

# Therapeutic Management of Nonhospitalized Adults With COVID-19

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Symptom management should be initiated for all nonhospitalized adults with mild to moderate COVID-19. For adults who are at high risk of progressing to severe disease, several antiviral therapeutic options are available to reduce the risk of hospitalization or death. The COVID-19 Treatment Guidelines Panel's (the Panel) recommendations on the use of these drugs for the treatment of COVID-19 are outlined in this section.

The main goal of therapeutic management for nonhospitalized patients is to prevent progression to severe disease, hospitalization, or death. Other goals may include accelerating symptom recovery and viral clearance and preventing long-term sequelae. Current data on the impact of therapy on these secondary goals are limited.

Several factors affect the selection of the best treatment option for a specific patient. These factors include the clinical efficacy and availability of the treatment option, the feasibility of administering parenteral medications, the potential for significant drug-drug interactions, the patient's pregnancy status, the time from symptom onset, and the *in vitro* activities of the available products against the currently circulating SARS-CoV-2 variants and subvariants.

Most of the data that support the use of the recommended treatment options come from clinical trials that enrolled individuals who were at high risk of disease progression and who had no pre-existing immunity from COVID-19 vaccination or prior SARS-CoV-2 infection. Accordingly, the proportion of hospitalizations and deaths in the placebo arms of these trials was high compared to what has been seen more recently in populations where most people are vaccinated or have had prior SARS-CoV-2 infection. Although these trials demonstrated the efficacy of using antiviral drugs in high-risk populations, it is difficult to know their precise effectiveness in the current setting because of the low rates of hospitalization and death among those who have been vaccinated.

Nevertheless, some patients continue to have an increased risk of disease progression, and it is in those people that therapies are most likely to be beneficial. Patients who are at the highest risk are older patients (i.e., those aged >50 years and especially those aged ≥65 years) and patients who are unlikely to have an adequate immune response to COVID-19 vaccines due to a moderate to severe immunocompromising condition or the receipt of immunosuppressive medications. Other risk factors include lack of vaccination or incomplete vaccination; a prolonged amount of time since the most recent vaccine dose (e.g., >6 months); and conditions such as obesity, diabetes, and chronic pulmonary, cardiac, or renal disease.<sup>1</sup>

People who are members of racial and ethnic minority groups have higher rates of hospitalization and death from COVID-19 than people who are White.<sup>2</sup> Disparities in the use of antiviral treatments in patients who are not White have been reported; therefore, attention to equitable access is critical.<sup>3,4</sup>

The Panel's recommendations reflect the available data on the benefits of using antiviral therapies to prevent progression to severe COVID-19. Table 2a outlines the Panel's recommendations for the therapeutic management of nonhospitalized adults with COVID-19. For the recommended doses for the agents listed in Table 2a, refer to Table 2b below.

**Table 2a. Therapeutic Management of Nonhospitalized Adults With Mild to Moderate COVID-19 Who Do Not Require Supplemental Oxygen**

| Patient Disposition  | Panel's Recommendations   |
|--|---|
| All Patients   | <ul style="list-style-type: none"> <li>Symptom management should be initiated for all patients (<b>AIII</b>).</li> <li>The Panel <b>recommends against</b> the use of <b>dexamethasone</b><sup>a</sup> or other systemic corticosteroids (<b>AIIb</b>), unless these agents are being used to treat an underlying condition (<b>AIII</b>).</li> </ul>   |
| Patients Who Are at High Risk of Progressing to Severe COVID-19 <sup>b,c,d</sup>   | <p><i>Preferred therapies. Listed in order of preference:</i></p> <ul style="list-style-type: none"> <li><b>Ritonavir-boosted nirmatrelvir (Paxlovid)</b><sup>e</sup> (<b>AIIa</b>). Start as soon as possible and within 5 days of symptom onset. See footnote on drug-drug interactions.<sup>f</sup></li> <li><b>Remdesivir</b><sup>e,g</sup> (<b>BIIa</b>). Start as soon as possible and within 7 days of symptom onset.</li> </ul> <p><i>Alternative therapy. For use when the preferred therapies are not available, feasible to use, or clinically appropriate.<sup>h</sup></i></p> <ul style="list-style-type: none"> <li><b>Molnupiravir</b><sup>e,i</sup> (<b>CIIa</b>). Start as soon as possible and within 5 days of symptom onset.</li> </ul> <p>There is insufficient evidence for the Panel to recommend either for or against initiating these antiviral agents after the timeframes listed above.</p> |
| Each recommendation in the Guidelines receives a rating for the strength of the recommendation (A, B, or C) and a rating for the evidence that supports it (I, IIa, IIb, or III). See <a href="#">Guidelines Development</a> for more information. |   |

<sup>a</sup> There is currently a lack of safety and efficacy data on the use of dexamethasone in outpatients with COVID-19. Using systemic glucocorticoids in outpatients with COVID-19 may cause harm.

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

<sup>c</sup> For a discussion of potential treatment options for patients who are immunocompromised and have prolonged COVID-19 symptoms and evidence of ongoing viral replication, see below and [Special Considerations in People Who Are Immunocompromised](#).

<sup>d</sup> Concerns about viral rebound or the recurrence of symptoms should not be a reason to avoid using antiviral therapies when their use is indicated. See Viral Rebound and Symptom Recurrence below for details.

<sup>e</sup> If a patient requires hospitalization after starting treatment, the full treatment course can be completed at the health care provider's discretion.

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

<sup>g</sup> Administration of remdesivir requires an IV infusion once daily for 3 days.

<sup>h</sup> Molnupiravir appears to have lower efficacy than the other options recommended by the Panel.

<sup>i</sup> The Panel **recommends against** the use of **molnupiravir** for the treatment of COVID-19 in pregnant patients unless there are no other options and therapy is clearly indicated (**AIII**).

**Key:** CDC = Centers for Disease Control and Prevention; IV = intravenous; the Panel = the COVID-19 Treatment Guidelines Panel

## Symptom Management

Treatment of symptoms includes using over-the-counter antipyretics, analgesics, or antitussives for fever, headache, myalgias, and cough. Patients should be advised to drink fluids regularly to avoid dehydration. Rest is recommended as needed during the acute phase of COVID-19, and ambulation and other forms of activity should be increased according to the patient's tolerance. Patients should be educated about the variability in time to symptom resolution and complete recovery. When possible, patients with symptoms of COVID-19 may be triaged via telehealth visits to determine whether they require COVID-19-specific therapy and in-person care.

Patients with persistent or progressive dyspnea, especially those who have an oxygen saturation measured by pulse oximetry  $\leq 94\%$  on room air at sea level or have symptoms that suggest high acuity (e.g., chest pain or tightness, dizziness, confusion, other mental status changes), should be evaluated by a health care provider (**AIII**). For more information, see [General Management of Nonhospitalized Adults With Acute COVID-19](#).

## Rationale for the Panel's Recommendations

The Panel's recommendations for the antiviral agents that are used to treat nonhospitalized patients with mild to moderate COVID-19 who are at high risk of disease progression are based on the results of clinical trials.

The Panel favors the use of ritonavir-boosted nirmatrelvir (Paxlovid) in most high-risk, nonhospitalized patients with mild to moderate COVID-19. When ritonavir-boosted nirmatrelvir is not clinically appropriate (e.g., because of significant drug-drug interactions), the Panel recommends using remdesivir. Ritonavir-boosted nirmatrelvir has high efficacy; has been shown to reduce hospitalization and death when administered to high-risk, unvaccinated, nonhospitalized patients within 5 days of symptom onset;<sup>5</sup> and is an oral medication, whereas remdesivir requires intravenous (IV) administration.

The Panel's recommendation for remdesivir is based on the results from a Phase 3, randomized, placebo-controlled trial that reported high clinical efficacy for remdesivir in high-risk, nonhospitalized patients with COVID-19 who were unvaccinated.<sup>6</sup> However, in some settings, daily IV administration of remdesivir for 3 days may be a logistical challenge.

The Panel recommends **molnupiravir** as a therapeutic option when the other recommended antiviral treatment options are not available, feasible to use, or clinically appropriate (**CIIa**). Molnupiravir appears to have lower clinical efficacy than the other treatment options, although no randomized studies have compared these therapies directly.

There is insufficient evidence for the Panel to recommend either for or against initiating these antiviral agents after the recommended timeframes. Because the drugs listed above were studied soon after symptom onset (i.e., within 5 days for molnupiravir and ritonavir-boosted nirmatrelvir and within 7 days for remdesivir), it is not known whether they would confer a clinical benefit if they were started beyond the recommended timeframe.

Currently, data on the use of combinations of antiviral agents for the treatment of COVID-19 are limited. Clinical trials are needed to determine whether combination therapy has a role in the treatment of COVID-19.

## Strategies for the Use of Ritonavir-Boosted Nirmatrelvir

Because ritonavir is a strong cytochrome P450 3A4 inhibitor and a P-glycoprotein inhibitor, it may increase blood concentrations of certain concomitant medications and increase the potential for serious drug toxicities. Therefore, the Food and Drug Administration (FDA) prescribing information includes a

boxed warning for significant drug-drug interactions with ritonavir-boosted nirmatrelvir.<sup>7</sup> Clinicians should consider both the potential benefits of treatment with ritonavir-boosted nirmatrelvir and the potential risks related to drug-drug interactions.

Many drug-drug interactions between ritonavir-boosted nirmatrelvir and concomitant medications (e.g., certain statins, calcium channel blockers, or direct oral anticoagulants) **can be safely managed**. If a significant drug-drug interaction is identified, prescribers should consider consulting with a pharmacist.

The following resources provide information on identifying and managing drug-drug interactions:

- [Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir \(Paxlovid\) and Concomitant Medications](#)
- The [Liverpool COVID-19 Drug Interactions website](#)
- The [University of Waterloo/University of Toronto drug interaction guide](#) for ritonavir-boosted nirmatrelvir
- The FDA [prescribing information](#) for ritonavir-boosted nirmatrelvir

The use of ritonavir-boosted nirmatrelvir may be challenging in patients with severe renal impairment. The FDA prescribing information states that ritonavir-boosted nirmatrelvir is not recommended for patients with an estimated glomerular filtration rate (eGFR) of <30 mL/min until more data are available to establish appropriate dosing.<sup>7</sup> Although data on dose adjustments are limited, some groups have proposed dosing adjustments for ritonavir-boosted nirmatrelvir in patients with an eGFR of <30 mL/min or in patients who require hemodialysis.<sup>8-11</sup>

The decision to prescribe ritonavir-boosted nirmatrelvir to patients who have received transplants and are taking calcineurin and mammalian target of rapamycin inhibitors should always be made in consultation with the patient's specialist providers. Among reports submitted to the FDA Adverse Event Reporting System, the most commonly reported concomitant medications that resulted in serious adverse reactions, including fatal events, were calcineurin inhibitors (e.g., tacrolimus).<sup>12</sup> Ritonavir-boosted nirmatrelvir may be prescribed to select patients if an expert in managing the interaction is available and close therapeutic drug monitoring is logistically feasible. Otherwise, an alternative therapy for COVID-19 should be considered. See the [American Society of Transplantation statement](#) for additional information.

Interactions between ritonavir-boosted nirmatrelvir and cancer chemotherapeutic agents should also be managed in consultation with the patient's specialist providers. For guidance on managing these interactions, refer to the FDA prescribing information for ritonavir-boosted nirmatrelvir and the prescribing information for the chemotherapeutic agent. The [University Health Network/Kingston Health Sciences Centre](#) provides an additional resource for evaluating drug-drug interactions between ritonavir-boosted nirmatrelvir and chemotherapeutic agents.

## Strategies for the Use of Remdesivir

Advanced planning (e.g., reserving infusion slots, identifying alternative infusion sites) may be needed to increase access to IV remdesivir. IV remdesivir can be administered in skilled nursing facilities, home health care settings, and outpatient facilities such as infusion centers. If treatment facilities cannot provide a 3-day course of remdesivir IV infusions to all eligible patients, prioritizing patients who will benefit the most from the therapy becomes necessary. The prioritization scheme below is based on 4 key elements: age, vaccination status, immune status, and clinical risk factors. For a list of risk factors, see the Centers for Disease Control and Prevention (CDC) webpage [Underlying Medical Conditions Associated With Higher Risk for Severe COVID-19](#). The groups are listed by tier in descending order of priority.

| 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,<sup>a</sup> regardless of vaccine status; <i>or</i></li> <li>Unvaccinated individuals at the highest risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 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 ≥65 years or anyone aged &lt;65 years with clinical risk factors)</li> </ul>  |
| 3    | <ul style="list-style-type: none"> <li>Vaccinated individuals at risk of severe disease (anyone aged ≥65 years or anyone aged &lt;65 years with clinical risk factors)<sup>b</sup></li> </ul>   |

<sup>a</sup> See the CDC webpage [COVID-19 Vaccines for People Who Are Moderately or Severely Immunocompromised](#) for a discussion of immunocompromising conditions.

<sup>b</sup> Vaccinated individuals who are not up to date with their immunizations are likely at higher risk of severe disease; patients within this tier who are in this situation should be prioritized for treatment. See the CDC webpage [Stay Up to Date With COVID-19 Vaccines](#) for more information.

See [Prioritization of Anti-SARS-CoV-2 Therapies for the Treatment of COVID-19 in Nonhospitalized Patients When There Are Logistical Constraints](#) for more information.

## Patients Who Are Immunocompromised and Have Prolonged COVID-19 Symptoms and Evidence of Ongoing Viral Replication

For patients who are immunocompromised and have prolonged COVID-19 symptoms and evidence of ongoing viral replication (e.g., those with a low cycle threshold value, as measured by a reverse transcription polymerase chain reaction result or with a positive rapid antigen test result) despite receiving a course of antiviral therapy, the optimal management is unknown. Case reports and case series have described the treatment of these patients with additional antiviral treatments, prolonged courses of antiviral treatments, high-titer COVID-19 convalescent plasma (CCP), or combination therapy.<sup>13-19</sup> The data for these approaches are not definitive, but some Panel members would use 1 or more of the following treatment options:

- Longer and/or additional courses of ritonavir-boosted nirmatrelvir
- Longer and/or additional courses of remdesivir
- 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

For further discussion of these potential treatment options, see [Special Considerations in People Who Are Immunocompromised](#).

## Additional Information on Ritonavir-Boosted Nirmatrelvir

Nirmatrelvir is an orally bioavailable protease inhibitor that is active against M<sup>PRO</sup>, a viral protease that plays an essential role in viral replication.<sup>20</sup> The FDA has approved ritonavir-boosted nirmatrelvir for the treatment of mild to moderate COVID-19 in nonhospitalized adults who are at high risk of progressing to severe COVID-19.<sup>7</sup>

Patients should complete the 5-day treatment course of ritonavir-boosted nirmatrelvir, which was shown to be efficacious in the EPIC-HR trial.<sup>5</sup> If a patient requires hospitalization after starting treatment, the full 5-day treatment course of ritonavir-boosted nirmatrelvir should be completed unless there are drug-drug interactions that preclude its use.

In the EPIC-HR trial, ritonavir-boosted nirmatrelvir reduced the risk of hospitalization or death by 89%



compared to placebo in unvaccinated, nonhospitalized adults with laboratory-confirmed SARS-CoV-2 infection.<sup>5</sup> This efficacy is comparable to the efficacies reported in similar patient populations for remdesivir (87% relative reduction)<sup>6</sup> and greater than the efficacy reported for molnupiravir in this setting (31% relative reduction).<sup>21</sup>

Because ritonavir-boosted nirmatrelvir has the potential for significant drug-drug interactions with concomitant medications, this regimen may not be the optimal choice for all patients (see [Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir \[Paxlovid\] and Concomitant Medications](#)). However, because ritonavir-boosted nirmatrelvir is the only highly effective oral antiviral available for the treatment of COVID-19, drug-drug interactions that can be safely managed should not preclude the use of this medication.

For more information on the use of ritonavir-boosted nirmatrelvir, see [Ritonavir-Boosted Nirmatrelvir \(Paxlovid\)](#). See Viral Rebound and Symptom Recurrence below for information regarding SARS-CoV-2 viral rebound in patients who have completed treatment with ritonavir-boosted nirmatrelvir.

### Additional Information on Remdesivir

Remdesivir is a nucleotide prodrug of an adenosine analog that inhibits SARS-CoV-2 replication. It is approved by the FDA for the treatment of COVID-19 in adults and children aged  $\geq 28$  days and weighing  $\geq 3$  kg who are hospitalized with COVID-19 and for those with mild to moderate COVID-19 who are not hospitalized and are at high risk of progressing to severe disease. In the PINETREE trial, nonhospitalized patients with mild to moderate COVID-19 who were unvaccinated and at high risk of progressing to severe disease received 3 days of IV remdesivir or placebo. The use of remdesivir resulted in an 87% relative reduction in the risk of hospitalization or death.<sup>6</sup>

Remdesivir should be administered in a setting where severe hypersensitivity reactions, such as anaphylaxis, can be managed. Patients should be monitored during the infusion and observed for at least 1 hour after the infusion as clinically appropriate.

For more information, see [Remdesivir](#).

### Additional Information on Molnupiravir

Molnupiravir is the oral prodrug of beta-D-N4-hydroxycytidine, a ribonucleoside that has shown antiviral activity against SARS-CoV-2 in vitro and in clinical trials.<sup>22-24</sup> The FDA issued an Emergency Use Authorization for molnupiravir for the treatment of mild to moderate COVID-19 in nonhospitalized patients aged  $\geq 18$  years who are at high risk of disease progression and for whom other antiviral treatment options are not accessible or clinically appropriate.

The MOVE-OUT trial enrolled high-risk, unvaccinated, nonhospitalized adults in the pre-Omicron era.<sup>21</sup> The study found that molnupiravir reduced the rate of hospitalization or death by 31% compared to placebo. A secondary analysis of patients who required hospitalization during the trial found a reduced need for respiratory interventions among those who received molnupiravir compared to those who received placebo.<sup>25</sup>

The PANORAMIC trial enrolled nonhospitalized adults with COVID-19 who were at high risk of severe disease during a period when the Omicron variant was circulating.<sup>26</sup> Ninety-four percent of the patients had received at least 3 doses of a COVID-19 vaccine. The study found that the use of molnupiravir plus usual care did not reduce the occurrence of the primary composite outcome of hospitalization or death compared to usual care alone. The proportion of patients who met this composite outcome was 1% in both arms. Molnupiravir plus usual care was superior to usual care alone for several secondary clinical endpoints. For example, the time to self-reported recovery was substantially shorter in people who

received molnupiravir plus usual care than in people who received usual care alone (median of 9 days vs. 15 days). Because the PANORAMIC trial was an open-label study with self-reported symptoms, the findings are less reliable than those from a placebo-controlled trial.

Although the different COVID-19 treatment options have not been directly compared in clinical trials, the Panel recommends using molnupiravir as an alternative therapy only when ritonavir-boosted nirmatrelvir and remdesivir are not available, feasible to use, or clinically appropriate, because molnupiravir appears to have lower clinical efficacy than these other options.

There is a theoretical risk that the molnupiravir metabolite beta-D-N4-hydroxycytidine could be incorporated into host DNA, leading to mutations. The available genotoxicity data and the 5-day duration of treatment led the FDA to conclude that molnupiravir has a low risk for genotoxicity.<sup>27</sup>

The Panel **recommends against** the use of **molnupiravir** for the treatment of COVID-19 in pregnant patients unless there are no other options and therapy is clearly indicated (**AIII**). People who engage in sexual activity that may result in conception should use effective contraception during and following treatment with molnupiravir.

Fetal toxicity has been reported in animal studies of molnupiravir.<sup>27</sup> However, when other therapies are not available, pregnant patients with COVID-19 who are at high risk of progressing to severe disease may reasonably choose molnupiravir after being fully informed of the risks, particularly if they are beyond the time of embryogenesis (i.e., >10 weeks' gestation). See [Pregnancy, Lactation, and COVID-19 Therapeutics](#) for more information.

For more information, see [Molnupiravir](#).

## Viral Rebound and Symptom Recurrence

Observational studies and the EPIC-HR and MOVE-OUT trials have described SARS-CoV-2 viral rebound and the recurrence of COVID-19 symptoms in some patients who have completed treatment with ritonavir-boosted nirmatrelvir or molnupiravir.<sup>7,27-30</sup> However, viral rebound can also occur in patients who have not received treatment for COVID-19.<sup>31</sup> Some observational studies have reported that patients who were treated with ritonavir-boosted nirmatrelvir had a higher frequency of viral rebound and symptom recurrence than those who did not receive treatment.<sup>32,33</sup> The re-emergence of culturable SARS CoV-2 has been reported in some individuals with viral rebound.

To date, virus detection and the recurrence of COVID-19 symptoms following the use of antiviral therapies have not been associated with progression to severe COVID-19.<sup>34,35</sup> Therefore, concerns about viral rebound or the recurrence of symptoms should not be a reason to avoid using antiviral therapies when their use is indicated.<sup>27,36-38</sup> There are insufficient data on whether a longer course of ritonavir-boosted nirmatrelvir or molnupiravir will prevent viral rebound or symptom recurrence. There also are insufficient data on the efficacy of administering a second course of antiviral therapy to treat viral rebound or symptom recurrence. However, a clinical trial that is evaluating the use of a second course of ritonavir-boosted nirmatrelvir to treat patients with viral rebound and symptom recurrence is underway (ClinicalTrials.gov Identifier [NCT05567952](#)).

## Immunomodulators

The Panel **recommends against** the use of **dexamethasone** or other systemic corticosteroids to treat outpatients with mild to moderate COVID-19 who do not require hospitalization or supplemental oxygen (**AIIb**). Patients with COVID-19 who are receiving **dexamethasone** or another corticosteroid for an underlying condition should continue this therapy as directed by their health care provider (**AIII**).

Medicare and FDA data show a significant increase in the number of prescriptions for systemic

corticosteroids among nonhospitalized patients with COVID-19<sup>39</sup> despite a lack of safety and efficacy data on the use of systemic corticosteroids in this setting. Systemic glucocorticoids may cause harm in nonhospitalized patients with COVID-19. Results from 1 randomized controlled trial and 1 observational cohort study did not demonstrate a clinical benefit of dexamethasone among hospitalized patients who did not require supplemental oxygen,<sup>40</sup> and dexamethasone may potentially cause harm in these patients.<sup>41</sup>

In the RECOVERY trial, the use of dexamethasone had no effect on mortality among hospitalized patients with COVID-19 who did not require supplemental oxygen (rate ratio 1.19; 95% CI, 0.91–1.55).<sup>40</sup> A large observational study of patients at Veterans Affairs hospitals showed that patients with COVID-19 who did not require supplemental oxygen and received dexamethasone had an increased risk of 90-day mortality (HR 1.76; 95% CI, 1.47–2.12).<sup>41</sup>

## Concomitant Medication Management

In general, a patient's usual medication and/or supplement regimen should be continued after the diagnosis of COVID-19 (see [Considerations for Using Concomitant Medications in Patients With COVID-19](#)). Patients should be advised to avoid the use of nebulized medications in the presence of others to avoid potential aerosolization of SARS-CoV-2.<sup>42</sup> In patients with HIV, an antiretroviral regimen should not be modified for the purpose of preventing or treating SARS-CoV-2 infection. For more information, see [Special Considerations in People With HIV](#).

When a patient is receiving an immunomodulating medication, the prescribing clinician or an expert in the subspecialty should be consulted about the risks and benefits associated with a temporary dose reduction or discontinuation. These risks and benefits will depend on the medication's indication and the severity of the underlying condition (see [Special Considerations in People Who Are Immunocompromised](#)).

Before prescribing ritonavir-boosted nirmatrelvir, clinicians should carefully review the patient's concomitant medications, including over-the-counter medications, herbal supplements, and recreational drugs, to evaluate potential drug-drug interactions.

**Table 2b. Dosing Regimens for the Drugs Recommended in Table 2a**

| Drug Name  | Dosing Regimen   | Comments   |
|--|--|--|
| <b>Ritonavir-Boosted Nirmatrelvir (Paxlovid)</b> | <p><b>eGFR ≥60 mL/min</b></p> <ul style="list-style-type: none"> <li>Nirmatrelvir 300 mg with RTV 100 mg PO twice daily for 5 days</li> </ul> <p><b>eGFR ≥30 to &lt;60 mL/min</b></p> <ul style="list-style-type: none"> <li>Nirmatrelvir 150 mg with RTV 100 mg PO twice daily for 5 days</li> </ul> <p><b>eGFR &lt;30 mL/min</b></p> <ul style="list-style-type: none"> <li><b>Not recommended</b></li> <li>For more information on the use of this agent in patients with eGFR &lt;30 mL/min, see <a href="#">Ritonavir-Boosted Nirmatrelvir (Paxlovid)</a>.</li> </ul> <p><b>Severe Hepatic Impairment (Child-Pugh Class C)</b></p> <ul style="list-style-type: none"> <li><b>Not recommended</b></li> </ul> | <p>Clinicians should evaluate potential drug-drug interactions. See <a href="#">Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications</a> for more information.</p> |
| <b>Remdesivir</b>                                | RDV 200 mg IV on Day 1, then RDV 100 mg IV once daily on Days 2 and 3. Administer each infusion over 30–120 minutes.   | Patients should be monitored for ≥1 hour after the infusion as clinically appropriate.   |
| <b>Molnupiravir</b>                              | MOV 800 mg PO every 12 hours for 5 days  | Before initiating MOV, assess the patient's pregnancy status as clinically indicated. See <a href="#">Molnupiravir</a> for more information.   |



**Key:** eGFR = estimated glomerular filtration rate; IV = intravenous; MOV = molnupiravir; PO = oral; RDV = remdesivir; RTV = ritonavir

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