Thank You for Joining Us!

The presentation will begin shortly. All participants are muted and video cameras are disabled for the duration of the presentation. If you would like to ask a question, please use the Q&A feature.

- All attendees are muted upon arrival. Please stay on mute throughout the meeting.
- Video cameras will be disabled except for speakers and panelists.
- Use the Q&A feature to ask questions. Type out your message and hit "Enter" to send.
- Ensure your surroundings are quiet. If not, consider headphones with a microphone.
Review of COVID Therapeutics

Regina Chinsio-Kwong, DO OCHCA Health Officer
May 25, 2022
Disclosure

I personally do not have a financial relationship or interest (currently or within the past 24 months) with any proprietary entity producing health care goods or services consumed by or used on patients related to the content of this CME.

I do however have an immediate family member with a few shares of Merck & Co.

I do not intend to discuss an unapproved/investigative use of a commercial product/device.
Special Thanks

- CDPH staff
- American Academy of Pediatrics- OC Chapter
- Orange County Medical Association
- California Academy of Family Physician
- Riverside County and Yuba/Sutter County Health Officers
Learning Objectives

- Current County COVID status
- COVID therapeutics (focus on outpatient therapeutic options)
  - Evusheld
  - Oral Antivirals
- Effective outpatient treatment options are more widely available for those with mild to moderate COVID-19 and should be offered to high-risk patients if they meet criteria
Current State

Linear Adjusted Case Rate per 100K: 13.7
Unadjusted Daily Case rate per 100K: 18.3

Case Positivity: 5.5% (2.4% in HPI 1)
# hospitalized: 131
# in ICU: 20

Cumulative # Deaths to date: 7030
It’s time to layer up on protection - regardless of vaccination status when in crowded areas/indoors!
Omicron

- More transmissible than prior variants-
  - Variants today have increased fitness compared to earlier in the pandemic!

- Still can cause severe illness - but more commonly in unvaccinated, immunocompromised, frail individuals

- Vaccines offer less protection to Omicron vs previous variants earlier in pandemic due to some immune escape

- Susceptibility to monoclonal antibodies appears to be lower for Omicron compared to Delta

- Bebtelovimab is presumed effective against Omicron Variants

- Evusheld effective is presumed effective against Omicron Variants

https://www.science.org/doi/10.1126/science.abm1208
COVID Prevention - Vaccines/Therapeutics

**Vaccines**

- **Pfizer (mRNA) – 5+**
  - EUA for 5+ Primary series and for first Booster 5+
  - EUA 2nd booster: Moderately-Severely immunocompromised age 12-49 y/o or age 50+ Should get a 2nd booster
  - FDA Approved for 16+ Primary Series

- **Moderna (mRNA) 18+**
  - EUA for 18+ Primary Series and Booster
  - EUA 2nd booster: Moderately-Severely immunocompromised age 18-49 y/o or age 50+ Should get a 2nd booster

- **J&J – 18+**
  - EUA for 18+ Primary Series
  - EUA booster: anyone 18+ who completed 1st dose advised to get booster with mRNA
  - EUA Moderately-Severely Immunocompromised: advised to get 2nd dose with mRNA, booster with mRNA

**Pre-Exposure Prophylaxis (PrEP)**

- **Tixagevimab + Cilgavimab (Evusheld)- Long-Acting Monoclonal Antibody (IM injection)**
  - Age 12+ and > 40kg
COVID-19 Vaccine Timing

COVID-19 Vaccine Timing by Age

Routine Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccine</th>
<th>Primary Doses</th>
<th>1st Booster Dose</th>
<th>2nd Booster Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-11</td>
<td>Pfizer-Pediatric (5-11)</td>
<td>1st Dose 3 weeks</td>
<td>2nd Dose 25 months</td>
<td>Booster</td>
</tr>
<tr>
<td>12+</td>
<td>Pfizer/Comirnaty (12+)</td>
<td>1st Dose 3 weeks (8 weeks for some people)</td>
<td>2nd Dose 25 months</td>
<td>1st Booster Ages 12-17: Pfizer</td>
</tr>
<tr>
<td>18+</td>
<td>Moderna/Spikevax</td>
<td>1st Dose 4 weeks (8 weeks for some people)</td>
<td>2nd Dose 25 months</td>
<td>18+ Moderna/Pfizer</td>
</tr>
</tbody>
</table>
| 18+| Johnson & Johnson (Pfizer/Moderna preferred) | 1st Dose >2 months | 2nd Dose >2 months | 2nd Booster |}

Note Timing Intervals Differ!

Schedule if Moderately or Severely Immunocompromised

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccine</th>
<th>Primary Doses</th>
<th>1st Booster Dose</th>
<th>2nd Booster Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-11</td>
<td>Pfizer-Pediatric (5-11)</td>
<td>1st Dose 3 weeks</td>
<td>2nd Dose &gt;4 weeks</td>
<td>3rd Dose &gt;3 months</td>
</tr>
<tr>
<td>12+</td>
<td>Pfizer/Comirnaty (12+)</td>
<td>1st Dose 3 weeks</td>
<td>2nd Dose &gt;4 weeks</td>
<td>3rd Dose &gt;3 months</td>
</tr>
<tr>
<td>18+</td>
<td>Moderna/Spikevax</td>
<td>1st Dose 4 weeks</td>
<td>2nd Dose &gt;4 weeks</td>
<td>3rd Dose &gt;3 months</td>
</tr>
<tr>
<td>18+</td>
<td>Johnson &amp; Johnson (Pfizer/Moderna preferred)</td>
<td>1st Dose 4 weeks</td>
<td>2nd Dose of Moderna or Pfizer</td>
<td>&gt;2 months</td>
</tr>
</tbody>
</table>

*Although use of mRNA COVID-19 vaccines is preferred, the Janssen vaccine may be offered in some situations.*

View Interim Clinical Considerations for Use of COVID-19 Vaccines for details. Schedule is subject to change.
<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>AstraZeneca</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDA EUA Date</td>
<td>2/24/22</td>
</tr>
<tr>
<td>Drug Type/Class/Mode of Action</td>
<td>Monoclonal Antibody (mAb) mAb against conserved epitope of spike protein; blocks viral entry</td>
</tr>
<tr>
<td>Reported efficacy data</td>
<td>77% reduction in developing symptomatic COVID-19</td>
</tr>
<tr>
<td>Indication</td>
<td>Pre-Exposure Prophylaxis for those with moderate to severe immunocompromise or for those who any EUA or approved vaccine is not recommended. Individual should not currently be infected or have recent exposure</td>
</tr>
<tr>
<td>Age/weight requirement</td>
<td>12+ (minimum 40 kg or 88 lb)</td>
</tr>
<tr>
<td>Rx window</td>
<td>Pre-Exposure Period for eligible individual</td>
</tr>
<tr>
<td>Duration of therapy</td>
<td>1 dose</td>
</tr>
<tr>
<td>Testing Requirements</td>
<td>none</td>
</tr>
<tr>
<td>Administration details</td>
<td>Administrer the IM injections at different injections sites (preferably one in each gluteal muscle, one after the other)</td>
</tr>
<tr>
<td>Adverse Events (if from clinical trials, incidence &gt; 1%)</td>
<td>Injection site reactions 1%: one case of anaphylaxis in clinical trial</td>
</tr>
<tr>
<td>Heart disease adverse events: 0.6% vs 2% in Evusheld and placebo groups respectively</td>
<td></td>
</tr>
<tr>
<td>How supplied</td>
<td>One carton has Two vials - 150mg/1.5 ml Tixagevimab - 150mg/1.5 ml Cilgavimab</td>
</tr>
<tr>
<td>Special Populations</td>
<td>Insufficient data in pregnancy or breastfeeding.</td>
</tr>
<tr>
<td>Cost</td>
<td>$200 administration fee</td>
</tr>
</tbody>
</table>
How to get access of Evusheld for eligible patients

Kaiser
- Fax- monitored M-F- once received, nurse will contact patient to schedule appt

UCI
- Chao Cancer Center, Orange
  - Schedule with cancer provider

Providence
- St. Joseph-
  - Center for Cancer Prevention and Treatment Infusion Center
- Mission Hospital
  - Leonard Cancer Center
  - Mission Heritage Antibiotic Infusion Center
  - By referral only to established criteria

CHOC
- Provider should email to request

Hoag
- By referral from Hoag providers

City of Hope
- By referral from City of Hope Providers
Why Treat Mild-Moderate COVID-19?
- Reduce risk of severe illness- hospitalization/death

1) Verify SARS-CoV-2 infection (antigen/PCR)
2) Verify days from initial onset of symptoms
3) Is the patient at high risk for developing severe illness?
4) Age

5) Cautions-
   1) If considering Paxlovid-
      Kidney: Does patient have renal insufficiency (eGFR < 30)?
      Liver – Severe hepatic impairment- Child-Pugh C?
      Medication Interactions?
   2) If considering Molnupiravir
      Is the patient potentially pregnant?
What is Mild to Moderate COVID-19 Illness?

<table>
<thead>
<tr>
<th>Mild Illness</th>
<th>Moderate Illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absence of Viral Pneumonia &amp; hypoxemia</td>
<td>+ Viral Pneumonia but without hypoxemia</td>
</tr>
<tr>
<td>Individuals who have any of the various signs and symptoms of COVID-19 (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>

https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/
Who is at High Risk for Severe COVID outcomes?

Age is the strongest risk factor for severe COVID-19 outcomes, people age 65+ accounted for 81% of US COVID-19 related deaths in 2020

- Cancer
- Chronic kidney disease
- Chronic lung disease
  - Interstitial lung disease, Pulmonary embolism, Pulmonary HTN, Bronchiectasis, COPD
  - Moderate-Severe Asthma
- Chronic liver disease
  - Cirrhosis, non-alcoholic fatty liver disease, alcoholic liver disease, autoimmune hepatitis
- Cystic fibrosis
- Primary immunodeficiencies
- Solid Organ or hematopoietic cell transplantation
- Tuberculosis
- HIV
- Use of corticosteroids or other immunosuppressive medications
- Diabetes- type 1 or 2
- Heart conditions (HF, CAD, Cardiomyopathies, congenital heart disease)
- Cerebrovascular disease
- Neurologic condition limited to dementia
- Disabilities (ADHD, Cerebral palsy, congenital malformations (birth defects), intellectual and developmental disabilities, learning disabilities, spinal cord injury
- Mental health disorders (mood disorder including depression, schizophrenia spectrum disorder)
- Sickle Cell Anemia/Thalassemia
- Pregnancy, recent pregnancy
- Smoking- Current/former
- Obesity > 30
- Physical Inactivity

**race/ethnicity, and socioeconomic or behavioral factors

2. **Suggestive higher risk** for severe COVID-19 outcomes is defined as an underlying medical condition or risk factor that neither has a published meta-analysis or systematic review nor completed the CDC systematic review process. The evidence is supported by mostly cohort, case-control, or cross-sectional studies. (Systematic reviews are available for some conditions for children with underlying conditions.)
   - Children with certain underlying conditions
   - Overweight (BMI ≥ 25 kg/m², but <30 kg/m²)
   - Sickle cell disease
   - Substance use disorders
   - Thalassemia

3. **Mixed evidence** is defined as an underlying medical condition or risk factor that has a published meta-analysis or systematic review or completing the CDC systematic review process. The meta-analysis or systematic review is inconclusive, either because the aggregated data on the association between an underlying condition and severe COVID-19 outcomes are inconsistent in direction or there are insufficient data (or limited) on the association between an underlying conditions and severe COVID-19 outcomes.
   - Alpha 1 antitrypsin deficiency
   - Asthma
   - Bronchopulmonary dysplasia
   - Hepatitis B
   - Hepatitis C
   - Hypertension*

Footnote: * indicates underlying conditions for which there is evidence for pregnant and non-pregnant people

Links for identifying Higher Risk individuals

Sites describing those at higher risk


CDC Patient handout:
Treatment in outpatient setting for Mild-Moderate COVID-19 illness

NIH guidance

- Clinical Management Summary (4/8/22)
COVID-19 OUTPATIENT TREATMENT GUIDELINES ROADMAP

Last Updated: April 5, 2022

The resource is intended to serve as a guide on available outpatient COVID-19 treatment options, with links to FDA Emergency Use Authorization information and guideline recommendations from national guideline-developing organizations, where available. It is not intended to endorse or otherwise promote a specific clinical recommendation or course of action. Additionally, it does not include other forms of guidance that may be available for specific subsets of populations. Finally, the guidelines referenced herein may not consider local allocation and availability of scarce resources. Additional information on where to access these therapies can be found at the National Inpatient Nurse Association and NPH.12

Risk factors for severe COVID-1911

- Age 65 years and older
- BMI of more than 25 kg/m²
- Pregnancy
- Chronic kidney disease
- Diabetes mellitus
- Immunosuppressing medications
- Cardiovascular disease or hypertension
- Chronic lung disease
- Sickle cell disease
- Neurodevelopmental disorders or conditions that can impair medical complexity
- Medical technological dependence, e.g., tracheostomy

When giving products under Emergency Use Authorization, providers must:

2. Inform patient of alternatives to treatment.
3. Inform patient that this is an unapproved drug.

When giving products under Emergency Use Authorization, providers must:

2. Inform patient of alternatives to treatment.
3. Inform patient that this is an unapproved drug.

Options depicted in gray should be considered AFTER other options, if other options are unavailable, or only in certain clinical situations.

Does your patient have COVID?

Positive results of direct SARS-CoV-2 testing

YES

NO

Has vaccine been given?

YES

NO

Is your patient hospitalized for COVID-19 or requiring increased O₂ for COVID-19?

YES

NO

Does your patient have any symptoms?

YES

NO

Has vaccine been given?

YES

NO

How many days since symptom onset?

> 8 DAYS

Outpatient treatment options not authorized or recommended. Supportive care only.

Does your patient have COVID?

Positive results of direct SARS-CoV-2 testing

YES

NO

Is your patient hospitalized for COVID-19 or requiring increased O₂ for COVID-19?

YES

NO

Does your patient have any symptoms?

YES

NO

Has vaccine been given?

YES

NO

How many days since symptom onset?

> 8 DAYS

Outpatient treatment options not authorized or recommended. Supportive care only.

Does your patient have COVID?

Positive results of direct SARS-CoV-2 testing

YES

NO

Is your patient hospitalized for COVID-19 or requiring increased O₂ for COVID-19?

YES

NO

Does your patient have any symptoms?

YES

NO

Has vaccine been given?

YES

NO

How many days since symptom onset?

> 8 DAYS

Outpatient treatment options not authorized or recommended. Supportive care only.

Does your patient have COVID?

Positive results of direct SARS-CoV-2 testing

YES

NO

Is your patient hospitalized for COVID-19 or requiring increased O₂ for COVID-19?

YES

NO

Does your patient have any symptoms?

YES

NO

Has vaccine been given?

YES

NO

How many days since symptom onset?

> 8 DAYS

Outpatient treatment options not authorized or recommended. Supportive care only.

Does your patient have COVID?

Positive results of direct SARS-CoV-2 testing

YES

NO

Is your patient hospitalized for COVID-19 or requiring increased O₂ for COVID-19?

YES

NO

Does your patient have any symptoms?

YES

NO

Has vaccine been given?

YES

NO

How many days since symptom onset?

> 8 DAYS

Outpatient treatment options not authorized or recommended. Supportive care only.

Does your patient have COVID?

Positive results of direct SARS-CoV-2 testing

YES

NO

Is your patient hospitalized for COVID-19 or requiring increased O₂ for COVID-19?

YES

NO

Does your patient have any symptoms?

YES

NO

Has vaccine been given?

YES

NO

How many days since symptom onset?

> 8 DAYS

Outpatient treatment options not authorized or recommended. Supportive care only.

Does your patient have COVID?

Positive results of direct SARS-CoV-2 testing

YES

NO

Is your patient hospitalized for COVID-19 or requiring increased O₂ for COVID-19?

YES

NO

Does your patient have any symptoms?

YES

NO

Has vaccine been given?

YES

NO

How many days since symptom onset?

> 8 DAYS

Outpatient treatment options not authorized or recommended. Supportive care only.
lab + COVID & symptomatic, not hospitalized, not requiring O2 for COVID

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Time From Symptom Onset*</th>
</tr>
</thead>
</table>
| Ritonavir-Boosted Nirmatrelvir (Paxlovid) | eGFR ≥50 mL/min:  
- Nirmatrelvir 300 mg with RTV 100 mg PO twice daily for 5 days  
- eGFR ≥30 to <50 mL/min:  
- Nirmatrelvir 150 mg with RTV 100 mg PO twice daily for 5 days | ≤5 days |
| Ritonavir-Boosted Nirmatrelvir (Paxlovid), continued | eGFR <30 mL/min:  
- Not recommended  
Severe Hepatic Impairment (Child-Pugh Class C):  
- Not recommended | ≤5 days |
| Remdesivir | RDV 200 mg IV on Day 1, followed by RDV 100 mg IV once daily on Days 2 and 3.  
Each infusion should be administered over 30–120 minutes.  
Patients should be observed for ≥1 hour after infusion as clinically appropriate. | ≤7 days |
| Bebtelovimab | BEB 175 mg as a single IV injection, administered over ≥30 seconds.  
Patients should be observed for ≥1 hour after injection. | ≤7 days |
| Molnupiravir | Molnupiravir 800 mg PO twice daily for 5 days | ≤5 days |

* Per EUA criteria or clinical trial entry criteria.

An eGFR <30 mL/min at screening or <90 days before screening was considered an exclusion criterion in the outpatient RDV study PINETREE, but only if a participant’s weight was <48 kg. See the Remdesivir section for a discussion of RDV use in patients with renal impairment.

If RDV is administered to patients who have a new or increasing need for supplemental oxygen but who are discharged from the ED because hospital resources are limited and inpatient admission is not possible, the total duration of therapy is ≤5 days.

**Key:** BEB = bebtelovimab; ED = emergency department; eGFR = estimated glomerular filtration rate; EUA = Emergency Use Authorization; IV = intravenous; PO = orally; RDV = remdesivir; RTV = ritonavir.
<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Nirmatrelvir/ritonavir (Paxlovid) Oral</th>
<th>Remdesivir (Veklury) IV</th>
<th>Bebtelovimab IV</th>
<th>Molnupiravir (Lagevrio) Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>Pfizer</td>
<td>Gilead</td>
<td>Eli Lilly and Company</td>
<td>Merck</td>
</tr>
<tr>
<td>FDA EUA Date</td>
<td>EUA 12/22/21</td>
<td>4/25/22: No longer on EUA - Fully Authorized for Pediatrics 28 days and older, and at least 3 kg (7lbs)</td>
<td>EUA 3/25/22</td>
<td>EUA 12/23/21</td>
</tr>
<tr>
<td>Drug Type/Class/MOA</td>
<td>Antiviral Viral protease inhibitor (Nirmatrelvir) and HIV protease inhibitor &amp; CYP3A inhibitor (ritonavir). Halts viral replication</td>
<td>Antiviral Nucleoside analog (RNA) polymerase inhibitor that halts viral replication</td>
<td>Monoclonal Antibody (mAb) mAb against spike, blocks viral attachment to host cells</td>
<td>Antiviral Nucleoside Analog that inhibits viral replication by viral mutagenesis</td>
</tr>
<tr>
<td>Reported efficacy data</td>
<td>88% reduction in hospitalizations/deaths</td>
<td>87% reduction in hospitalizations/deaths</td>
<td>Symptomatic improvement and Day 5 reduction in viral load vs placebo</td>
<td>30% reduction in hospitalization/deaths</td>
</tr>
<tr>
<td>Indication</td>
<td>Treatment mild-moderate COVID for at risk patients</td>
<td>Treatment of Hospitalized pt with COVID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age/weight requirement</td>
<td>12+ (minimum 40 kg or 88 lb)</td>
<td>&gt; 28 days old (min 3.5 kg, 7lbs), &gt; 12 years of age (minimum 40 kg, 88lbs)</td>
<td>12+ (minimum 40 kg or 88 lb)</td>
<td>18+ (Adults ONLY)</td>
</tr>
<tr>
<td>Rx window</td>
<td>Within 5 days symptom onset</td>
<td>Within 7 days symptom onset</td>
<td>Within 7 days symptom onset</td>
<td>Within 5 days symptom onset</td>
</tr>
<tr>
<td>Duration of therapy</td>
<td>5 days</td>
<td>3 days - not hospitalized, mild-moderate COVID-19. 5 days - hospitalized, not on mech vent/ECMO (extend to 10 days if not improving)</td>
<td>1 Time dose</td>
<td>5 days</td>
</tr>
<tr>
<td>Testing Requirements And lab considerations</td>
<td>Positive direct SARS-CoV 2 viral test</td>
<td>Positive direct SARS-CoV 2 viral test</td>
<td>Positive direct SARS-CoV 2 viral test</td>
<td>Positive direct SARS-CoV 2 viral test</td>
</tr>
<tr>
<td>History requirements</td>
<td>Not specified</td>
<td>Baseline renal function required under EUA for pediatric patients</td>
<td>As clinically appropriate- perform renal/hepatic lab testing, assess PTT</td>
<td>Not specified</td>
</tr>
<tr>
<td>Family planning</td>
<td>Not specified Ritonavir may reduce efficacy of combined hormonal contraceptives. Pt should use effective alternative contraceptive method or additional barrier method of contraception.</td>
<td>Not specified</td>
<td>Not specified</td>
<td>Assess pregnancy status- not recommended during pregnancy, if childbearing potential, advise of potential risk to fetus, use reliable contraception correctly and consistently for duration of treatment and 4 days after last dose. Males of reproductive potential should use reliable contraception correctly/consistently x 3 months after last dose.</td>
</tr>
</tbody>
</table>

Adapted from https://aspr.hhs.gov/COVID-19/Therapeutics/Documents/side-by-side-overview.pdf
<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Dose</th>
<th>Administration details</th>
<th>How supplied</th>
<th>Dosing for Special Population: Pediatrics</th>
<th>Dosing for Special Population: Renal</th>
<th>Dosing for Special Population: Hepatic</th>
<th>Adverse Events (if from clinical trials, incidence ≥ 1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nirmatrelvir/ritonavir (Paxlovid) Oral</td>
<td>300 mg nirmatrelvir with 100 mg ritonavir. Take all 3 tablets PO BID with or without food. (although eating with fatty meal enhances absorption)</td>
<td></td>
<td>5 daily dose blister cards *renal impairment dose packs available</td>
<td></td>
<td></td>
<td></td>
<td>Dysguesia (altered taste sensation) 6%, diarrhea 3%, hypertension 1%, myalgia 1%</td>
</tr>
<tr>
<td>Remdesivir (Veklury) IV</td>
<td>Adults/Peds 12+ at least 40 Kg: Single loading dose 200mg Day 1 IV, then maintenance daily dose 100mg IV</td>
<td>Reconstitute powder by adding 19 ml sterile water. See recommended dilution instructions in package insert. Monitoring recommended 1 hour after infusion for hypersensitivity reaction or infusion reaction</td>
<td>Single Dose Vial 100 mg Remdesivir as lyophilized powder in single dose vial (no reconstituted) 100mg/20ml (5mg/ml) after reconstitution.</td>
<td>Dosing for Special Population: Pediatrics: If eligible, no dosage adjustment</td>
<td>Dosing for Special Population: Renal: No dosage adjustment</td>
<td>Dosing for Special Population: Hepatic: No dosage adjustment for mild hepatic impairment</td>
<td>Nausea 10.8%, Headache 5.7%, Cough 3.6%, diarrhea 3.9%, dyspnea 2.5%, fatigue 3.6%, ageusia 2.9%, anosmia 3.2%, dizziness 1.8%, chills 2.2% Lab abnormalities: (10.8%)</td>
</tr>
<tr>
<td>Bebtelovimab IV</td>
<td>Severe renal impairment eGFR &lt; 30: Not recommended 28+ day old full term neonate with serum creatinine greater than or equal to 1mg/dL. Not recommended</td>
<td>Administer entire contents via IV injection over at least 30 seconds. See recommended storage/handling instructions in package insert. Monitoring recommended 1 hour after infusion for hypersensitivity reaction or infusion reaction</td>
<td>Single Dose Vial</td>
<td></td>
<td></td>
<td></td>
<td>Infusion-related: 0.3%, pruritis 0.3%, rash 0.8% Nausea 0.8%, vomiting 0.7%</td>
</tr>
<tr>
<td>Molnupiravir (Lagevrio) Oral</td>
<td>800 mg PO q 12 hours (4 capsules per dose)</td>
<td></td>
<td>Bottle (40 capsules)</td>
<td>Dosing for Special Population: Pediatrics: Not eligible, as it may affect bone and cartilage growth.</td>
<td></td>
<td></td>
<td>Diarrhea 2%, nausea 1%, dizziness 1% Lab abnormality: ALT, AST, creatinine, lipase, hemoglobin, platelets, leukocytes &lt; 2% Post auth experience: Hypersensitivity: anaphylaxis, angioedema Skin disorder: Erythema, rash, urticaria</td>
</tr>
<tr>
<td>Generic Name</td>
<td>Nirmatrelvir/ritonavir (Paxlovid) Oral</td>
<td>Remdesivir (Veklury) IV</td>
<td>Bebtelovimab IV</td>
<td>Molnupiravir (Lagevrio) Oral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------------------</td>
<td>--------------------------------------</td>
<td>------------------------</td>
<td>-----------------</td>
<td>-----------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potential Drug-Drug Interactions</td>
<td>Moderate/High- see prescribing information</td>
<td>Low- See prescribing information</td>
<td>unlikely</td>
<td>None identified</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal Dose Adjustment</td>
<td>For eGFR 30-60, lower dose advised, not recommended for those with eGFR &lt; 30 ml/min</td>
<td>Not recommended for those with eGFR &lt; 30 ml/min</td>
<td>none</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatic Dose Adjustment</td>
<td>Avoid in severe hepatic impairment (Child-Pugh Class C)</td>
<td>None- but should monitor LFT before and during treatment</td>
<td>none</td>
<td>none</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contraindications</td>
<td>Hypersensitivity to ingredients CYP3A4 drug-drug interactions</td>
<td>Hypersensitivity to Veklury or any of its components</td>
<td>none listed</td>
<td>None listed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warnings/drug interactions</td>
<td>Beware of drug interactions, hepatotoxicity, HIV-1 drug resistance in patients with HIV-1 infection</td>
<td>Possible hypersensitivity/infusion related reaction.</td>
<td>Possible hypersensitivity/infusion related reaction.</td>
<td>Embryo-fetal toxicity, bone and cartilage toxicity- not recommended for patients &lt; 18 because of potential effects on bone/cartilage growth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Many drug interactions (statins, blood thinners, OCP, seizure medications, St. John’s Wort) should use drug interaction checker tool</td>
<td></td>
<td>Clinical worsening after SARS-CoV-2 administration</td>
<td>Not recommended for use during pregnancy. No drug interactions identified to date</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hypersensitivity reactions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Special Populations</td>
<td>No human data on use in pregnancy or breastfeeding</td>
<td>Insufficient human data on use during pregnancy or breastfeeding</td>
<td>Insufficient human data on use during pregnancy or breastfeeding</td>
<td>Not recommended in pregnancy. Not recommended if breastfeeding (has pregnancy surveillance program)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cost</td>
<td>$530 per course</td>
<td>$390-520 per dose, or $2,340-3,120 for 5 day tx (hospital)</td>
<td>$ 1,250 per dose</td>
<td>$712 per course</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generic Name</td>
<td>FDA</td>
<td>Activity against Omicron</td>
<td>Product Website</td>
<td>FDA Factsheets for HCP</td>
<td>FDA Factsheets for patients, parents, caregivers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------------------------</td>
<td>----------------------------------</td>
<td>----------------------------------------------------</td>
<td>----------------------------------------------</td>
<td>------------------------------------------------</td>
<td>--------------------------------------------------</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adapted from ASPR HHS Side by Side Overview of Therapeutics Authorized or Approved for the Prevention of COVID-19 Infection or Treatment of Mild-Moderate COVID-19: [Side-by-Side Overview of Outpatient Therapies Authorized for Treatment of Mild-Moderate COVID-19](https://hhs.gov)


Study showing maintained in vitro potency Molnupiravir and Remdesivir against Omicron Variant: [https://www.biorxiv.org/content/10.1101/2022.01.17.476685v1](https://www.biorxiv.org/content/10.1101/2022.01.17.476685v1)


[https://www.hrsa.gov/CovidUninsuredClaim](https://www.hrsa.gov/CovidUninsuredClaim)
As a healthcare provider, you should:

- Inform patients that Paxlovid™ may interact with some drugs and is contraindicated for use with some drugs
- Obtain a complete medication list from your patient (including nonprescription drugs and herbals)
- Check for clinically significant drug interactions:
  - Section 7.3 of the EUA Fact Sheet: [https://www.fda.gov/media/155050/download](https://www.fda.gov/media/155050/download)

- Based on the drug interactions, decide if:
  - Paxlovid™ use is appropriate versus an alternative authorized treatment
  - If appropriate, whether your patient should hold, change, or dose-reduce other medications while taking Paxlovid™, or if additional monitoring may be needed
Do Not Give Paxlovid.
Prescribe/refer to other treatments based on local availability in this order:
1) Remesivir 2) monoclonal antibody tx 3) molnupiravir

Ok to Prescribe Paxlovid
Hold medications on this table while on paxlovid if clinically appropriate. Consult Liverpool website on when to restart concomitant medication(s)

Ok to Prescribe Paxlovid
Consider adjusting dose or if cannot be adjusted, withhold medication listed on this table while patient is on Paxlovid. Consult Liverpool website.

---

Table: Alternative COVID-19 Therapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Alternative Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>Flecainide</td>
</tr>
<tr>
<td>Amiloride</td>
<td>Hydrochlorothiazide</td>
</tr>
<tr>
<td>Benzquinamide</td>
<td>Lumaractone</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Lumaractone/xavacort</td>
</tr>
<tr>
<td>Chlorpropamide</td>
<td>Lumaractone</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Lumaractone</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>Meperidine (pethidine)</td>
</tr>
<tr>
<td>Dofetilide</td>
<td>Midafoxol (oral)</td>
</tr>
<tr>
<td>Dronedarone</td>
<td>Phenoxyloplast</td>
</tr>
<tr>
<td>Enalapril</td>
<td>Phenylbutazone</td>
</tr>
<tr>
<td>Eplerenone</td>
<td>Pimozide</td>
</tr>
<tr>
<td>Ergot derivatives</td>
<td>Pimodone</td>
</tr>
</tbody>
</table>

---

Table: Temporarily Withhold Concomitant Medication, If Clinically Appropriate

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

---

Table: Adjust Concomitant Medication Dose and Monitor for Adverse Effects

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.

---

6 Reduced effectiveness of clopidogrel is likely. Do not coadminister clopidogrel in patients who are at a very high risk of thrombosis (e.g., those who are within 6 weeks of coronary stenting); consider prescribing an alternative antiplatelet (i.e., prasugrel) or an alternative COVID-19 therapy. For other indications, it may be acceptable to continue clopidogrel if the benefit of ritonavir-boosted nirmatrelvir treatment outweighs the risk of reduced clopidogrel effectiveness.

8 Additional resources include the EUA fact sheet for ritonavir-boosted nirmatrelvir and the FDA prescribing information for the concomitant medication. These may be consulted for medications that are not found on the Liverpool COVID-19 Drug Interactions website.
Paxlovid and determining Drug-Drug Interactions

University of Liverpool

Prescribing Resources:
https://www.covid19-druginteractions.org/prescribing_resources
Paxlovid™ Summary

• Paxlovid™ was authorized on 12/22/21 for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older and ≥40 kg) who are at high risk for progression to severe COVID-19*.

• Paxlovid™ reduced COVID-19 related hospitalization and death by 88% when given within 5 days of symptom onset, without concerning safety findings, in the clinical trial EPIC-HR.

• Key Things to Remember When Prescribing:
  – Multiple drug interactions
  – Reduced dose for moderate renal impairment
  – Not recommended with severe renal impairment or severe hepatic impairment

*Paxlovid™ may be used regardless of COVID-19 vaccination status under EUA
What about COVID-19 Rebound after Paxlovid Treatment

CDC Health Advisory May 24, 2022
https://emergency.cdc.gov/han/2022/han00467.asp

Paxlovid treatment helps prevent hospitalization and death due to COVID-19. COVID-19 rebound has been reported to occur between 2 and 8 days after initial recovery and is characterized by a recurrence of COVID-19 symptoms or a new positive viral test after having tested negative.

A brief return of symptoms may be part of the natural history of SARS-CoV-2 (the virus that causes COVID-19) infection in some persons, independent of treatment with Paxlovid and regardless of vaccination status.

Recommendations for Healthcare Providers

For patients with COVID-19 rebound

• There is currently no evidence that additional treatment for COVID-19 is needed for COVID-19 rebound. Based on data available at this time, patient monitoring continues to be the most appropriate management for patients with recurrence of symptoms after completion of a treatment course of Paxlovid.
• Advise people with COVID-19 rebound to follow CDC’s guidance on isolation and take precautions to prevent further transmission. Patients should re-isolate for at least 5 days. Per CDC guidance, they can end their re-isolation period after 5 full days if fever has resolved for 24 hours (without the use of fever-reducing medication) and symptoms are improving. The patient should wear a mask for a total of 10 days after rebound symptoms started.
• Consider clinical evaluation of patients who have COVID-19 rebound and symptoms that persist or worsen.
• Healthcare providers are encouraged to report cases of COVID-19 rebound to Pfizer after Paxlovid treatment using the following online tool: Pfizer Safety Reporting external icon and to FDA MedWatch. Complete and submit a MedWatch form external icon, or complete and submit FDA Form 3500 (health professional) by fax (1-800-FDA-0178). Call 1-800-FDA-1088 for questions.
MOV is not recommended for use during pregnancy
- Based on animal data, MOV may cause fetal harm when administered to pregnant individuals

However, if a healthcare provider determines that the benefits outweigh the risks for an individual pregnant patient, they must:
- Counsel the patient regarding the known and potential benefits and potential risks of MOV use during pregnancy
- Document that the patient is aware of the known and potential benefits and potential risks of MOV use during pregnancy
- Make the individual aware of the pregnancy surveillance program
- If the pregnant individual agrees to participate in the pregnancy surveillance program and allows the prescribing healthcare provider to disclose patient specific information to Merck, the prescribing healthcare provider must provide the patient’s name and contact information to Merck at 1-877-888-4231 or https://pregnancyreporting.msd.com
3) Molnupiravir- Prescriber Requirements

- Provide an electronic or hard copy of patient fact sheet and document that patient has received an electronic or hard copy of the patient fact sheet
- Review the information contained within the patient factsheet with the patient and counsel patient on the known and potential benefits and risks of MOV
- Assess whether an individual of childbearing potential is pregnant or not, if clinically indicated
- Advise individuals of childbearing potential to use contraception for the duration of treatment and for 4 days after the last dose of MOV
- Advise sexually active individuals with partners of childbearing potential to use contraception during treatment and for at least 3 months after the last dose of MOV
- Make individuals of childbearing potential aware of pregnancy surveillance program
- Report all medication errors and serious adverse events potentially related to MOV within 7 calendar days from the healthcare provider’s awareness of the event
  - www.fda.gov/medwatch/report.htm
  - or call 1-800-FDA-1088
- See prior slide for requirements for use in pregnancy
Therapeutic Algorithm for Covid-19 Patient with Mild-Moderate Symptoms

At high-risk for progression to severe disease if COVID-19 positive? **This is regardless of vaccination status.**

**NO** STOP

Within 5 Days of Symptoms Onset?

**NO**

If within 7 days of symptoms onset, refer for monoclonal antibody treatment.

**YES**

If eGFR > 30 and not in Child-Pugh C

**NO**

Can consider Molnupiravir after careful review of safety profile in EUA. Contraindicated in pregnant women

**YES**

Mild-moderate symptoms = does not require hospitalization or supplemental oxygen

**Medical Conditions at High-Risk for Progression to Severe Disease if COVID-19 Positive**

- Cancer
- Chronic Kidney Disease
- Chronic Liver Disease
- Cystic Fibrosis
- Dementia or other Neurological Conditions
- Diabetes (Type 1 or 2)
- Disabilities
- Heart Conditions
- HIV Infection
- Immunocompromised State (Weakened Immune System)
- Mental Health Conditions
- Overweight And Obesity
- Substance Use Disorders
- Stroke or Cerebrovascular Disease
- Solid or Blood Stem Cell Transplant
- Smoking, Current or Former
- Sickle Cell Disease or Thalassemia
- Tuberculosis


Also, anyone age 65 years and older, regardless of vaccination status, should be considered.
Supply of therapeutics in California is currently NOT limited!
Doses are more readily available across the county
All patients who are eligible for treatment with COVID-19 treatments should be offered treatment to reduce potential for hospitalization
If therapeutics become scarce, clinicians should use NIH treatment guidelines to prioritize higher risk individuals

Where to find doses

- HHS Therapeutic Locator: https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com
- HHS Test to Treat: https://covid-19-test-to-treat-locator-dhhs.hub.arcgis.com
Test to Treat

- Federal initiative launched in March to provide quick access to free treatment for COVID-19
- One-Stop Test to Treat sites where people are able to get tested and if they are positive and treatments are appropriate, can also receive a prescription from a health care provider (either on site or through telehealth) and have their prescription filled all at one location
- “One-Stop Test to Treat” sites are available at thousands of locations nationwide, including pharmacy-based clinics, federally-funded health centers, long-term care facilities, and community-based sites.
- In May, the program was expanded to include federally-supported Test to Treat sites.

Note, even if a “Test to Treat” site is not available in a given location
- Health care providers throughout the county who can appropriately assess individuals and have prescribing abilities can prescribe the oral viral therapeutics to pharmacy sites that carry the oral antivirals.
Finding Therapeutics

Test to Treat locator for Patients

[Image: Find COVID-19 Medication]

**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.

Need help finding a place to get medication? Call 1-800-232-0233 (TTY 888-720-7489)


COVID-19 Therapeutics Locator for Clinicians

[Image: COVID-19 Therapeutics Locator]

The national map below displays public locations that have received supplies of U.S. Government-sponsored COVID-19 therapeutics under U.S. Food and Drug Administration (FDA) Emergency Use Authorization (EUA) authority. The biologic antibody treatments, bamlanivimab and casirivimab-escimmab (Relexdal), and the monoclonal antibody treatment, lenzilumab-mp1 (Renral), are products authorized by the FDA for either prevention [prevention or treatment] (Relexdal and Lenzilumab-mp1) and [treatment] (Renral). Distribution was suspended due to the major preventions of the EUA due to the potential of the EUA due to the potential of the EUA.

Therapeutic Distribution Locator for Provider Use

[Map: COVID-19 Therapeutics Locator]

### Case Discussions

#### Case 1:
66 y/o M  
**Sx:** 3 days fever/cough + home antigen test  
**PMH:** no renal/hepatic impairment  
**Meds:** none

---

**What if the case was 45 y/o? M Vs F**  
**Ethnicity:** non-White unsheltered?

---

<table>
<thead>
<tr>
<th><strong>Paxlovid Candidate?</strong></th>
<th><strong>Verify SARS-CoV-2 infection (antigen/PCR), mild-moderate illness</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Verify &lt; 5 days from symptom onset</td>
</tr>
<tr>
<td>2</td>
<td>Is the patient at high risk for developing severe illness?</td>
</tr>
<tr>
<td>3</td>
<td>Age/weight appropriate for paxlovid?</td>
</tr>
<tr>
<td>4</td>
<td><strong>Cautions</strong></td>
</tr>
<tr>
<td>5</td>
<td>1) eGFR &gt; 30? eGFR 31-60? &gt; 60</td>
</tr>
<tr>
<td>6</td>
<td>2) No severe hepatic impairment (Child-Pugh C)?</td>
</tr>
<tr>
<td>7</td>
<td>3) Med Interactions? Can meds be adjusted?</td>
</tr>
</tbody>
</table>

**Good Paxlovid Candidate!**  
Prescribe regular Paxlovid pack!  
Can consider at high risk with ethnicity/unsheltered status!
Case Discussion

Case 2:
48 y/o F, fully vaccinated and boosted
Sx: 3 days sore throat, headache, + home antigen test
PMH: BMI 25, HTN, DM, HLP
Moderate renal impairment eGFR 45
Meds: amlodipine, saxagliptin, simvastatin

Case 3:
45 y/o F, fully vaccinated and boosted
Pregnant
Sx: 3 days sore throat, headache, + home antigen test
PMH: BMI 25, HTN, DM, HLP
Moderate renal impairment eGFR 45
Meds: Hydralazine, regular insulin

Paxlovid Candidate?
1) Verify SARS-CoV-2 infection (antigen/PCR), mild-moderate illness
2) Verify < 5 days from symptom onset
3) Is the patient at high risk for developing severe illness?
4) Age/weight appropriate for paxlovid?
5) Cautions
   1) eGFR > 30? eGFR 31-60? > 60
   2) No severe hepatic impairment (Child-Pugh C)?
6) Med Interactions? Can meds be adjusted?

Consider
1) Paxlovid - renally dosed, adjust HTN/DM meds, temporarily hold Simvastatin
2) Remdesivir
Case 2 - If 1 and 2 not available, then mAb or MOV
Case 3 - consider mAb if 1 and 2 not available
Case 3: 35 y/o F, fully vaccinated and boosted
Sx: 3 days sore throat, headache, + home antigen test
PMH: BMI 25, HTN, DM, HLP eGFR < 30
Meds: Metformin, Simvastatin, Amlodipine, OCP

Paxlovid Candidate?
1) Yes
2) Yes
3) High risk - PMH
4) Meets age requirement
5) + renal/hepatic impairment
6) + med interactions

Not a good candidate for paxlovid or Remdesivir - eGFR < 30

Consider Bebtelovimab
If not available, Consider Molnupiravir
continue OCP! Inform about embryo-fetal toxicity risk
Case Discussion - Peds

Case 4: 12 yr/0 M, 95 lbs
Sx: 3 days fever/cough + home antigen test
PMH: ADHD, moderate-severe asthma, sickle cell disease, obese
Meds: Albuterol inhaler, Adderall, prednisone

Case 5: 6 month old
Fever, appears hydrated + COVID-19 molecular test
PMH: Congenital heart disease

Case 4: Paxlovid candidate
Or Remdesivir

Case 5: Remdesivir Candidate (ped dose)

Paxlovid Candidate?
1) Verify SARS-CoV-2 infection (antigen/PCR), mild-moderate illness
2) Verify < 5 days from symptom onset
3) Is the patient at high risk for developing severe illness?
4) Age/weight appropriate for paxlovid?
5) Cautions
   1) eGFR > 30? eGFR 31-60? > 60
   2) No severe hepatic impairment (Child-Pugh C)?
6) Med Interactions? Can meds be adjusted?

Remdesivir Candidate?

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.

Case Discussion - Peds

Case 4: 12 yr/0 M, 95 lbs
Sx: 3 days fever/cough + home antigen test
PMH: ADHD, moderate-severe asthma, sickle cell disease, obese
Meds: Albuterol inhaler, Adderall, prednisone

Case 5: 6 month old
Fever, appears hydrated + COVID-19 molecular test
PMH: Congenital heart disease

Case 4: Paxlovid candidate
Or Remdesivir

Case 5: Remdesivir Candidate (ped dose)
Question and Answer
Resources

Treatment

- NIH Guidance: https://www.covid19treatmentguidelines.nih.gov
- COVID-19 Drug Interaction Tool: https://covid19-druginteractions.org/checker
- CDPH Webpage: 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

Locating Therapeutic Options

- HHS Therapeutic Locator: https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com
- HHS Test to Treat: https://covid-19-test-to-treat-locator-dhhs.hub.arcgis.com

Fact Sheets for Providers

- Paxlovid: https://www.fda.gov/media/155050/download
- Remdesivir:
  - Use in <12 years of age: https://www.fda.gov/media/137566/download
- Bebtelovimab: https://www.fda.gov/media/156152/download
- Molnupiravir: https://www.fda.gov/media/155054/download

Fact Sheets for Patients:

- Paxlovid: https://www.fda.gov/media/155051/download
- Bebtelovimab: https://www.fda.gov/media/156153/download
- Molnupiravir: https://www.fda.gov/media/155055/download
- FDA Patient information: https://www.fda.gov/consumers/consumer-updates/know-your-treatment-options-covid-19
Resources- Clinician Webinars

CDC/IDSA COVID-19 Clinician Calls
  • April 11, 2022- All About Paxlovid; Plus Variants Update
  • March 18, 2022- The Latest on COVID-19 Treatment; Plus Variants Update
  • February 28, 2022- Update on Serology Testing
  • February 7, 2022- Outpatient Therapeutics: Addressing Operational Barriers to Delivery & Access; Omicron Update

CDC Clinician Outreach and Communication Activity (COCA)
• https://emergency.cdc.gov/coca/
  • COCA Call: May 5, 2022: Evaluating and Supporting Patients Presenting with Cognitive Symptoms Following COVID
  • COCA Now: April 4, 2022: New COVID-19 Test to Treat Initiative and Locator Tool
  • COCA Now: March 25, 2022: New CDC COVID-19 Quarantine and Isolation (Q&I) Calculator
  • COCA Now: February 24, 2022: Updated List of High-Risk Medical Conditions for Severe COVID-19 Outcomes
  • COCA Call: February 24, 2022: Updated Guidance for Clinicians on COVID-19 Vaccines
  • COCA Call: February 10, 2022: COVID-19 Updates: What Clinicians Need to Know About Multisystem Inflammatory Syndrome in Children
  • COCA Now: February 01, 2022: Ivermectin Products are Not Approved by FDA to Prevent or Treat COVID-19
  • COCA Now: January 31, 2022: How to Talk with Parents and Caregivers about COVID-19 Vaccination
  • COCA Call: January 13, 2022: Updates to CDC’s COVID-19 Quarantine and Isolation Guidelines in Healthcare and Non-Healthcare Settings
  
  → COCA Call: January 12, 2022: What Clinicians Need to Know About the New Oral Antiviral Medications for COVID-19
    • https://emergency.cdc.gov/coca/ppt/2022/011222_slide.pdf
Details for each COVID-19 Therapeutic
Evusheld- Pre-Exposure Prophylaxis

Long-Acting Monoclonal Antibody

EUA for Pre-exposure prophylaxis (prevention) of COVID-19 in certain adults and pediatric patients (12+ and weighing at least 40 kg) who do not have current infection or recent exposure and

- who have moderate-to-severe immune compromise due to a medical condition or who have received immunosuppressive medications or treatments and may not mount an adequate immune response to COVID-19 vaccination or
- for whom vaccination with any available approved or authorized COVID-19 vaccine is not recommended due to a history of severe adverse reaction (e.g., severe allergic reaction) to a COVID-19 vaccine(s) and/or COVID-19 vaccine component(s).

Activity against Omicron

- Retained activity against Omicron BA.1 and BA.1.1
- Reduced viral burden and limited inflammation in lungs for all three variants BA.1, BA.1.1, BA.2

2. Fajnzylber, J et al. SARS-CoV-2 viral load is associated with increased disease severity and mortality. Available at https://www.nature.com/articles/s41467-020-19057-5/ [Last accessed March 2022]
**Evusheld Dosage and Administration**

**Initial Dose:** 300 mg Tixagevimab and 300 mg of Cilgavimab
Administered as 2 separate consecutive IM injections

**Dosing for Individuals Who Initially Received 150 mg of Tixagevimab and 150 mg Cilgavimab**

For individuals who initially received 150 mg tixagevimab and 150 mg cilgavimab:
- Initial dose ≤3 months prior: 150 mg tixagevimab and 150 mg cilgavimab.
- Initial dose >3 months prior: 300 mg Tixagevimab and 300 mg Cilgavimab

**Repeat dose:** The SARS-CoV-2 variants that will be circulating in the United States when EVUSHELD may need to be re-dosed are not known at this time and therefore repeat dosing recommendations cannot be made; the Fact Sheets will be revised with repeat dosing recommendations in the future when more data are available.

Prior to 2/24/22, Evusheld had EUA authorization, at lower dose of 150mg Tixagevimab and 150 mg Cilgavimab. On 2/24/22, FDA adjusted recommendations. Based on data during Omicron Surge, Evusheld was found to be less active against certain Omicron subvariants. Dosing regimen was increased because available data indicated that higher dose of may prevent infection of COVID-19 Omicron subvariants BA.1 and BA.1.1 than the originally authorized Evusheld dose.
Contraindications and Risks and use in Specific Populations

Contraindication:
- Individuals with previous severe hypersensitivity reactions, including anaphylaxis to any component of EVUSHELD

Warnings and Precautions:
- Hypersensitivity including anaphylaxis
- Clinically significant bleeding disorders (since IM injection, give with caution to individuals with thrombocytopenia or any coagulation disorder)
- Cardiovascular Events
  • A higher proportion of subjects who received EVUSHELD versus placebo reported myocardial infarction and cardiac failure serious adverse events. All of the subjects with events had cardiac risk factors and/or a prior history of cardiovascular disease at baseline. A causal relationship between EVUSHELD and these events has not been established. Consider the risks and benefits prior to initiating EVUSHELD in individuals at high risk for cardiovascular events and advise individuals to seek immediate medical attention if they experience any signs or symptoms suggestive of a cardiovascular event.

Adverse Reactions:
- The most common adverse events are headache, fatigue and cough.

Use in Specific Populations:

Pregnancy
There are insufficient data to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. EVUSHELD should only be used during pregnancy if the potential benefit outweighs the potential risk for the mother and the fetus.

Lactation
There are no available data on the presence of tixagevimab or cilgavimab in human milk or animal milk, the effects on the breastfed infant, or the effects of the drug on milk production. Maternal IgG is known to be present in human milk.
1) Nirmatrelvir + Ritonavir (Paxlovid)

**EUA 12/22/22 for:**
- Treatment of mild-to-moderate COVID-19 in adults & pediatric patients (+ lab confirmed)
- 12 years of age and older weighing at least 40 kg
- And who are at high risk for progression to severe COVID-19, including hospitalization or death
- May be used regardless of vaccination status

**NOT authorized for:**
- Patients requiring hospitalization
- < age 12, < 40 kg
- Pre-exposure or post-exposure treatment
- Use for longer than 5 days

**Dose:**
- **Normal renal function (eGFR 60+):**
  - two 150 mg tab Nirmatrelvir & 100 mg tab of ritonavir PO BID
  (with or without food, high fat meal increases nirmatrelvir absorption by 15%)
- **Impaired renal function, eGFR: 30-60:**
  - One 150 mg tab Nirmatrelvir & one Ritonavir PO BID
    *New Dose pack coming soon. If not yet available, can ask patient to take one 150mg nirmatrelvir with one 100 mg ritonavir PO BID x 5 days*

**Possible Side Effects:**
- Dysgeusia (altered taste) (6% compared to placebo < 1%), diarrhea (3% vs 2%),
  hypertension (1% vs <1%), myalgia (1% vs < 1%) , muscle aches

**Contraindications**
- eGFR < 30, severe hepatic impairment (Child-Pugh Class C)
- Co-administration with drugs highly dependent on CYP3A for clearance or potent CYP3A inducers

*eGFR calculated using CKD-Epi formula*
1) Nirmatrelvir + Ritonavir (Paxlovid)

**Warnings/Precautions**

- **Drug-Drug Interaction**
  - CYP3A inhibitor and can increase medications metabolized by CYP3A
  - Medications that inhibit or induce CYP3A may increase or decrease Paxlovid concentrations
  - These interactions can lead to clinically significant adverse reactions, including fatal events
  - Loss of therapeutic effect of Paxlovid and possible viral resistance from decreased Paxlovid exposure

- **Allergic reactions/hypersensitivity** have been reported- if any allergic reaction/hypersensitivity- immediately discontinue, provider should treat accordingly

- **Hepatotoxicity** has occurred in patients receiving ritonavir

- **HIV-1** Use of Paxlovid may lead to risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled, undiagnosed HIV-1 infection

- The **Liverpool COVID-19 Drug Interactions website**, and the EUA fact sheet for ritonavir-boosted nirmatrelvir can be used to identify and manage drug-drug interactions

**Special Populations**

**Hepatic Impairment**

- No dosage adjustment needed for mild/moderate hepatic impairment.
- For Severe hepatic impairment (Child-Pugh Class C, paxlovid is NOT recommended due to lack of pharmacokinetic and safety data for nirmatrelvir or ritonavir in that population

**Pregnancy and Lactation**

- No available clinical data on use in pregnancy or with breastfeeding
- Animal studies- reduced fetal body weights seen at ~10x the nirmatrelvir exposure seen in humans with the authorized dose; no other adverse developmental effects were seen.

**Pediatrics**

- No available clinical data in children. The authorized adult dose is expected to result in comparable serum exposures in patients 12 years of age and older and weighing at least 40 kg.
# Efficacy Results in Non-Hospitalized Adults with COVID-19 Dosed within 5 Days of Symptom Onset who Did Not Receive COVID-19 mAb Treatment at Baseline

<table>
<thead>
<tr>
<th></th>
<th>PAXLOVID™ (N=1,039)</th>
<th>PLACEBO (N=1,046)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary endpoint: COVID-19 related hospitalization or death from any cause through Day 28, n(%)</td>
<td>8 (.08%)</td>
<td>66 (6.3%)</td>
</tr>
<tr>
<td>Reduction relative to placebo for primary endpoint[^a^] [95%, CI], %</td>
<td>-5.62 (-7.21, -4.03)</td>
<td></td>
</tr>
<tr>
<td>All-cause mortality through Day 28, %</td>
<td>0</td>
<td>12 (1.1%)</td>
</tr>
</tbody>
</table>

\[^a^]\ The estimated cumulative proportion of participants with COVID-19 related hospitalization or death from any cause through Day 28 was calculated for each treatment group using the Kaplan-Meier method, where subjects without hospitalization and death status through Day 28 were censored at the time of study discontinuation.

- **88% (95% CI: 75%, 94%)** relative risk reduction for the primary endpoint (proportion of subjects with COVID-19 related hospitalization or death from any cause through Day 28)
- Treatment effect was generally consistent across subgroups, including baseline serology status.
# 1) Nirmatrelvir + Ritonavir (Paxlovid)

<table>
<thead>
<tr>
<th>Dosing Regimens</th>
<th>Adverse Events</th>
<th>Monitoring Parameters</th>
<th>Drug-Drug Interaction Potential</th>
<th>Comments and Links to Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ritonavir-Boosted Nirmatrelvir (Paxlovid)</td>
<td>• Dysgeusia <strong>Diarrhea</strong></td>
<td>• Monitor for potential AEs due to drug-drug interactions with concomitant medication(s).</td>
<td>• RTV-boosted nirmatrelvir has significant and complex drug-drug interactions. Before prescribing RTV-boosted nirmatrelvir, carefully review concomitant medications, including OTC medicines, herbal supplements, and recreational drugs. See Ritonavir-Boosted Nirmatrelvir (Paxlovid) for more information.</td>
<td>• Both nirmatrelvir and RTV tablets can be taken with or without food.</td>
</tr>
</tbody>
</table>

**EUA Dose for COVID-19**

**Dosing Based on eGFR:**
- **≥60 mL/min:** Nirmatrelvir 300 mg (two, 150-mg tablets) with RTV 100 mg (one, 100-mg tablet) twice daily for 5 days
- **≥30 to 60 mL/min:** Nirmatrelvir 150 mg (one, 150-mg tablet) with RTV 100 mg (one, 100-mg tablet) twice daily for 5 days
- **<30 mL/min:** Not recommended

**Dosing for Patients with Severe Hepatic Impairment (Child-Pugh Class C):**
- Not recommended

---

As a healthcare provider, you should:

- Inform patients that Paxlovid™ may interact with some drugs and is contraindicated for use with some drugs
- Obtain a complete medication list from your patient (including nonprescription drugs and herbals)
- Check for clinically significant drug interactions:
  - Section 7.3 of the EUA Fact Sheet: [https://www.fda.gov/media/155050/download](https://www.fda.gov/media/155050/download)
  - [https://www.covid19-druginteractions.org/checker](https://www.covid19-druginteractions.org/checker)
- Based on the drug interactions, decide if:
  - Paxlovid™ use is appropriate versus an alternative authorized treatment
  - If appropriate, whether your patient should hold, change, or dose-reduce other medications while taking Paxlovid™, or if additional monitoring may be needed
Paxlovid™ Summary

• Paxlovid™ was authorized on 12/22/21 for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older and ≥40 kg) who are at high risk for progression to severe COVID-19*.

• Paxlovid™ reduced COVID-19 related hospitalization and death by 88% when given within 5 days of symptom onset, without concerning safety findings, in the clinical trial EPIC-HR.

• Key Things to Remember When Prescribing:
  – Multiple drug interactions
  – Reduced dose for moderate renal impairment
  – Not recommended with severe renal impairment or severe hepatic impairment

*Paxlovid™ may be used regardless of COVID-19 vaccination status under EUA
What about COVID-19 Rebound after Paxlovid Treatment

CDC Health Advisory May 24, 2022
https://emergency.cdc.gov/han/2022/han00467.asp

Paxlovid treatment helps prevent hospitalization and death due to COVID-19. COVID-19 rebound has been reported to occur between 2 and 8 days after initial recovery and is characterized by a recurrence of COVID-19 symptoms or a new positive viral test after having tested negative.

A brief return of symptoms may be part of the natural history of SARS-CoV-2 (the virus that causes COVID-19) infection in some persons, independent of treatment with Paxlovid and regardless of vaccination status.

Recommendations for Healthcare Providers

For patients with COVID-19 rebound

• There is currently no evidence that additional treatment for COVID-19 is needed for COVID-19 rebound. Based on data available at this time, patient monitoring continues to be the most appropriate management for patients with recurrence of symptoms after completion of a treatment course of Paxlovid.
• Advise people with COVID-19 rebound to follow CDC’s guidance on isolation and take precautions to prevent further transmission. Patients should re-isolate for at least 5 days. Per CDC guidance, they can end their re-isolation period after 5 full days if fever has resolved for 24 hours (without the use of fever-reducing medication) and symptoms are improving. The patient should wear a mask for a total of 10 days after rebound symptoms started.
• Consider clinical evaluation of patients who have COVID-19 rebound and symptoms that persist or worsen.
• Healthcare providers are encouraged to report cases of COVID-19 rebound to Pfizer after Paxlovid treatment using the following online tool: Pfizer Safety Reporting external icon and to FDA MedWatch. Complete and submit a MedWatch form external icon, or complete and submit FDA Form 3500 (health professional) by fax (1-800-FDA-0178). Call 1-800-FDA-1088 for questions.
2) Remdesivir- (Veklury)

- Adenosine nucleotide analogue prodrug
- Broad-spectrum against several RNA viruses

**FDA: (updated April 25, 2022)**
- Treatment of COVID-19 in individuals aged 28 days of age or older, weighing at least 3 kg (7 lbs) with positive results of direct SARS-CoV-2 viral testing who are
  - hospitalized or,
  - not hospitalized and have mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death.

**Dose:**

**Pediatric 3 kg or less than 40 kg**
- Single loading dose 5 mg/kg on Day 1 followed by once daily maintenance doses of Veklury 2.5mg/kg from Day 2 via IV.

**Adult and Pediatric patients weighing at least 40 kg**
- Single loading dose of 200 mg on Day 1 followed by once daily maintenance dose 100 mg from day 2 via IV

**Duration of treatment**
- 3 days treatment course for Non-Hospitalized patients with mild-moderate COVID 19 at risk for progression to severe COVID-19
- 10 day treatment course for hospitalized patients requiring invasive mechanical ventilation and/or ECMO
- 5 days treatment course for hospitalized patients not requiring invasive Mechanical Ventilation and/or ECMO

**Possible Side Effects:**
- Nausea (5%), increased ALT and AST (5%)
- Less common adverse reactions: hypersensitivity reactions, seizure, rash

**Contraindications**
- History of clinically significant hypersensitivity reactions to Veklury or any components of the product
2) Remdesivir (Veklury)

Warnings/Precautions

• Allergic reactions/hypersensitivity have been reported- if any allergic reaction/hypersensitivity- immediately discontinue, provider should treat accordingly

• Increased risk of transaminase elevations. Perform hepatic lab testing in all patients. Consider discontinuing if ALT levels increase > 10x ULN. Discontinue Veklury if ALT elevation is accompanied by signs or symptoms of liver inflammation

• Risk of reduced antiviral activity when co-administered with chloroquine or hydroxychloroquine. Coadministration with chloroquine phosphate or hydroxychloroquine sulfate is not recommended.

• Should not be given to patient with ALT > 5x Upper limit of normal or ALT elevation associated with increase conjugated bilirubin, alkaline phosphatase or INR

Special Populations

Renal Impairment

• Not recommended for individuals with eGFR < 30 ml/min

Pregnancy and Lactation

• No available clinical data on use in pregnancy or with breastfeeding
## Remdesivir- Veklury

### Dosing Regimens

The doses listed here are for approved indications or from reported experiences or clinical trials.

<table>
<thead>
<tr>
<th>Adults and Children (Aged ≥12 Years and Weighing ≥40 kg):</th>
<th>Adverse Events</th>
<th>Monitoring Parameters</th>
<th>Drug-Drug Interaction Potential</th>
<th>Comments and Links to Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>RDV 200 mg IV on Day 1, than RDV 100 mg IV once daily from Day 2</td>
<td>Nausea</td>
<td>Monitor patients for infusion reactions during the infusion and observe them for ≥1 hour after the infusion as clinically appropriate.</td>
<td>Clinical drug-drug interaction studies of RDV have not been conducted.</td>
<td>RDV should be administered in settings in which health care providers have immediate access to medications to treat a severe infusion-related reactions or HSR, such as anaphylaxis, and the ability to activate the emergency medical system. A list of clinical trials is available: <a href="https://remdesivir.niddk.nih.gov">Remdesivir</a></td>
</tr>
<tr>
<td>RDV 5 mg/kg IV on Day 1, then RDV 2.5 mg/kg IV once daily from Day 2</td>
<td>ALT and AST elevations, Hypersensitivity, Increases in prothrombin time, Drug vehicle is SBECO, which has been associated with renal and liver toxicity. SBECO accumulation may occur in patients with moderate or severe renal impairment. Each 100 mg vial of RDV lyophilized powder contains 3 g of SBECO, and each 100 mg/20 mL vial of RDV solution contains 6 g of SBECO. Clinicians may consider preferentially using the lyophilized powder formulation (which contains less SBECO) in patients with renal impairment.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Treatment Duration: Nonhospitalized patients: 3 days, Hospitalized patients: 5 days or until hospital discharge</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Approved by the FDA for the treatment of COVID-19 in individuals aged ≥12 years and weighing ≥40 kg.

“Our data show that remdesivir was superior to placebo in shortening the time to recovery in adults who were hospitalized with COVID-19 and had evidence of lower respiratory tract infection.”

3) (Alternative Treatment) Bebtelovimab

<table>
<thead>
<tr>
<th>Dosing Regimens</th>
<th>Adverse Events</th>
<th>Monitoring Parameters</th>
<th>Drug-Drug Interaction Potential</th>
<th>Comments and Links to Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bebtelovimab (Anti-SARS-CoV-2 Monoclonal Antibody)</td>
<td>Nausea</td>
<td>Only for administration in healthcare settings by qualified healthcare providers who have immediate access to emergency medical services and medications to treat severe infusion reactions.</td>
<td>Drug-drug interactions are unlikely between BEB and medications that are renally excreted or that are CYP substrates, inhibitors, or inducers.</td>
<td>Availability:</td>
</tr>
<tr>
<td>Dose Recommended in FDA EUA for Treatment of COVID-19 in Adults and Pediatric Patients Aged ≥12 Years and Weighing ≥40 kg:</td>
<td>Vomiting</td>
<td>Monitor during IV injection and for ≥1 hour after injection is completed.</td>
<td>Under the FDA EUA, BEB is available for the treatment of high-risk outpatients with mild to moderate COVID-19. See Anti-SARS-CoV-2 Monoclonal Antibodies for a list of high-risk conditions.</td>
<td>• A list of clinical trials is available: Bebtelovimab</td>
</tr>
<tr>
<td>• BEB 175 mg as an IV injection over ≥at least 30 seconds</td>
<td>Pruritus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rash</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypersensitivity, including anaphylaxis and infusion-related reactions</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

[https://files.covid19treatmentguidelines.nih.gov/guidelines/covid19treatmentguidelines.pdf Table 3c, page 228 (updated 4/8/22)]
Third Line alternatives after Paxlovid and Remdesivir

Beptelovimab
Molnupiravir

If ritonavir-boosted nirmatrelvir, sotrovimab, or remdesivir are not available, feasible to deliver, or clinically appropriate, the Panel recommends using either beptelovimab (CIII) or molnupiravir (CIIa). The Panel’s recommendation on beptelovimab is primarily based on laboratory data showing its potent activity against the Omicron VOC, its BA.1 and BA.2 subvariants, and other VOCs and on limited clinical trial data. The assessment of the clinical efficacy of beptelovimab is limited to 1 small, Phase 2, randomized, placebo-controlled trial in patients at low risk of disease progression and 1 small randomized controlled trial that compared beptelovimab to an anti-SARS-CoV-2 mAb combination of bamlanivimab, etesevimab, and beptelovimab in patients at high risk of disease progression (described below). The MOVE-OUT trial that compared the use of molnupiravir to placebo reported a 30% reduction in rate of hospitalization or death in the molnupiravir recipients, which is markedly lower than the rate reduction reported with the use of ritonavir-boosted nirmatrelvir, sotrovimab, or remdesivir.4 More detailed information regarding these therapies can be found in Therapeutic Management of Nonhospitalized Adults With COVID-19.
3) Alternative therapy- Bebtelovimab

**Drug Class- Monoclonal antibody**
- Recombinant neutralizing human mAb that binds to the spike protein of SARS-CoV-2
- broad activity against SARS-CoV-2 variants, including Omicron variant and its BA.1, BA.1.1, BA.2 subvariants

**EUA 3/25/22**
- Treatment of mild to moderate coronavirus disease COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg), with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death

**NIH panel** recommends using Bebtelovimab 175 mg IV in those age 12+ ONLY when Paxlovid and remdesivir are not available, feasible to use, or clinically appropriate. Treatment should be initiated as soon as possible and within 7 days of symptom onset

**Dose:**
175 mg/2ml IV over 30 seconds followed by flushing injection line with 0.9% Sodium Chloride
*(same for adults and pediatric patients age 12+ weighing at least 40 kg)*
Observe x 1 hour after infusion for infusion reaction/hypersensitivity

**Contra-Indications:**
- Hypersensitivity including anaphylaxis and infusion-related reactions
- Clinical worsening after SARS-CoV-2 Monoclonal Antibody Administration
- Limitations of benefit and potential for Risk in patients with Severe COVID-19

**Adverse Reactions:**
- Infusion related reactions (0.3%), pruritis (0.3%), rash (0.8%)

**Drug Interactions:**
- None known (Not renally excreted or metabolized by Cytochrome P450 enzymes)

---


NIH Panel guidance- From Coronavirus Disease 2019 (COVID-19) Treatment Guidelines (nih.gov) page 61
3) Alternative therapeutic- Bebtelovimab

Warnings/Precautions

• Allergic reactions/hypersensitivity reactions including anaphylaxis have been reported- if any allergic reaction/hypersensitivity- immediately discontinue, provider should treat accordingly
• Infusion-related reactions which may occur up to 24 hours after injection
• Signs and symptoms of infusion-related reactions may include:
  • fever, difficulty breathing, reduced oxygen saturation, chills, fatigue, arrhythmia (e.g., atrial fibrillation, sinus tachycardia, bradycardia), chest pain or discomfort, weakness, altered mental status, nausea, headache, bronchospasm, hypotension, hypertension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, vasovagal reactions (e.g., pre-syncpe, syncope), dizziness and diaphoresis.
• Clinical worsening after SARS-CoV-2 monoclonal antibody administration
  • Has been reported- may include fever, hypoxia or increased respiratory difficulty, arrhythmia, fatigue, and altered mental status. Some of these events require hospitalization. It is not known if these events were related to the monoclonal antibody use or were due to progression of COVID-19

Special Populations

• Pregnancy/Lactation- insufficient or not data
• Pediatric Use- Not authorized < 12 or weighing < 40 kg. Safety and effectiveness have not been assessed in pediatric patients.
• Geriatric Use- Of 602 patients receiving bebtelovimab in BLAZE-4, 10.5% were 65 years of age and older and 3.3% were 75 years of age and older. No difference in the pharmacokinetics in geriatric patients compared to younger patients.

LIMITATIONS OF AUTHORIZED USE

Bebtelovimab is not authorized for treatment of mild-to-moderate COVID-19 in geographic regions where infection is likely to have been caused by a non-susceptible SARS-CoV-2 variant based on available information including variant susceptibility to this drug and regional variant frequency.
• FDA's determination and any updates will be available at: https://www.fda.gov/emergencypreparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-useauthorization#coviddrugs.

Bebtelovimab is not authorized for use in patients, who:
• are hospitalized due to COVID-19, OR o require oxygen therapy and/or respiratory support due to COVID-19, OR
• require an increase in baseline oxygen flow rate and/or respiratory support due to COVID-19 and are on chronic oxygen therapy and/or respiratory support due to underlying non-COVID-19 related comorbidity'
Bebtelovimab and activity against other COVID Variants

Table 2: Bebtelovimab Pseudotyped Virus-Like Particle Neutralization Data for SARS-CoV-2 Spike Protein Variants

<table>
<thead>
<tr>
<th>Lineage with Spike Protein Substitution</th>
<th>Country First Identified</th>
<th>WHO Nomenclature</th>
<th>Key Substitutions Tested</th>
<th>Fold Reduction in Susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.1.1.7</td>
<td>UK</td>
<td>Alpha</td>
<td>N501Y</td>
<td>No change</td>
</tr>
<tr>
<td>B.1.351</td>
<td>South Africa</td>
<td>Beta</td>
<td>K417N + E484K + N501Y</td>
<td>No change</td>
</tr>
<tr>
<td>P.1</td>
<td>Brazil</td>
<td>Gamma</td>
<td>K417T + E484K + N501Y</td>
<td>No change</td>
</tr>
<tr>
<td>B.1.617.2/AY.3</td>
<td>India</td>
<td>Delta</td>
<td>L452R + T478K</td>
<td>No change</td>
</tr>
<tr>
<td>AY.1/AY.2 (B.1.617.2 sublineages)</td>
<td>India</td>
<td>Delta + [K417N]</td>
<td>L452R + T478K + K417N</td>
<td>No change</td>
</tr>
<tr>
<td>B.1.427/1.429</td>
<td>USA (California)</td>
<td>Epsilon</td>
<td>L452R</td>
<td>No change</td>
</tr>
<tr>
<td>C.37</td>
<td>Peru</td>
<td>Lambda</td>
<td>L452Q + E484Q</td>
<td>No change</td>
</tr>
<tr>
<td>B.1.821</td>
<td>Colombia</td>
<td>Mu</td>
<td>R346K + E484K + N501Y</td>
<td>5.3</td>
</tr>
<tr>
<td>B.1.1.529/BA.1</td>
<td>South Africa</td>
<td>Omicron</td>
<td>G339D + S371L + S373P + S375F + K417N + N440K + G446S + G443L + T478K + E484A + G483R + G496S + G498R + N501Y + Y505H</td>
<td>No change</td>
</tr>
</tbody>
</table>

* Key substitutions occurring in the receptor binding domain of spike protein are listed. Pseudotyped VLP containing the E46-length spike protein reflects the consensus sequence for each of the variant lineages were tested.
* No change: <5-fold reduction in susceptibility.
* No change: <5-fold reduction in susceptibility.
* No change: <5-fold reduction in susceptibility.
* No change: <5-fold reduction in susceptibility.
* No change: <5-fold reduction in susceptibility.
* No change: <5-fold reduction in susceptibility.
* No change: <5-fold reduction in susceptibility.
* No change: <5-fold reduction in susceptibility.
* No change: <5-fold reduction in susceptibility.
* No change: <5-fold reduction in susceptibility.

Table 3: Authentic SARS-CoV-2 Neutralization Data for Bebtelovimab

<table>
<thead>
<tr>
<th>Lineage with Spike Protein Substitution</th>
<th>Country First Identified</th>
<th>WHO Nomenclature</th>
<th>Key Substitutions Tested</th>
<th>Fold Reduction in Susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.1.1.7</td>
<td>UK</td>
<td>Alpha</td>
<td>N501Y</td>
<td>No change</td>
</tr>
<tr>
<td>B.1.351</td>
<td>South Africa</td>
<td>Beta</td>
<td>K417N, E484K, N501Y</td>
<td>No change</td>
</tr>
<tr>
<td>P.1</td>
<td>Brazil</td>
<td>Gamma</td>
<td>K417T, E484K, N501Y</td>
<td>No change</td>
</tr>
<tr>
<td>B.1.617.2/AY.3</td>
<td>India</td>
<td>Delta</td>
<td>L452R, T478K</td>
<td>No change</td>
</tr>
<tr>
<td>B.1.427/1.429</td>
<td>USA (California)</td>
<td>Epsilon</td>
<td>L452R</td>
<td>No change</td>
</tr>
<tr>
<td>B.1.526</td>
<td>USA (New York)</td>
<td>iota</td>
<td>E484K</td>
<td>No change</td>
</tr>
<tr>
<td>C.37</td>
<td>Peru</td>
<td>Lambda</td>
<td>L452Q + E484Q</td>
<td>No change</td>
</tr>
<tr>
<td>B.1.821</td>
<td>Colombia</td>
<td>Mu</td>
<td>R346K + E484K + N501Y</td>
<td>5.3</td>
</tr>
<tr>
<td>B.1.1.529/BA.1</td>
<td>South Africa</td>
<td>Omicron</td>
<td>G339D + S371L + S373P + S375F + K417N + N440K + G446S + G443L + T478K + E484A + G483R + G496S + G498R + N501Y + Y505H</td>
<td>No change</td>
</tr>
</tbody>
</table>

* The B.1.1.7, B.1.351, B.1.617.2, and B.1.1.529/BA.1 variants were assessed using cell culture-replicating viral isolates and tested using a plaque reduction assay; the B.1.351, P.1, B.1.617.2, B.1.1.529/BA.1 and BA.1.1 variants were assessed using cell culture-expanded isolates and tested using a microneutralization assay with a CPE-based endpoint (to determine the IC50). The B.1.529/E484K and B.1.427/1.429/E484K substitutions were assessed using recombinant SARS-CoV-2 (USA/WA/1/2020 isolate with E484K or L452R) and tested using a plaque reduction assay.
* Key substitutions occurring in receptor binding domain of spike protein which are associated with each lineage.
* No change: <5-fold reduction in susceptibility when compared to ancestral control isolate using the same methodology.
* No change: <5-fold reduction in susceptibility.
* No change: <5-fold reduction in susceptibility.
* No change: <5-fold reduction in susceptibility.
* No change: <5-fold reduction in susceptibility.

From EUA Factsheet for HCP- [lilly.com](http://lilly.com)
3) Alternative therapy- Molnupiravir (Lagevrio)

- Nucleoside analogue that inhibits replication by viral mutagenesis

**EUA**
  - With positive results of direct SARS-CoV-2 viral testing, and
  - Who are at high risk for progression to severe COVID-19, including hospitalization or death, and
  - For whom alternative COVID-19 treatment options approved or authorized by FDA are not accessible or clinically appropriate.

*Molnupiravir is not authorized:*
- for use in patients who are less than 18 years of age
- for initiation of treatment in patients hospitalized due to COVID-19. Benefit of treatment with LAGEVRIIO has not been observed in subjects when treatment was initiated after hospitalization due to COVID-19
- for use for longer than 5 consecutive days
- for pre-exposure or post-exposure prophylaxis for prevention of COVID-19

**Dose:**
800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days, with or without food

**Possible Side Effects:**
diarrhea, nausea, dizziness

**Contraindications**
- No contraindications have been identified based on limited available data on emergency use (per label)
3) Alternative Therapy - Molnupiravir (Lagevrio)

Warnings/Precautions

• Embryo-Fetal Toxicity: not recommended for use during pregnancy.
• Hypersensitivity reactions, including anaphylaxis have been reported with LAGEVRI. If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue LAGEVRI.
• Bone and Cartilage Toxicity: LAGEVRI is not authorized for use in patients less than 18 years of age because it may affect bone and cartilage growth.

Special Populations

Renal Impairment
• No dosage adjustment in patients with any degree of renal impairment is recommended

Hepatic Impairment
• No dosage adjustments in patients with hepatic impairment is recommended.

Pregnancy
• Not recommended during pregnancy - causes fetal harm - do not use in pregnant individuals
• Advise females of childbearing potential to use effective contraception correctly and consistently, as applicable for the duration of treatment and for 4 days after the last day of treatment. 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

Lactation
• Breastfeeding is not recommended during treatment and for 4 days after the last dose. A lactating individual may consider interrupting breastfeeding and may consider pumping and discarding breast milk during treatment and for 4 days after the last dose.
**Trial P002 (MOVe-OUT): Efficacy Results**

<table>
<thead>
<tr>
<th>Medical Event</th>
<th>Molnupiravir (N=709) n(%)</th>
<th>Placebo (N=699) n(%)</th>
<th>Adjusted Risk Difference % (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause hospitalization ≥24 hours for acute care or death through Day 29</td>
<td>48 (6.8%)</td>
<td>68 (9.7%)</td>
<td>-3.0 (-5.9%, -0.1%)</td>
</tr>
<tr>
<td>All-cause mortality through Day 29</td>
<td>1 (0.1%)</td>
<td>9 (1.3%)</td>
<td></td>
</tr>
</tbody>
</table>

*The determination of primary efficacy was based on a planned interim analysis of 762 subjects. At the interim analysis, 7.3% of participants who received molnupiravir were either hospitalized or died through Day 29 (28/385), compared with 14.1% of placebo-treated participants (53/377). The adjusted risk difference was -6.8% with a 95% CI of (-11.3%, -2.4%) and 2-sided p-value = 0.0024.*

**Adjusted relative risk reduction of molnupiravir compared to placebo for all randomized participants was 30% (95% CI: 1%, 51%).**

Analyses are adjusted by the stratification factor of time of COVID-19 symptom onset (≤3 days vs. >3 [4-5] days).
### 3) Alternative Therapeutic - Molnupiravir

<table>
<thead>
<tr>
<th>Dosing Regimens</th>
<th>Adverse Events</th>
<th>Monitoring Parameters</th>
<th>Drug-Drug Interaction Potential</th>
<th>Comments and Links to Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Molnupiravir</strong> Authorised under FDA EUA for the treatment of mild to moderate COVID-19 in high-risk individuals aged ≥18 years.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| **Dose Recommended in FDA EUA:**  
- MOV 800 mg (four, 200-mg capsules) PO every 12 hours for 5 days | • Diarrhea  
• Nausea  
• Dizziness  
- Per the FDA, the 5-day course of MOV has a low risk for genotoxicity. See the Molnupiravir section for details. | • Before initiating MOV, assess pregnancy status as clinically indicated.  
• Monitor for potential AEs. | • Clinical drug-drug interaction studies of MOV have not been conducted.  
- Drug-drug interactions related to hepatic metabolism are not expected. | • MOV can be taken with or without food.  
- Sexually active individuals of reproductive potential should use effective contraception during and following treatment with MOV. See the Molnupiravir section for details.  
- If MOV is prescribed for a pregnant individual, the prescribing clinician should document that the risks and benefits were discussed and that the patient chose this therapy. Pregnant patients should also be informed of the pregnancy surveillance program and if they agree to participate, be enrolled in the program. See the Molnupiravir section for details.  
- During MOV treatment and for 4 days after the final dose, lactating people should not breastfeed their infants.  
- MOV is not authorized for use in children aged <18 years due to potential effects on bone and cartilage growth.  
- A list of clinical trials is available: [Molnupiravir](https://clinicaltrials.gov) |
3) Alternative Therapeutic- Molnupiravir

- **MOV is not recommended for use during pregnancy**
  - Based on animal data, MOV may cause fetal harm when administered to pregnant individuals

- However, if a healthcare provider determines that the benefits outweigh the risks for an individual pregnant patient, they must:
  - Counsel the patient regarding the known and potential benefits and potential risks of MOV use during pregnancy
  - Document that the patient is aware of the known and potential benefits and potential risks of MOV use during pregnancy
  - Make the individual aware of the pregnancy surveillance program
  - If the pregnant individual agrees to participate in the pregnancy surveillance program and allows the prescribing healthcare provider to disclose patient specific information to Merck, the prescribing healthcare provider must provide the patient’s name and contact information to Merck at 1-877-888-4231 or [https://pregnancyreporting.msd.com](https://pregnancyreporting.msd.com)
3) Molnupiravir- Prescriber Requirements

- Provide an electronic or hard copy of patient fact sheet and document that patient has received an electronic or hard copy of the patient fact sheet
- Review the information contained within the patient factsheet with the patient and counsel patient on the known and potential benefits and risks of MOV
- Assess whether an individual of childbearing potential is pregnant or not, if clinically indicated
- Advise individuals of childbearing potential to use contraception for the duration of treatment and for 4 days after the last dose of MOV
- Advise sexually active individuals with partners of childbearing potential to use contraception during treatment and for at least 3 months after the last dose of MOV
- Make individuals of childbearing potential aware of pregnancy surveillance program
- Report all medication errors and serious adverse events potentially related to MOV within 7 calendar days from the healthcare provider’s awareness of the event
  - www.fda.gov/medwatch/report.htm
  - or call 1-800-FDA-1088
- See prior slide for requirements for use in pregnancy
Extra slides/resources
Susceptibility to monoclonal antibodies appears to be lower for Omicron compared to Delta.

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>MONOCLONAL ANTIBODIES (mAbs)</th>
<th>IV ANTIVIRALS</th>
<th>ORAL ANTIVIRALS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preventative (PrEP)</td>
<td>Treatment</td>
<td>Prevention</td>
</tr>
<tr>
<td></td>
<td>Evusheld (ixegestimab/digemtivmab)</td>
<td>sotrovimab</td>
<td>VELPURY* (remdesivir)</td>
</tr>
<tr>
<td>Date of Latest Update to Emergency Use Authorization (EUA) and Prescribing Information (PI)</td>
<td>EUA: 02/24/22</td>
<td>EUA: 02/21/22</td>
<td>EUA: 02/21/22</td>
</tr>
<tr>
<td>Mechanism of Action</td>
<td>mAb against conserved epitope of spike protein; blocks viral entry</td>
<td>mAb against spike protein; blocks viral attachment to host cells</td>
<td>Nucleotide analog ribonucleic acid (RNA) polymerase inhibitor that halts viral replication</td>
</tr>
<tr>
<td>Treatment Efficacy per Clinical Trials</td>
<td>77% reduction in developing symptomatic COVID-19</td>
<td>Symptomatic improvement and Day 5 reduction in viral load vs. placebo</td>
<td>87% reduction in hospitalizations/deaths</td>
</tr>
<tr>
<td>Activity Against SARS-CoV-2 Variants</td>
<td>Omicron variant: Likely active</td>
<td>Omicron variant: Likely active</td>
<td>Omicron variant: Likely active</td>
</tr>
<tr>
<td>Eligible Population(s)</td>
<td>Adult and pediatric patients (at least 12 years of age and older weighing at least 40 kg) who are not currently infected with SARS-CoV-2 and who have not had a known recent exposure to an individual infected with SARS-CoV-2, and who have moderate to severe immune compromise or for those who any EUA or approved vaccine is not recommended.</td>
<td>Adult and pediatric patients (at least 12 years of age and older weighing at least 40 kg) at high risk for progressing to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options approved or authorized by the U.S. Food and Drug Administration (FDA) are not accessible or clinically appropriate</td>
<td>FDA-approved for: Adults and pediatric patients (12 years of age and older weighing at least 40 kg) who are (1) hospitalized or (2) not hospitalized and at high risk for progression to severe COVID-19, including hospitalization or death</td>
</tr>
</tbody>
</table>

*Precautions/Warnings: Please consult prescribing information for full details.

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Manufacturer</th>
<th>FDA EUA Date</th>
<th>Drug Type/Class/MOA</th>
<th>Reported efficacy data</th>
<th>Indication</th>
<th>Age/weight requirement</th>
<th>Rx window</th>
<th>Duration of therapy</th>
<th>Testing Requirements And lab considerations</th>
<th>History requirements</th>
<th>Family planning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tixagevimab/Cilgavimab (Evusheld), PrEP</td>
<td>AstraZeneca</td>
<td>2/24/22</td>
<td>Monoclonal Antibody (mAb) mAb against conserved epitope of spike protein; blocks viral entry</td>
<td>77% reduction in developing symptomatic COVID-19</td>
<td>Pre-Exposure Prophylaxis for those with moderate to severe immunocompromise or for those who any EUA or approved vaccine is not recommended. Individual should not currently be infected or have recent exposure</td>
<td>12+ (minimum 40 kg or 88 lb)</td>
<td>PreExposure Period for eligible individual</td>
<td>5 days</td>
<td>none</td>
<td>Not specified</td>
<td></td>
</tr>
<tr>
<td>Nirmatrelvir/ritonavir (Paxlovid) Oral</td>
<td>Pfizer</td>
<td>EUA 12/22/21</td>
<td>Antiviral Viral protease inhibitor (Nirmatrelvir) and HIV protease inhibitor &amp; CYP3A inhibitor (ritonavir). Halts viral replication</td>
<td>88% reduction in hospitalizations/deaths</td>
<td>Treatment mild-moderate COVID for at risk patients</td>
<td>12+ (minimum 40 kg or 88 lb)</td>
<td>Within 5 days symptoms onset</td>
<td>3 days - not hospitalized, mild/mod COVID-10. 5 days - hospitalized, not on mech vent/ECMO (extend to 10 days if not improving)</td>
<td>Positive direct SARS-CoV 2 viral test</td>
<td>Positive direct SARS-CoV 2 viral test</td>
<td></td>
</tr>
<tr>
<td>Remdesivir (Veklury) IV</td>
<td>Gilead</td>
<td>4/25/22- No longer on EUA. Fully Authorized for Pediatrics 28 days and older, and at least 3 kg (7lbs)</td>
<td>Antiviral Nucleoside analog (RNA) polymerase inhibitor that halts viral replication</td>
<td>87% reduction in hospitalizations/deaths</td>
<td>Treatment of Hospitalized pt with COVID</td>
<td>&gt; 28 days old (min 3.5 kg, 7lb), &gt; 12 years of age (minimum 40 kg, 88lbs)</td>
<td>Within 7 days symptom onset</td>
<td>10 days - hospitalized, on mech vent/ECMO</td>
<td>Baseline renal function required under EUA for pediatric patients</td>
<td>Baseline renal function required under EUA for pediatric patients</td>
<td></td>
</tr>
<tr>
<td>Bebtelovimab IV</td>
<td>EUA 3/25/22</td>
<td></td>
<td>Monoclonal Antibody (mAb) mAb against spike, blocks viral attachment to host cells</td>
<td>Symptomatic improvement and Day 5 reduction in viral load vs placebo</td>
<td></td>
<td>&gt; 12+ (minimum 40 kg or 88 lb)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Molnupiravir (Lagevrio) Oral</td>
<td>Merck</td>
<td>EUA 12/23/21</td>
<td>Antiviral Nucleoside Analog that inhibits viral replication by viral mutagenesis</td>
<td>30% reduction in hospitalization/deaths</td>
<td></td>
<td>18+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Dose

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Tixagevimab/Cilgavimab (Evusheld), PrEP</th>
<th>Nirmatrelvir/ritonavir (Paxlovid) Oral</th>
<th>Remdesivir (Veklury) IV</th>
<th>Bebtelovimab IV</th>
<th>Molnupiravir (Lagevrio) Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose</strong></td>
<td>300 mg of tixagevimab (100 mg/mL) and 300 mg of cilgavimab (100 mg/mL) via two separate 3.0 mL consecutive intramuscular (IM) injections of each product.</td>
<td>300 mg nirmatrelvir with 100 mg ritonavir Take all 3 tablets PO BID with or without food (although eating with fatty meals enhances absorption)</td>
<td>Adults/Peds 12+ at least 40 Kg: Single loading dose 200mg Day 1 IV, then maintenance daily dose 100mg IV</td>
<td>175 mg/2ml (87.5 mg/ml) administered via IV injection over 30 seconds</td>
<td>800 mg PO q 12 hours (4 capsules per dose)</td>
</tr>
<tr>
<td><strong>How supplied</strong></td>
<td>One carton has Two vials - 150mg/1.5 ml Tixagevimab - 150mg/1.5 ml Cilgavimab</td>
<td>5 daily dose blister cards *renal impairment lower dose packs available</td>
<td>Single Dose Vial 100 mg Remdesivir as lyophilized powder in single dose vial (no reconstituted) 100mg/20ml (5mg/ml) after reconstitution.</td>
<td>Single Dose Vial</td>
<td>Bottle (40 capsules)</td>
</tr>
<tr>
<td><strong>Administration details</strong></td>
<td>Monitor for 1 hour after injection for hypersensitivity</td>
<td>Monitor for 1 hour after injection for hypersensitivity</td>
<td>Monitoring recommended 1 hour after infusion - for hypersensitivity reaction or infusion reaction</td>
<td>Monitoring recommended 1 hour after infusion - for hypersensitivity reaction or infusion reaction</td>
<td>Ok to take with or without food, pills cannot be crushed</td>
</tr>
<tr>
<td><strong>Adverse Events (if from clinical trials, incidence &gt; 1%)</strong></td>
<td>Injection site reactions 1%: one case of anaphylaxis in clinical trial</td>
<td>Dysgeusia (altered taste sensation) 6%, diarrhea 3%, hypertension 1%, myalgia 1%</td>
<td>Nausea 10.8%, Headache 5.7%, Cough 3.6%, diarrhea 3.9%, dyspnea 2.5%, fatigue 3.6%, ageusia 2.9%, anosmia 3.2%, dizziness 1.8%, chills 2.2%</td>
<td>Infusion-related: 0.3%, pruritis 0.3%, rash 0.8%</td>
<td>Diarrhea 2%, nausea 1%, dizziness 1%</td>
</tr>
</tbody>
</table>

### Dosing for Special Population:

- **Pediatric patients at least 12 years or older,** and weighing at least 40 kg: no dosage adjustment
- **Pediatric patients 12+ and at least 40 kg:** no dosage adjustment
- **Pregnancy or Lactation:** No dosage adjustment
- **Renal:** No dosage adjustment
- **Hepatic:** Not specified

### How supplied

- One carton has Two vials
- 150mg/1.5 ml Tixagevimab
- 150mg/1.5 ml Cilgavimab

### Administration details

- Monitor for 1 hour after injection for hypersensitivity
- Ok to take with or without food, but high fat meal increases absorption 15%, pills cannot be crushed
- Reconstitute powder by adding 19 ml sterile water.
- See recommended dilution instructions in package insert.
- See recommended storage/handling instructions in package insert.

### Adverse Events (if from clinical trials, incidence > 1%)

- **Injection site reactions 1%:** one case of anaphylaxis in clinical trial
- **Headache 6%, fatigue 4%, cough 3%, insomnia 1%, dizziness 1%:** Injection site reaction 1%
- **Injection site reaction 1%**
- **Cardiac serious adverse events:** 0.6% vs 2% in Evusheld and placebo groups respectively
- **Dysgeusia (altered taste sensation) 6%, diarrhea 3%, hypertension 1%, myalgia 1%**
- **Nausea 10.8%, Headache 5.7%, Cough 3.6%, diarrhea 3.9%, dyspnea 2.5%, fatigue 3.6%, ageusia 2.9%, anosmia 3.2%, dizziness 1.8%, chills 2.2%**
- **Lab abnormalities:** (10.8%)
<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Tixagevimab/Cilgavimab (Evusheld), PrEP</th>
<th>Nirmatrelvir/ritonavir (Paxlovid) Oral</th>
<th>Remdesivir (Veklury) IV</th>
<th>Bebtelovimab IV</th>
<th>Molnupiravir (Lagevrio) Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Potential Drug-Drug Interactions</strong></td>
<td>Unlikely</td>
<td>Moderate/High- see prescribing information</td>
<td>Low- See prescribing information</td>
<td>unlikely</td>
<td>None identified</td>
</tr>
<tr>
<td><strong>Renal Dose Adjustment</strong></td>
<td>For eGFR 30-60, lower dose advised, not recommended for those with eGFR &lt; 30 ml/min</td>
<td>Not recommended for those with eGFR &lt; 30 ml/min</td>
<td>none</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td><strong>Hepatic Dose Adjustment</strong></td>
<td>Avoid in severe hepatic impairment (Child-Pugh Class C)</td>
<td>None- but should monitor LFT pre and during treatment</td>
<td>none</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Previous severe hypersensitivity reactions, including anaphylaxis to any components of Evusheld</td>
<td>Hypersensitivity to ingredients CYP3A4 drug-drug interactions</td>
<td>Hypersensitivity to Veklury or any of its components</td>
<td>none listed</td>
<td>None listed</td>
</tr>
<tr>
<td><strong>Warnings/drug interactions</strong></td>
<td>Beware of drug interactions, hepatoxicity, HIV-1 drug resistance in patients with HIV-1 infection</td>
<td>Possible hypersensitivity/infusion related reaction. Clinical worsening after SARS-CoV-2 administration</td>
<td>Embryo-fetal toxicity, bone and cartilage toxicity- not recommended for patients &lt; 18 because of potential effects on bone/cartilage growth Not recommended for use during pregnancy. No drug interactions identified to date Hypersensitivity reactions</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Special Populations</strong></td>
<td>Insufficient data in pregnancy or breastfeeding.</td>
<td>No human data on use in pregnancy or breastfeeding</td>
<td>Insufficient human data on use during pregnancy or breastfeeding</td>
<td>Insufficient human data on use during pregnancy or breastfeeding</td>
<td>Not recommended in pregnancy. Not recommended if breastfeeding (has pregnancy surveillance program)</td>
</tr>
<tr>
<td><strong>cost</strong></td>
<td>$200 administration fee</td>
<td>$530 per course</td>
<td>$390-520 per dose, or $2,340-3,120 for 5 day tx (hospital)</td>
<td>$1,250 per dose</td>
<td>$712 per course</td>
</tr>
</tbody>
</table>
### Resources

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Oral Antivirals</th>
<th>FDA</th>
<th>Activity against Omicron</th>
<th>Product Website</th>
<th>FDA Factsheets for HCP</th>
<th>FDA Factsheets for patients, parents, caregivers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tixagevimab/Cilgavimab (Evusheld), PrEP</td>
<td>Nirmatrelvir/ritonavir (Paxlovid Oral)</td>
<td>Remdesivir (Veklury IV)</td>
<td>Bebtelovimab IV</td>
<td>Molnupiravir (Lagevrio Oral)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other variants: See Section 12.4 of <a href="https://www.fda.gov/media/154701/download">https://www.fda.gov/media/154701/download</a></td>
<td>Other variants: See Section 12.4 of <a href="https://www.fda.gov/media/153050/download">https://www.fda.gov/media/153050/download</a></td>
<td>Other Variants- see section 15 of <a href="https://www.fda.gov/media/147566/download">https://www.fda.gov/media/147566/download</a> see section 12.4 of <a href="https://www.gilead.com/-/media/files/pdfs/medicines/COVID-19/veklury/veklury_pi.pdf">https://www.gilead.com/-/media/files/pdfs/medicines/COVID-19/veklury/veklury_pi.pdf</a></td>
<td>Other variants: See Section 12.4 of <a href="https://www.fda.gov/media/156152/download">https://www.fda.gov/media/156152/download</a></td>
<td>Other variants: See Section 12.4 of <a href="https://www.fda.gov/media/155054/download">https://www.fda.gov/media/155054/download</a></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Study showing maintained in vitro potency Molnupiravir and Remdesivir against Omicron Variant: [https://www.biorxiv.org/content/10.1101/2022.01.17.476685v1](https://www.biorxiv.org/content/10.1101/2022.01.17.476685v1)


[https://www.hrsa.gov/CovidUninsuredClaim](https://www.hrsa.gov/CovidUninsuredClaim)