COVID-19 Outpatient Therapeutics

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CDPH
Main Points

• **Effective treatment** for outpatients with mild to moderate COVID-19 is available and **should be offered to all high-risk patients** if they meet criteria for treatment based on EUAs.

• We are **not in a state of scarcity**, all patients at high risk for disease progression with a COVID-19 positive test (PCR or antigen) who are within the treatment window should be offered treatment.

• Providers should **review product EUAs** as well as the **NIH Treatment Guidelines** prior to using outpatient therapeutics.

• **Clinical guidance is available** to assist in the selection of an appropriate COVID-19 therapeutic as well the navigation of some of the clinical complexities of using these drugs (i.e. Paxlovid drug interactions).
Available Outpatient Therapies at Each Disease Stage

<table>
<thead>
<tr>
<th>Treatment Options</th>
<th>SARS-CoV-2 Negative (-)</th>
<th>SARS-CoV-2 Positive (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not Exposed</td>
<td>Exposed</td>
</tr>
<tr>
<td>Pre-Exposure Prophylaxis (PrEP)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Long-Acting Monoclonal Antibody</td>
<td>Currently no authorized treatments*</td>
</tr>
<tr>
<td></td>
<td>• Tixagevimab/cilgavimab (Evusheld)</td>
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<tr>
<td>Post-Exposure Prophylaxis (PEP)</td>
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</tbody>
</table>

*The anti-SARS-CoV-2 monoclonal antibodies bamlanivimab/etevimab and casirivimab/imdevimab (REGEN COV) were previously FDA authorized for PEP and treatment, but these are not effective against the Omicron variant and are currently not authorized for use in any US state per the FDA. This may change in the future depending on the prevailing variant.

**Sotrovimab has reduced effectiveness against BA.2; distribution of Sotrovimab was paused to California on 3/29/2022
Treatment of Acutely Ill Outpatients
### Available Anti-SARS-COV-2 Treatments: Antivirals

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Age groups authorized for treatment</th>
<th>Timing of Treatment</th>
<th>Effectiveness</th>
<th>Activity Against Variants Currently Circulating</th>
<th>Clinical considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nirmatrelvir 300 mg with ritonavir 100 mg (Paxlovid)</td>
<td>Oral</td>
<td>12 years and older and weighing at least 40 kg</td>
<td>As soon as possible, but within 5 days of symptom onset</td>
<td>Compared to placebo, a relative risk reduction of 89% in hospitalizations or deaths.</td>
<td>Effective against Delta and Omicron</td>
<td>Drug interactions; Caution if concern for undiagnosed HIV; Renally dosed; Caution if severe hepatic impairment</td>
</tr>
<tr>
<td>Remdesivir (Veklury)</td>
<td>Intravenous</td>
<td>FDA approved in 12 years and older and weighing at least 40 kg; EUA for &lt;12 years of age weighing 3.5 to 40 kg</td>
<td>As soon as possible, but within 7 days of symptom onset</td>
<td>Compared to placebo, a relative risk reduction of 87% in hospitalizations or deaths.</td>
<td>Effective against Delta and Omicron</td>
<td>Caution in renal or hepatic impairment</td>
</tr>
<tr>
<td>Molnupiravir (Legevrio) 800 mg</td>
<td>Oral</td>
<td>18 years and older</td>
<td>As soon as possible, but within 5 days of symptom onset</td>
<td>Compared to placebo, a relative risk reduction of 30% in hospitalizations or deaths.</td>
<td>Effective against Delta and Omicron</td>
<td>Caution in individuals of reproductive age; require use of reliable method of contraception</td>
</tr>
</tbody>
</table>

# Available Anti-SARS-COV-2 Treatments: Monoclonal Antibodies

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Age groups authorized for treatment</th>
<th>Timing of Treatment</th>
<th>Treatment Effectiveness</th>
<th>Activity Against Variants Currently Circulating</th>
<th>Clinical considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bebtelovimab 175 mg</td>
<td>Intravenous</td>
<td>12 years and older and weighing at least 40 kg</td>
<td>As soon as possible, but within 7 days of symptom onset</td>
<td>Only phase 1/2 data; no risk reduction data</td>
<td>Effective against Delta and Omicron</td>
<td>Caution if any history of hypersensitivity</td>
</tr>
</tbody>
</table>


"Vaccinate ALL 58"
### What is Mild to Moderate Illness?

<table>
<thead>
<tr>
<th>Mild Illness</th>
<th>Moderate Illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.</td>
<td>Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO2) ≥94% on room air at sea level.</td>
</tr>
</tbody>
</table>
Who is High Risk?


- Age is the strongest risk factor for severe COVID-19 outcomes, people aged 65 years or older accounted for 81% of U.S. COVID-19 related deaths in 2020

Text of EUAs

**Conditions:**

- Older age (for example, age ≥65 years of age)
- <1 year old
- Obesity or being overweight
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or treatment
- Cardiovascular disease or hypertension
- Chronic lung disease
- Sickle cell disease
- Neurodevelopmental disorders
- Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation)

Other medical conditions or factors (for example, race or ethnicity) may also place individual patients at high risk for progression to severe COVID-19, and authorization under the EUA is not limited to the medical conditions or factors listed above.
Prescribing Treatment for Mild to Moderate Disease

Mild to moderately ill outpatient with positive direct viral test

Evaluate if candidate for outpatient therapy

Select treatment option

Use of oral option

Healthcare provider identifies dispensing location that has received shipment of Paxlovid or molnupiravir

Communicate with dispensing location to ensure stock available

Send prescription to dispensing location

Use of IV option

Identify infusion center if healthcare provider’s facility does not have product

Regardless of treatment medication or route, patients should be reminded not to delay initiating treatment!

See NIH Treatment Guidelines and product EUAs for:
- Guidance regarding patient eligibility
- Prioritization of therapeutic options

To find dispensing locations, see:
- HHS Therapeutics Locator with map of locations with quantities in stock (based on daily reporting)
- HHS Therapeutics Locator for infusion centers to find locations

NIH Treatment Guidelines: https://www.covid19treatmentguidelines.nih.gov/

HHS Therapeutics Locators: https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/
NIH Prioritization of Treatment Options

In order of preference, the NIH recommends using one of the following treatment options (taking into account a patient’s full clinical status, including drug-drug interactions) for mild to moderate infection:

1. **Nirmatrelvir 300 mg with ritonavir 100 mg (Paxlovid)** orally twice daily for 5 days, initiated as soon as possible and within 5 days of symptom onset in those aged ≥12 years and weighing ≥40 kg

2. **Sotrovimab 500 mg*** as a single IV infusion, administered as soon as possible and within 10 days of symptom onset in those aged ≥12 years and weighing ≥40 kg

3. **Remdesivir 200 mg** IV on Day 1, followed by remdesivir 100 mg IV daily on Days 2 and 3, initiated as soon as possible and within 7 days of symptom onset in those aged ≥12 years and weighing ≥40 kg; EUA in children under the age of 12 years. Doses should be adjusted for pediatric patients.

4. **Bebtelovimab 175 mg** as a single IV injection OR **Molnupiravir 800 mg** orally twice daily for 5 days, initiated as soon as possible and within 5 days of symptom onset in those aged ≥18 years

   *Use bebtelovimab or molnupiravir ONLY when none of the above options can be used*

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*Sotrovimab has reduced effectiveness against BA.2; use of product in California has been paused by HHS*
COVID-19 Outpatient Therapeutics
Clinical Decision Aid for Ages 12+

Adult or pediatric patient (ages 12 and older weighing at least 40 kg) with mild to moderate COVID-19 and at high risk for progression to severe disease.

Is patient:
- Hospitalized for COVID-19
- OR
- Requiring $O_2$
- OR
- Requiring an increase in baseline home $O_2$ due to COVID-19

Symptom onset within the past 5-7 days?

Does patient have severe renal impairment (eGFR <30 mL/min) OR Severe hepatic impairment (Child-Pugh Class C)?

Consider:
- Sotrovimab: 500 mg IV begun ASAP within 7 days of symptom onset
- OR
- Molnupiravir: 800 mg by mouth every 12h for 5 days begun ASAP within 5 days of symptom onset
- OR
- Bebeto: 175 mg single IV injection ASAP within 7 days of symptom onset

Consider one of the following therapeutics, if available:
- Paxlovid: within 5 days of symptom onset
  - eGFR ≥ 60 mL/min: 300 mg nirmatrelvir taken with 100 mg ritonavir twice daily for 5 days
  - eGFR ≥ 30 to < 60: 150 mg nirmatrelvir taken together with 100 mg ritonavir twice daily for 5 days
  - Evaluate concomitant use of CYP3A inducers and medications with high dependency on CYP3A for clearance as these may be contraindicated
- Sotrovimab: 500 mg IV begun ASAP within 7 days of symptom onset
  OR
- Veklury (remdesivir): 200 mg IV x 1 dose on Day 1, 100 mg IV x 1 on Days 2-3 begun ASAP within 7 days of symptom onset

Is patient age 18 or older AND possibility of pregnancy, if applicable, ruled out?

Consider:
- Molnupiravir: 800 mg by mouth every 12h for 5 days begun ASAP within 5 days of symptom onset
  - Prescribers must review and comply with the mandatory requirements outlined in the molnupiravir EUA
- Bebeto: 175 mg single IV injection ASAP within 7 days of symptom onset

Treatment of symptoms, management per NIH & CDC Guidelines

Sotrovimab has reduced effectiveness against BA.2; Distribution has been paused in California.
COVID-19 Outpatient Therapeutics
Clinical Decision Aid for Ages 12+

Adult or pediatric patient (ages 12 and older weighing at least 40 kg) with mild to moderate COVID-19 and at high risk for progression to severe disease

Is patient:
• Hospitalized for COVID-19
• Requiring O₂
• Requiring an increase in baseline home O₂ due to COVID-19?

Symptom onset within the past 5–7 days?

Does patient have severe renal impairment (eGFR <30 mL/min)
• OR
• Severe hepatic impairment (Child-Pugh Class C)?

Consider:
• sotrovimab³ 500 mg IV begun ASAP within 7 days of symptom onset
• OR
• bebtelovimab² 175 mg single IV injection ASAP within 7 days of symptom onset

Consider one of the following therapeutics, if available¹,²:
• Paxlovid with 5 days of symptom onset
  • eGFR ≥ 60 mL/min: 300 mg nirmatrelvir taken with 100 mg ritonavir twice daily for 5 days
  • eGFR ≥ 30 to < 60: 150 mg nirmatrelvir taken together with 100 mg ritonavir twice daily for 5 days
• Evaluate concomitant use of CYP3A inducers and medications with high dependency on CYP3A for clearance as these may be contraindicated³⁴

Veklury (remdesivir)⁵ 200 mg IV x 1 dose on Day 1, 100 mg IV x 1 on Days 2–3 begun ASAP within 7 days of symptom onset

If none of these therapeutics are available, feasible to deliver, or clinically appropriate for patient treatment:

Is patient age 18 or older AND possibility of pregnancy, if applicable, ruled out?

Consider molnupiravir⁶ 800 mg by mouth every 12h for 5 days begun ASAP within 5 days of symptom onset
Prescribers must review and comply with the mandatory requirements outlined in the molnupiravir EUA³

Consider bebtelovimab² 175 mg single IV injection ASAP within 7 days of symptom onset

Treatment of symptoms, management per NIH & CDC Guidelines

Sotrovimab has reduced effectiveness against BA.2; Distribution has been paused in California

COVID-19 Outpatient Therapeutics
Clinical Decision Aid for Ages 12+

Adult or pediatric patient (ages 12 and older weighing at least 40 kg) with mild to moderate COVID-19 and at high risk for progression to severe disease.

Is patient:
- Hospitalized for COVID-19
  - OR
  - Requiring $O_2$
  - OR
  - Requiring an increase in baseline home $O_2$ due to COVID-19?

Symptom onset within the past 5–7 days?

Does patient have severe renal impairment (eGFR <30 mL/min) OR Severe hepatic impairment (Child-Pugh Class C)?

Consider:
- sotrovimab: 500 mg IV begun ASAP within 7 days of symptom onset
  - OR
  - molnupiravir: 800 mg by mouth every 12h for 5 days begun ASAP within 5 days of symptom onset

Is patient age 18 or older AND possibility of pregnancy, if applicable, ruled out?

Consider:
- nirmatrelvir: 100 mg ritonav twice daily for 5 days
  - OR
  - nirmatrelvir: 150 mg ritonav twice daily for 5 days
  - OR
  - Evaluate concomitant use of CYP3A inducers and medications with high dependency on CYP3A for clearance as these may be contraindicated

Veklury (remdesivir): 200 mg IV x 1 dose on Day 1, 100 mg IV x 1 on Days 2–3 begun ASAP within 7 days of symptom onset

If none of these therapeutics are available, feasible to deliver, or clinically appropriate for patient treatment:

Treatment of symptoms, management per NIH & CDC Guidelines

Consider one of the following therapeutics, if available:
- Paxlovid within 5 days of symptom onset
  - eGFR ≥ 60 mL/min: 300 mg nirmatrelvir taken with 100 mg ritonav twice daily for 5 days
  - eGFR ≥ 30 to < 60: 150 mg nirmatrelvir taken together with 100 mg ritonav twice daily for 5 days

Sotrovimab has reduced effectiveness against BA.2; Distribution has been paused in California
Clinical Decision Aid for Pediatric Patients

Outpatient 3.5 kg to less than 40 kg or younger than 12 years of age weighing at least 3.5 kg, with mild to moderate COVID-19 and at high risk for progression to severe disease

- Symptom onset within the past 7 days?
  - NO
  - YES
    - Pediatric patient (greater than 28 days old) with severe renal impairment (eGFR <30 mL/min)
    - OR
      - Full-term neonate (7 to 28 days old) with serum creatinine greater than or equal to 1 mg/dL?
        - YES
          - Consider Veklury (remdesivir)*1 begun ASAP within 7 days of symptom onset
            - Pediatric patients younger than 12 years and weighing 40 kg or greater: 200 mg IV x 1 dose on Day 1, 100 mg IV x 1 on Days 2–3
            - Pediatric patients 3.5 kg to less than 40 kg or pediatric patients younger than 12 years weighing at least 3.5 kg: 5 mg/kg IV on Day 1, 2.5 mg/kg on Days 2–3
          - *Use 100 mg lyophilized vial for EUA pediatric use
        - NO
          - Treatment of symptoms, management per NIH & CDC Guidelines
Drug Interactions With Paxlovid

- Paxlovid has significant and complex drug-drug interactions, primarily due to the ritonavir component of the combination
- Ritonavir is a strong Cytochrome P450 3A4 (CYP3A4) inhibitor
- CYP3A4 oxidizes small foreign organic molecules such as drugs so that they can be removed from the body
- Additionally, ritonavir is an inhibitor, inducer, and substrate of various other drug-metabolizing enzymes and/or drug transporters.
- CYP3A4 inhibition occurs rapidly after initiating ritonavir, with maximum inhibition occurring within 48 hours
- After ritonavir is discontinued, 80% to 90% of CYP3A4 inhibition resolves within 3 days.
Drug Interactions With Paxlovid

- Drug interactions that can be safely managed should not preclude the use of Paxlovid
- Multiple resources are available to guide prescribers through potential interactions and suggest mitigating steps:
  - NIH Treatment Guidelines: https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ritonavir-boosted-nirmatrelvir--paxlovid-
## Drug Interactions With Paxlovid

### Prescribe an alternative COVID-19 therapy

For cases where drug-drug interaction management strategies are not possible or feasible, or the potential risks of such strategies outweigh the potential benefits.

<table>
<thead>
<tr>
<th>Drug Interactions</th>
<th>Alternative Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>Flecainide</td>
</tr>
<tr>
<td>Apalutamide</td>
<td>Quinidine</td>
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<tr>
<td>Bosentan</td>
<td>Rifampin</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Rifapentine</td>
</tr>
<tr>
<td>Clopidogrel&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Sildenafil for PH</td>
</tr>
<tr>
<td>Clozapine</td>
<td>St. John's wort</td>
</tr>
<tr>
<td>Disopyramide</td>
<td>Tadalafil for PH</td>
</tr>
<tr>
<td>Dofetilide</td>
<td>Tolvaptan</td>
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<tr>
<td>Dronedarone</td>
<td>Vardenafil for PH</td>
</tr>
<tr>
<td>Enalaprilatide</td>
<td>Voscorporin</td>
</tr>
<tr>
<td>Ergot derivatives</td>
<td></td>
</tr>
</tbody>
</table>

### Start Paxlovid and temporarily hold or adjust the dosing of medication(s) that might be problematic

Temporarily Withhold Concomitant Medication, If Clinically Appropriate

For guidance on restarting the concomitant medication, consult the Liverpool COVID-19 Drug Interactions website.<sup>2</sup> If withholding is not clinically appropriate, use an alternative concomitant medication or COVID-19 therapy.

<table>
<thead>
<tr>
<th>Drug Interactions</th>
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</thead>
<tbody>
<tr>
<td>Alfuzosin</td>
<td>Estazolam&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Alikiren</td>
<td>Everolimus&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>Finerenone</td>
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<tr>
<td>Avanefil</td>
<td>Fibanserin</td>
</tr>
<tr>
<td>Chemotherapy&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Flurazepam&lt;sup&gt;g&lt;/sup&gt;</td>
</tr>
<tr>
<td>Clonazepam&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Lomitapide</td>
</tr>
<tr>
<td>Clorazepate&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Lovastatin</td>
</tr>
<tr>
<td>Colchicine&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Naloxegol</td>
</tr>
<tr>
<td>Diazepam&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Ranolazine</td>
</tr>
<tr>
<td>Eletriptan</td>
<td>Rimogepant</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Rivaroxaban&lt;sup&gt;f&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>Rosuvastatin</td>
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<td></td>
<td>Salmeterol</td>
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<td></td>
<td>Silodosin</td>
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<tr>
<td></td>
<td>Simvastatin</td>
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<tr>
<td></td>
<td>Sirolimus&lt;sup&gt;f&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>Suvorexant</td>
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<tr>
<td></td>
<td>Tacrolimus&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Ticagrelor</td>
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<tr>
<td></td>
<td>Triazolam&lt;sup&gt;d&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>Ubrogepant</td>
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<tr>
<td></td>
<td>Vorapaxar</td>
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</tbody>
</table>

### Adjust Concomitant Medication Dose and Monitor for Adverse Effects

Consult the Liverpool COVID-19 Drug Interactions website<sup>2</sup> for guidance. If the dose of the concomitant medication cannot be adjusted, withhold the medication (if clinically appropriate) or use an alternative concomitant medication or COVID-19 therapy.

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Alprazolam&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Digoxin</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>Elexacaftor/tezacaftor/ivacaftor</td>
</tr>
<tr>
<td>Apixaban</td>
<td>Eluxadoline</td>
</tr>
<tr>
<td>Anipirazole</td>
<td>Fentanyl</td>
</tr>
<tr>
<td>Brexpiprazole</td>
<td>Iloperidone</td>
</tr>
<tr>
<td>Buspirone</td>
<td>Itraconazole</td>
</tr>
<tr>
<td>Caripazine</td>
<td>Ivacaftor</td>
</tr>
<tr>
<td>Chloridazepoxide&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Ketoconazole</td>
</tr>
<tr>
<td>Clobazam&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Maraviroc</td>
</tr>
<tr>
<td>Cisplatinolomycyn</td>
<td>Melexetine</td>
</tr>
<tr>
<td>Ciocazolam&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Oxycodone</td>
</tr>
<tr>
<td>Cyclosporine&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Pimavanserin</td>
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<tr>
<td>Darifenacin</td>
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<tr>
<td>Quadipine</td>
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<tr>
<td>Rifabutin</td>
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<tr>
<td>Rociguat</td>
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<tr>
<td>Saxaglitin</td>
<td></td>
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<tr>
<td>Sildenafil for ED</td>
<td></td>
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<tr>
<td>Ruxolitinib</td>
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<tr>
<td>Tadalafil for ED</td>
<td></td>
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<tr>
<td>Tamsulosin</td>
<td></td>
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<tr>
<td>Tezacaftor/ivacaftor</td>
<td></td>
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<tr>
<td>Trazodone</td>
<td></td>
</tr>
<tr>
<td>Vardenafil for ED</td>
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</tbody>
</table>

For full details, see the Liverpool COVID-19 Drug Interaction Tool: [https://covid19-druginteractions.org/checker](https://covid19-druginteractions.org/checker)

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<sup>1</sup>For cases where drug-drug interaction management strategies are not possible or feasible, or the potential risks of such strategies outweigh the potential benefits.

<sup>2</sup>For guidance on restarting the concomitant medication, consult the Liverpool COVID-19 Drug Interactions website for guidance. If the dose of the concomitant medication cannot be adjusted, withhold the medication (if clinically appropriate) or use an alternative concomitant medication or COVID-19 therapy.
Considerations for HIV Patients with COVID-19

• Triage, management, and treatment of COVID-19 in people with HIV are generally the same as those for the general population.

• People with HIV who are taking ritonavir-based or cobicistat-based antiretroviral therapy (ART) can receive ritonavir-boosted nirmatrelvir (Paxlovid) to treat COVID-19 without altering or interrupting their ART.
Molnupiravir Considerations

- Because of bone and cartilage toxicity, NOT authorized for use in individuals <18 years of age
- Causes fetal harm, do not use in pregnant individuals
- Breast feeding is not recommended during treatment with molnupiravir and for 4 days after the last dose
- Individuals of childbearing potential must use effective contraception:
  - Females: use a reliable method of contraception correctly and consistently, as applicable, for the duration of treatment and for 4 days after the last dose
  - Males: Males of reproductive potential who are 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
Test to Treat Sites

Get medication for COVID-19

COVID-19 medications are now available through your doctor, local pharmacies, and health clinics. If you have COVID-19 symptoms, do not wait to get treated. You must take oral COVID-19 medication within 5 days of your first COVID-19 symptoms. Use the tool below to find a location that is right for you.

Find COVID-19 Medication

Alameda County, CA, USA

<table>
<thead>
<tr>
<th>Location</th>
<th>Distance</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVS Store #09251</td>
<td>3530 m</td>
<td>1</td>
</tr>
</tbody>
</table>

Locate with testing, medical visits, and medication (Test-to-Treat)

- CVS Store #09251

How to get medication

1. Locations to get testing, medical visits, and medication (Test-to-Treat)

Some pharmacy clinics and health centers can prescribe and give you medication at the same location. Learn more about the Test-to-Treat program.

2. Locations to fill a prescription

Any healthcare provider can evaluate and prescribe you COVID-19 medication just as they normally would. You can fill those prescriptions at any location in this tool.

Data available for download at HealthData.gov

Need help finding a place to get medication? Call 1-800-232-0233 (TTY 888-370-7449)
Prophylaxis for COVID-19
Post-Exposure Prophylaxis

• Currently we have no FDA authorized or approved therapeutics for post-exposure prophylaxis
• Bam/Ete and REGEN COV are the only drugs with EUAs for post-exposure prophylaxis and neither are effective against Omicron
• As of January 24, 2022:
  ◦ The FDA has revised bam/ete and REGEN COV EUAs to limit use to patients who are likely to have been exposed or infected to a variant that is susceptible to these treatments
  ◦ Use of bam/ete and REGEN COV are not authorized for use in any US state
# Pre-Exposure Prophylaxis: Evusheld

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Age groups authorized for treatment</th>
<th>Pre-Exposure Prophylaxis Effectiveness</th>
<th>Activity Against Variants Currently Circulating</th>
<th>Clinical Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tixagevimab 300 mg / cilgavimab 300 mg (Evusheld)</td>
<td>Intramuscular</td>
<td>12 years and older and weighing at least 40 kg</td>
<td>Reduced the risk of developing symptomatic COVID-19 by 77% compared to placebo.</td>
<td>Effective against Delta and Omicron</td>
<td>Use with caution if history of hypersensitivity</td>
</tr>
</tbody>
</table>

Given as two separate consecutive injections

Redose every 6 months

Pre-Exposure Prophylaxis: Evusheld

• Use of Evusheld as a pre-exposure prophylaxis (PrEP) is authorized for adults and adolescents (aged ≥12 years and weighing ≥40 kg) who do not have SARS-CoV-2 infection, who have not been recently exposed to an individual with SARS-CoV-2 infection, AND who:

  ◦ Are moderately to severely immunocompromised and may have inadequate immune response to COVID-19 vaccination; or
  ◦ Are not able to be fully vaccinated with any available COVID-19 vaccines due to a history of severe adverse reaction to a COVID-19 vaccine or any of its components.

Evusheld is not a substitute for COVID-19 vaccination and should not be used in unvaccinated individuals for whom COVID-19 vaccination is recommended and who are anticipated to have an adequate response.
Therapeutic Allocation and Supply
Current Supply of COVID-19 Outpatient Therapeutics

- Supply of therapeutic products in California is currently **not** limited; we are currently **not** in a state of scarcity
- At this time, **all patients** who are eligible for treatment with COVID-19 treatments should be offered treatment
- Should product ever be scarce in the future, the NIH Treatment Guidelines provide direction on patient prioritization: https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/nonhospitalized-adults-therapeutic-management/
Clinical Cases
Clinical Cases #1: The Straightforward Patient

66 yo obese male on no medications with 3 days of fever and cough; positive SARS-CoV-2 on home antigen test. No history of renal or hepatic impairment.
COVID-19 Outpatient Therapeutics
Clinical Decision Aid for Ages 12+

Adult or pediatric patient (ages 12 and older weighing at least 40 kg) with mild to moderate COVID-19 and at high risk for progression to severe disease

Is patient:
- Hospitalized for COVID-19
- OR
- Requiring O₂
- OR
- Requiring an increase in baseline home O₂ due to COVID-19?

Symptom onset within the past 5–7 days?

Does patient have severe renal impairment (eGFR <30 mL/min):
- OR
- Severe hepatic impairment (Child-Pugh Class C)?

Consider:
- Sotrovimab: 500 mg IV begun ASAP within 7 days of symptom onset
- OR
- Bebtelovimab: 175 mg single IV injection ASAP within 7 days of symptom onset

Is patient age 18 or older AND possibility of pregnancy, if applicable, ruled out?

Consider:
- Molnupiravir: 800 mg by mouth every 12h for 5 days begun ASAP within 5 days of symptom onset
- Prescribers must review and comply with the mandatory requirements outlined in the molnupiravir EUA

Consider:
- Paxlovid: within 5 days of symptom onset
- OR
- Evaluate concomitant use of CYP3A inducers and medications with high dependency on CYP3A for clearance as these may be contraindicated

Sotrovimab has reduced effectiveness against BA.2; Distribution has been paused in California
Clinical Case #1: The Straightforward Patient

66 yo obese male on no medications with 3 days of fever and cough; positive SARS-CoV-2 on home antigen test. No history of renal or hepatic impairment.

Paxlovid
Clinical Case #2: Patient on Multiple Medications

50 yo male with history of diabetes, high blood pressure, obesity, and high cholesterol presenting with 3 days of fever and cough; positive SARS-CoV-2 on home antigen test. No history of renal or hepatic impairment.

Medications:
Metformin
Simvastatin
Amlodipine
Clinical Case #2: Patient on Multiple Medications

COVID-19 Outpatient Therapeutics
Clinical Decision Aid for Ages 12+

Adult or pediatric patient (ages 12 and older weighing at least 40 kg) with mild to moderate COVID-19 and at high risk for progression to severe disease

Is patient:
- Hospitalized for COVID-19
- Requiring O₂
- Requiring an increase in baseline home O₂ due to COVID-19

Symptom onset within the past 5–7 days?

Does patient have severe renal impairment (eGFR <30 mL/min) OR Severe hepatic impairment (Child-Pugh Class C)?

Consider:
- sotrovimab® 500 mg IV begun ASAP within 7 days of symptom onset
- molnupiravir® 800 mg by mouth every 12h for 5 days begun ASAP within 5 days of symptom onset

Paxlovid® within 5 days of symptom onset
- eGFR ≥60 mL/min: 300 mg nirmatrelvir taken with 100 mg ritonavir twice daily for 5 days
- eGFR ≥30 to <60: 150 mg nirmatrelvir taken together with 100 mg ritonavir twice daily for 5 days
- Evaluate concomitant use of CYP3A inducers and medications with high dependency on CYP3A for clearance as these may be contraindicated

Sotrovimab has reduced effectiveness against BA.2; Distribution has been paused in California

Clinical Case #2: Patient on Multiple Medications

50 yo male with history of diabetes, high blood pressure, obesity, and high cholesterol presenting with 3 days of fever and cough; positive SARS-CoV-2 on home antigen test. No history of renal or hepatic impairment.

Medications:
- Metformin
- Simvastatin
- Amlodipine
- Paxlovid
- Remdesivir
- Bebtelovimab
- Molnupiravir

https://www.covid19treatmentguidelines.nih.gov/special-populations/hiv/
Clinical Case #2: Patient on Multiple Medications

<table>
<thead>
<tr>
<th>COVID Drugs</th>
<th>Co-medications</th>
<th>Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paxlo</td>
<td>Metformin</td>
<td></td>
</tr>
<tr>
<td>A-Z</td>
<td>A-Z</td>
<td></td>
</tr>
</tbody>
</table>

- **Nirmatrelvir/ritonavir** (Please read the interaction details as management of these interactions may be complex.)
- **Simvastatin**
- **Amlodipine**

**Potential Interaction**

- **Nirmatrelvir/ritonavir** (Please read the interaction details as management of these interactions may be complex.)
- **Amlodipine**

**No Interaction Expected**

- **Nirmatrelvir/ritonavir** (Please read the interaction details as management of these interactions may be complex.)

[https://covid19-druginteractions.org/checker](https://covid19-druginteractions.org/checker)
Clinical Case #2: Patient on Multiple Medications

<table>
<thead>
<tr>
<th>Drugs that should not be coadministered (RED)</th>
<th>Hold simvastatin, resume 3 days after last dose of Paxlovid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nirmatrelvir/ritonavir (Please read the interaction details as management of these interactions may be complex.) + Simvastatin</td>
<td></td>
</tr>
<tr>
<td>Coadministration of simvastatin and potent CYP3A4 inhibitors, such as ritonavir, is contraindicated due to the high risk of presenting serious reactions such as risk of myopathy including rhabdomyolysis. It is highly advised to stop simvastatin during nirmatrelvir/ritonavir treatment. The pragmatic approach to stop temporarily simvastatin (or any other statins) is acceptable considering that it will not negatively affect the therapeutic effect but can minimize the risk for adverse events related to a drug interaction. Given the mechanism-based inhibition of nirmatrelvir/ritonavir, simvastatin treatment will have to be resumed 3 days after the last dose of nirmatrelvir/ritonavir.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Potential clinically significant interaction - likely to require additional monitoring, alteration of drug dosage or timing of administration (AMBER)</th>
<th>Reduce amlodipine dose by 50% OR monitor blood pressure and stop drug if low</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nirmatrelvir/ritonavir (Please read the interaction details as management of these interactions may be complex.) + Amlodipine</td>
<td></td>
</tr>
<tr>
<td>Coadministration has not been studied. Amlodipine is metabolized by CYP3A4. Nirmatrelvir/ritonavir is predicted to increase amlodipine exposure by ~2-fold based on drug-drug interactions studies with amlodipine and indinavir/ritonavir or paritaprevir/ritonavir leading to the recommendation to reduce amlodipine dosage by 50%. However, a dose adjustment can be optional in the case of amlodipine given that patients can be advised to monitor for symptoms of hypotension and to temporarily pause the antihypertensive drug if needed. The inhibitory effect of ritonavir is expected to last up to 3 days after the last administered dose of nirmatrelvir/ritonavir.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No clinically significant interaction expected (GREEN)</th>
<th>No change to metformin dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nirmatrelvir/ritonavir (Please read the interaction details as management of these interactions may be complex.) + Metformin</td>
<td></td>
</tr>
</tbody>
</table>

https://covid19-druginteractions.org/checker
Clinical Case #2: Patient on Multiple Medications

50 yo male with history of diabetes, high blood pressure, obesity, and high cholesterol presenting with 3 days of fever and cough; positive SARS-CoV-2 on home antigen test. No history of renal or hepatic impairment.

Medications:
Metformin
Simvastatin
Amlodipine

<table>
<thead>
<tr>
<th>Drug</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paxlovid</td>
<td>Drug interactions, but all manageable</td>
</tr>
<tr>
<td>Remdesivir</td>
<td>Infusion center required, three days of treatment</td>
</tr>
<tr>
<td>Bebtelovimab</td>
<td>Infusion center required; less clinical data</td>
</tr>
<tr>
<td>Molnupiravir</td>
<td>Oral, but least effective medication</td>
</tr>
</tbody>
</table>
Clinical Case #3: Patient With Longer Symptom Duration

50 yo male with history of diabetes, high blood pressure, obesity, and high cholesterol presenting with 6 days of fever and cough; positive SARS-CoV-2 on home antigen test. No history of renal or hepatic impairment.

**Medications:**
- Metformin
- Simvastatin
- Amlodipine
Clinical Case #3: Patient With Longer Symptom Duration

50 yo male with history of diabetes, high blood pressure, obesity, and high cholesterol presenting with 6 days of fever and cough; positive SARS-CoV-2 on home antigen test. No history of renal or hepatic impairment.

Medications:
Metformin
Simvastatin
Amlodipine

Remdesivir  Infusion center required, three days of treatment
Bebtelovimab  Infusion center required; less clinical data
Clinical Case #4: Patient on Hemodialysis

50 yo male with history of diabetes, end stage renal disease and on hemodialysis M-W-Fri, high blood pressure, obesity, and high cholesterol presenting with 3 days of fever and cough; positive SARS-CoV-2 on home antigen test.
Clinical Case #4: Patient on Hemodialysis

COVID-19 Outpatient Therapeutics
Clinical Decision Aid for Ages 12+

Adult or pediatric patient (ages 12 and older weighing at least 40 kg) with mild to moderate COVID-19 and at high risk for progression to severe disease

Is patient:
- Hospitalized for COVID-19
  - OR
  - Requiring O₂
  - OR
  - Requiring an increase in baseline home O₂ due to COVID-19?

Symptom onset within the past 5–7 days?

Does patient have severe renal impairment (eGFR <30 mL/min) OR Severe hepatic impairment (Child-Pugh Class C)?

Consider:
- sotrovimab: 500 mg IV begun ASAP within 7 days of symptom onset
  - OR
  - molnupiravir: 800 mg by mouth every 12h for 5 days begun ASAP within 5 days of symptom onset

- Paxlovid: within 5 days of symptom onset
  - eGFR ≥ 60 mL/min: 300 mg nirmatrelvir taken with 100 mg ritonavir twice daily for 5 days
  - eGFR ≥ 30 to < 60: 150 mg nirmatrelvir taken together with 100 mg ritonavir twice daily for 5 days
  - Evaluate concomitant use of CYP3A inducers and medications with high dependency on CYP3A for clearance as these may be contraindicated

- Veklury (remdesivir): 200 mg IV x 1 dose on Day 1, 100 mg IV x 1 on Days 2–3 begun ASAP within 7 days of symptom onset

If none of these therapeutics are available, feasible to deliver, or clinically appropriate for patient treatment:

Is patient age 18 or older AND possibility of pregnancy, if applicable, ruled out?

Treatment of symptoms, management per NIH & CDC Guidelines

Consider one of the following therapeutics, if available:

- sotrovimab: 500 mg IV begun ASAP within 7 days of symptom onset
- molnupiravir: 800 mg by mouth every 12h for 5 days begun ASAP within 5 days of symptom onset

Prescribers must review and comply with the mandatory requirements outlined in the molnupiravir EUA.

Sotrovimab has reduced effectiveness against BA.2; Distribution has been paused in California
Clinical Case #4: Patient on Hemodialysis

50 yo male with history of diabetes, end stage renal disease and on hemodialysis M-W-Fri, high blood pressure, obesity, and high cholesterol presenting with 3 days of fever and cough; positive SARS-CoV-2 on home antigen test.

Bebtelovimab
Infusion center required; less clinical data

Molnupiravir
Oral, but likely least effective medication of the two options
Clinical Case #5: Pregnant Patient

35 yo female who is 24 weeks pregnant with history of sickle cell disease with 3 days of fever and cough; positive SARS-CoV-2 on home antigen test. No history of liver or kidney problems.
Clinical Case #5: Pregnant Patient

COVID-19 Outpatient Therapeutics
Clinical Decision Aid for Ages 12+

Adult or pediatric patient (ages 12 and older weighing at least 40 kg) with mild to moderate COVID-19 and at high risk for progression to severe disease

Is patient:
- Hospitalized for COVID-19
- OR
- Requiring \( O_2 \)
- OR
- Requiring an increase in baseline home \( O_2 \) due to COVID-19?

NO → Treatment of symptoms, management per NIH & CDC Guidelines

YES → Symptom onset within the past 5–7 days?

NO → NO

YES → Does patient have severe renal impairment (eGFR < 30 mL/min) OR Severe hepatic impairment (Child-Pugh Class C)?

NO → NO

YES → Consider:
- sotrovimab<sup>3</sup> 500 mg IV begun ASAP within 7 days of symptom onset
- OR
- molnupiravir<sup>6</sup> 800 mg by mouth every 12h for 5 days begun ASAP within 5 days of symptom onset

Is patient age 18 or older AND possibility of pregnancy, if applicable, ruled out?

NO → Consider: sotrovimab<sup>3</sup> 500 mg IV begun ASAP within 7 days of symptom onset

YES → Consider:
- molnupiravir<sup>6</sup> 800 mg by mouth every 12h for 5 days begun ASAP within 5 days of symptom onset
- OR
- bebtelovimab<sup>2,7</sup> 175 mg single IV injection ASAP within 7 days of symptom onset

Consider one of the following therapeutics, if available:<sup>1,2</sup>
- Paxlovid<sup>2</sup> within 5 days of symptom onset
  - eGFR ≥ 60 mL/min: 300 mg nirmatrelvir taken with 100 mg ritonavir twice daily for 5 days
  - eGFR 30 to < 60: 150 mg nirmatrelvir taken together with 100 mg ritonavir twice daily for 5 days
- Evaluate concomitant use of CYP3A inducers and medications with high dependency on CYP3A for clearance as these may be contraindicated<sup>3,4</sup>
- sotrovimab<sup>3</sup> 500 mg IV begun ASAP within 7 days of symptom onset
- OR
- Veklury (remdesivir)<sup>5,9</sup> 200 mg IV x 1 dose on Day 1, 100 mg IV x 1 on Days 2–3 begun ASAP within 7 days of symptom onset

If none of these therapeutics are available, feasible to deliver, or clinically appropriate for patient treatment:


Sotrovimab has reduced effectiveness against BA.2; Distribution has been paused in California
Clinical Case #5: Pregnant Patient

35 yo female who is 24 weeks pregnant with history of sickle cell disease with 3 days of fever and cough; positive SARS-CoV-2 on home antigen test. No history of liver or kidney problems.

Patients Should be Counseled Regarding:

- COVID-19 in pregnancy is associated with adverse maternal and fetal outcomes, including preeclampsia, eclampsia, preterm birth, premature rupture of membranes, venous thromboembolic disease, and fetal death.
- For all drugs, insufficient data to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.
Clinical Case #6: Pediatric Case

8 yo female with cerebral palsy presenting with 3 days of fever and chills. Found to be SARS-CoV-2 PCR positive. No history of liver or kidney problems
Clinical Case #6: Pediatric Case

Clinical Decision Aid for Pediatric Patients

Outpatient 3.5 kg to less than 40 kg or younger than 12 years of age weighing at least 3.5 kg, with mild to moderate COVID-19 and at high risk for progression to severe disease

Symptom onset within the past 7 days?

YES

Pediatric patient (greater than 28 days old) with severe renal impairment (eGFR <30 mL/min)

OR

Full-term neonate (7 to 28 days old) with serum creatinine greater than or equal to 1 mg/dL?

NO

YES

Consider Veklury (remdesivir)*1 begun ASAP within 7 days of symptom onset

Pediatric patients younger than 12 years and weighing 40 kg or greater: 200 mg IV x 1 dose on Day 1, 100 mg IV x 1 on Days 2–3

Pediatric patients 3.5 kg to less than 40 kg or pediatric patients younger than 12 years weighing at least 3.5 kg: 5 mg/kg IV on Day 1, 2.5 mg/kg on Days 2–3

*Use 100 mg lyophilized vial for EUA pediatric use

Treatment of symptoms, management per NIH & CDC Guidelines

8 yo female with cerebral palsy presenting with 3 days of fever and chills. Found to be SARS-CoV-2 PCR positive. No history of liver or kidney problems.
Resources and Summary Points
Summary Points

- **Effective treatment** for outpatients with mild to moderate COVID-19 is available and *should be offered to all high-risk patients* if they meet criteria for treatment based on EUAs.

- We are **not in a state of scarcity**, all patients at high risk for disease progression with a COVID-19 positive test (PCR or antigen) who are within the treatment window should be offered treatment.

- Providers should review product EUAs as well as the **NIH Treatment Guidelines** prior to using outpatient therapeutics.

- **Clinical guidance is available** to assist in the selection of an appropriate COVID-19 therapeutic as well the navigation of some of the clinical complexities of using these drugs (i.e. Paxlovid drug interactions).
**Resources**

- **Treatment**
  - CDPH Webpage: [https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/COVID-19/Treatments.aspx](https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/COVID-19/Treatments.aspx)
  - HHS: [https://www.phe.gov/emergency/events/COVID19/therapeutics/Pages/healthcare-professionals.aspx](https://www.phe.gov/emergency/events/COVID19/therapeutics/Pages/healthcare-professionals.aspx)

- **Locating Therapeutic Options**

- **Information on Billing**
  - CMS Infusion Billing: [https://www.cms.gov/monoclonal](https://www.cms.gov/monoclonal)

- **Fact Sheets for Providers**
  - Paxlovid: [https://www.fda.gov/media/155050/download](https://www.fda.gov/media/155050/download)
  - Remdesivir:
    - Use in <12 years of age: [https://www.fda.gov/media/137566/download](https://www.fda.gov/media/137566/download)
  - Bebtelovimab: [https://www.fda.gov/media/156152/download](https://www.fda.gov/media/156152/download)
  - Molnupiravir: [https://www.fda.gov/media/155054/download](https://www.fda.gov/media/155054/download)
  - Evusheld: [https://www.fda.gov/media/154701/download](https://www.fda.gov/media/154701/download)

- **Fact Sheets for Patients**
  - Paxlovid: [https://www.fda.gov/media/155051/download](https://www.fda.gov/media/155051/download)
  - Remdesivir: [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) and for pediatric patients: [https://www.fda.gov/media/137565/download](https://www.fda.gov/media/137565/download)
  - Bebtelovimab: [https://www.fda.gov/media/156153/download](https://www.fda.gov/media/156153/download)
  - Molnupiravir: [https://www.fda.gov/media/155055/download](https://www.fda.gov/media/155055/download)
  - Evusheld: [https://www.fda.gov/media/154702/download](https://www.fda.gov/media/154702/download)