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Use of Outpatient COVID-19 Therapeutics in California

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Introduction

As supply of therapeutics has increased and overall COVID-19 cases have decreased across California, there is no longer a limited supply of COVID-19 therapeutic treatments in most locations.

As of this writing, all outpatients with mild to moderate COVID-19 who are at risk for disease progression should be offered treatment if eligible based on the product Emergency Use Authorizations (EUAs). Treatment should be offered regardless of vaccination status. Because of the predominance of the Omicron sub-variant BA.2, sotrovimab is no longer authorized for use in California.

Available Outpatient Therapeutic Options for COVID-19

Currently authorized therapeutics for COVID-19 are summarized below with routes of administration (IM = intramuscular; IV = intravenous; PO = oral):

	SARS-CoV-2 Negative (-)		**SARS-CoV-2 Positive (+)**
	Not Exposed *Pre-Exposure Prophylaxis (PrEP)*	**Exposed** *Post-Exposure Prophylaxis (PEP)*	**Mild to Moderate Illness** *Treatment*
Outpatient Treatment Options	*Long-Acting Monoclonal Antibody* • Tixagevimab/cilgavimab (Evusheld) (IM)	*Currently no authorized treatments****	*Monoclonal Antibodies*†* • Bebtelovimab (IV) *Antivirals* • Niramtrelivr/ritonavir (Paxlovid) (PO) • Remdesivir (Veklury) (IV) • Molnupiravir (Lagevrio) (PO)

****The anti-SARS-CoV-2 monoclonal antibodies bamlanivimab/etesevimab 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 the Omicron BA.2 sub-variant. US Health and Human Services (HHS) paused distribution of sotrovimab to California on 3/29/2022 and the drug is no longer authorized in California as of 3/30/2022 per the FDA.

Providers should review the US Food and Drug Administration's (FDA) Healthcare Provider Fact Sheets for each drug (linked below) prior to using outpatient therapeutics.

Sotrovimab and The Omicron Sub-variant BA.2

On 3/25/2022, the FDA revised the EUA for sotrovimab to reflect decreased activity against the Omicron BA.2 sub-variant. Due to increases in BA.2 in California, the FDA updated the sotrovimab EUA on 3/30/2022 and the drug is no longer authorized for use in California and other regions of the US where BA.2 is the predominant variant.

Providers should prioritize the use of Paxlovid and remdesivir for the treatment of mild to moderate COVID-19 in outpatients at risk for disease progression. If an anti-SARS-CoV-2 monoclonal antibody is indicated over these options, providers should use bebtelovimab.

Prioritization of COVID-19 Treatments

Preferred COVID-19 Treatments (listed in order of preference) per the NIH COVID-19 Treatment Guidelines are:

- **Nirmatrelvir 300 mg with ritonavir 100 mg (Paxlovid)** orally twice daily for 5 days, initiated as soon as possible within 5 days of symptom onset in those aged ≥12 years and weighing ≥40 kg; *or*
- **Remdesivir** 200 mg IV on Day 1, followed by **remdesivir 100 mg** IV once daily on Days 2 and 3, initiated as soon as possible within 7 days of symptom onset in those aged ≥12 years and weighing ≥40 kg. Indications and dosage for outpatients <12 years of age can be found in the remdesivir EUA fact sheet.

If none of the preferred therapies for high-risk, non-hospitalized patients are available, feasible to deliver, or clinically appropriate (e.g., due to drug-drug interactions, concerns related to renal or hepatic function), the NIH recommends using one of the two following therapies (listed in alphabetical order):

- **Bebtelovimab** 175 mg as a single IV infusion, administered as soon as possible within 7 days of symptom onset in those aged ≥12 years and weighing ≥40 kg; *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

If patients are to receive molnupiravir, they should be counseled regarding its decreased effectiveness compared to other treatment options and, if of childbearing potential, should be counseled in the use of effective contraceptives (see EUA for full details).

Pre-Exposure Prophylaxis

Evusheld (tixagevimab/cilgavimab) is available as pre-exposure prophylaxis in immunocompromised patients administered as two separate consecutive intramuscular (IM) injections of 300 mg of tixagevimab and 300 mg of cilgavimab. Evusheld is not approved as a treatment for COVID-19 and is not a replacement for vaccination.

Evusheld is authorized for pre-exposure prophylaxis (PrEP) in 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 documented history of severe adverse reaction to a COVID-19 vaccine or any of its components.

Locating Outpatient Therapeutics

The Health and Human Services' (HHS) COVID-19 Therapeutics Locator tool displays pharmacy locations and infusion centers that have received shipments of federally-procured Covid-19 therapeutic agents and have reported available treatment courses in the last 7 days. Prescribers should refer to this tool when writing prescriptions for outpatient COVID-19 treatments.

The US federal government recently announced a new Test to Treat initiative, and Test to Treat sites can both test for SARS-CoV-2 and dispense COVID-19 treatments. Current sites participating in the federal program can be found on the new HHS Test to Treat Locator, which went live on 3/30/2022.

Further Resources and Clinical Guidance

As the COVID-19 therapeutics landscape changes rapidly, we encourage all local health jurisdictions and medical providers to regularly refer to the following resources for updates:

- CDPH COVID-19 Therapeutics site: COVID-19 Treatments (ca.gov)
- NIH COVID-19 Treatment Guidelines: What's New | COVID-19 Treatment Guidelines (nih.gov)
- Health and Human Services ASPR: COVID-19 Therapeutics | HHS/ASPR