](https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf)

## Needs for space to prepare infusion:

- Dedicated preparation area for sterile preparation

## Acceptable equipment for Veklury drug storage:

- Refrigerated storage (2-8 °C)
- Temperature control mechanism including temperature monitoring process

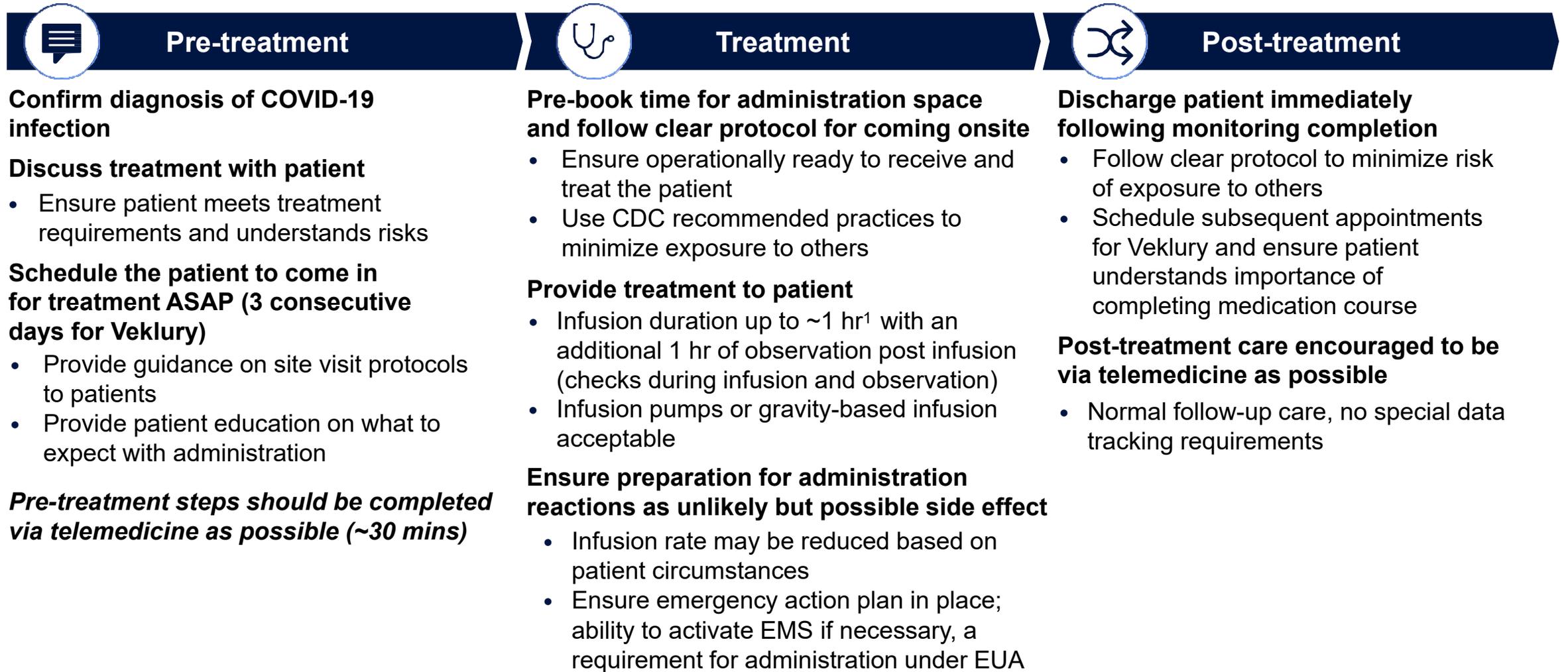
*Note: product can be prepared for infusion bedside by any qualified medical professional*

[Official Veklury Website](https://www.vekluryhcp.com/dosing-and-admin/) <https://www.vekluryhcp.com/dosing-and-admin/>

# Veklury (remdesivir): Product Information

- **FDA Approved for certain COVID19 indications, outpatient and inpatient**
- **Procurement/Ordering:**
  - Commercially available through [Gilead Pharmaceuticals](https://www.gilead.com/remdesivir) <https://www.gilead.com/remdesivir>
  - Veklury is available through multiple distributors.
    - Outpatient distribution: Amerisource Bergen and Cardinal
      - Non-hospital entities that can attest to the proper administration of Veklury in accordance with the label can order Veklury for outpatient use.
    - Inpatient hospital distribution: Hospitals should continue ordering Veklury through AmerisourceBergen Specialty Division, Cardinal Specialty, and McKesson Plasma & Biologics.
  - Treatment Locator Tool include outpatients Veklury (remdesivir) providers that allows visibility of Veklury outpatient infusion sites on the [-Treatments Locator \(hhs.gov\)](https://treatments.hhs.gov/) to assist in matching patients at high risk of severe COVID-19 to the medications that can prevent disease progression [Treatments Locator \(hhs.gov\)](https://treatments.hhs.gov/) <https://treatments.hhs.gov/>
- Infusion sites can **opt in** using [this simple online form](https://hpop.hhs.gov/ords/r/ohrr/voluntary). All that is needed from provider is location information and agreement to participate) <https://hpop.hhs.gov/ords/r/ohrr/voluntary>
  - For provider sites that want to be removed from the locator, follow the [opt in link](https://hpop.hhs.gov/ords/r/ohrr/voluntary), fill out the form and select to opt out before re-submitting. In order to opt out, please ensure you use the EXACT information previously used when provider opted in. [HPoP Voluntary Reporting \(hhs.gov\)](https://hpop.hhs.gov/ords/r/ohrr/voluntary) <https://hpop.hhs.gov/ords/r/ohrr/voluntary>
- Sites are encouraged to offer outpatient Veklury, especially in collaboration with tertiary centers treating immunocompromised patients for whom Paxlovid may not be clinically appropriate (e.g., transplant centers, oncology, etc.) and for vulnerable pediatric patients not eligible for other outpatient treatments.

# Example of Patient Flow for Outpatient Intravenous Product



<sup>1</sup>Contingent on product dilution, reference EUA fact sheet or prescribing information for dilution and infusion timing

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# **Products for Treatment of Mild-to-Moderate COVID-19: Alternative Therapies**

# Lagevrio (molnupiravir) – Merck Oral Antiviral (Alternative)



[Lagevrio \(molnupiravir\) Product Information](https://www.molnupiravir-us.com/)

<https://www.molnupiravir-us.com/>

# Lagevrio (molnupiravir) Product Information

- FDA Fact Sheets
  - [Lagevrio \(molnupiravir\) provider fact sheet](https://www.fda.gov/media/155054/download)  
https://www.fda.gov/media/155054/download
  - [Lagevrio \(molnupiravir\) patient fact sheet](https://www.fda.gov/media/155055/download) https://www.fda.gov/media/155055/download
  - Lagevrio (molnupiravir) patient fact sheet (Spanish): N/A
- Manufacturer's Resources:
  - [Website for Healthcare Providers](https://www.molnupiravir-us.com/hcp/) https://www.molnupiravir-us.com/hcp/
  - [Website for Patients](https://www.molnupiravir-us.com/patients/) https://www.molnupiravir-us.com/patients/
- Safety Reporting:
  - [DHCP Letter](https://www.fda.gov/media/165071/download) https://www.fda.gov/media/165071/download
  - [Report a Pregnancy Exposure](https://covid-pr.pregistry.com) https://covid-pr.pregistry.com
  - [FDA MedWatch](https://www.accessdata.fda.gov/scripts/medwatch/index.cfm) https://www.accessdata.fda.gov/scripts/medwatch/index.cfm
  - [Safety Reporting Email](mailto:dpoc.usa@msd.com) dpoc.usa@msd.com

# Lagevrio (molnupiravir) Authorization

- Lagevrio (molnupiravir) has been authorized by FDA under an EUA, for the treatment of mild-to-moderate COVID-19 in adults who are at high-risk for progression to severe COVID-19, including hospitalization or death, for whom alternative COVID-19 outpatient treatment options approved or authorized by FDA are not accessible or clinically appropriate.
- Not authorized for:
  - Patients less than 18 years of age
  - Initiation of treatment in patients requiring hospitalization due to COVID-19
  - Use longer than 5 consecutive days
- Lagevrio (molnupiravir) may only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under state law to prescribe drugs in the therapeutic class to which Lagevrio (molnupiravir) belongs (i.e., anti-infectives).

# Lagevrio (molnupiravir)

## Dosage and Administration

- **800 mg (four 200 mg capsules)** taken orally every 12 hours for 5 days, with or without food.
- Take Lagevrio (molnupiravir) as soon as possible after a diagnosis of COVID-19 has been made, and within 5 days of symptom onset.
- Not authorized for use for longer than 5 consecutive days.
- For administration via nasogastric (NG) or orogastric (OG) Tube (12F or larger), refer to instructions within the EUA Fact Sheet, Section 2.3

## Contraindications and Precautions

- No contraindications have been identified based on the limited available data on the emergency use of Lagevrio (molnupiravir) authorized under the EUA.
- Not recommended for use during pregnancy and not authorized for use in patients under 18 years of age.
- Hypersensitivity reactions, including anaphylaxis have been reported with Lagevrio (molnupiravir).
- If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue Lagevrio (molnupiravir).

# Lagevrio (molnupiravir) Checklist Tool for Prescribers

## Patient Eligibility

- Current diagnosis of mild to moderate COVID-19
- Age  $\geq$  18 years
- Alternate COVID-19 treatment options approved or authorized by FDA are not accessible or clinically appropriate
- High-risk<sup>1</sup> criteria met
- Symptom onset within **5 days\***
- Not hospitalized due to COVID-19

\*Prescriber is encouraged to include a note to the pharmacist in the prescription stating:

Please fill prescription by [insert date]. This prescription fill by date is within 5 days from symptom onset and complies with the patient eligibility criteria under the EUA.

1. [CDC Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Professionals](https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html): <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html>  
[Molnupiravir Checklist Tool for Prescribers](https://www.fda.gov/media/155118/download): <https://www.fda.gov/media/155118/download>

# Lagevrio (molnupiravir) Checklist Tool for Prescribers (continued)

## Prescriber Requirements – All Patients

- Provide electronic or hard copy of patient fact sheet
- Document\* that patient has received an electronic or hard copy of the patient fact sheet
- Review the information contained within the patient factsheet with the patient and counsel patient on the known and potential benefits and risks of Lagevrio (molnupiravir)
- Advise patients on need for contraception use as appropriate
  - Females of childbearing potential treated: should use a reliable method of contraception correctly and consistently, as applicable, for the duration of treatment and for 4 days after the last dose of Lagevrio (molnupiravir)
  - Males of reproductive potential treated: if sexually active with females of childbearing potential, should use a reliable method of contraception correctly and consistently during treatment and for at least 3 months after the last dose
- The prescribing healthcare provider and/or the provider's designee must report all medication errors and serious adverse events potentially related to Lagevrio (molnupiravir) within 7 calendar days from the healthcare provider's awareness of the event

\*How and where documentation occurs is at the discretion of the prescribing health care provider and their clinical site.

[Molnupiravir Checklist Tool for Prescribers](https://www.fda.gov/media/155118/download): <https://www.fda.gov/media/155118/download>

# Lagevrio (molnupiravir) Checklist Tool for Prescribers (continued)

## Prescriber Requirements – Individuals of Childbearing Potential

- Assess whether pregnant or not
  - Report of LMP in an individual who has regular menstrual cycles, uses a reliable method of contraception correctly and consistently or has had a negative pregnancy test
  - Negative pregnancy test (recommended but not required if other criteria are not met)
- If pregnant:
- Counsel the patient regarding the known and potential benefits and potential risks of molnupiravir use during pregnancy
  - Document that the patient is aware of the known and potential benefits and potential risks of molnupiravir use during pregnancy
  - Make the individual aware of the [pregnancy registry](https://covid-pr.pregistry.com/) or 1-800-616-3791
- If not pregnant:
  - Make the individual aware of the pregnancy registry program and encourage them to participate should they become pregnant

# Viral RNA Rebound

- Viral RNA Rebound Post-treatment increases in SARS-CoV-2 RNA shedding levels (i.e., viral RNA rebound) in nasopharyngeal samples were observed on Day 10, Day 15, and/or Day 29 in a subset of Lagevrio and placebo recipients in the Phase 3 MOVE-OUT trial. **Approximately 1% of both Lagevrio and placebo recipients had evidence of recurrent COVID-19 symptoms coinciding with a rebound in viral RNA levels in nasopharyngeal samples.**
- Post-treatment viral RNA rebound **was not associated with the primary clinical outcome of hospitalization or death** through Day 29 following the single 5-day course of Lagevrio treatment. Post-treatment viral RNA rebound **also was not associated with the detection of cell culture infectious virus** in nasopharyngeal swab samples
- Viral RNA rebound is not specific to Lagevrio or Paxlovid and has been seen in placebo recipients

**\*\*\*Not exclusive to Lagevrio\*\*\***

See Microbiology (12.4): Viral RNA Rebound of [Fact Sheet for Healthcare Providers: EUA for Lagevrio](https://www.fda.gov/media/155054/download) <https://www.fda.gov/media/155054/download>

# Lagevrio (molnupiravir): Product Information & Ordering Logistics

- **EUA Status:** Currently under Emergency Use Authorization
- **Procurement:** USG purchased and commercially available
- **Eligibility information:**
  - [ASPR Lagevrio page](https://aspr.hhs.gov/COVID-19/Therapeutics/Products/Lagevrio/Pages/default.aspx)  
https://aspr.hhs.gov/COVID-19/Therapeutics/Products/Lagevrio/Pages/default.aspx
  - [Frequently Asked Questions: FDA EUA for Lagevrio \(FDA\)](https://www.fda.gov/media/155056/download)  
https://www.fda.gov/media/155056/download
- **To order:**
  - [Process for Ordering COVID-19 Therapeutics | HHS/ASPR](https://aspr.hhs.gov/HPOP/Pages/default.aspx)  
https://aspr.hhs.gov/HPOP/Pages/default.aspx
- **Where to find:**
  - [Treatments Locator \(hhs.gov\)](https://treatments.hhs.gov/)  
https://treatments.hhs.gov/

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# **Module 3: Oral Antiviral Administration**

# Patient Flow for Antiviral Oral Therapies

(When product not available onsite)



## Assessment and Prescribing

**Confirm diagnosis of COVID-19 infection**

**Discuss treatment with patient**

- Ensure patient meets treatment requirements and understands risks

**Prescribe therapy for patient & provide the medication fact sheet (for product under EUA)**



## Visit Discharge

**Prescription provided to the patient**

- Ensure patient understands medication therapy being provided
- Ensure medication therapy being dispensed complies with federal/state dispensing laws

**Discuss treatment with patient**

- Ensure patient meets treatment requirements and understands risks

**Prescribe therapy for patient & provide the medication fact sheet (for product under EUA)**

- Document required patient assessment in medical record
- Provide patient education on medication therapy being prescribed

**Determine locations medication is available in local area.**



## Post-visit

**Pharmacist receives or prescribes patient prescription**

- Pharmacy should prioritize the prescription fill and ensure timely turnaround to support same day start for therapy
- Pharmacist verifies prescription is appropriate for patient. Any concerns are clarified with prescribing provider

**Pharmacy staff dispenses product to the patient**

- Patient is counseled on medication therapy and reminded to start immediately

**Patient to begin prescribed therapy immediately and continue x 5 days**

**Patient to report any adverse effect to FDA MedWatch**

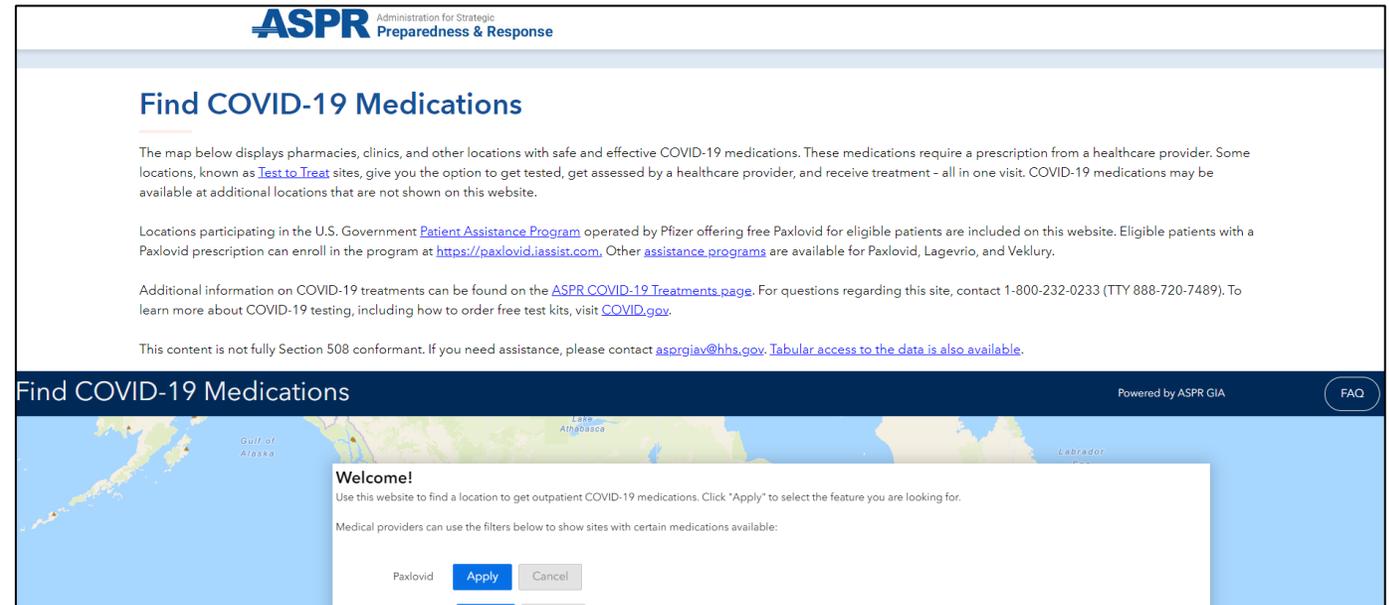
- Patients that present for hospital visit may continue their prescribed antiviral during hospitalization (at discretion of provider)

# Test to Treat: About the Program

- Overall goal of Test to Treat program is to increase access to COVID-19 oral therapeutics, **particularly for individuals who don't have ready access to a health care provider**
- **Sites with Test to Treat services give patients the option to get tested, get assessed by a healthcare provider, and receive treatment – all in one visit.**
- COVID-19 treatments delivered as part of Test to Treat Program (Paxlovid and Lagevrio) must be taken within 5 days of initial COVID-19 symptoms.
- Helps close gap between positive COVID-19 test and receiving treatment for those eligible
- An individual's healthcare providers remain the first option for care; Test to Treat sites are one additional access point.
- Find Test to Treat locations on the [Treatments Locator](http://treatments.hhs.gov/) <http://treatments.hhs.gov/>

# Treatments Locator

- The Treatments Locator displays pharmacies, clinics, and other locations with safe and effective COVID-19 medications.
- Users can find locations offering Test to Treat, telehealth, home delivery, and testing services for eligible patients
- Locations participating in the U.S. Government [Patient Assistance Program](https://paxlovid.iassist.com/) operated by Pfizer offering free Paxlovid for eligible patients are included on this website.  
<https://paxlovid.iassist.com/>
- For questions regarding this site, contact 1-800-232-0233 (TTY 888-720-7489).



[Treatments Locator](https://treatments.hhs.gov)  
Treatments.hhs.gov

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# **Module 4: Facilitating Patient Access**

# Access to OAVs

- Pharmacy partners are encouraged to **order commercial product to ensure that there is adequate supply to meet demand for oral antivirals**
  - There should be no gap between depletion of USG-distributed product and commercial product
- Anyone facing difficulty in access at the pharmacy counter should be directed to the patient assistance programs available to support access to [Paxlovid \(PAXCESS\)](https://www.paxlovid.com/paxcess) <https://www.paxlovid.com/paxcess> and [Lagevrio \(Merck Helps\)](https://www.merckhelps.com/LAGEVRIO) <https://www.merckhelps.com/LAGEVRIO>
- Through the Paxlovid PAP operated by Pfizer, individuals covered under federal programs, such as Medicare or Medicaid, and uninsured patients have a free access option to Paxlovid through 2024. -Eligible uninsured and uninsured have a free access option beyond 2024
- Commercially insured can access the co-pay savings program
- **Medical professionals, pharmacy and plan partners should take steps to ensure patients understand the full range of options**
  - **Guide patients to enroll** – to ensure little to no cost for patient, encourage enrollment/awareness at every opportunity (eg, prior to pharmacy engagement)

# Continued Access to Paxlovid

- **Medicare, Medicaid, and uninsured patients will continue to receive Paxlovid at no charge** through December 2024 using the USG Patient Assistance Program (USG PAP) operated by Pfizer
  - Includes all patients publicly insured through Medicare (with or without Part D, Part B, or Part C and inclusive of Medicare Advantage), Medicaid/CHIP, TRICARE, and patients insured through the VA Community Care Network
  - Uses USG-procured supply (commercial, NDA-labeled)
- Separately, **federal entities (HRSA, IHS, VA, DoD, others) will have continued access to USG-procured Paxlovid supply for their patients**, similar to how they have accessed Paxlovid to date
- USG-procured Paxlovid may also be used to support state, local, tribal, or territorial **special programs targeting vulnerable populations on a case-by-case basis**
  - Reach out to your [ASPR regional staff by email](mailto:covid19.therapeutics@hhs.gov) covid19.therapeutics@hhs.gov
- Concurrently, Pfizer is operating a [Paxlovid Co-Pay Savings Program](https://www.paxlovid.com/enroll-in-co-pay-program) for eligible privately (commercially) insured patients <https://www.paxlovid.com/enroll-in-co-pay-program>
  - Accessible through [Paxlovid for patients](https://www.paxlovid.com/) <https://www.paxlovid.com/> and [Paxlovid for health care providers](https://paxlovid.pfizerpro.com/) <https://paxlovid.pfizerpro.com/> or Phone 1-877-C19-PACK (1-877-219-7225) IVR & Live Operator Support

# Continued Access to Lagevrio

- The [Merck Patient Assistance Program](https://merckhelps.com/LAGEVRIO) (a 501c3 non-profit organization) provides Lagevrio free of charge to patients who meet its eligibility criteria and who, without assistance, could not otherwise afford the product.  
<https://merckhelps.com/LAGEVRIO>
  - This product is **ONLY available through an URGENT NEED request**. Your **Health Care Provider must call 800-727-5400** and tell the program representative that they are making an Urgent Need Request for LAGEVRIO. The program representative will provide necessary instructions. Your Health Care Provider must follow the program representative's instructions to make your request. You may also check your eligibility on [MerckHelps](https://merckhelps.com/LAGEVRIO). <https://merckhelps.com/LAGEVRIO>
- In addition, USG-procured Lagevrio will continue to be distributed to certain federal entities, including HRSA-supported health centers, Indian Health Service, and others until USG supply is depleted.

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# Module 5: Reimbursement

# CMS Guidance for Oral Antivirals

- Oral antivirals for COVID-19 that meet the statutory requirements at section 1860D-2(e) of the Social Security Act and are not otherwise excluded from coverage **must be covered** by Part D plans, either as a formulary product or through the formulary exception process consistent with 42 CFR § 423.578(b).
- Consistent with the November 4, 2022, memorandum CMS continues to encourage Part D sponsors to add at least one oral antiviral for COVID-19 that meets the definition of a Part D drug to their Contract Year (CY) 2024 formulary on a preferred or \$0 cost-sharing tier, as available in the plan benefit structure.

[CMS Commercial COVID-19 oral antivirals memo](https://www.cms.gov/files/document/commercialcovid19oralantiviralsmemofinal.pdf)

<https://www.cms.gov/files/document/commercialcovid19oralantiviralsmemofinal.pdf>

# CMS Resources: Veklury Billing

- **CMS created HCPCS (Healthcare Common Procedure Coding System) code J0248 for Veklury**
  - J0248 represents 1mg, and you should report units to reflect the dosage you administered for each patient.
- Outpatient Billing Example: a provider administering Veklury (remdesivir) in the outpatient setting would bill J0248 for the product and could use the following CPT code for its administration:
- 96365 (Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour)
  - and if needed use: 96366 (Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)).
- Medicare Part B will provide payment for the drug and its administration under the applicable Medicare Part B payment policy when you provide it in the outpatient setting, according to the FDA approval and authorization. In most cases, your patient's yearly Part B deductible and 20% co-insurance apply.
- [CMS COVID-19 FAQs](https://www.cms.gov/files/document/03092020-covid-19-faqs-508.pdf) (https://www.cms.gov/files/document/03092020-covid-19-faqs-508.pdf) Veklury FAQs begin on page 146

# CMS Resources

## CMS Resources:

- [CMS COVID-19 Monoclonal Antibodies](https://www.cms.gov/monoclonal) <https://www.cms.gov/monoclonal>
- [CMS COVID-19 toolkits](https://www.cms.gov/covidvax) <https://www.cms.gov/covidvax>
- [Guidance for the Expiration of the COVID-19 Public Health Emergency \(PHE\)](https://www.cms.gov/files/document/qso-23-13-all.pdf)  
<https://www.cms.gov/files/document/qso-23-13-all.pdf>
- Oral Antiviral NDC Numbers:
  - Paxlovid: **0069-1085-06, 0069-1085-30, 0069-0345-06, 0069-0345-30**
  - Reduced Dose (Renal) Paxlovid: **0069-1101-20**
  - Lagevrio (molnupiravir): **0006-5055-06, 0006-5055-07**
- Veklury (remdesivir) NDC Numbers: **61958-2901-2** (lyophilized powder for injection), **61958-2902-2** (aqueous-based solution for injection)

Continue to check [CMS website](http://www.CMS.gov) for most up to date information ([www.CMS.gov](http://www.CMS.gov))

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# Module 6: Product Returns

# Inventory and Disposal Management for Transition to Traditional Commercial Distribution

## Lagevrio

- USG-distributed supply should be dispensed to patients until depletion or expiration, whichever comes first
- USG-distributed supply cannot be returned/disposed of unless expired (first expiry February 2024, [ASPR searchable expiry database](#))  
<https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/Product-Expiry.aspx>
- Once expired, should be disposed of through manufacturer's return process or on site in accordance with all federal, state, and local regulations

## Paxlovid

- Unexpired USG-distributed supply can be dispensed to patients while provider obtains commercial supply
- Providers with excess USG-distributed, EUA-labeled Paxlovid are encouraged to return product through the Pfizer returns process to facilitate a credit to USG. All returns should be initiated by mid February 2024, to ensure the product is received by February 29, 2024
- Any expired product (Pfizer's [searchable expiry database](#)), should be disposed of through manufacturer's return process or on site in accordance with all federal, state, and local regulations <https://www.paxlovidlotexpiry.com/>

## [COVID-19 Therapeutics Transition Guide](#)

<https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/COVID19-Tx-Transition-Guide.aspx>

# Data Reporting Requirements

In accordance with the COVID-19 Therapeutics Provider Agreement, providers are responsible for adhering to all requirements outlined in the agreement while dispensing USG-distributed product.

- **Providers are expected to provide reporting of all USG-distributed courses** that they received and should report inventory, administration/dispensing, and disposal data **until the provider's USG product inventory is fully reconciled.**
- USG supply used to support the Paxlovid USG PAP program is ***not*** subject to provider agreement reporting requirements.

Learn more in the [COVID-19 Therapeutics Transition Guide](https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/COVID19-Tx-Transition-Guide.aspx)

<https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/COVID19-Tx-Transition-Guide.aspx>

# Guidelines for Product Return/Disposal

- All USG distributed COVID19 Therapeutics are property of USG and must be used in accordance with the EUA.
  - Sites of care cannot donate products to entities outside the U.S. or for use outside the U.S.
  - After checking for true expiration date online, dispose of any expired product.
  - Non-expired product *not currently authorized for use* is eligible for disposal or returns to the manufacturer if no longer able to be stored.
  - **No returns or disposal of non-expired product currently in distribution by the USG.**
- 
- Jurisdictions can transfer product to other jurisdictions/states/territories
  - Doses of USG-product discarded on site and doses returned **need to be recorded in HPOP**
  - **If undamaged product needs to be disposed of, destroy it on-site in accordance with the HPOP attestation, or follow the returns instructions below:**
    - **Updated:** For Paxlovid, visit [Inmar](#) or contact [PaxlovidEUareturns@inmar.com](mailto:PaxlovidEUareturns@inmar.com), 800-967-6148 <http://www.paxlovideuareturns.com/>
    - **Updated:** For [Lagevrio](#) select “Return Merchandise” or call the Merck Order Management Center at 800-MERCK-RX (800-637-2579). <http://www.merckorders.com/>
    - For bam and bam/ete, see [The Lilly Return Goods Procedure](#) for detailed guidance. Bebtelovimab returns are not being accepted. <https://www.lillytrade.com/>
    - For REGEN-COV, call 844-734-6643
    - For sotrovimab, see the [GSK Returns Goods Policy](#) <http://www.gsk-ecs.com/>
    - Visit [Evusheld](#) or call 1-833-EVUSHLD <https://www.evusheld.com/>

# On Site Destruction of Expired or Unauthorized Product

- For licensed provider locations with destruction procedures in place that follow all federal, state, and local regulations, therapeutics can be destroyed on site only if:
  - Guidelines are followed on what product can be destroyed
    - Only expired product or unauthorized product that can no longer be stored
    - No unexpired product that is currently authorized for use can be destroyed
  - Sites are to follow established protocols for destruction and attest in HPOP to following all regulations
  - Quantities of any product destroyed is recorded in HPOP
- The established returns process for each product is still an option for sites who do not have an established method for proper destruction or otherwise prefer to go through the returns process
  - Returned product must also be recorded in HPOP
  - This process has been enabled in HPOP

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# Module 7: Additional Resources

# COVID-19 Vaccination after mAb Administration

## Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Approved or Authorized in the US

- Non-hospitalized COVID-19 patients who previously received passive antibody therapy
  - There is no longer any need to delay vaccination following receipt of monoclonal antibody or convalescent plasma *beyond recovery from the acute illness (if symptoms were present) and criteria to discontinue isolation have been met.*
- Hospitalized COVID-19 patients
  - Follow guidelines from [CDC Advisory Committee on Immunization Practices](https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#CoV-19-vaccination)  
<https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#CoV-19-vaccination>

# FOR USG PROCUREMENT REPORTING GUIDANCE

For sotrovimab, bam/ete,  
REGEN-COV, bebtelovimab, Evusheld



Reporting required  
**once a month by 11:59 pm ET  
on the last day of the month**

For Paxlovid and Lagevrio



Reporting required  
**at least twice a month by 11:59 pm ET  
on the 15th and last day of the month**

- **Reporting stock on hand is the minimal requirement** if a therapeutic has not been administered, transferred, or wasted within the reporting period
  - Please ensure accurate reporting, including when there is a significant change to stock on hand, e.g., if a specific lot of therapeutics expires and is wasted

Sites with inventory of USG-purchased COVID-19 therapeutics must provide information on product utilization, wastage, returns, and stock on hand

# Opting in to the Treatments Locator

- USG has developed a mechanism for providers to **report commercial treatment locations voluntarily** that will be visible in an expanded treatments locator tool.
  - As of November 27, sites could voluntarily upload commercially acquired inventory data for Paxlovid, Lagevrio, and outpatient Veklury via HPOP.
  - HPOP users can leverage their existing accounts to report, while non-HPOP users can report using the [HPOP volunteer reporting website](https://hpop.hhs.gov/voluntary). <https://hpop.hhs.gov/voluntary>
  - If a site opts in, that site will become publicly visible on the [Treatments Locator](https://treatments.hhs.gov/). <https://treatments.hhs.gov/>
  - We encourage sites to report commercial therapeutics as often as possible; reporting commercially distributed therapeutics at least every 14 days is requested to ensure the locator remains accurate.
  - After 60 days, sites will fall off the locator until commercial inventory is reported again.
  - Separately, USG-distributed product should continue to be entered in the appropriate HPOP reporting fields.

Learn more in the [COVID-19 Therapeutics Transition Guide](https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/COVID19-Tx-Transition-Guide.aspx)

<https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/COVID19-Tx-Transition-Guide.aspx>

# Voluntary Reporting of Commercial Therapeutics

- HPOP users can use HPOP for voluntary reporting.
- Non-HPOP users can use the [HPOP Volunteer Reporting](https://hpop.hhs.gov/voluntary) website to voluntarily report availability of commercial therapeutics. <https://hpop.hhs.gov/voluntary>

The screenshot shows the 'HPOP Voluntary Reporting' form. At the top left is the ASPR logo (Administration for Strategic Preparedness & Response, Health Partner Order Portal) and the title 'HPOP Voluntary Reporting'. The main heading is 'HPOP Voluntary Reporting'. Below this are several input fields: 'First Name' (containing 'Tester', marked 'Required'), 'Last Name' (containing 'One', marked 'Required'), 'Job Title', 'Email' (containing 'testerone@test.com', marked 'Required'), and three fields for 'Phone', 'Phone Ext...', and 'Fax'. A 'Continue' button is at the bottom right. A note states: 'Phone number, Phone Extension, and Fax will only accept numeric input.' Three red arrows point to the 'First Name', 'Last Name', and 'Email' fields.

# COVID-19 Therapeutic Resources

- [Administration for Strategic Preparedness and Response](https://ASPR.HHS.gov)  
<https://ASPR.HHS.gov>
- For the latest information on all COVID-19 therapeutics, refer to:
  - [FDA's COVID-19 EUA Information](https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization) <https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization>
  - [ASPR's COVID-19 Therapeutics Resources](https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/default.aspx) <https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/default.aspx>
- Still have questions? Reach out to [HHS COVID 19 Therapeutics Email](mailto:covid19therapeutics@hhs.gov)  
[covid19therapeutics@hhs.gov](mailto:covid19therapeutics@hhs.gov)

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# Module 8: Appendices

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# **Appendix A: Outpatient Infusion Site Resources**

# Sample Staffing Models for Parenteral Therapeutic Administration

Examples of staff plans (*recommended positions may vary depending on the State's scope of practice for Paramedics as it related to Subcutaneous and or Intravenous administration of medications*)

- 8 - 10 bed infusion/observation site
  - 1 physician / advanced practitioner (present or available via telemedicine)
  - 2 Nurses
  - 1 Nurse or Paramedic
  - 2 Paramedics
  - 1 flex position – administrative/ logistics/ runner
- Single station or mobile visit Subcutaneous administration site
  - 1 physician / advanced practitioner (present or available via telemedicine)
  - 1 Nurse / Paramedic per single mobile visit or single station

Average patient (door to door) visit can range from 80-120 minutes

# Infused Outpatient Therapeutics Site Suggested Supplies

## Infrastructure

- Seating area with appropriate spacing for patients to receive infusion
- Steel table for product preparation
- Privacy screens if needed
- Protocol/outline for patient flow (written protocol not required however patient flow and infection control should be addressed at each administration site)
- Emergency response plan (written plan not required, however all staff should be aware of the plan for emergency response)

## General supplies

- Infusion Reaction Kit
- Refrigerator
  - *Optional to store prepared solution onsite*
- Sharps container
- Biohazard disposal bag
- Trash bins and liners
- Disposable disinfecting wipes
- Hand sanitizer
- Thermometer probe covers (*if required*)
- 70% alcohol wipes
- Paper towels

## PPE

- NIOSH-certified, disposable N95 filter facepiece respirators or better
- Gloves in appropriate sizes
- Gowns
- Surgical face masks for patients
- Eye and face protection (e.g., goggles, safety glasses, face shields)

## Patient Intake

- Vital signs machine
- Pulse oximeter
- Thermometer
- Copies of eligibility checklist for treatment/PEP

## Administrative

- Site-specific documentation
- Patient fact sheets to provide each patient (copies in English, Spanish and other appropriate languages)

## Administration Supplies-Subcutaneous

- Alcohol wipes
- 3 or 5 mL luer lock syringes (4 required for each patient for subcutaneous administration)
- Appropriate needles for product preparation and subcutaneous administration
  - 21-gauge 1.5-inch needles for product transfer
  - 25- or 27-gauge needles for subcutaneous administration (4 per each patient course)

## Administration Supplies-Intravenous

- IV poles
- Alcohol wipes
- 2x2 gauze pads
- Adhesive bandages
- Medical tape
- Tegaderm bio-occlusive dressing
- Absorbent underpads (blue pads)
- Normal saline bags for mixing/administration- 50-250 mL
- IV administration sets:
  - *For monoclonal antibody infusion: PVC infusion set with/without DEHP containing 0.2- or 0.22-micron polyethersulfone (PES) in-line filter*
- IV catheters
- IV extension set tubing
- 3mL saline syringes
- Needles – stainless steel 18ga
- *Optional: Transilluminator (vein finder)*

# Site Preparation for Infused Outpatient COVID-19 Therapeutic Administration

- Collect administration site location(s), address, and points of contact
  - For mobile or deployed teams, identify the point of contact at the administration site and make contact
  - Site will need dedicated space for isolation of COVID-19 patients<sup>1</sup>
  - Rededication of existing clinical space is permitted under the CMS Hospital Without Walls Initiative
- Ensure a patient scheduling and referral process is in place
- Identify and understand which therapeutics will be administered
- Determine who is responsible for ordering infused therapeutic administration
  - Referring provider
  - On-site or telemedicine provider
  - Standing order
- Brief administration team with site objectives
- Team training
  - Site workflow
  - Therapeutic Administration
  - Managing adverse reactions with rescue medications on site as applicable



<sup>1</sup> For more info reference [CDC guidelines](https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-controlrecommendations.html) <https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-controlrecommendations.html>

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# Appendix B: COVID-19 Convalescent Plasma

# COVID-19 Convalescent Plasma EUA<sup>1</sup>

- Eligibility Criteria
  - The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved product, COVID-19 convalescent plasma with high titers of anti-SARS-CoV-2 antibodies, for the treatment of COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment, in either the outpatient or inpatient setting.
- Not authorized for
  - Treatment of immunocompetent patients with COVID-19 infection
- Contraindications
  - Individuals with a history of severe allergic reactions or anaphylaxis to plasma transfusion
- Administration Considerations
  - Administer according to standard institutional medical and nursing practices for the administration of plasma<sup>2</sup>

<sup>1</sup> [Emergency Use Authorization of COVID-19 Convalescent Plasma](https://www.fda.gov/media/141478/download) <https://www.fda.gov/media/141478/download>

<sup>2</sup> [Circular of Information for the Use of Human Blood and Blood Components](http://www.aabb.org/tm/coi/Documents/coi1017.pdf) <http://www.aabb.org/tm/coi/Documents/coi1017.pdf>  
[Fact Sheet for Healthcare Providers download \(fda.gov\)](https://www.fda.gov/media/141478/download) <https://www.fda.gov/media/141478/download>

# NIH Guidelines Panel- COVID-19 Convalescent Plasma<sup>1</sup>

- There is insufficient evidence for the Panel to recommend either for or against the use of high-titer CCP for the treatment of COVID-19 in hospitalized or nonhospitalized patients who are **immunocompromised**
  - Some panel members would use CCP to treat an immunocompromised patient with significant symptoms attributable to COVID-19 and with signs of active SARS-CoV-2 replication and who is having an inadequate response to available therapies. In these cases, clinicians should attempt to obtain high-titer CCP from a vaccinated donor who recently recovered from COVID-19 likely caused by a SARS-CoV-2 variant similar to the variant causing the patient's illness
- There is insufficient evidence for the Panel to recommend either for or against the use of high-titer CCP for the treatment of COVID-19 in nonhospitalized patients who are **immunocompetent**
- The panel recommends **against** the use of CCP for the treatment of COVID-19 in hospitalized patients who are **immunocompetent**

<sup>1</sup>NIH Guidelines: COVID-19 Convalescent Plasma <https://www.covid19treatmentguidelines.nih.gov/therapies/antivirals-including-antibody-products/covid-19-convalescent-plasma/>

# Outpatient COVID-19 Convalescent Plasma (CCP) Resources

- [Emergency Use Authorization of COVID-19 Convalescent Plasma](https://www.fda.gov/media/141478/download)  
https://www.fda.gov/media/141478/download
- [Implementation of an Outpatient Covid-19 Convalescent Plasma Administration Program](https://onlinelibrary.wiley.com/doi/full/10.1111/trf.16871)  
https://onlinelibrary.wiley.com/doi/full/10.1111/trf.16871
- [Early Outpatient Treatment for COVID-19 with Convalescent Plasma-NEJM](https://www.nejm.org/doi/full/10.1056/NEJMoa2119657)  
https://www.nejm.org/doi/full/10.1056/NEJMoa2119657
- [New COVID-19 Treatments Add-On Payment \(NCTAP\) | CMS](https://www.cms.gov/medicare/covid-19/new-covid-19-treatments-add-payment-nctap)  
https://www.cms.gov/medicare/covid-19/new-covid-19-treatments-add-payment-nctap
  - ICD-10-PCS Code: XW13325, XW14325 (*Only applies to inpatient use*)
- [Addendum A and Addendum B Updates | CMS](https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalOutpatientPPS/Addendum-A-and-Addendum-B-Updates)  
https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalOutpatientPPS/Addendum-A-and-Addendum-B-Updates
  - APC Code: 9540 / HCPCS Code: C9507 (*Only applies to outpatient use*)

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# Appendix C: Formerly-Authorized Products

# EUA Products Not Currently Authorized

HHS continuously monitors emerging variants to assess their potential impacts on testing, treatments and vaccines, including susceptibility to therapeutics. There is potential for paused products to play a role in addressing future COVID-19 variants. Sites are encouraged to retain all product in the event that the below authorizations change in the future. For current variant data, refer to [CDC Nowcast Projections](https://covid.cdc.gov/covid-data-tracker/#variant-proportions) <https://covid.cdc.gov/covid-data-tracker/#variant-proportions>.

Product	Latest Status
Evusheld	as of 26 January 2023, <a href="https://www.fda.gov/drugs/drug-safety-and-availability/fda-announces-evusheld-not-currently-authorized-emergency-use-us">not currently authorized for emergency use in the US</a> <a href="https://www.fda.gov/drugs/drug-safety-and-availability/fda-announces-evusheld-not-currently-authorized-emergency-use-us">https://www.fda.gov/drugs/drug-safety-and-availability/fda-announces-evusheld-not-currently-authorized-emergency-use-us</a>
Bebtelovimab	as of 30 November 2022, <a href="https://aspr.hhs.gov/COVID-19/Therapeutics/updates/Pages/important-update-30November2022.aspx">not authorized in any US region</a> <a href="https://aspr.hhs.gov/COVID-19/Therapeutics/updates/Pages/important-update-30November2022.aspx">https://aspr.hhs.gov/COVID-19/Therapeutics/updates/Pages/important-update-30November2022.aspx</a>
Sotrovimab	as of 05 April 2022, <a href="https://aspr.hhs.gov/COVID-19/Therapeutics/updates/Pages/important-update-5April2022.aspx">not authorized in any US region</a> <a href="https://aspr.hhs.gov/COVID-19/Therapeutics/updates/Pages/important-update-5April2022.aspx">https://aspr.hhs.gov/COVID-19/Therapeutics/updates/Pages/important-update-5April2022.aspx</a>
Bamlanivimab plus etesevimab	as of 14 of December 2023, <a href="https://www.fda.gov/media/174884/download?attachment">EUA status revoked in US region</a> <a href="https://www.fda.gov/media/174884/download?attachment">https://www.fda.gov/media/174884/download?attachment</a>
Casirivimab plus imdevimab (REGEN-COV)	as of 24 January 2022, <a href="https://aspr.hhs.gov/COVID-19/Therapeutics/updates/Pages/important-update-24January2022.aspx">not authorized in any US region</a> <a href="https://aspr.hhs.gov/COVID-19/Therapeutics/updates/Pages/important-update-24January2022.aspx">https://aspr.hhs.gov/COVID-19/Therapeutics/updates/Pages/important-update-24January2022.aspx</a>
Bamlanivimab alone	as of 16 April 2021, <a href="https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-monoclonal-antibody-bamlanivimab">EUA status revoked for product when administered alone</a> <a href="https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-monoclonal-antibody-bamlanivimab">https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-revokes-emergency-use-authorization-monoclonal-antibody-bamlanivimab</a>

[COVID-19 Therapeutic Product Expiration Database \(hhs.gov\)](https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/Product-Expiry.aspx) <https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/Product-Expiry.aspx>

# Product Expiration Date Summary

- **Paxlovid:** First lot expiry July 31, most in field supply expiry is later
- **Lagevrio:** No lots have reached expiry, first expiry is Feb 9, 2024, last is Feb 27, 2025

Therapeutic	First expiry	Last expiry	Extension
Bamlanivimab <sup>1</sup>	09/5/2022	5/22/2023	No further extension
Etesevimab <sup>1</sup>	4/8/2022	5/16/2023	No further extension
Regen-COV <sup>1</sup>	12/31/2022	12/31/2023	No further extension
Evusheld	6/30/2023	8/31/2024	No further extension
Sotrovimab	8/31/2023	8/31/2024	Extension possible
Bebtelovimab	7/11/2023	8/28/2024	Extension possible

<sup>1</sup>All lots have expired. No expiry extension expected. Dispose of all product.

- For Paxlovid (nirmatrelvir co-packaged with ritonavir): Pfizer's [searchable expiry data](https://www.paxlovidlotexpiry.com/)  
https://www.paxlovidlotexpiry.com/
- For up-to-date information on expiration dates of all products: [ASPR searchable expiry database](https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/Product-Expiry.aspx)  
https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/Product-Expiry.aspx

# Bamlanivimab and etesevimab reporting in HPOP

- **Bamlanivimab and etesevimab can now be reported separately** in HPOP, when needed
  - The products should be reported separately only when there is an excess of one component relative to a patient course
  - **When reporting separately**, each component should be reported **in proportion to the amount of the product previously used in a patient course**
  - In HPOP: 1 vial bam = 1 course bam ; 2 vials ete = 1 course ete
  - When remaining product is proportional to the previously used patient course, it should be reported together as bam/ete
    - In HPOP: 1 vial bam and 2 vials ete = 1 course bam/ete