This guidance document was developed by the San Francisco Department of Public Health (SFDPH) for local use. It will be posted at www.sfcdcp.org/.

AUDIENCE: Clinical prescribing providers in San Francisco.

PURPOSE: To guide clinicians prescribing available outpatient therapies for treatment and prevention of COVID-19.

BACKGROUND: Outpatient therapeutics are available in San Francisco. Therapies to treat COVID-19 help mild to moderately symptomatic non-hospitalized individuals with COVID-19, who are at higher risk of progressing to severe disease. Higher risk of disease progression includes those who are not vaccinated, not up to date with vaccination or are not expected to mount sufficient vaccine response. Therapies to prevent COVID-19 infection provide greatest benefit to those who cannot receive the vaccine due to severe allergic reaction or who have immune compromise that may limit their response to the vaccine. With improved supply, expanded eligibility for medications now includes many common conditions.” This guide was created to help providers prescribing these therapies.

The following guidelines have been adapted from those utilized and shared throughout the San Francisco Health Network and based on the performance of therapies against current variants. Individual provider or practice may adjust their evaluation and prescribing practices based on changing conditions of the disease.

Available Therapies

For Treatment: The following therapies in Table 1 can be considered for mild to moderately symptomatic non-hospitalized individuals with COVID-19 at risk of progression to severe disease. Of note, individuals who are hospitalized for a non-COVID indication and who meet these criteria may also be considered for these treatments. See the below table for the mechanism of action, administration instructions, evidence for efficacy, and clinical considerations for each treatment. The NIH and CDC have ranked them in terms of first-line and second-line therapies. Recommendations for isolation with COVID-19 infection do not change if a patient is given a COVID-19 therapy.

Of note, the FDA recently (March 2022) began limiting use of Sotrovimab in regions where the BA.2 Omicron subvariant is dominant due to decreased efficacy. California, which is in HHS region 9, surpassed this threshold on March 30th. Therefore Sotrovimab should not currently be used in San Francisco¹ and has been removed from this guidance document.
### Table 1: Recommended COVID-19 Therapeutics for the outpatient setting

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Mechanism &amp; Administration</th>
<th>Clinical Considerations</th>
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</thead>
<tbody>
<tr>
<td><strong>1st Line</strong></td>
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</table>
| Nirmatrelvir/Ritonavir (Paxlovid) | • Antiviral  
• **Oral:** Nirmatrelvir 300mg (two 150 mg tablets) with ritonavir 100mg (one 100mg tablet)- three tablets taken twice daily x 5 days within 5 days of symptom onset  
• Dose reduce for renal impairment. For eGFR 30-60 ml/min-decrease dose to 150mg nirmatrelvir (one 150mg tablet) and 100mg ritonavir (one 100mg tablet) twice daily x 5 days. Formulations in renal dosing are available. Do not prescribe for eGFR <30 ml/min.  
• Do not use in severe hepatic impairment (ie Child-Pugh C, history of decompensated cirrhosis). | • Numerous drug interactions due to inhibitor of CYP3A4. Many interacting medications should be held or dose reduced for the 5 days of Paxlovid and 2 days after Paxlovid completion*  
• Limited data in pregnancy, but per EUA, should not be withheld in pregnancy  
• For use in individuals >12 years of age  
• May cause some GI symptoms  
• Evidence: 88% reduction in hospitalization and death² |
| Remdesivir (Veklury) | • Antiviral  
• **Intravenous:** 200mg x1 day, then 100mg x 2 days within 7 days of symptom onset.  
• Limited data in eGFR < 30 ml/min. Weigh risks and benefits.  
• Do not use in severe hepatic impairment  

*May only be given in inpatient or skilled nursing home settings at this time* | • Limited drug interactions. Minor CYP3A4 inhibitor.*  
• Limited data in pregnancy but generally considered safe.  
• For use in individuals >12 years of age  
• Evidence: 87% reduction in hospitalization and death³ |
| **2nd Line** | | |
| Molnupiravir (Lagevrio) | • Antiviral  
• **Oral:** 800mg (4 tablets of 200mg) twice daily for 5 days 5 days of symptom onset.  
• No adjustments for renal or hepatic insufficiency | • No drug interactions*  
• Contraindicated in pregnancy or while breastfeeding. Patients of childbearing potential should use contraception during and 4 days after use. Individuals with partners of childbearing potential should use contraception during and 3 months after use.  
• For use in individuals >18 years of age  
• May cause some GI symptoms  
• Evidence: 30% reduction in hospitalization and death⁴ |
Bebtelovimab

- Monoclonal antibody with presumed activity against Omicron
- **Intravenous**: 175mg x 1 dose *within 7 days of symptom onset.*
- No adjustments for renal or hepatic insufficiency

- Drug interactions unlikely*
- Limited data in pregnancy or during lactation but generally considered safe
- For use in individuals >12 years of age weighing at least 40kg
- Risk of an allergic reaction so should be monitored for 60 minutes after infusion
- **Evidence**: Reduced time to symptom resolution. Data in low-risk individuals did not show reduction in hospitalization and death.

*Drug interactions for COVID-19 medications can be found here: [https://www.covid19-druginteractions.org/](https://www.covid19-druginteractions.org/)

**For Pre-exposure Prophylaxis:** The following therapies in Table 2 can be considered for individuals who have moderate to severe immune compromise and may not be able to mount an adequate response to COVID-19 vaccination OR for whom vaccination is not recommended due to history of severe adverse reaction. See the below table for the mechanism of action, administration instructions, evidence for efficacy, and clinical considerations for each treatment.

**Table 2: Recommended COVID-19 Therapeutics for Pre-exposure Prophylaxis**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Mechanism &amp; Administration</th>
<th>Clinical Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tixagevimbocilgavimab</td>
<td>• Monoclonal antibody</td>
<td>• Drug interactions unlikely*</td>
</tr>
<tr>
<td>(Evusheld)</td>
<td>• <strong>Intramuscular</strong>: two IM injections of tixagevimbocilgavimab 300 mg and cilgavimab 300 mg</td>
<td>• Limited data in pregnancy or during lactation. Should weight risks and benefits.</td>
</tr>
<tr>
<td></td>
<td>• No adjustments for renal or hepatic insufficiency</td>
<td>• For use in individuals &gt;12 years of age weighing at least 40kg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Risk of an allergic reaction so should be monitored for 60 minutes after infusion.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• <strong>Evidence</strong>: 77% reduction in infection with COVID-19</td>
</tr>
</tbody>
</table>

*Drug interactions for COVID-19 medications can be found here: [https://www.covid19-druginteractions.org/](https://www.covid19-druginteractions.org/)*
Prioritizing High-Risk Patients When There is Limited Supply of Therapeutics

The National Health Institute (NIH) has developed guidance on allocation of these therapies during times of low supply or high demand. In times of scarcity, COVID-19 therapies should be directed towards the patients who will have the greatest potential benefit based on vaccination status, age and comorbidities (Table 3). This framework provides a guideline that individual health systems may choose to interpret differently to best serve their patients when supply is low or demand is high. Allocation of a scarce resource often poses equity concerns. The CDC released data that racial and ethnic minorities are less likely to receive certain outpatient treatments against COVID-19 which clinicians should consider in their practice.

The California Department of Public Health (CDPH) and SFDPH will be monitoring availability and prescribing practices and will adjust allocations and provider outreach as needed to enhance equitable access. Providers may choose to follow local and state Health Alerts to determine current availability and eligibility criteria for COVID-19 treatments. Health advisories and alerts are posted at www.sfcdcp.org/health-alerts-emergencies/health-alerts/.

Table 3: Risk Groups for COVID-19 Therapeutic Prioritization for Treatment of COVID-19

<table>
<thead>
<tr>
<th>Tier 1</th>
<th>Tier 2</th>
<th>Tier 3***</th>
<th>Tier 4***</th>
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<tbody>
<tr>
<td>• Moderately or severely Immunocompromised patient not expected to have mounted response to the vaccine*&lt;br&gt;• Unvaccinated individuals either 1) age &gt;75; or 2) age &gt;65 with clinical risk factors**</td>
<td>• Unvaccinated patients at risk of severe disease due to 1) age &gt;65; or 2) age &lt;65 with clinical risk factors**</td>
<td>• Vaccinated patients at high risk of severe disease due to 1) age &gt;75; or 2) age &gt;65 with clinical risk factors**</td>
<td>• Vaccinated patients at risk of severe disease due to 1) age &gt;65; or 2) age &lt;65 with clinical risk factors**</td>
</tr>
</tbody>
</table>

*Immunocompromising Conditions:

CDC lists conditions that qualify an individual as moderately or severely immunocompromised.

However, given supply may not reach all moderately to severely immunocompromised individuals, the following should be prioritized per NIH guidance:

- Patients within 1 year of receiving B-cell depleting therapies (rituximab, ocrelizumab, ofatumumab, alemtuzumab)
- Patients receiving tyrosine kinase inhibitors
- Chimeric antigen receptor T cell recipients
- Post-hematopoietic cell transplant recipients with chronic graft versus host disease or who are taking immunosuppressives
- Patients with hematologic malignancies on active therapy
- Most solid organ transplant recipients (see NIH guidance below for specifics)
- Patients with severe combined immunodeficiencies
- Patients with untreated HIV with CD4 counts <50

**Clinical risk factors can be found here: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html

*** Vaccinated individuals who have not received the booster should be prioritized.
Pre-exposure prophylaxis should not be used for unvaccinated individuals unless they have a severe allergy to ingredients of the vaccine or a severe allergy to prior doses of the vaccine. Therapies used for pre-exposure should be allocated in the following priority groups per CDPH guidance.

- Priority 1: People who are severely immunocompromised by NIH treatment guidelines (list above)
- Priority 2: If adequate supply exists, then can be used for those who are moderately immunocompromised and not expected to mount an appropriate response.
- Priority 3: If adequate supply exists to meet the above demands, healthy people with no immunocompromising conditions but history of severe adverse reactions to the COVID-19 vaccine

Prescribing Therapies for Your Eligible Patients in San Francisco

Prescriptions can now be sent to any Walgreens, CVS, and Safeway to reduce barriers. Medications will either be stocked or redistributed internally.

Walgreens offers free delivery: request on prescription
- MediCal: free DoorDash same day if received by 11am
- All others: free 1-2 day FedEx delivery, or $9.99 delivery by DoorDash

A full list of pharmacies and clinics can be found at Covid.gov

Most prescriptions should be placed electronically through your EHR. However, if having difficulty, some pharmacies can accommodate phone prescriptions.

If you are a provider who works at University of California San Francisco (UCSF), Kaiser Permanente, California Pacific Medical Center (CPMC), Northeast Medical Services (NEMS) or Zuckerberg San Francisco General (ZSFG), you may access therapies within your own health system as well. Contact your department to determine which internal pharmacies have supplies.

Your prescription must include the date of patient’s symptom onset, if relevant and their eligibility criteria as can be found in Table 3.

Patients without insurance or a healthcare provider

Test to Treat sites can both test for SARS-CoV-2 and dispense COVID-19 treatments regardless of insurance status.

- Sites providing test to treat in San Francisco can be found on: https://sf.gov/get-treated-covid-19
- Current sites participating in the federal program can be found on the new HHS Test to Treat Locator, which can be found here: https://covid-19-test-to-treat-locator-dhhs.hub.arcgis.com.
Additional Resources

- NIH Guidance: “The COVID-19 Treatment Guidelines Panel’s Interim Statement on Patient Prioritization for Outpatient Anti-SARS-CoV-2 Therapies or Preventive Strategies When There Are Logistical or Supply Constraints”
- CDC Paxlovid Eligibility Screening Checklist for Providers
  https://www.fda.gov/media/158165/download

References

6. Administration. UFaD. FACT SHEET FOR HEALTHCARE PROVIDERS: EMERGENCY USE AUTHORIZATION FOR EVUSHIELD (tixagevimab co-packaged with cilgavimab). Available at: https://www.fda.gov/media/154701/download.