New: Updated COVID-19 Treatment Guidelines

- **August 8, 2022** – Updates posted by the COVID-19 Treatment Guidelines Panel; all recommendations included in the Guidelines are endorsed by a majority of Panel members (see Guidelines Development for additional details on the development process)
- Guidelines are updated in step with the rapid pace and growing volume of information regarding the treatment of COVID-19.
- **What's New in the Guidelines**
  - Special Considerations in People Who Are Immunocompromised
  - Clinical Management of Children
  - Clinical Spectrum of SARS-CoV-2 Infection
  - Prevention of SARS-CoV-2 Infection
  - Therapeutic Management of Nonhospitalized Adults With COVID-19
  - Kinase Inhibitors: Janus Kinase Inhibitors and Bruton's Tyrosine Kinase Inhibitors

Reminder: Paxlovid Access

- **August 1, 2022** - In our continued efforts to increase oral antiviral dispensing in vulnerable areas, a new initiative was launched to pre-position Paxlovid in areas of high social vulnerability
  - Goal is to pre-position Paxlovid at provider sites (EDs, physician offices, clinics/urgent cares) in areas of the country that are most vulnerable to COVID-19
  - Emails were sent to nearly 9000 providers to invite a one-time distribution request of 20 courses of Paxlovid
    - Targeted outreach to sites in counties/parishes with high SVI and low dispensing rates of oral antivirals
    - ASPR regional teams will be sharing targeted counties with jurisdictions
- Effort intended to make product more readily available to quickly treat patients in vulnerable communities where they are engaging providers
- Paxlovid supply used for this effort is separate from jurisdictional thresholds

Paxlovid EUA Update

- **August 5, 2022** – additional post-authorization requirements for Pfizer to conduct:
  - A clinical trial in patients with "COVID-19 rebound"
    - To evaluate a subsequent 5-day treatment in patients with rebound
  - A clinical trial evaluating different durations of treatment in immunocompromised patients with mild-to-moderate COVID-19
    - To evaluate safety and efficacy for either 5, 10, or 15 days of treatment

Paxlovid Wrong Dosing Reports

As a reminder, PAXLOVID contains two different drugs (nirmatrelvir tablets and ritonavir tablets) that are co-packaged in a daily blister card for oral use.

PAXLOVID is available in the following two packaging configurations.

1. **300 mg; 100 mg Dose Pack:** This packaging configuration should be used for patients with normal renal function or mild renal impairment (eGFR* ≥60 ml/min).

   The 300 mg; 100 mg Dose Pack is a carton containing 5 daily blister cards. Each blister card contains a daily morning dose and evening dose, with each dose consisting of **300 mg nirmatrelvir** (two oval, pink 150 mg tablets) and **100 mg ritonavir** (one white to off-white film-coated 100 mg tablet).

2. **150 mg; 100 mg Dose Pack:** This packaging configuration should be used for patients with **moderate renal impairment** (eGFR ≥30 to <60 mL/min).

   The 150 mg; 100 mg Dose Pack is a carton containing 5 daily blister cards. Each blister card contains a daily morning dose and evening dose, with each dose consisting of **150 mg nirmatrelvir** (one oval, pink 150 mg tablet) and **100 mg ritonavir** (one white to off-white film-coated 100 mg tablet).

PAXLOVID is not recommended in patients with severe renal impairment (<30 mL/min) as the appropriate dose has not been determined.

https://www.fda.gov/media/155071/download

Reminder: CDC Health Advisory COVID-19 Rebound After Paxlovid Treatment

The Centers for Disease Control and Prevention (CDC) is issuing this Health Alert Network (HAN) Health Advisory to update healthcare providers, public health departments, and the public on the potential for recurrence of COVID-19 or "COVID-19 rebound."

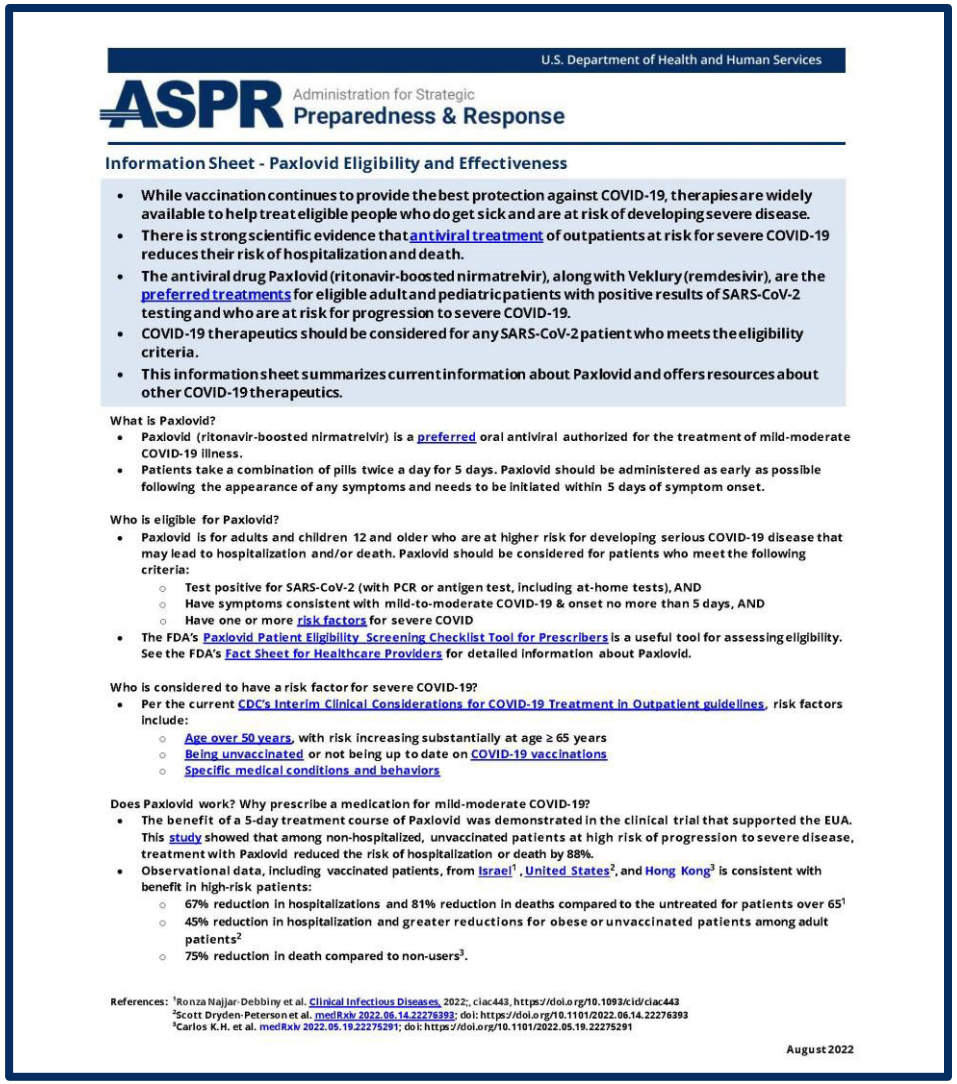
- **Paxlovid continues to be recommended for early-stage treatment of mild to moderate COVID-19 among persons at high risk for progression to severe disease**.
- Paxlovid treatment helps prevent hospitalization and death due to COVID-19. COVID-19 rebound has been reported to occur between 2 and 8 days 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**.
- Limited information currently available from case reports suggests that persons treated with Paxlovid who experience COVID-19 rebound have had mild illness; there are no reports of severe disease.

COVID-19 Rebound After Paxlovid Treatment (cdc.gov)

New Paxlovid Resource!

Information Sheet for Providers

- This information sheet summarizes current information about **Paxlovid** and offers resources about other COVID-19 therapeutics.
- There is strong scientific evidence that antiviral treatment of outpatients at risk for severe COVID-19 reduces their risk of hospitalization and death.
- The antiviral drug **Paxlovid (ritonavir-boosted nirmatrelvir)**, along with Veklury (remdesivir), are the preferred treatments for eligible adult and pediatric patients with positive results of SARS-CoV-2 testing and who are at risk for progression to severe COVID-19.
- COVID-19 therapeutics should be considered for any SARS-CoV-2 patient who meets the eligibility criteria.



U.S. Department of Health and Human Services

ASPR Administration for Strategic Preparedness & Response

Information Sheet - Paxlovid Eligibility and Effectiveness

- While vaccination continues to provide the best protection against COVID-19, therapies are widely available to help treat eligible people who do get sick and are at risk of developing severe disease.
- There is strong scientific evidence that antiviral treatment of outpatients at risk for severe COVID-19 reduces their risk of hospitalization and death.
- The antiviral drug Paxlovid (ritonavir-boosted nirmatrelvir), along with Veklury (remdesivir), are the preferred treatments for eligible adult and pediatric patients with positive results of SARS-CoV-2 testing and who are at risk for progression to severe COVID-19.
- COVID-19 therapeutics should be considered for any SARS-CoV-2 patient who meets the eligibility criteria.
- This information sheet summarizes current information about Paxlovid and offers resources about other COVID-19 therapeutics.

What is Paxlovid?

- Paxlovid (ritonavir-boosted nirmatrelvir) is a preferred oral antiviral authorized for the treatment of mild-moderate COVID-19 illness.
- Patients take a combination of pills twice a day for 5 days. Paxlovid should be administered as early as possible following the appearance of any symptoms and needs to be initiated within 5 days of symptom onset.

Who is eligible for Paxlovid?

- Paxlovid is for adults and children 12 and older who are at higher risk for developing serious COVID-19 disease that may lead to hospitalization and/or death. Paxlovid should be considered for patients who meet the following criteria:
  - Test positive for SARS-CoV-2 (with PCR or antigen test, including at-home tests), AND
  - Have symptoms consistent with mild-to-moderate COVID-19 & onset no more than 5 days, AND
  - Have one or more risk factors for severe COVID
- The FDA's Paxlovid Patient Eligibility Screening Checklist Tool for Prescribers is a useful tool for assessing eligibility. See the FDA's Fact Sheet for Healthcare Providers for detailed information about Paxlovid.

Who is considered to have a risk factor for severe COVID-19?

- Per the current CDC's Interim Clinical Considerations for COVID-19 Treatment in Outpatient guidelines, risk factors include:
  - Age over 50 years, with risk increasing substantially at age ≥ 65 years
  - Being unvaccinated or not being up to date on COVID-19 vaccinations
  - Specific medical conditions and behaviors

Does Paxlovid work? Why prescribe a medication for mild-moderate COVID-19?

- The benefit of a 5-day treatment course of Paxlovid was demonstrated in the clinical trial that supported the EUA. This study showed that among non-hospitalized, unvaccinated patients at high risk of progression to severe disease, treatment with Paxlovid reduced the risk of hospitalization or death by 88%.
- Observational data, including vaccinated patients, from Israel[1], United States[2], and Hong Kong[3] is consistent with benefit in high-risk patients:
  - 67% reduction in hospitalizations and 81% reduction in deaths compared to the untreated for patients over 65[1]
  - 45% reduction in hospitalization and greater reductions for obese or unvaccinated patients among adult patients[2]
  - 75% reduction in death compared to non-users[3].

References: [1]Ronza Najjar-Debbiny et al. Clinical Infectious Diseases, 2022;; ciac443, https://doi.org/10.1093/cid/ciac443
[2]Scott Dryden-Peterson et al. medRxiv 2022.06.14.22276393; doi: https://doi.org/10.1101/2022.06.14.22276393
[3]Carlos K.H. et al. medRxiv 2022.05.19.22275291; doi: https://doi.org/10.1101/2022.05.19.22275291

August 2022

Reminder: Paxlovid Shelf-Life Extension

- Upon EUA, Paxlovid was issued a 12-month product shelf-life
- Four lots of Paxlovid manufactured prior to the EUA issuance were labeled with a 9-month expiry
- FDA authorized extended expiration dates for these lots to reflect the 12-month product shelf-life (see Table), when stored according to the storage conditions detailed in the authorized Fact Sheet for Health Care Providers and the Letter of Authorization for Emergency Use Authorization (EUA) 105 for Paxlovid.
- This information is now posted on the FDA's website.

Lot#	Extended Expiry Date
FL4516 FL4517 FR7229	The initial 3 lots were extended from 7/31 to 10/31/22.
FR9088	4th lot was extended from 8/31 to 11/30/22

Evusheld Remains Readily Available for Use!

- Call line for Evusheld product and ordering information: **1-833-EVUSHLD** (833-388-7453)

- Additional pathway established for **small volume ordering**:
  - For individual providers seeking small quantities of product (1-3 patient courses)
  - OrderEvusheld.com

- Evusheld is **available at some Federal Pharmacy Partner locations**:
  - Albertsons, including Albertsons, Acme, Jewel-Osco, Pavilions, Randalls, Safeway, Star Market, and Vons
  - CPESN
  - Hy-Vee, including Amber Specialty Pharmacy
  - Managed Healthcare Associates (MHA), including Thrifty White
  - Good Neighbor Pharmacy (select locations)

- Locator tool updates: Central Partners are encouraged to **update information for Evusheld providers** so that accurate information is reflected in the COVID-19 Therapeutics Locator tool.

Evusheld Reporting

- Evusheld reporting on inventory and administration is required, just as it is for all therapeutic products received from the federal government
  - Reporting is required in HPOP, at a minimum of twice per week

- To stay consistent with historical reporting, we ask that you continue to report Evusheld inventory and administrations per 300mg units (1 carton)
  - Thus, **one patient dose with 600mg should be reported as 2 administrations**!!
  - Administrations reporting should always be an even number
  - 2 patients dosed ➔ report in HPOP as "4" (2 patients, 4 cartons, 8 vials)
  - 6 patients dosed ➔ report in HPOP as "12" (6 patients, 12 cartons, 24 vials)

- If you have been reporting differently (as 600mg units), please reach out. We will work with you to correct.

Transition of Bebtelovimab to Commercial Market

- **August 15:** last USG distribution at full threshold

- **August 22:** USG distribution at lower threshold (likely ~15,000 doses; dependent on current ordering rates)

- **August 29**: HPOP ordering for bebtelovimab will close temporarily for one week
  - One week pause will allow final accounting of inventory; please update all inventory and utilization numbers
  - **Any unordered doses will come back into the USG supply** to be used for a final allocation the week of Sept 6

- **September 6:** USG allocates remaining supply of bebtelovimab to jurisdictions based on population
  - Jurisdictions are expected to use this supply to cover under and uninsured patients
  - Ordering against this final allocation will be open for an extended period of time; at least 2 weeks lead time will be given before ordering closes

Transition of Bebtelovimab to Commercial Market

- Bebtelovimab will be commercially available for purchase as USG supply ends
  - Bebtelovimab will be commercially available for purchase starting **the week of Aug 15th**
  - States/territories and providers will be eligible to purchase directly through AmerisourceBergen
  - FDA Letter of Authorization was updated on August 5th allowing Lilly to start commercial distribution of bebtelovimab
  - As commercial product becomes available, USG supply should be used to fill in gaps for the underinsured and uninsured within your jurisdictions

- HPOP reporting of all USG supply is still mandatory twice a week until all supply is reconciled (all doses delivered are accounted for)
  - USG is working to determine how to capture data for commercially purchased supply

- There can be no cost of drug payment for USG distributed product
  - Commercially purchased supply will have unique batch numbers relative to USG supply

Current Medicare Payment Structure for Bebtelovimab

- Payment Allowances and Effective Dates for COVID-19 Monoclonal Antibodies and their Administration During the Public Health Emergency
- CMS updated COVID-19 Toolkit for Healthcare Providers and Medicare COVID-19 Monoclonal Antibodies Toolkit
- Medicare product payment amount of $2394.00 when sites purchase the product
- No product payment for bebtelovimab received for free from the USG

HCPCS Code	HCPCS Short Descriptor	Labeler Name	National Payment Allowance Effective for Claims with DOS on or after 05/6/2021	National Payment Allowance Effective for Claims with DOS through 05/5/2021	Effective Dates
Q0222	Bebtelovimab 175 mg	Eli Lilly	$2394 [1] [1a]	Code not active during this time period	02/11/2022 - TBD
M0222	Bebtelovimab injection	Eli Lilly	$350.50[3]	Code not active during this time period	02/11/2022 - TBD
M0223	Bebtelovimab injection (home)	Eli Lilly	$550.50[3]	Code not active during this time period	02/11/2022 - TBD

[1] Providers shouldn't bill for the product if they received it for free through the USG-purchased inventory.
[1a] Payment rate effective for dates of service on or after August 15, 2022. Providers should only bill Medicare for commercially-purchased products.
[3] These rates will be geographically adjusted for many providers. For providers and suppliers with payments that are geographically adjusted by the methodology used by the Medicare Physician Fee Schedule (MPFS), files with the geographically adjusted payment rates for monoclonal antibody administration are included in the "Additional Resources" section below. Certain settings utilize other payment methodologies, such as payment based on reasonable costs

AmerisourceBergen

Bebtelovimab Commercial Access

Existing AmerisourceBergen Accounts:

- Immediate access to Bebtelovimab will be granted to all existing AmerisourceBergen accounts
  - Excluding retail pharmacies

Sites Without an AmerisourceBergen Account

- Sites will need to register for an AmerisourceBergen account
  - Contact service@asdhealthcare.com
  - AmerisourceBergen will sell to licensed and approved customers regardless of current HPOP participation

Ordering Details

- Please note that to limit the potential for overstocking, **no returns will be accepted for bebtelovimab**
- There will be a maximum order limit of 270 doses per week per provider site, there is no minimum order limit
- Exceptions, including for states, for weekly dose quantities beyond 270 will be evaluated on a case-by-case basis

Additional Support

- For any questions regarding access to Bebtelovimab
  - Contact c19therapies@amerisourcebergen.com

New! Update to Fact Sheet: Lagevrio (molnupiravir)

- **August 5, 2022:** FDA updated Lagevrio Fact Sheet
- Updated Section - Microbiology (Section 12.4)
  - Addition of viral RNA rebound
  - Viral RNA Rebound Post-treatment increases in SARS-CoV-2 RNA shedding levels (i.e., viral RNA rebound) in nasopharyngeal samples were observed on Day 10, Day 15, and/or Day 29 in a subset of LAGEVRIO and placebo recipients in the Phase 3 MOVe-OUT trial. **Approximately 1% of both LAGEVRIO and placebo recipients had evidence of recurrent COVID-19 symptoms coinciding with a rebound in viral RNA** levels in nasopharyngeal samples. Post-treatment viral RNA rebound **was not associated with the primary clinical outcome of hospitalization or death** through Day 29 following the single 5-day course of LAGEVRIO treatment. Post-treatment viral RNA rebound **also was not associated with the detection of cell culture infectious virus** in nasopharyngeal swab samples

NIH Guidelines for Therapeutic Management of Non-Hospitalized Adults with COVID-19

Updated August 8, 2022

Patient Disposition	Panel's Recommendations
Does Not Require Hospitalization or Supplemental Oxygen	**For All Patients:** • All patients should be offered symptomatic management **(AIII)**. • The Panel **recommends against** the use of **dexamethasone**[a] or **other systemic corticosteroids** in the absence of another indication **(AIIb)**. **For Patients Who Are at High Risk of Progressing to Severe COVID-19**[b] *Preferred therapies. Listed in order of preference:* • **Ritonavir-boosted nirmatrelvir (Paxlovid)**[c,d] **(AIIa)** • **Remdesivir**[d,e] **(BIIa)** *Alternative therapies. For use ONLY when neither of the preferred therapies are available, feasible to use, or clinically appropriate. Listed in alphabetical order:* • **Bebtelovimab**[f] **(CIII)** • **Molnupiravir**[d,g] **(CIIa)**
Discharged from Hospital Inpatient Setting in Stable Condition and Does Not Require Supplemental Oxygen	The Panel **recommends against** continuing the use of **remdesivir (AIIa)**, **dexamethasonea (AIIa)**, or **baricitinib (AIIa)** after hospital discharge.
Discharged from Hospital Inpatient Setting and Requires Supplemental Oxygen *For those who are stable enough for discharge but still require oxygen*[h]	There is insufficient evidence to recommend either for or against the continued use of remdesivir or dexamethasone.
Discharged from ED Despite New or Increasing Need for Supplemental Oxygen *When hospital resources are limited, inpatient admission is not possible, and close follow-up is ensured*[i]	The Panel recommends using **dexamethasone** 6 mg PO once daily for the duration of supplemental oxygen (dexamethasone use **should not exceed** 10 days) with careful monitoring for AEs **(BIII)**.
	Because remdesivir is recommended for patients with similar oxygen needs who are hospitalized,[j] clinicians may consider using it in this setting. As remdesivir requires IV infusions for up to 5 consecutive days, there may be logistical constraints to administering remdesivir in the outpatient setting.
Rating of Recommendations: A = Strong; B = Moderate; C = Weak **Rating of Evidence:** I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion	

NIH Therapeutic Management of Non-hospitalized Adults With COVID-19