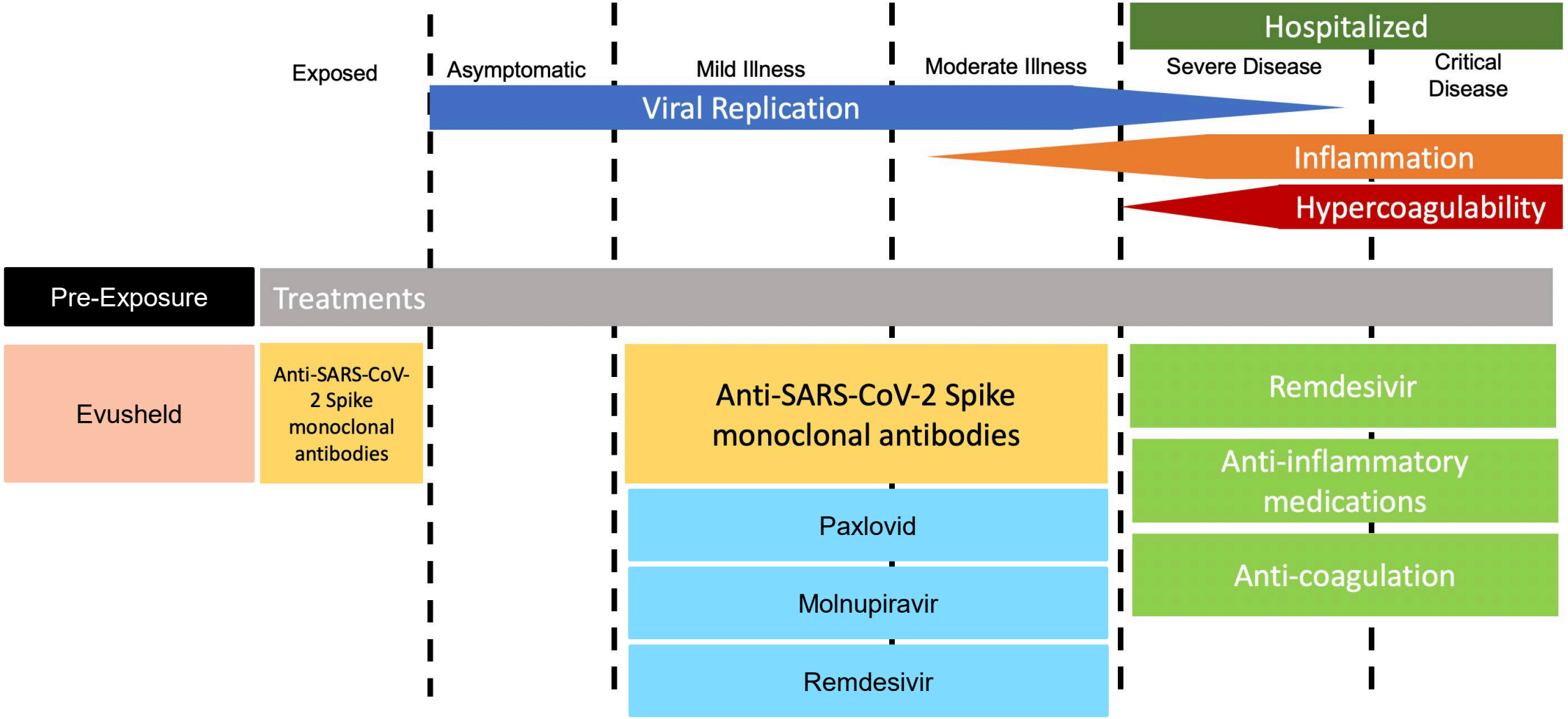
SARS-CoV-2 Outpatient Therapeutics

Updated: January 19, 2022

Illness Stages and Available Treatments



Currently Available Anti-SARS-COV-2 Monoclonal Antibodies: Treatment and PEP

Drug	Route of Administration	Treatment Effectiveness	Post-Exposure Prophylaxis Effectiveness	Activity Against Variants Currently Circulating
Bamlanivimab 700 mg plus etesevimab 1,400 mg	Intravenous	Compared to placebo, receipt of Bam/Ete was associated with a 4.8% absolute reduction and **70% relative reduction** in COVID-19-related hospitalizations or all-cause deaths.	In skilled nursing facility resident population incidence of mild or worse COVID-19 was **8.8% in the bamlanivimab arm** compared to **22.5% in the placebo arm** (OR 0.20; 95% CI, 0.08–0.49; P < 0.001)	Not effective against Omicron
Casirivimab 600 mg plus imdevimab 600 mg (REGEN COV)	Intravenous or subcutaneous infusion	Compared to placebo, receipt of REGEN-COV was associated with a 2.2% absolute reduction and **70% relative risk reduction** in COVID-19-related hospitalizations or all-cause deaths.	In a trial enrolling household contacts of a SARS-COV-2 positive case, there was a significant reduction in the risk of symptomatic SARS-CoV-2 infection when compared with placebo **81.4% risk reduction** (P < 0.001).	Not effective against Omicron
Sotrovimab 500 mg	Intravenous	Compared to placebo, receipt of SOT was associated with a 6% absolute reduction and **85% relative risk reduction** in all-cause hospitalizations or deaths.	Not authorized for use	Yes

*https://www.fda.gov/media/151719/download

https://www.covid19treatmentguidelines.nih.gov/tables/table-3a/, https://www.ncbi.nlm.nih.gov/pubmed/34081073
https://www.ncbi.nlm.nih.gov/pubmed/34347950
*https://www.fda.gov/media/151719/download

Currently Available Antiviral Outpatient Therapies: Treatment

Drug	Mechanism	Administration Route	Potential Use	Effectiveness
Molnupiravir	Ribonucleoside analog	Oral	Treatment of mild to moderately ill high-risk outpatients Trial results pending for post-exposure prophylaxis	**Treatment:** Molnupiravir reduced the risk of hospitalization or death from 9.7% in the placebo group (68/699) to 6.8% (48/709) in the molnupiravir group, for an absolute risk reduction of 3.0% (95% confidence interval [CI]: 0.1, 5.9; nominal p-value=0.0218) and a **relative risk reduction of 30%** (relative risk 0.70; 95% CI: 0.49, 0.99)
Paxlovid, co-administered with ritonavir	Protease inhibitor	Oral	Treatment of mild to moderately ill high-risk outpatients	**Treatment:** Analysis showed an **89% reduction in risk of COVID-19-related hospitalization or death** from any cause compared to placebo in patients treated within three days of symptom onset. 0.8% of patients who received paxlovid were hospitalized through Day 28 following randomization (3/389 hospitalized with no deaths), compared to 7.0% of patients who received placebo and were hospitalized or died (27/385 hospitalized with 7 subsequent deaths.
Remdesivir	Interferes with RNA-dependent polymerase	IV	Treatment of mild to moderately ill high-risk outpatients	**Treatment:** Among nonhospitalized patients who were at high risk for Covid-19 progression, a **3-day course** of remdesivir had an acceptable safety profile and resulted in an **87% lower risk of hospitalization or death than placebo**.

Molnupiravir: https://www.merck.com/news/merck-and-ridgeback-biotherapeutics-provide-update-on-results-from-move-out-study-of-molnupiravir-an-investigational-oral-antiviral-medicine-in-at-risk-adults-with-mild-to-moderate-covid-19/; Paxlovid: https://www.pfizer.com/news/press-release/press-release-detail/pfizers-novel-covid-19-oral-antiviral-treatment-candidate

Anti-SARS-COV-2 Monoclonal Antibody for PrEP

Drug	Mechanism	Administration Route	Use	Effectiveness
Evusheld (Tixagevimab /cilgavimab)	Anti-SARS-COV-2 monoclonal antibody	Intramuscular	Pre-exposure prophylaxis in high-risk individuals not expected to respond to vaccines; duration of action = 6 months	**Pre-exposure prophylaxis:** Reduced the risk of developing symptomatic COVID-19 by **77%** (95% confidence interval (CI): 46, 90) compared to placebo. **Post-exposure prophylaxis:** Failed to meet the primary endpoint of post-exposure prevention of symptomatic COVID-19 with AZD7442 compared to placebo. **Treatment:** Reduced the risk of developing severe COVID-19 or death (from any cause) by **50%** compared to placebo in outpatients who had been symptomatic for seven days or less.

https://www.astrazeneca.com/media-centre/press-releases/2021/update-on-azd7442-storm-chaser-trial.html, https://www.astrazeneca.com/media-centre/press-releases/2021/azd7442-prophylaxis-trial-met-primary-endpoint.html, https://www.astrazeneca.com/media-centre/press-releases/2021/azd7442-phiii-trial-positive-in-covid-outpatients.html; https://www.fda.gov/media/154701/download

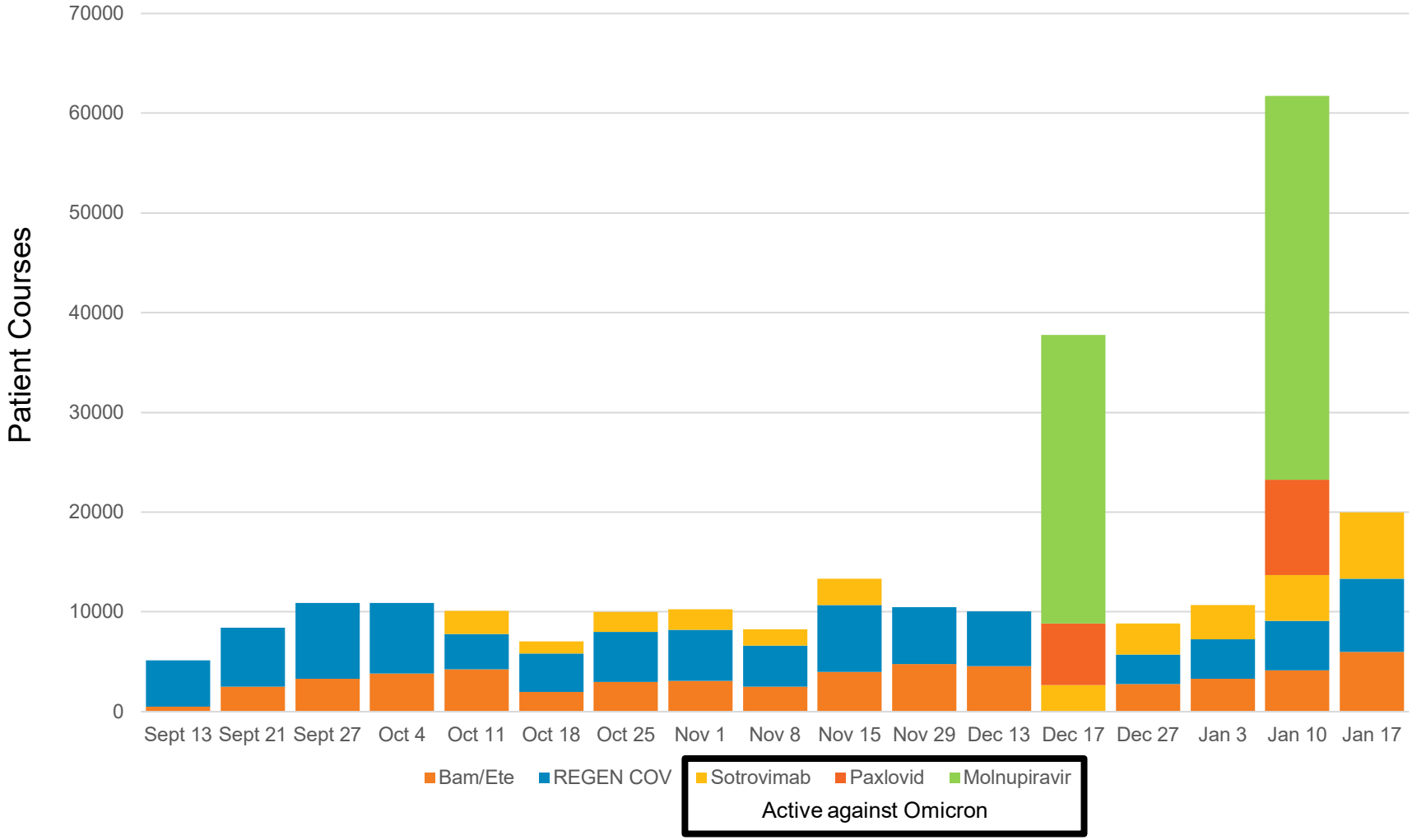
Prioritization of Treatment Options for Omicron

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):

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 who live in areas with a high prevalence of the Omicron VOC
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
4. **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 **ONLY** when none of the above options can be used

https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-therapies-for-high-risk-nonhospitalized-patients/

Anti-SARS-COV-2 Monoclonal Antibody Allocation for Treatment: California



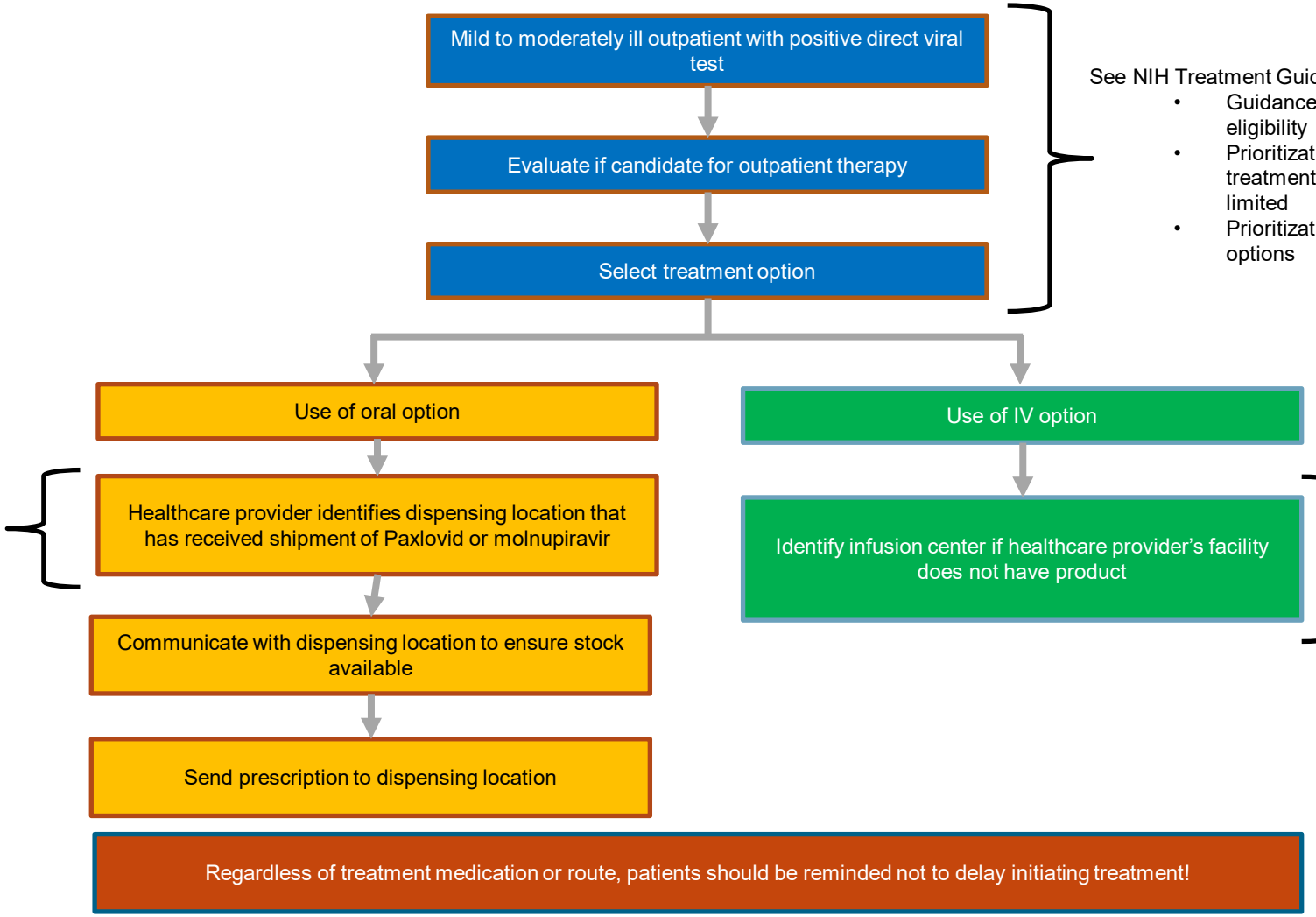
- Extremely limited supply of the most effective options against Omicron (Paxlovid and sotrovimab)
- Allocation of bam/ete and REGEN-COV continue, but these drugs are not effective against Omicron
- However, they may be used in areas where Delta prevalence is estimated to be >20% AND if no other treatment options are available they may be offered to patients as an alternative option with the caveat that they may not work

Distribution

Product and Route	Distribution Point	Allocation Scheme
Sotrovimab IV anti-SARS-CoV-2 monoclonal antibody	Facilities able to provide infusion services and monitor patients; number of courses for each site determined by Medical Health Operational Area Coordinators at county level	Allocated to counties Based on new cases (7 day average) and new COVID-19 hospitalizations (7 day average). Weighted 75% to cases; 25% to hospitalizations.
Paxlovid Oral protease inhibitor	Allocated to a limited number of pharmacies that can dispense in each county, final list determined by local jurisdictions	Allocated to counties Based on new COVID-19 cases (7 day average) and Health Places Index (HPI); with 50% weighted to cases and 50% weighted to HPI. Within the 50% allocated by HPI, 40% to Q1 (most disadvantaged); 30% to Q2; 20% to Q3; 10% to Q4.
Molnupiravir Oral nucleoside analogue		
Evusheld IM anti-SARS-CoV-2 monoclonal antibody	Distributed to mutual aid regions (6 regions), with instructions to send courses to transplant and cancer centers	Allocated to mutual aid regions Within each region, allocation based on share of the population in different equity quartiles; 40% of state allocation to Q1; 30% to Q2; 20% to Q3; 10% to Q4.

For the most up-to-date distribution numbers by cycle, see:
https://www.phe.gov/emergency/events/COVID19/therapeutics/distribution/Pages/data-tables.aspx

Operationalizing



See NIH Treatment Guidelines for:

- Guidance regarding patient eligibility
- Prioritization of patients for treatment when supplies are limited
- Prioritization of therapeutic options

To find dispensing locations, see:

- HHS Therapeutics Locator with map of locations with quantities in stock (based on daily reporting, not a guarantee of availability)

- Use HHS Treatment Locator for infusion centers to find locations

NIH Treatment Guidelines: https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-therapies-for-high-risk-nonhospitalized-patients/; HHS Therapeutics Locators (orals and Evusheld): https://healthdata.gov/Health/COVID-19-Public-Therapeutic-Locator/rxn6-qnx8/data; Infusion Centers (sotrovimab): https://protect-public.hhs.gov/pages/therapeutics-distribution