What Clinicians Need to Know About the New Oral Antiviral Medications for COVID-19

Clinician Outreach and Communication Activity (COCA) Call

Wednesday, January 12, 2022

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  - Click on the “Q&A” button
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- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.

Today's Presenters

- **Lauri Hicks, DO**
  CAPT, U.S. Public Health Service
  Chief Medical Officer, COVID-19 Response
  Director, Office of Antibiotic Stewardship
  Division of Healthcare Quality Promotion
  Centers for Disease Control and Prevention

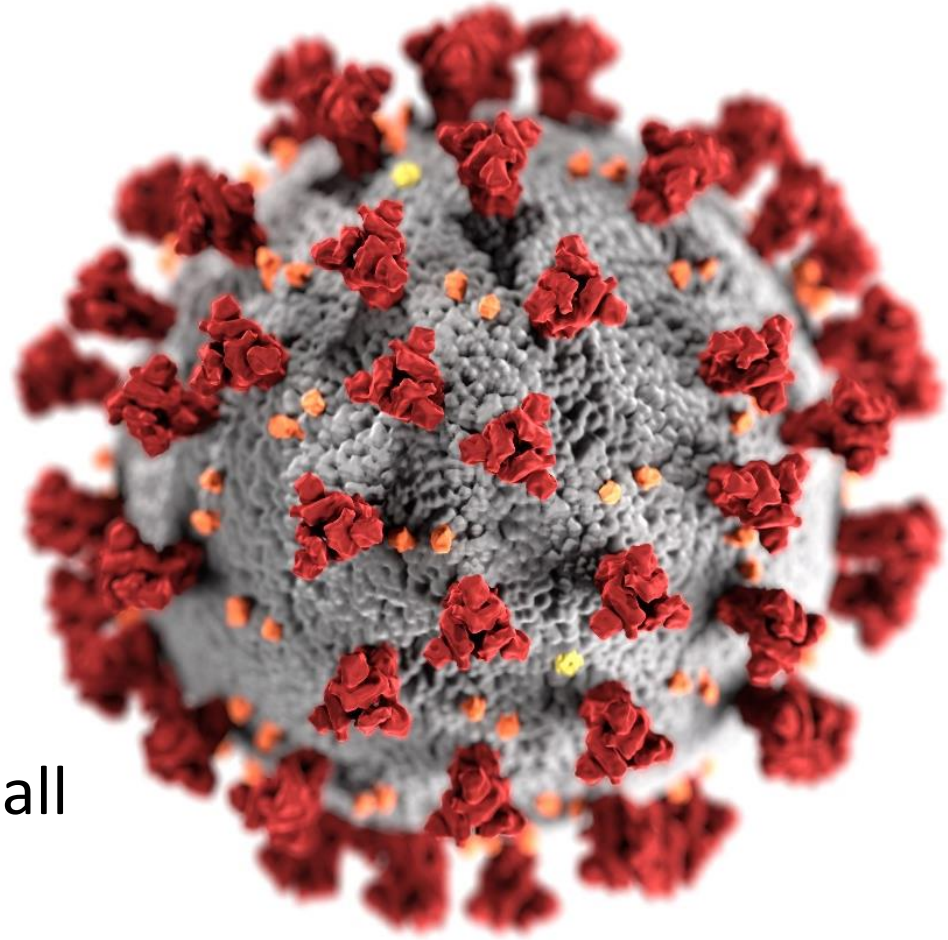
- **Colin Shepard, MD**
  CDC Liaison to the Assistant Secretary for Preparedness and Response (ASPR)
  Center for Preparedness and Response
  Centers for Disease Control and Prevention

- **Stephanie Troy, MD**
  Senior Medical Officer
  Division of Antivirals
  Center for Drug Evaluation and Research
  U.S. Food and Drug Administration

- **Aimee Hodowanec, MD**
  Senior Medical Officer
  Division of Antivirals
  Center for Drug Evaluation and Research
  U.S. Food and Drug Administration

- **Alice K. Pau, PharmD**
  Executive Secretary, NIH COVID-19 Treatment Guidelines Panel
  Staff Scientist (Clinical)
  Clinical Pharmacy Specialist
  Division of Clinical Research
  National Institute of Allergy & Infectious Diseases
  National Institutes of Health

What Clinicians Need to Know About the New Oral Antiviral Medications for COVID-19



January 12, 2022

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Update on the Omicron Variant

CAPT Lauri Hicks, DO
Chief Medical Officer
CDC COVID-19 Response
Centers for Disease Control and Prevention

January 12, 2022
Clinician Outreach and Communication Activity Call

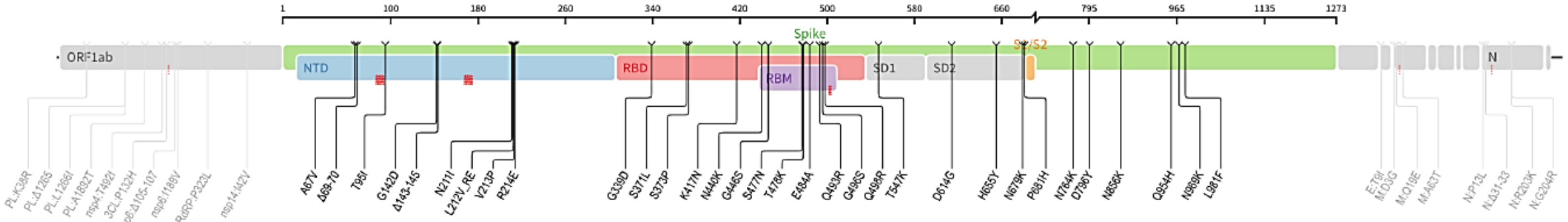
What are the key questions we're trying to answer?

- How **transmissible** is Omicron?
- How **severe** is Omicron compared to other variants?
- How well do vaccines and prior infection **protect** against infection, transmission, clinical disease, and death due to Omicron?
- What therapeutics are available to **treat** Omicron infections?

https://www.who.int/publications/m/item/enhancing-readiness-for-omicron-(b.1.1.529)-technical-brief-and-priority-actions-for-member-states

Transmissibility

B.1.1.529 Lineage Mutation Profile



- Unusually large number of mutations across the SARS-CoV-2 genome
  - **45-52 amino acid changes, deletions, or insertions: 15 within receptor binding domain**
- Some mutations well characterized with known phenotypic impact might allow Omicron to:
  - Be more infectious and transmissible than the Delta variant
  - Resist neutralization by vaccine- and infection-induced antibodies
  - Resist treatment with therapeutics
  - Evade innate immunity

NGS-SA Network for Genomic Surveillance in South Africa

COVID-19 cases rapidly increased since the first U.S. Omicron case was reported on December 1, 2021

January 22, 2020* - January 05, 2022

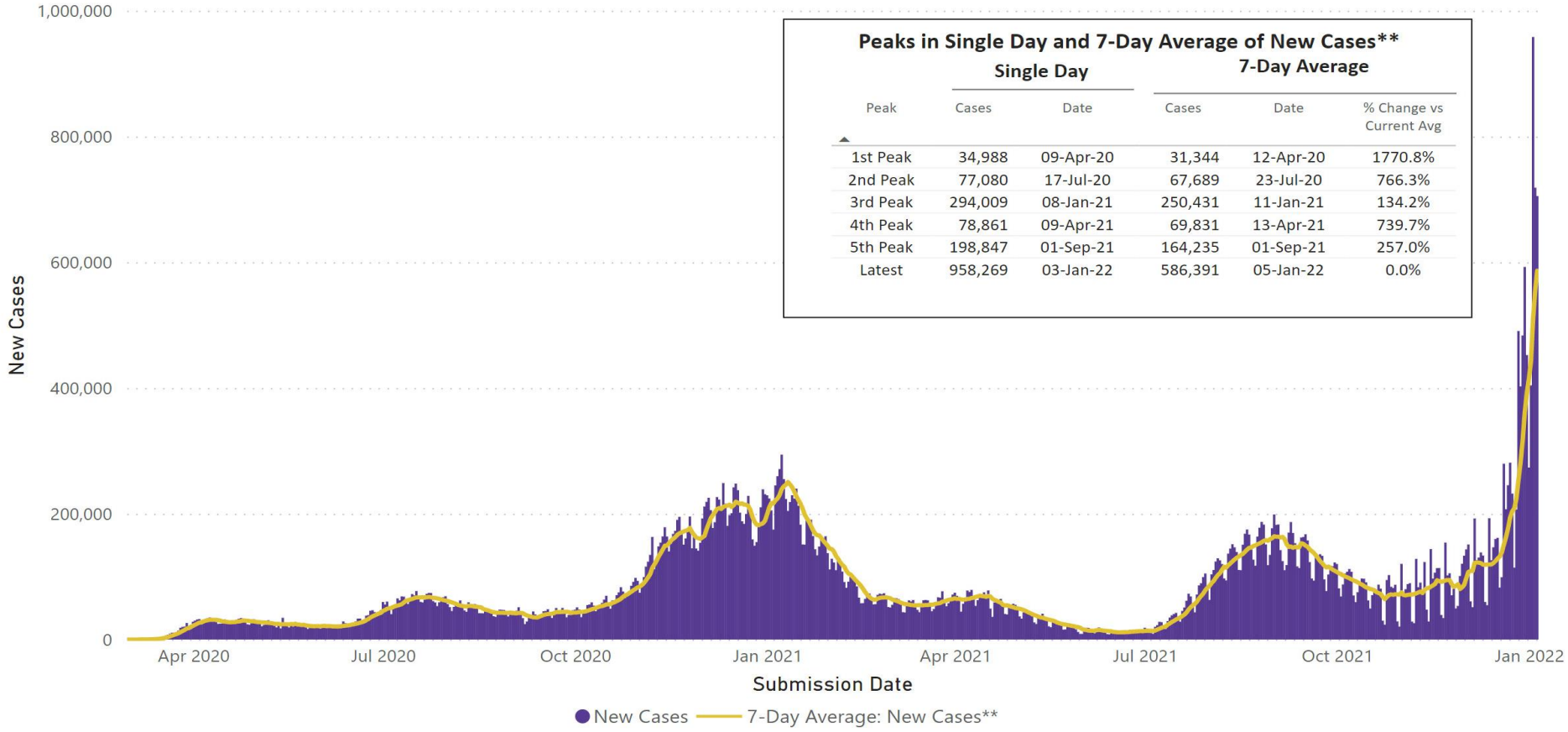
57,898,239
Total Cases Reported

705,264
New Cases Reported**

586,391
Current 7-Day Average**
Dec 30, 2021 - Jan 05, 2022

315,851
Prior 7-Day Average**
Dec 23, 2021 - Dec 29, 2021

85.7%
Change in 7-Day Average



Peaks in Single Day and 7-Day Average of New Cases**

Peak	Single Day Cases	Single Day Date	7-Day Average Cases	7-Day Average Date	% Change vs Current Avg
1st Peak	34,988	09-Apr-20	31,344	12-Apr-20	1770.8%
2nd Peak	77,080	17-Jul-20	67,689	23-Jul-20	766.3%
3rd Peak	294,009	08-Jan-21	250,431	11-Jan-21	134.2%
4th Peak	78,861	09-Apr-21	69,831	13-Apr-21	739.7%
5th Peak	198,847	01-Sep-21	164,235	01-Sep-21	257.0%
Latest	958,269	03-Jan-22	586,391	05-Jan-22	0.0%

*Graph displays data for Mar 01, 2020, to date. The totals include cases reported since Jan 22, 2020.

** The histogram, total of new cases in the last 24 hours, and 7-day averages do not include historical cases retroactively that are not yet attributed to the correct date of report. Of 352,811 historical cases reported retroactively, none were reported on the most recent submission date; 134 in the current week; and 621 in the prior week.

https://covid.cdc.gov/covid-data-tracker/#trends

Data suggest higher household transmissibility of Omicron compared with Delta among vaccinated persons (Denmark, 2021)

	Omicron households (N=2225)		Delta households (N=9712)	
Vaccine Status	**2° attack rate for Omicron (# 2° cases)**	**Odds ratio for Omicron transmissibility (95% CI)**	**2° attack rate for Delta (# 2° cases)**	**Odds ratio for Delta transmissibility (95% CI)**
Unvaccinated	29% (340)	1.04 (0.87-1.24)	28% (2044)	2.31 (2.09-2.55)
Fully vaccinated	32% (1057)	ref	19% (2714)	ref
Booster-vaccinated	25% (77)	0.54 (0.40-0.71)	11% (165)	0.38 (0.32-0.46)

SARS-CoV-2 Omicron VOC Transmission in Danish Households: https://www.medrxiv.org/content/10.1101/2021.12.27.21268278v1.full.pdf

Severity

U.S. hospitalizations with confirmed COVID-19 are surpassing peaks from last winter

3,773,704
Total New Admissions
Aug 01, 2020 – Jan 04, 2022

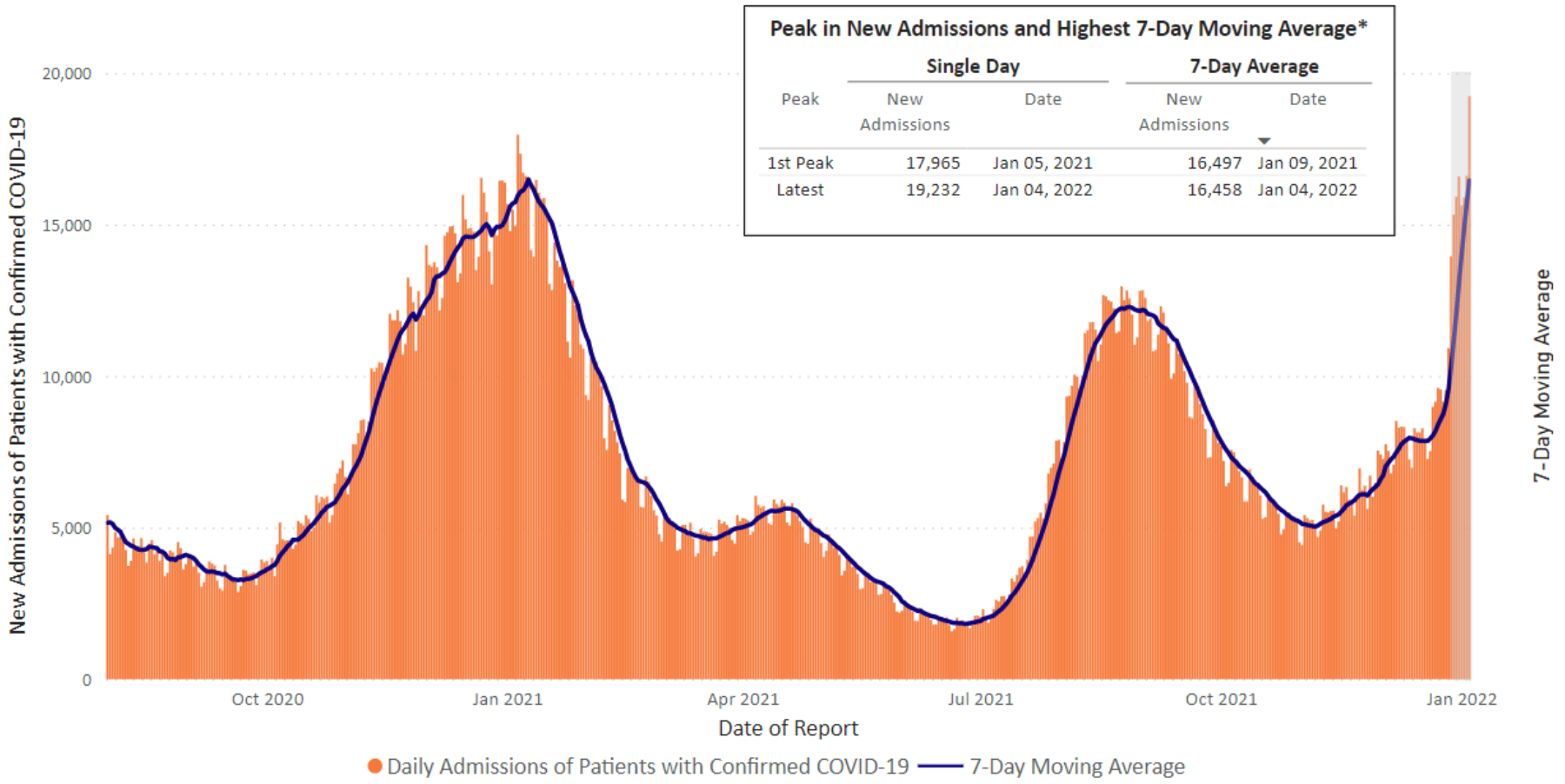
19,232
New Admissions
Jan 04, 2022

16,458
Current 7-Day Average
Dec 29, 2021 – Jan 04, 2022

10,271
Prior 7-Day Average
Dec 22, 2021 – Dec 28, 2021

+60.2%
Change in 7-Day Average

-0.2%
Change Since Peak 7-Day Average



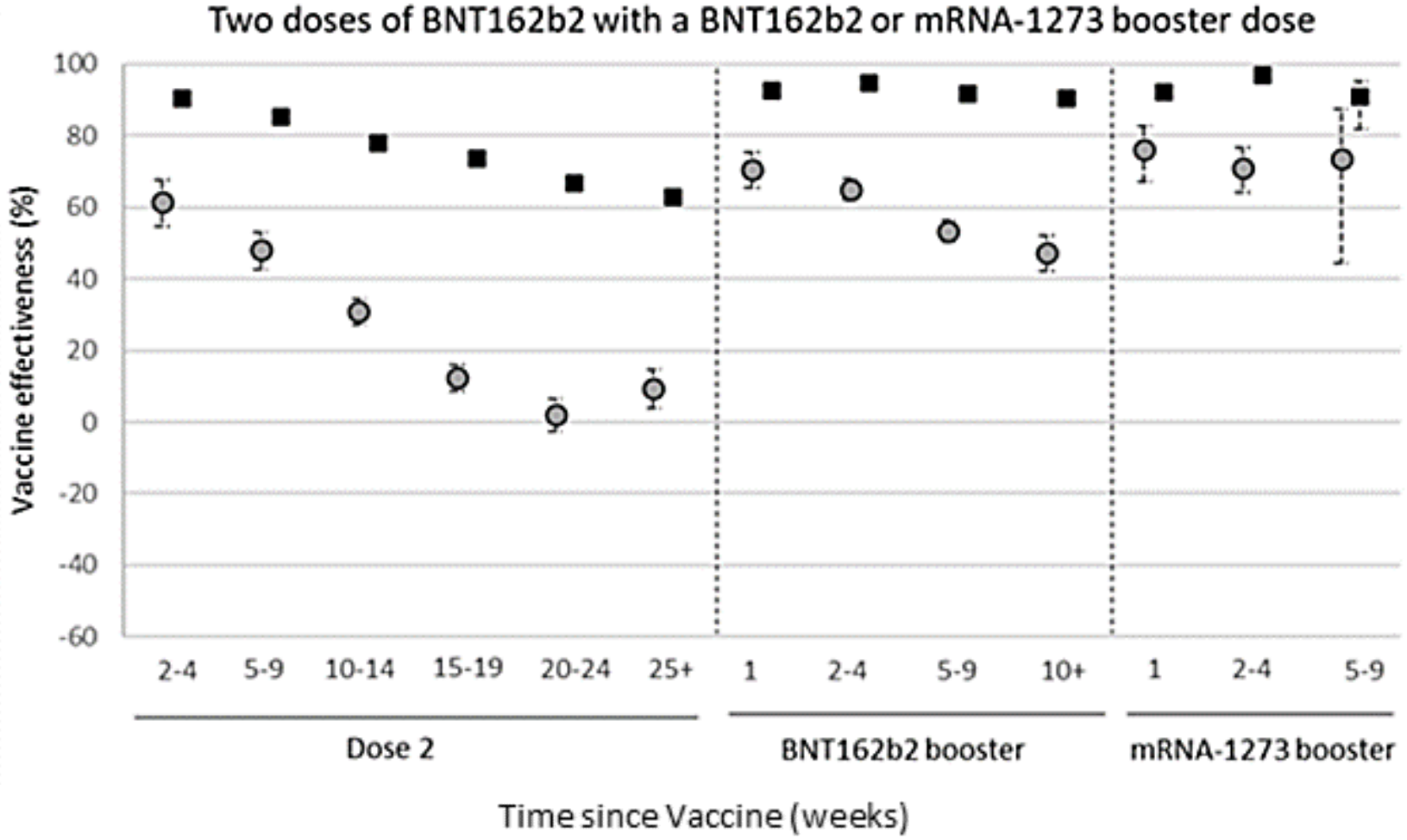
https://covid.cdc.gov/covid-data-tracker/#new-hospital-admissions

Vaccine Effectiveness

Neutralization of the Omicron variant is reduced compared with ancestral and Delta strains

Sera from persons with different vaccination and infection scenarios	Time of collection after last vaccine dose	Neutralization of Omicron and range reduction compared with ancestral and Delta strains	References
Infection-naïve, primary mRNA vaccine series	0.5–6 months	Undetectable to 11–127x lower for Omicron	Wilhelm et al https://www.medrxiv.org/content/10.1101/2021.12.07.21267432v1.full.pdfCele et al https://www.ahri.org/wp-content/uploads/2021/12/MEDRXIV-2021-267417v1-Sigal.pdf Denjnirattisai et al https://www.medrxiv.org/content/10.1101/2021.12.10.21267534v1 Aggarwal et al https://www.medrxiv.org/content/10.1101/2021.12.14.21267772v1.full.pdf Zeng et al https://www.biorxiv.org/content/10.1101/2021.12.16.472934v1 Lu et al https://pubmed.ncbi.nlm.nih.gov/34915551/ Edara et al https://www.biorxiv.org/content/10.1101/2021.12.20.473557v1.full.pdf Schmidt et al https://www.nejm.org/doi/full/10.1056/NEJMc2119641?query=RP Basile et al https://www.biorxiv.org/content/10.1101/2021.12.12.472252v1.full.pdf Planas et al https://www.biorxiv.org/content/10.1101/2021.12.14.472630v1.full.pdf Rossler et al https://www.medrxiv.org/content/10.1101/2021.12.08.21267491v1.full
Infection-naïve, primary mRNA vaccine series + booster (homologous or heterologous)	0.5–3 months	Increased compared with primary series alone but 3–37x lower for Omicron	Basile et al https://www.biorxiv.org/content/10.1101/2021.12.12.472252v1.full.pdf Planas et al https://www.biorxiv.org/content/10.1101/2021.12.14.472630v1.full.pdf
Previous infection and vaccination (1 or 2 doses of mRNA vaccine)	1–6 months	Increased compared with infection or vaccination alone but 18–44x lower for Omicron	Rossler et al https://www.medrxiv.org/content/10.1101/2021.12.08.21267491v1.full

Pfizer mRNA vaccine effectiveness (VE) is lower for symptomatic infection due to Omicron compared to Delta



Delta

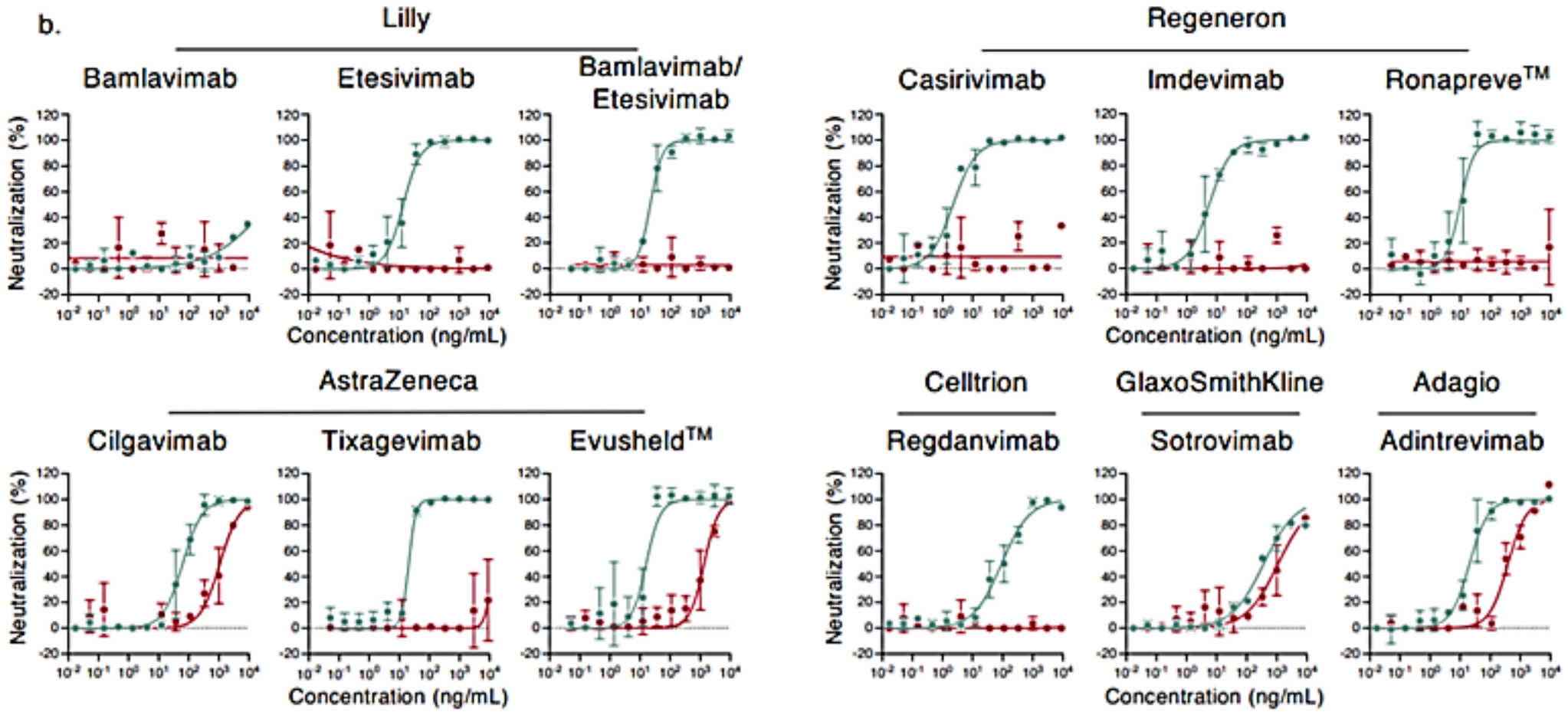
Omicron

- **Post 2-dose**: increased waning immunity for Omicron (~15%) vs. Delta (~60%) at 25+ weeks post 2nd dose
- **Booster**: ~65% VE against Omicron 2 weeks; decreases to 45% at 10+ weeks

SARS-CoV-2 variants of concern and variants under investigation: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1043807/technical-briefing-33.pdf

Therapeutics

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



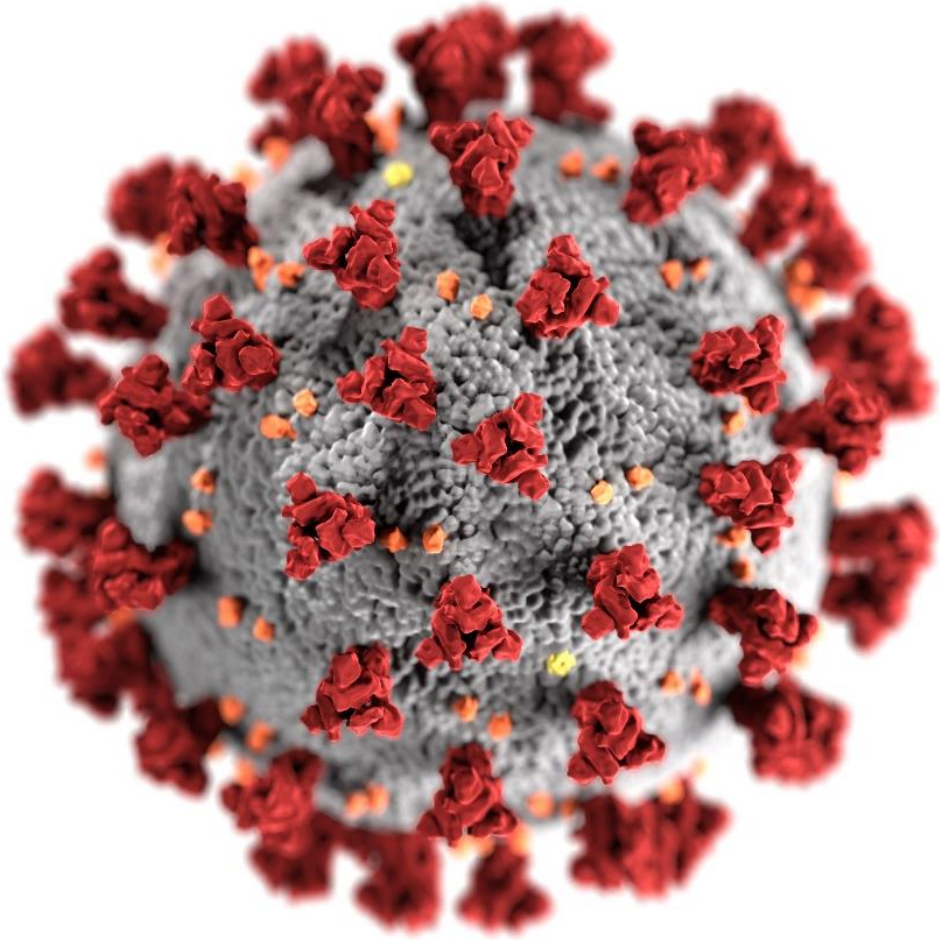
Considerable escape of SARS-CoV-2 variant Omicron to antibody neutralization: https://www.biorxiv.org/content/10.1101/2021.12.14.472630v1.full.pdf

Summary

- Accumulating evidence suggests that the Omicron variant is more transmissible but causes less severe disease.
- Currently authorized vaccines offer less protection against infection due to Omicron compared to ancestral strains and previous variants but still provide benefit—important to increase uptake of primary vaccination and boosters in eligible populations to optimize protection.
- Susceptibility to monoclonal antibodies appears to be lower for Omicron compared to Delta; sotrovimab is likely effective.

Disclaimer

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC).



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Distribution of Oral Antivirals for COVID-19 – Update from ASPR

Colin Shepard, MD

Medical Officer

U.S. Department of Health and Human Services (HHS)

CDC Liaison to the Office of the Assistant Secretary for Preparedness and Response, HHS

January 12, 2022

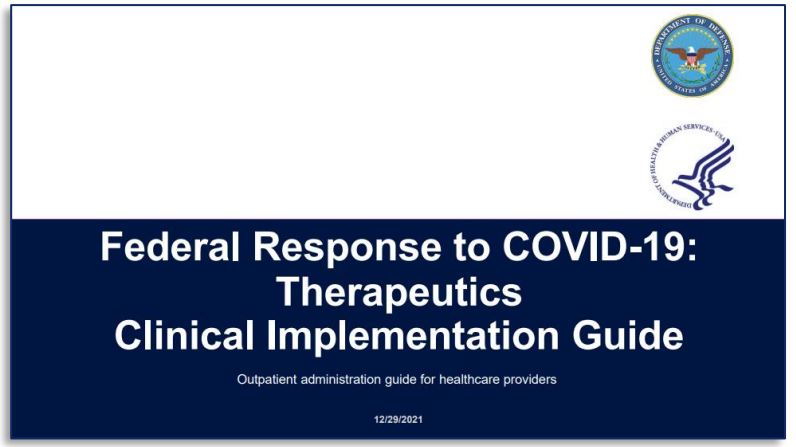
Unclassified/For Public Use

These medications are not a substitute for vaccination.

Clinical Implementation Guide

Federal Response to COVID-19: Therapeutics Clinical Implementation Guide

- Updated periodically with EUA changes
- More information
  - COVID-19 Therapeutics: PHE.gov/COVIDTherapeutics
  - Side-by-Side Overview of Outpatient Therapies Authorized for Treatment of Mild-Moderate COVID-19: https://www.phe.gov/emergency/events/COVID19/therapeutics/Pages/Side-by-Side-Overview-of-mAbs-Treatment.aspx



Please contact **COVID19Therapeutics@hhs.gov** with any questions.

Weekly Stakeholder Engagements

- **Office Call: Discussion with FRPTP Participants (Pharmacy Group)**
  - Tuesdays (12:00–12:30PM EST)
- **Office Call Sessions: HHS/ASPR Distribution and Administration of COVID-19 Therapeutics—open to all with equity in the process**
  - Tuesdays and Thursdays (2:00–2:30PM EST)
- **Stakeholder Call: State, Local, Tribal, and Territorial Health Officials**
  - Wednesdays (2:00–3:00PM EST)
- **Stakeholder Call: National Healthcare and Medical Orgs and Associations**
  - Wednesdays (3:15–4:15PM EST)
- **Federal COVID Response: Therapeutics 210 Webinar**
  - For new administration sites, health officials: Every other Friday (12:00–1:00PM EST) https://hhsasproea.zoomgov.com/j/1617536991?pwd=NjFMcnJOUENuSFhtRFFtaWltejYzZz09

Please email COVID19Therapeutics@hhs.gov to request Zoom links for these calls.

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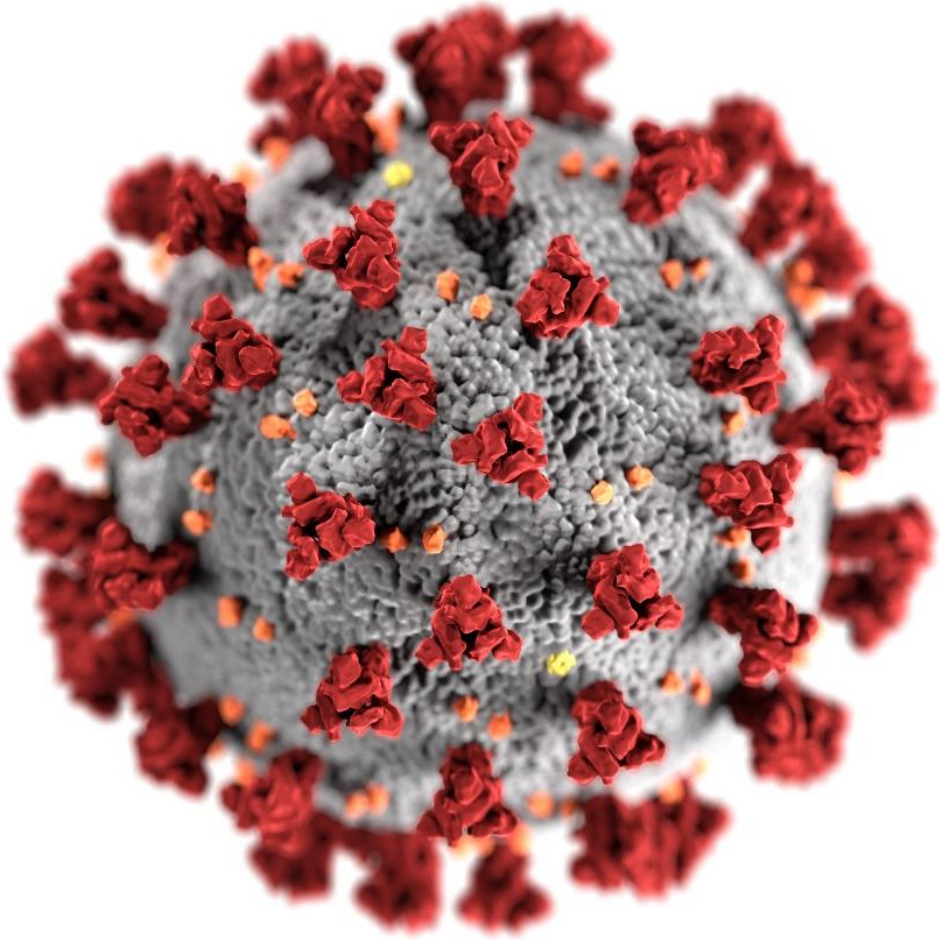

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Paxlovid™ Emergency Use Authorization for COVID-19: An Overview for Clinicians

Stephanie Troy, MD
Senior Medical Officer, Division of Antivirals
Center for Drug Evaluation and Research
US Food and Drug Administration

CDC COCA Call

January 12, 2022

Content

- What is Paxlovid™?
- How Paxlovid™ is Dosed/Supplied
- Paxlovid™'s Authorized Use and Limitations of Use
- Data Supporting the Emergency Use Authorization
- What Clinicians Need to Know:
  - Drug Interactions
  - Specific Populations
- Summary and Useful Links

What is Paxlovid™?

- Nirmatrelvir + Ritonavir
  - Nirmatrelvir is a SARS-CoV-2 main protease inhibitor (aka Mpro, 3CLpro, or nsp5 protease inhibitor)
  - Ritonavir is a CYP3A inhibitor included to increase nirmatrelvir plasma levels
    - Ritonavir alone has no activity against SARS-CoV-2
    - Ritonavir at higher doses was previously used as an HIV-1 protease inhibitor

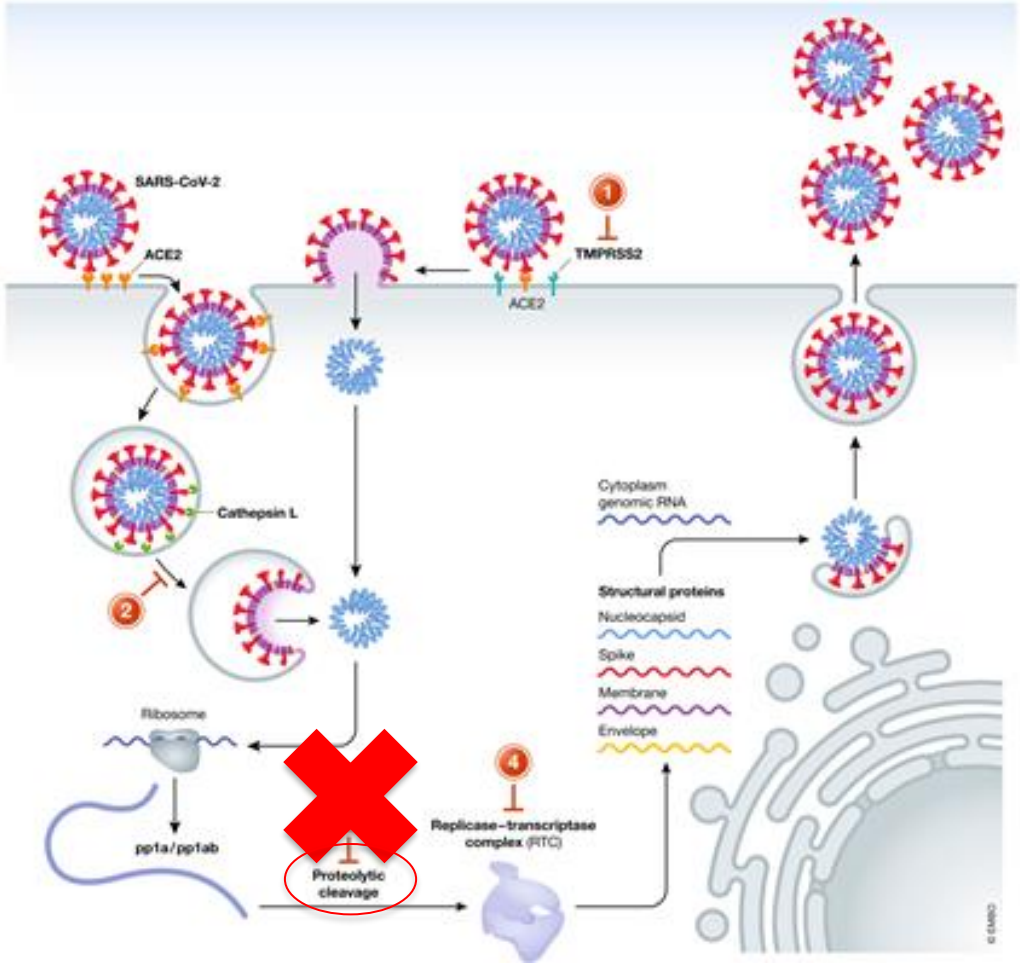
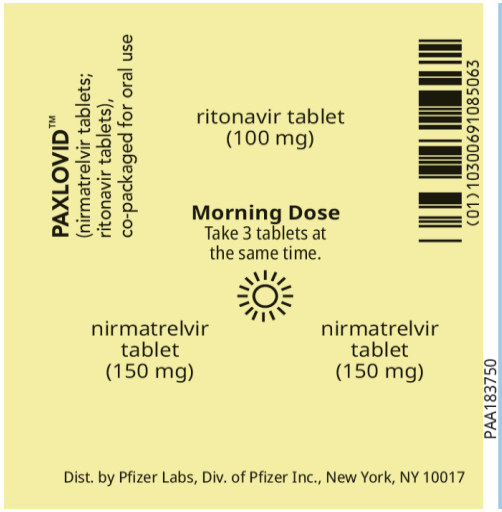
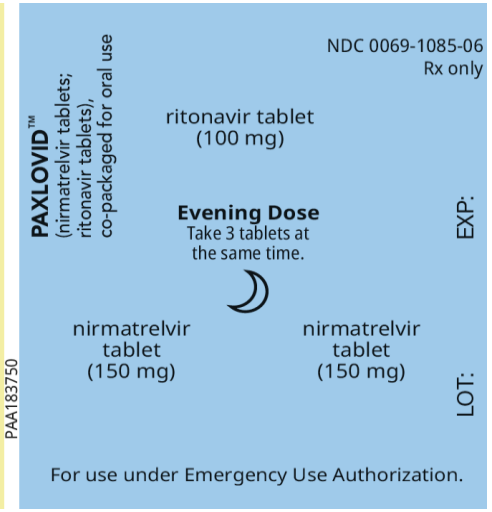


Figure adapted from "A comparative analysis of remdesivir and other repurposed antivirals against SARS-CoV-2", EMBO Mol Med, Volume: 13, Issue: 1, First published: 04 October 2020, DOI: (10.15252/emmm.202013105).

How Paxlovid™ is Dosed/Supplied

- Authorized dose: **two** 150 mg tablets (300 mg) nirmatrelvir with **one** 100 mg tablet ritonavir orally **bid x 5 days**
  - without regard to food
  - as soon as possible after COVID-19 diagnosis and within 5 days of symptom onset
- Each carton contains five blister packs, one for each day
  - Dose reduction needed for **moderate renal impairment**





Authorized Use under EUA

Paxlovid™ is authorized for the treatment of mild-to-moderate 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[1] for progression to severe COVID-19, including hospitalization or death.

[1]For information on medical conditions and factors associated with increased risk for progression to severe COVID-19, see the CDC website on extra precautions for people with medical conditions (https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html)

For more information on Paxlovid™, see the FDA Paxlovid™ Fact Sheet for Healthcare Providers: https://www.fda.gov/media/155050/download

Limitations of Authorized Use

Paxlovid™ is not authorized for:

- Initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19[2].
- Use as pre-exposure or post-exposure prophylaxis for prevention of COVID-19.
- Use for longer than 5 consecutive days.

[2]Patients requiring hospitalization due to severe or critical COVID-19 after starting treatment with Paxlovid™ may complete the full 5-day treatment course per the healthcare provider's discretion.

Data on Efficacy: EPIC-HR*

- Phase 2/3 double-blind study in 2,246 non-hospitalized, symptomatic adults with a laboratory-confirmed SARS-CoV-2 infection who were randomized 1:1 to receive Paxlovid™ or placebo for 5 days.
- Population:
  - Enrolled within 5 days of symptom onset
  - ≥1 risk factor for progression to severe disease
  - No prior COVID-19 vaccine receipt or prior COVID-19 infection
  - Standard of care treatment allowed, but the primary analysis population was limited to subjects who did not receive COVID-19 monoclonal antibodies (mAbs)
- 98% of SARS-CoV-2 variants identified in EPIC-HR were Delta.

*More information about the study EPIC-HR: https://clinicaltrials.gov/ct2/show/NCT04960202

Data on Efficacy: EPIC-HR, continued

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

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

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.

Data on Safety: EPIC-HR*

- Adverse events (AEs) seen in ≥1% of Paxlovid™ recipients (n=1,109) with a higher frequency (≥5 subject difference) versus placebo recipients (n=1,115):
  - Dysgeusia (6% versus <1%)
  - Diarrhea (3% versus 2%)
  - Hypertension (1% versus <1%)
  - Myalgia (1% versus <1%)

*The study population excluded children, pregnant women, individuals with GFR <45 mL/min/1.73 m^2, individuals with active liver disease, and individuals taking concomitant medications that could have clinically significant drug interactions with Paxlovid™.

Drug Interactions

- Paxlovid™ is a CYP3A inhibitor and is also metabolized by CYP3A
  - Paxlovid™ may increase plasma concentrations of medications metabolized by CYP3A
  - Medications that inhibit or induce CYP3A may increase or decrease Paxlovid™ concentrations
- These interactions may lead to:
  - Clinically significant adverse reactions, including fatal events, from greater exposures of concomitant medications
  - Loss of therapeutic effect of Paxlovid™ and possible viral resistance from decreased Paxlovid™ exposures

Drug Interactions, continued

- 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
    - **NIH Statement on Paxlovid™ Drug-Drug Interactions:** https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-paxlovid-drug-drug-interactions/
  - 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

Specific Populations: Renal Impairment

eGFR*	PAXLOVID™ Dose
Greater than 60 mL/min (normal renal function or mild renal impairment)	300 mg nirmatrelvir with 100 mg ritonavir, taken twice daily for 5 days
≥30 to ≤60 mL/min (moderate renal impairment)	150 mg nirmatrelvir with 100 mg ritonavir, taken twice daily for 5 days
<30mL/min (severe renal impairment)	PAXLOVID™ is not recommended (the appropriate dose has not been determined)

*eGFR = estimated glomerular filtration rate based on the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) formula

As a healthcare provider, you should:

- Determine the appropriate Paxlovid™ dose for your patient
- Specify the numeric dose of each active ingredient (nirmatrelvir and ritonavir) in the Paxlovid™ prescription
- Counsel patients with moderate renal impairment about renal dosing instructions and inform them that the blister cards will be altered by the pharmacist to remove unneeded tablets
  - Instructions for pharmacists and sticker packs accompany each shipment of Paxlovid™

Other Specific Populations

- Hepatic Impairment
  - No dosage adjustment needed for mild or 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 Paxlovid™ in pregnancy or with breast feeding.
  - In animal studies, reduced fetal body weights were 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 for Paxlovid™ 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.

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

Helpful Links

- EUA Documents:
  - https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs
- Scientific Review Documents:
  - https://www.fda.gov/drugs/coronavirus-covid-19-drugs/cder-scientific-review-documents-supporting-emergency-use-authorizations-drug-and-biological
- For questions on how to obtain products under EUA, please go to COVID-19 Therapeutics Locator (https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/) or contact COVID19therapeutics@hhs.gov

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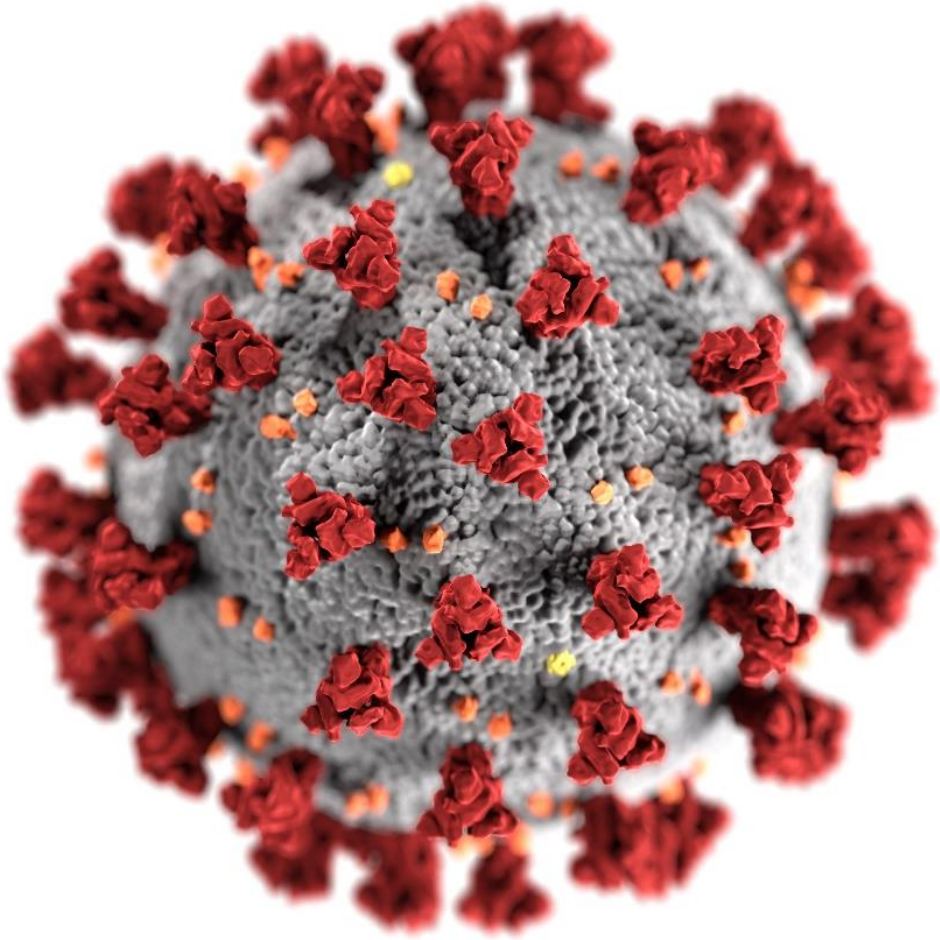

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Molnupiravir Emergency Use Authorization for COVID-19: An Overview for Clinicians

Aimee Hodowanec, MD
Senior Medical Officer, Division of Antivirals
Center for Drug Evaluation and Research
US Food and Drug Administration

CDC COCA Call

January 12, 2022

Content Overview for Molnupiravir

- Mechanism of Action
- Authorized Use
- Limitations of Authorized Use
- Dosage and Administration
- Data Supporting the Emergency Use Authorization
- What Clinicians Need to Know
- Prescriber Requirements

Mechanism of Action

- Molnupiravir (MOV) is a nucleoside analogue that inhibits SARS-CoV-2 replication by viral mutagenesis

Authorized Use Statement

MOV is authorized for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults with positive results of direct SARS-CoV-2 viral testing who are at high risk* for progression to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate.

*See the CDC website on extra precautions for people with medical conditions Healthcare providers should consider the benefit-risk for an individual patient: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

Molnupiravir Fact Sheet For Healthcare Providers: https://www.fda.gov/media/155054/download

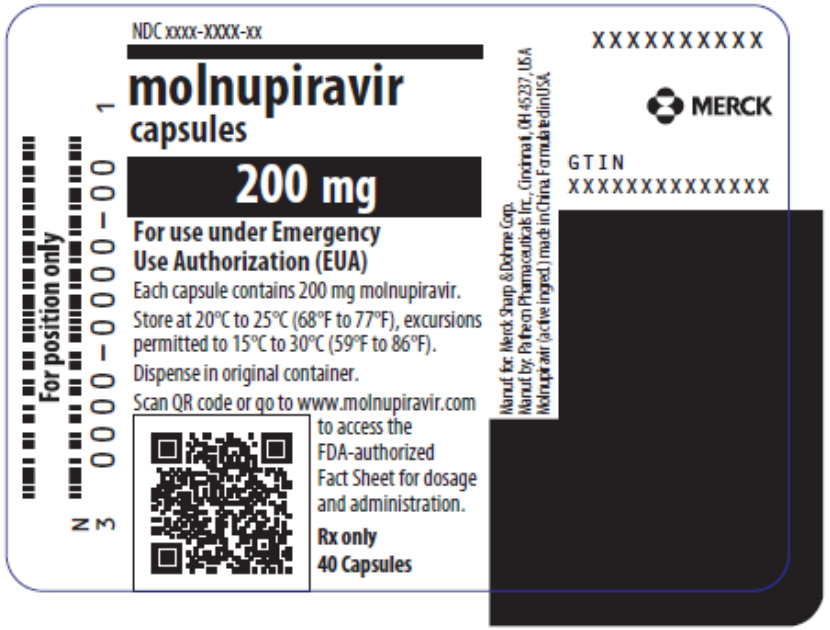
MOV Limitations of Authorized Use

MOV is not authorized

- for use in patients less than 18 years of age
- for initiation of treatment in patients requiring hospitalization due to COVID-19
  - Benefit of treatment with MOV has not been observed in subjects when treatment was initiated after hospitalization due to COVID-19
  - Should a patient require hospitalization after starting treatment with MOV, the patient may complete the full 5-day treatment course per the healthcare provider's discretion
- for use for longer than 5 consecutive days
- for pre-exposure or post-exposure prophylaxis for prevention of COVID-19

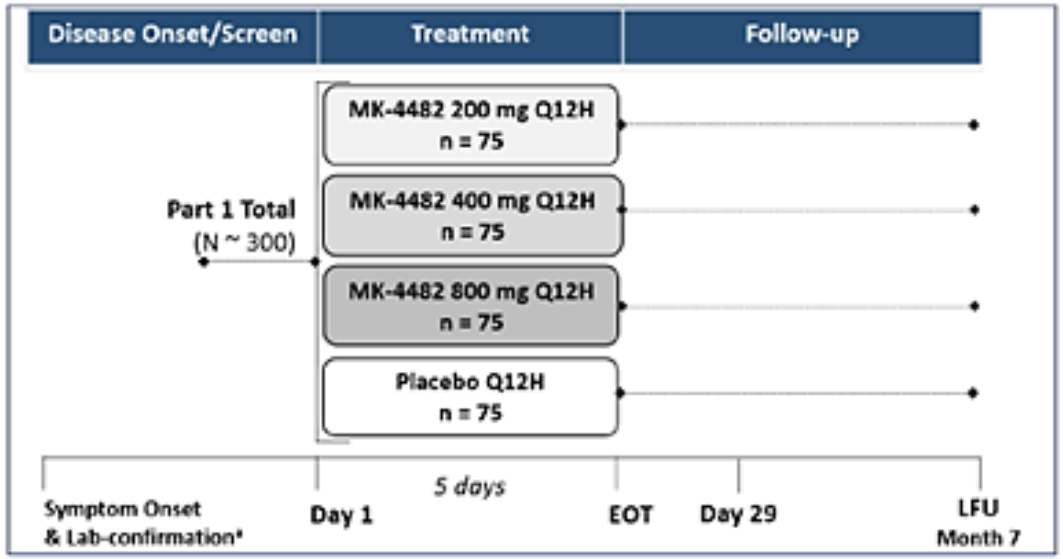
Authorized MOV Dosage

- 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days, with or without food
- Take as soon as possible after a diagnosis of COVID-19 has been made, and within 5 days of symptom onset
- Completion of the full 5-day treatment course and continued isolation in accordance with public health recommendations are important to maximize viral clearance and minimize transmission of SARS-CoV-2



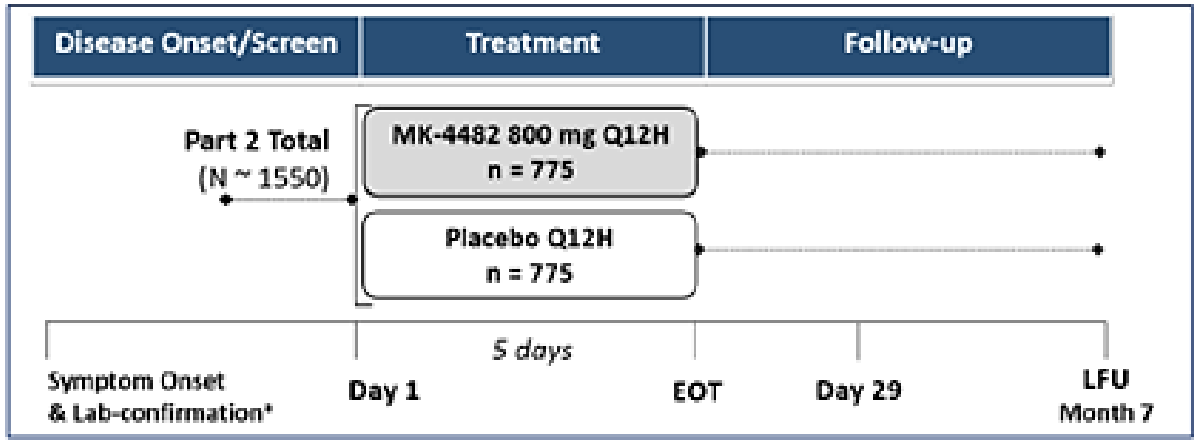
Trial P002 (MOVe-OUT): A Phase 2/3 Randomized, Placebo-Controlled, Double-Blind Clinical Study to Evaluate MOV in Non-Hospitalized Adults with COVID-19

Part 1
Dose Ranging
(Phase 2)



Primary Endpoint: The percentage of participants who were hospitalized or died through Day 29 due to any cause

Part 2
Evaluation of
Selected Dose
(Phase 3)



Trial P002 (MOVe-OUT): Eligibility Criteria

- Outpatient adults with mild or moderate COVID-19
  - Laboratory-confirmed SARS-CoV-2 infection with sample collection and onset of COVID-19 symptoms ≤5 days prior to randomization
- All participants at increased risk for severe illness from COVID-19
  - >60 years of age, active cancer, CKD, COPD, obesity (BMI ≥ 30), serious heart conditions (CAD, heart failure, cardiomyopathies), DM
- SARS-CoV-2 vaccines were prohibited any time prior to randomization and through Day 29
- Pregnant individuals excluded and contraception was required

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus

Trial P002 (MOVe-OUT): Efficacy Results

	Molnupiravir (N=709) n(%)	**Placebo (N=699) n(%)**	**Adjusted Risk Difference % (95%CI)**
All-cause hospitalization ≥24 hours for acute care or death through Day 29	48 (6.8%)	68 (9.7%)	-3.0 (-5.9%, -0.1%)
All-cause mortality through Day 29	1 (0.1%)	9 (1.3%)	

*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).

Trial P002 (MOVe-OUT) Safety: Adverse Reactions Occurring in ≥ 1% of Participants Receiving Molnupiravir

	Molnupiravir N=710	Placebo N=701
Diarrhea	2%	2%
Nausea	1%	1%
Dizziness	1%	1%

Frequencies of adverse reactions are based on all adverse events attributed to study intervention by the investigator.

What Clinicians Need to Know

- **MOV is not authorized for use in patients < 18 years of age**
  - May affect bone and cartilage growth
- MOV may be used regardless of COVID-19 vaccination status
- Breastfeeding is not recommended during treatment with MOV and for 4 days after the final dose
- No drug interactions have been identified based on the limited available data
- No dosage adjustment is recommended in patients with any degree of renal or hepatic impairment

What Clinicians Need to Know: Use in Pregnancy

- **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

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

MOV Helpful Links

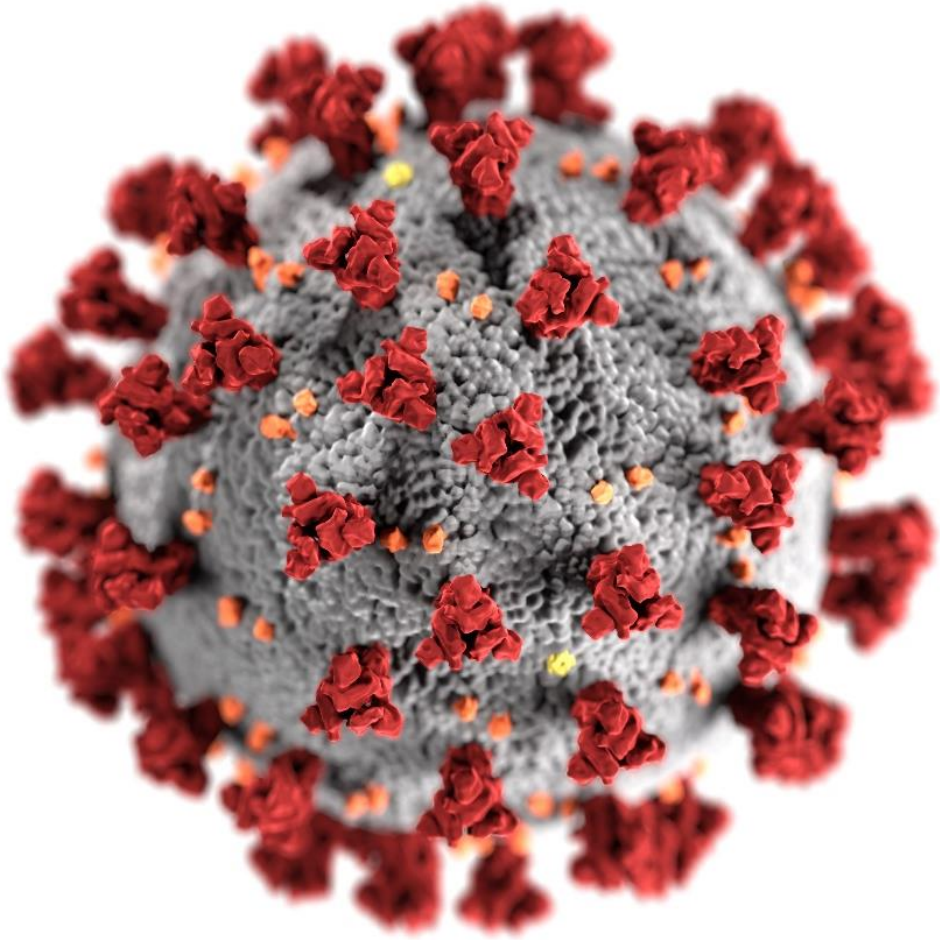
- EUA Documents:
  - https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs

- Scientific Review Documents:
  - https://www.fda.gov/drugs/coronavirus-covid-19-drugs/cder-scientific-review-documents-supporting-emergency-use-authorizations-drug-and-biological

- For questions on how to obtain products under EUA, please go to COVID-19 Therapeutics Locator (https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/)or contact COVID19therapeutics@hhs.gov

Disclaimer Reminder

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC).



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Therapies for Nonhospitalized Patients with COVID-19 and Prioritization Based on Patient Factors

Alice K Pau, Pharm.D.
Staff Scientist (Clinical), NIAID, NIH
Executive Secretary
NIH COVID-19 Treatment Guidelines

January 12, 2022

Goals of Therapy for Outpatients with COVID-19

- Prevent progression to serious disease, thereby reducing
  - Visits to urgent care setting
  - Hospitalizations
  - Deaths
- Reduce duration of illness
- Reduce infectivity and ongoing transmission
- Minimize the potential of overwhelming the healthcare system

Given the limited drug supplies – highest priority should be given to patients with the highest risk of progression to severe disease

Panel's Recommendations for Nonhospitalized Patients Who are at **High Risk of Clinical Progression**

Before Feb 2021

- Symptomatic management, no specific therapy

Feb – Dec 23, 2021

Anti-SARS-CoV-2 monoclonal antibodies (mAb) -

- Bamlanivimab + etesivimab (BAM + ETE)
- Casirivimab + imdesvimab (CAS + IMD or REGEN-COV)
- Sotrovimab (July 2021)

https://www.covid19treatmentguidelines.nih.gov

Panel's Recommendations for Nonhospitalized Patients Who are at **High Risk of Clinical Progression**

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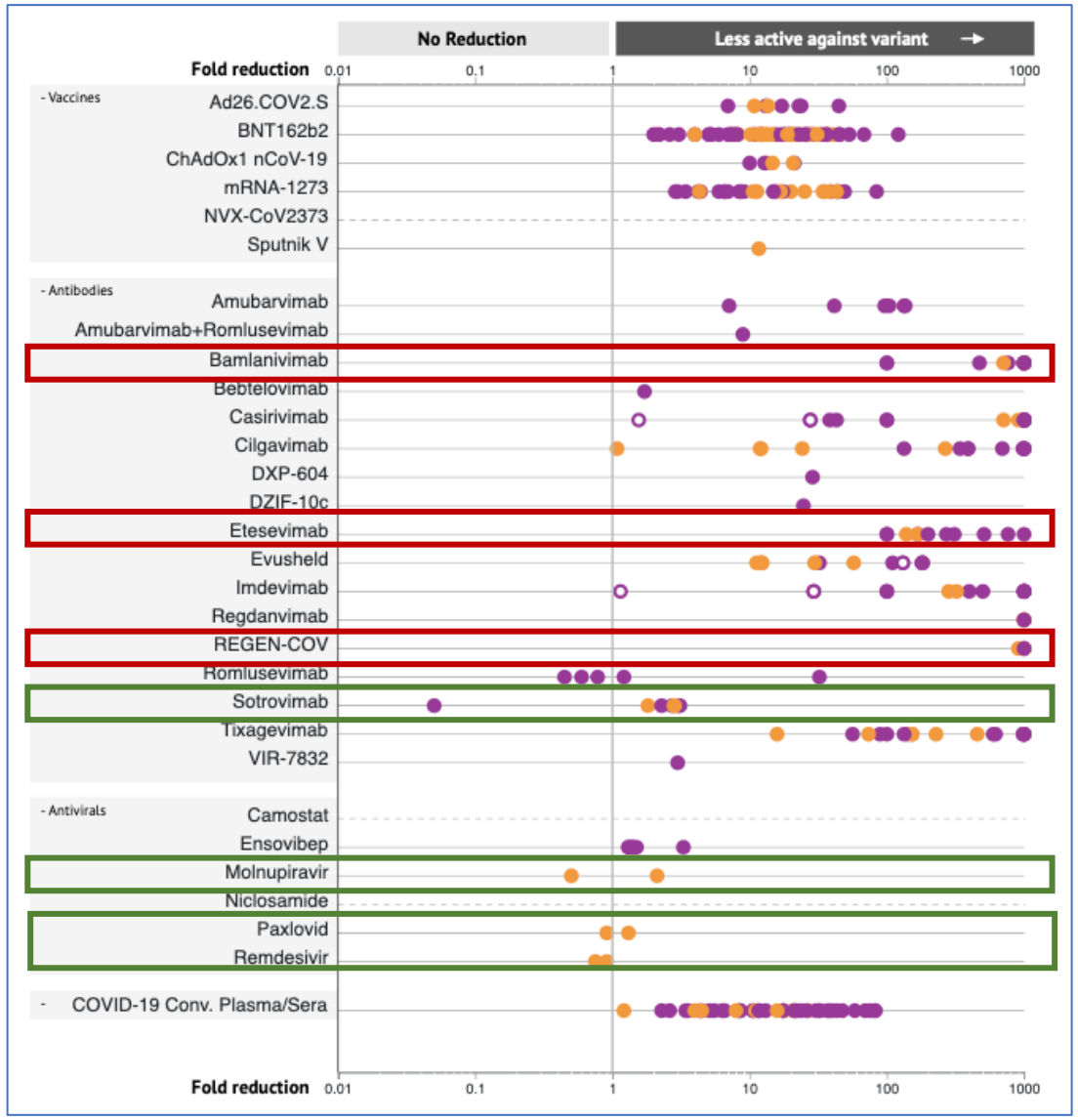
- Sotrovimab (July 2021)

Dec 23, 2021

- Sotrovimab
- Remdesivir (IV x 3 days)

https://www.covid19treatmentguidelines.nih.gov

December 23, 2021 - Change in Recommendations in Response to Increased Prevalence of the Omicron Variant COVID GL Omicron Rec 12.23.21



- **BAM/ETE and REGEN-COV -** Removed from the list of recommended anti-SARS-CoV-2 mAbs -
  - Except in regions where there is still a significant proportion of Delta variant
- **Sotrovimab** was recommended as the primary anti-SARS-CoV-2 mAb
- **Remdesivir** IV x 3 days was added as a treatment option –
  - Based on results from the PINETREE trial
  - Due to limited supply of Sotrovimab; and on December 23, Paxlovid™ and Molnupiravir were not yet available for general use

https://opendata.ncats.nih.gov/variant/activity, Accessed Jan 6, 2022

The COVID-19 Treatment Guidelines Panel's Statement on Therapies for High-Risk, Nonhospitalized Patients With Mild to Moderate COVID-19

Last Updated: December 30, 2021

The COVID-19 Treatment Guidelines Panel's Statement on Potential Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications

Last Updated: December 30, 2021

https://www.covid19treatmentguidelines.nih.gov

Continued:

Panel's Recommendations for Nonhospitalized Patients Who are at **High Risk of Clinical Progression**

Before Feb 2021

- Symptomatic management, no specific therapy

Feb – Dec 23, 2021

Anti-SARS-CoV-2 mAbs -

- Bamlanivimab + etesivimab (BAM + ETE)
- Casirivimab + imdesvimab (CAS + IMD or REGEN-COV)
- Sotrovimab (July 2021)

Dec 23, 2021

- Sotrovimab
- Remdesivir (IV x 3 days)

Dec 30, 2021 (list in order of preference)

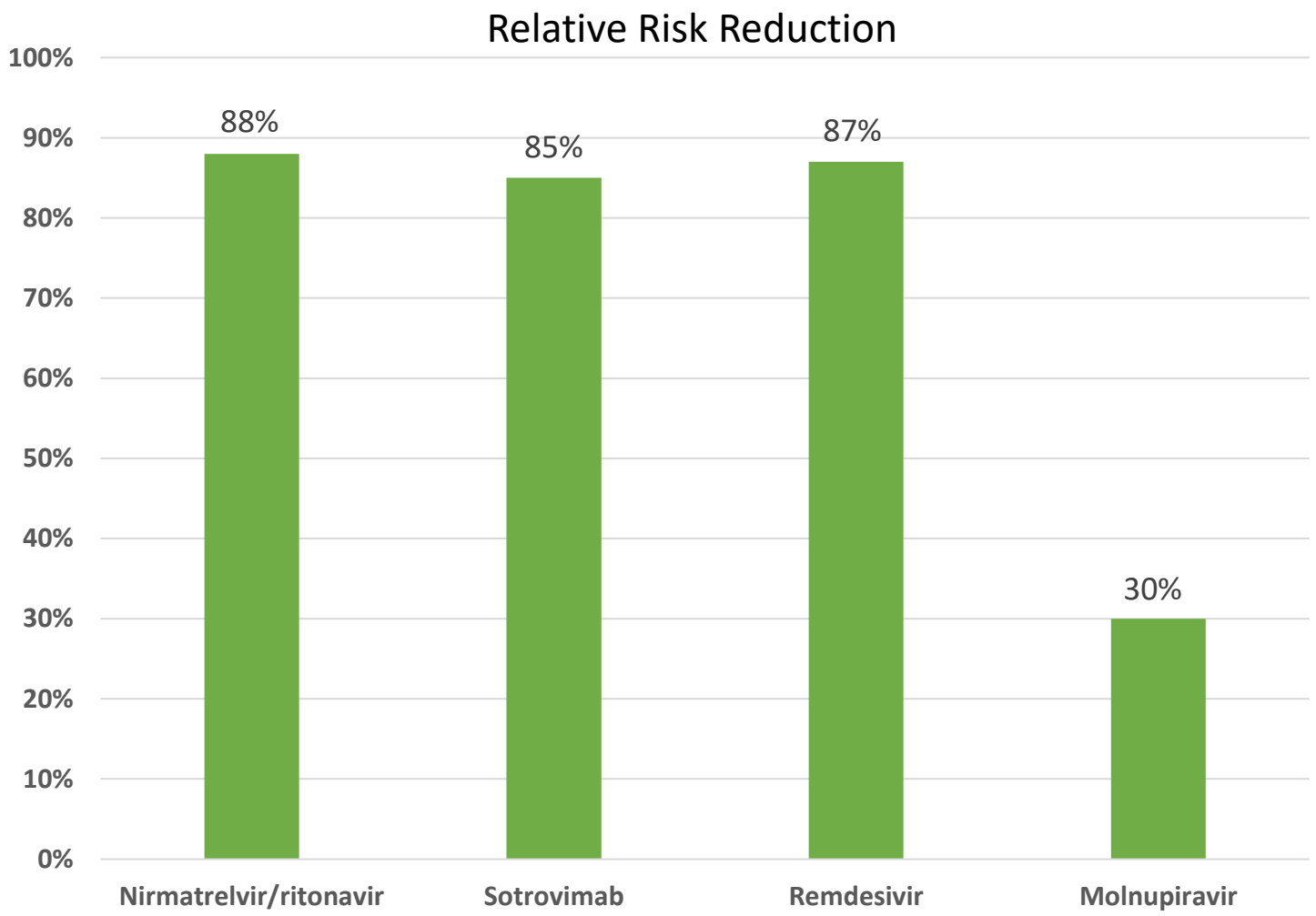
1. **Paxlovid™**
2. **Sotrovimab**
3. **Remdesivir**
4. **Molnupiravir**

https://www.covid19treatmentguidelines.nih.gov

Factors Used in Determining Preferential Recommendations for the Available Therapeutics

- Clinical Efficacy (reduction in hospitalizations or deaths) - as demonstrated in clinical trials
- Convenience/Logistics (PO vs. IV, and duration of therapy)
- Availability for General Population (including children and pregnancy)
- Drug Interaction Potential

Clinical Efficacy Comparison



Events* (%) Drug vs. placebo	0.8% vs. 6.3%	1% vs. 7%	0.7% vs. 5.3%	6.8% vs. 9.7%

*Events = hospitalizations or deaths

Comparisons of Recommended Outpatient Therapies

	Paxlovid™ (1)	Sotrovimab (2)	Remdesivir (3)	Molnupiravir (4)
Age allowed for use	≥ 12 yr	≥ 12 yr	≥ 12 yr	≥18 yr
Initiate within # days of symptom onset	< 5 days	< 10 days	< 7 days	< 5 days
Route of Administration	PO	IV	IV	PO
Duration of Therapy	5 days	1 time	3 days	5 days
Pros	-High efficacy -Oral	-High efficacy -Single IV infusion	-High efficacy -Greater experience	-Oral -No drug-drug interaction concerns
Cons	Ritonavir-related drug-drug interactions	Requires IV infusion	-Requires 3 days of IV infusion -Not FDA approved for outpatient	-Low efficacy -Not authorized for age 12-17 years -Not approved for pregnancy -Concerns for mutagenciity
Supply Availability	Limited supply	Limited supply	Commercially available	More supply than Paxlovid™ & Sotrovimab

The COVID-19 Treatment Guidelines Panel's Interim Statement on Patient Prioritization for Outpatient Anti-SARS-CoV-2 Therapies or Preventive Strategies When There Are Logistical or Supply Constraints

Last Updated: December 23, 2021

https://www.covid19treatmentguidelines.nih.gov

When will Prioritization be Necessary?

- **DEMANDS** → **Supplies**
- Logistic resources are limited - personnel, space, equipment, time slots
- Cost becomes prohibitive

The COVID-19 Treatment Guidelines Panel's Interim Statement on Patient Prioritization for Outpatient Anti-SARS-CoV-2 Therapies or Preventive Strategies When There Are Logistical or Supply Constraints

Last Updated: December 23, 2021

Goal

- When resources are limited, provide therapy to individuals who may derive the most benefits from the treatment – i.e., individuals who are at the highest risk for progression to severe or critical diseases

Reasons for the statement

- Rapidly rising cases of COVID-19 due to the Omicron variant
- As BAM-ETE and REGEN-COV are not active against Omicron, sotrovimab is the only effective anti-SARS-CoV-2 mAb therapy
- Available therapies in short supply

Factors used to determine who may be at highest risk for progression –

- **Age** – Older → Younger
- **Vaccination status** – Unvaccinated or Unable to mount response → Vaccinated
- **Immune status** – Severely immunocompromised → immunocompetent
- **Clinical factors** – Obesity, diabetes, CV disease, etc. → no risk factor

Patient Prioritization Risk Groups

Tier	Characteristics
1	• **Immunocompromised**, not expected to mount an adequate immune response to COVID-19 vaccine or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccine status; or • **Unvaccinated individuals at the highest risk of severe disease** (anyone aged ≥75 years or anyone aged ≥65 years with additional risk factors).
2	• **Unvaccinated individuals at risk of severe disease not included in Tier 1** (anyone aged ≥65 years or anyone aged <65 years with clinical risk factors)
3	• **Vaccinated individuals at high risk of severe disease** (anyone aged ≥75 years or anyone aged ≥65 years with clinical risk factors) **Note:** Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.
4	• **Vaccinated individuals at risk of severe disease** (anyone aged ≥65 years or anyone aged <65 with clinical risk factors) **Note:** Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.

https://www.covid19treatmentguidelines.nih.gov

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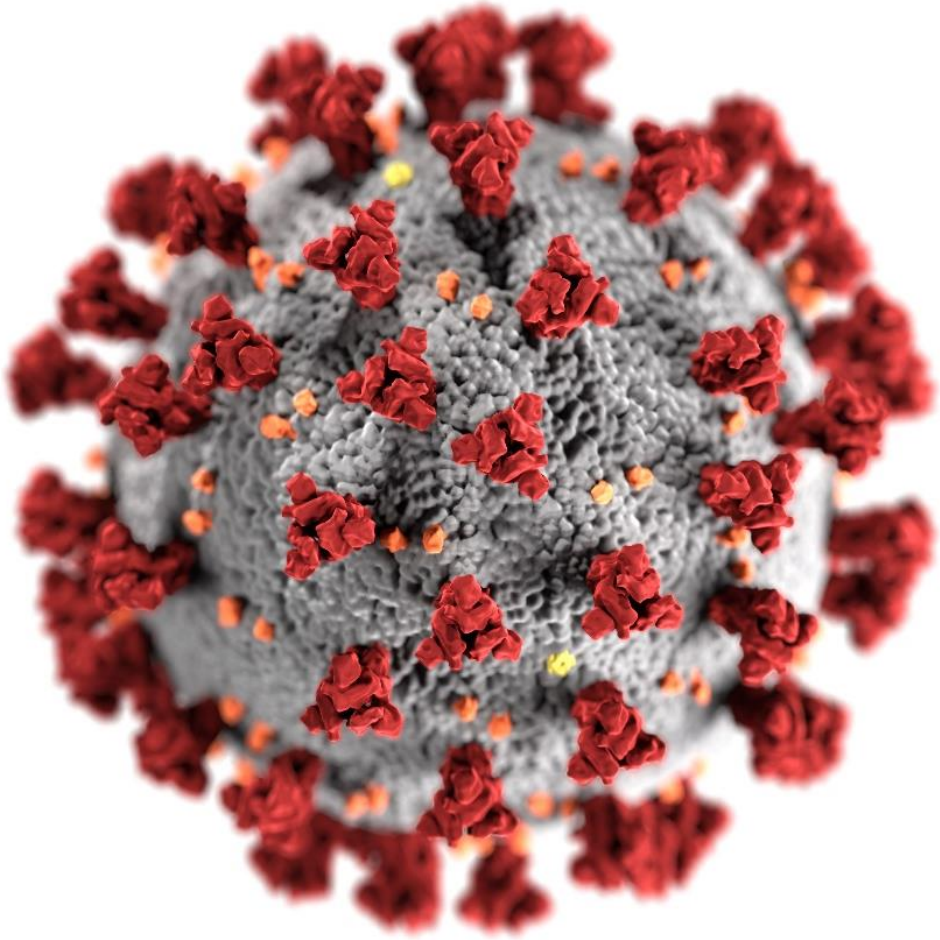

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Thank you

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  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
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- **When:** A few hours after the live call
- **What:** Video recording
- **Where:** On the COCA Call webpage at

https://www.emergency.cdc.gov/coca/calls/2022/callinfo_011222.asp

Next COCA Call

- **Date:** Thursday, January 13, 2022
- **Time:** 2:00–3:00 P.M. ET
- **Topic:** Updates to CDC's COVID-19 Quarantine and Isolation Guidelines in Healthcare and Non-healthcare Settings
- **Website:** (https://www.emergency.cdc.gov/coca/calls/2022/callinfo_011322.asp)

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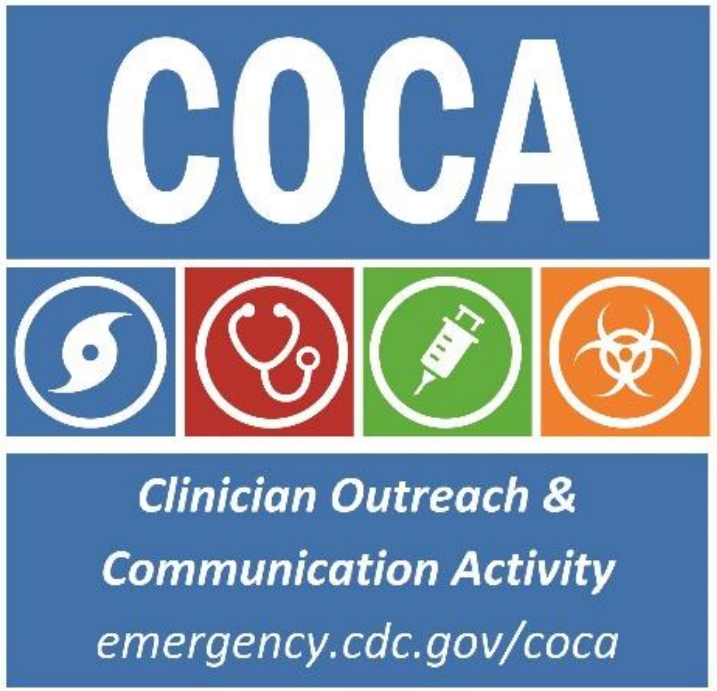

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