U.S. Department of Health and Human Services

ASPR Administration for Strategic Preparedness & Response

HHS/ASPR COVID-19 Therapeutics Clinical Rounds

COVID-19 Landscape and Paxlovid

January 6, 2023

Unclassified/For Public Distribution

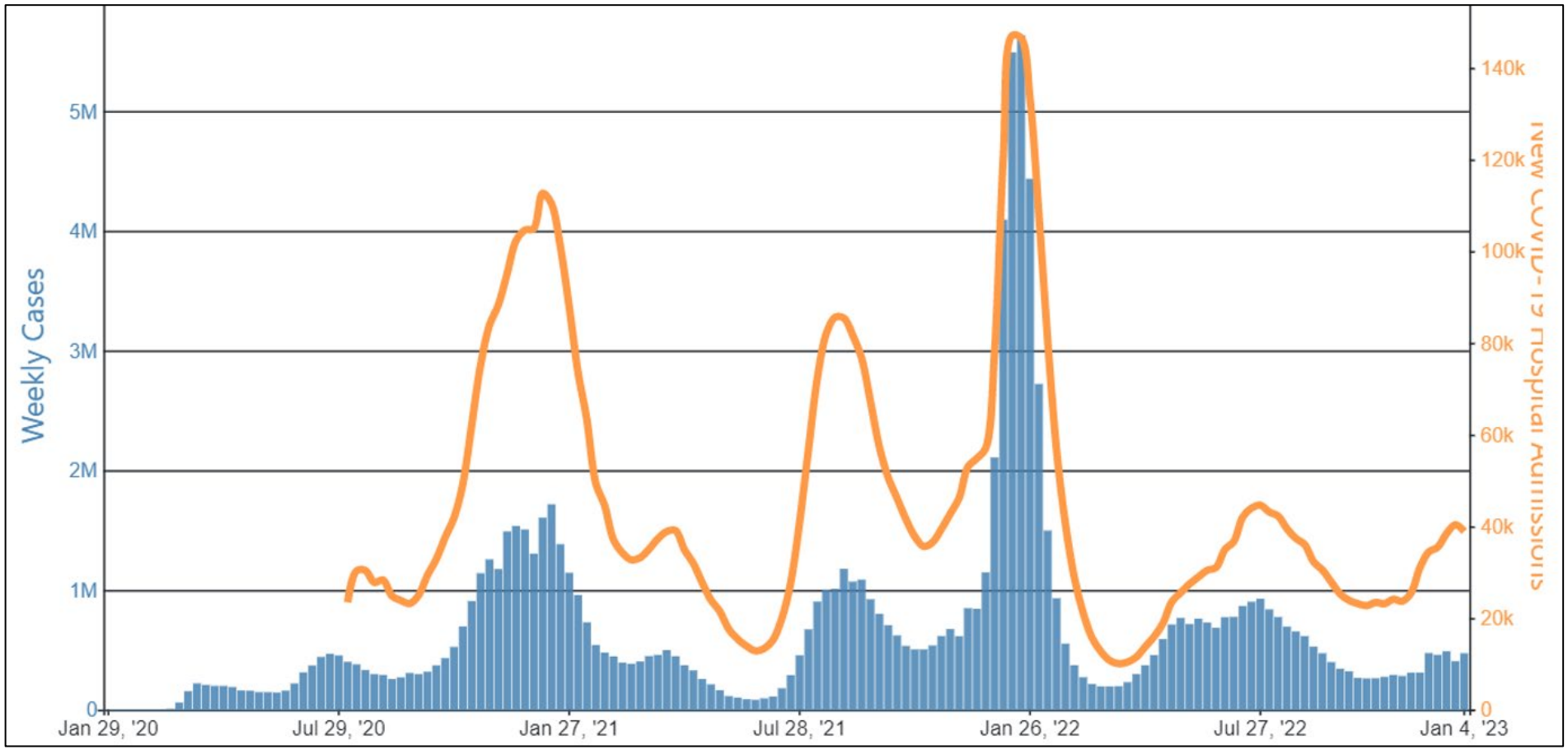
Agenda

- **Administrative Remarks**
- **Opening Remarks/Welcome**
- **COVID-19 Therapeutics Updates**
  - Dr. Meg Sullivan, ASPR Chief Medical Officer
- **Presentation**
  - Dr. Florin Draica, Pfizer Medical Affairs
- **Case Scenarios**
- **Q&A and Discussion**
- **Closing Remarks**

COVID-19 Therapeutics Updates

COVID-19 Data Tracker

Weekly trends in the number of cases and number of new patients admitted to hospital with confirmed COVID-19 per week in the United States reported to the CDC



https://covid.cdc.gov/covid-data-tracker/#datatracker-home

New: NIH Guidelines Panel Updates

- **Dec. 28, 2022** - Updates Regarding the Use of Bebtelovimab
  - Due to the increasing prevalence of SARS-CoV-2 Omicron subvariants that are anticipated to be resistant to bebtelovimab (i.e., BQ.1, BQ.1.1, XBB), bebtelovimab is not currently authorized by the Food and Drug Administration (FDA) for the treatment of COVID-19 in any region of the United States. The Panel **recommends against** the use of **bebtelovimab** for the treatment of non-hospitalized patients with COVID-19 who are at high risk of progressing to severe COVID-19 **(All)**.

https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/

New: NIH Guidelines Panel Updates

Table 2a. Therapeutic Management of Nonhospitalized Adults With Mild to Moderate COVID-19 Who Do Not Require Supplemental Oxygen

Last Updated: December 28, 2022

Patient Disposition	Panel's Recommendations
All Patients	• All patients should be offered symptom management (AIII). • The Panel **recommends against** the use of **dexamethasone**[a] or **other systemic corticosteroids** in the absence of another indication (AIIb).
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 therapy. For use when the preferred therapies are not available, feasible to use, or clinically appropriate:* • **Molnupiravir**[d,f,g] (CIIa)
Each recommendation in the Guidelines receives 2 ratings that reflect the strength of the recommendation and the quality of the evidence that supports it. See Guidelines Development for more information.	

https://www.covid19treatmentguidelines.nih.gov/tables/therapeutic-management-of-nonhospitalized-adults/

Reminder: NIH Guidelines Panel Updates December 6

Minor updates were made to the following Guidelines sections:

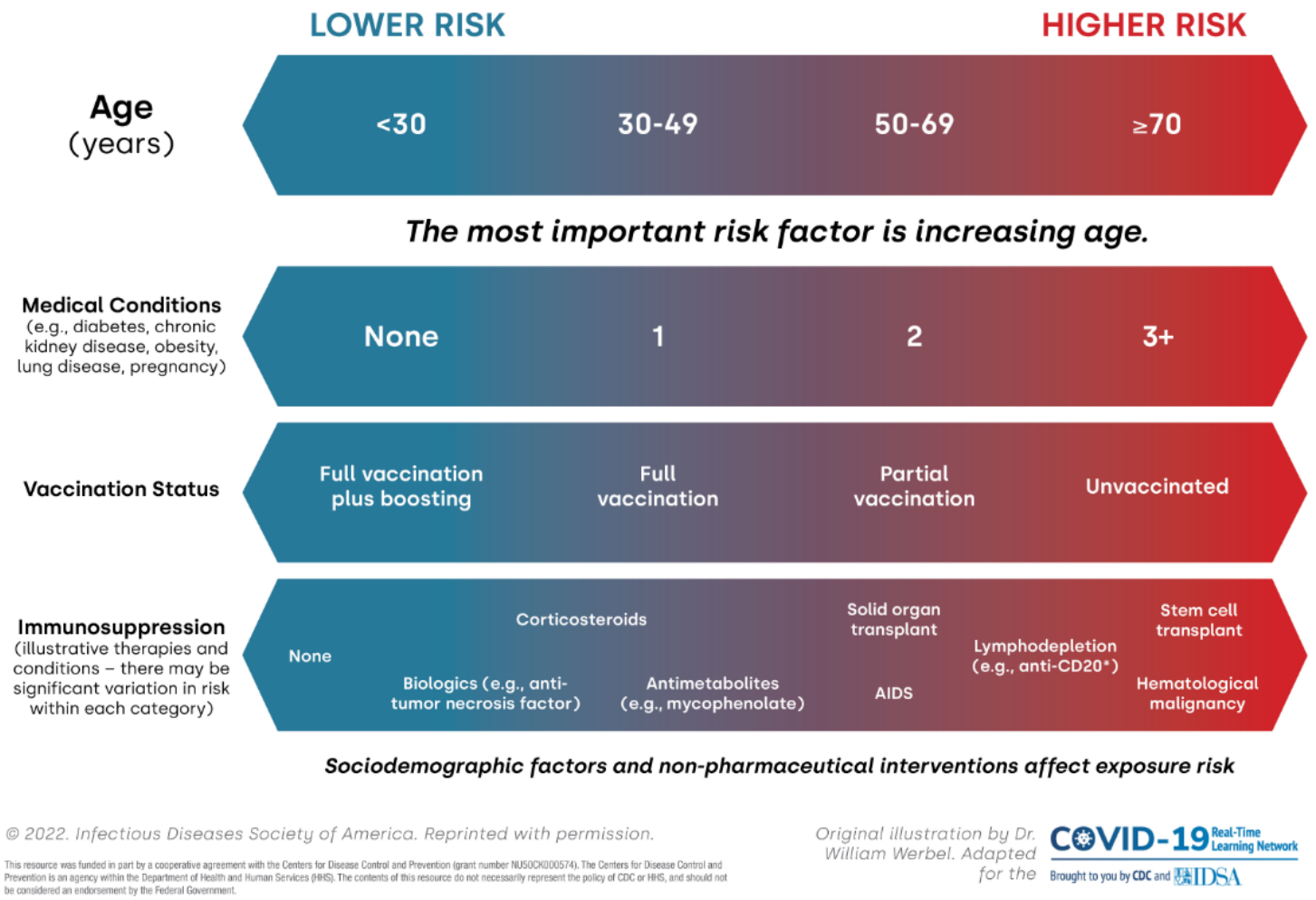
- Remdesivir
- Ritonavir-Boosted Nirmatrelvir (Paxlovid)
- Antithrombotic Therapy in Patients with COVID-19
- Special Considerations in People Who are Immunocompromised
- Special Considerations in Adults and Children with Cancer
- Special Considerations in Solid Organ Transplant, Hematopoietic Cell Transplant, and Cellular Immunotherapy Candidates, Donors, and Recipients
- Intravenous Immunoglobulin

https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/

New Report: COVID-19 Antivirals Utilization: Geographic and Demographic Patterns of Treatment in 2022

- Dec. 23, 2022 – HHS Office of the Assistant Secretary for Planning and Evaluation issued report that examines the utilization of oral antiviral medications, Paxlovid and Lagevrio, for the treatment of COVID-19.
- Analyses include an examination of time trends of COVID-19 antiviral use as well as breakdowns by age cohorts and gender.
- Report finds that utilization in the U.S. of both Paxlovid and Lagevrio rose sharply in the spring of 2022, rising more than tenfold for all age groups between March and July 2022.
- Utilization rates were higher among older adults and those in long-term care settings. Paxlovid utilization rates per 100,000 people were highest for those in long-term care (LTC) settings, exceeding any population-based age group in retail settings. Lagevrio usage was even more concentrated in LTC settings, where residents may more frequently have contraindications to Paxlovid.
- Report notes wide variation in COVID-19 antiviral medication use by state.
- Paxlovid utilization (but not Lagevrio) was statistically significantly higher in states with higher vaccination rates, while utilization of both medications increased in association with higher statewide COVID-19 case rates.
- Read the full report here.

Who Is At Risk for Severe COVID-19?



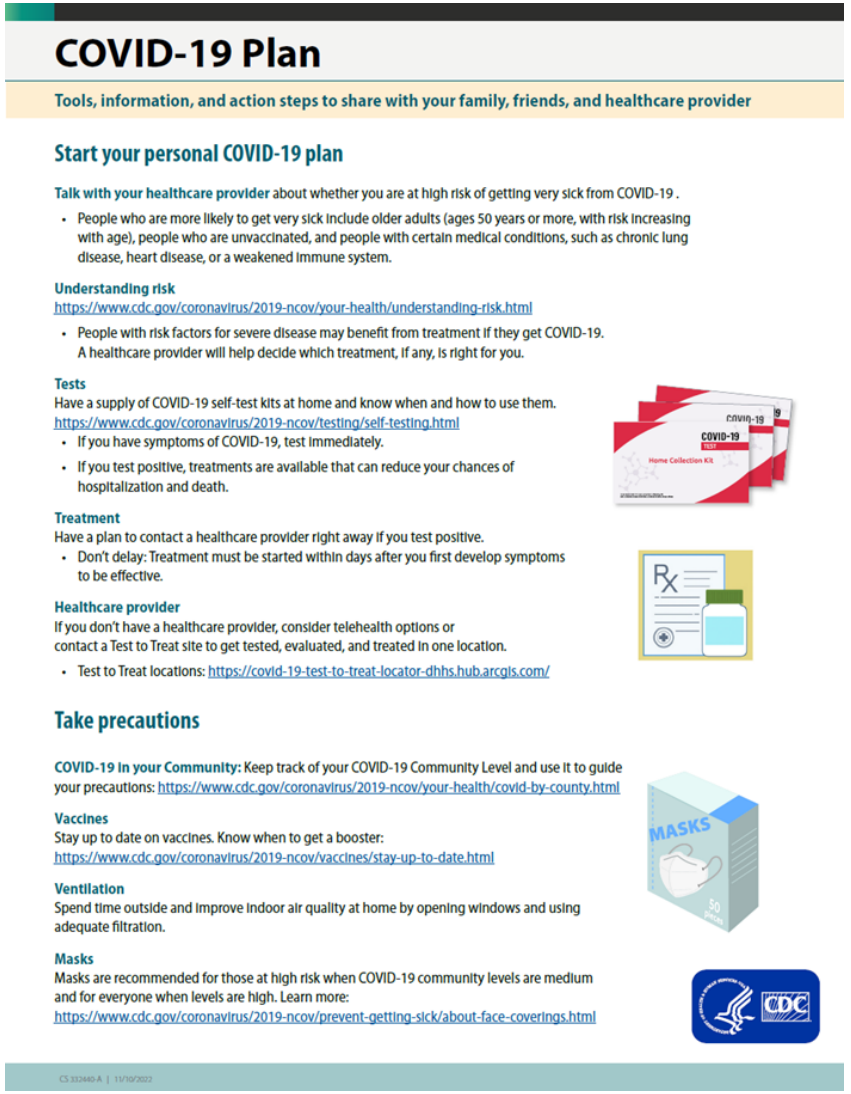
This resource was funded in part by a cooperative agreement with the Centers for Disease Control and Prevention (grant number NU50CK000574). The Centers for Disease Control and Prevention is an agency within the Department of Health and Human Services (HHS). The contents of this resource do not necessarily represent the policy of CDC or HHS, and should not be considered an endorsement by the Federal Government.

Original illustration by Dr. William Werbel. Adapted for the COVID-19 Real-Time Learning Network. Brought to you by CDC and IDSA

IDSA Immunocompromised Populations: https://www.idsociety.org/covid-19-real-time-learning-network/special-populations/immunocompromised-populations/
CDC Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Professionals: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html#anchor_1618433687270

Reminder! COVID-19 Action Plan

- Guidance to help individuals put together a COVID-19 plan so that all information needed is on hand if a person or a member of their household gets sick with COVID-19
- Downloadable guide that can be edited, saved, and shared with family, friends, and healthcare providers
- Additional information also available regarding COVID-19 prevention actions
- Access COVID Action Plan guidance at:
  - COVID-19 Personal Plan (cdc.gov)
  - How to Protect Yourself and Others | CDC



COVID-19 Plan

Tools, information, and action steps to share with your family, friends, and healthcare provider

Start your personal COVID-19 plan

Talk with your healthcare provider about whether you are at high risk of getting very sick from COVID-19 .

- People who are more likely to get very sick include older adults (ages 50 years or more, with risk increasing with age), people who are unvaccinated, and people with certain medical conditions, such as chronic lung disease, heart disease, or a weakened immune system.

Understanding risk
https://www.cdc.gov/coronavirus/2019-ncov/your-health/understanding-risk.html

- People with risk factors for severe disease may benefit from treatment if they get COVID-19. A healthcare provider will help decide which treatment, if any, is right for you.

Tests
Have a supply of COVID-19 self-test kits at home and know when and how to use them.
https://www.cdc.gov/coronavirus/2019-ncov/testing/self-testing.html

- If you have symptoms of COVID-19, test immediately.
- If you test positive, treatments are available that can reduce your chances of hospitalization and death.

Treatment
Have a plan to contact a healthcare provider right away if you test positive.

- Don't delay: Treatment must be started within days after you first develop symptoms to be effective.

Healthcare provider
If you don't have a healthcare provider, consider telehealth options or contact a Test to Treat site to get tested, evaluated, and treated in one location.

- Test to Treat locations: https://covid-19-test-to-treat-locator-dhhs.hub.arcgis.com/

Take precautions

COVID-19 in your Community: Keep track of your COVID-19 Community Level and use it to guide your precautions: https://www.cdc.gov/coronavirus/2019-ncov/your-health/covid-by-county.html

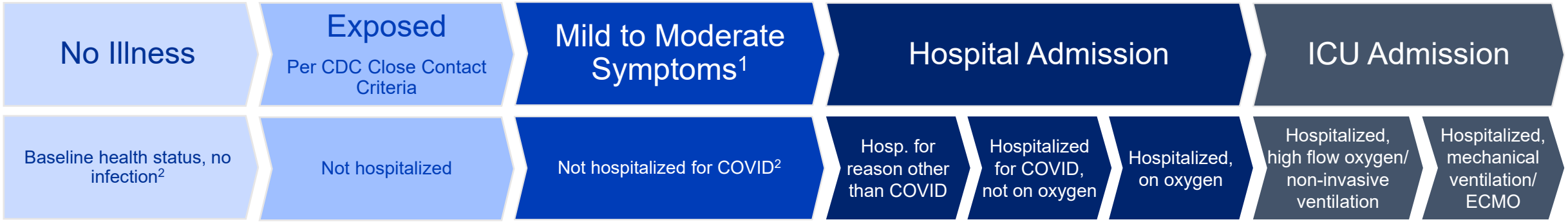
Vaccines
Stay up to date on vaccines. Know when to get a booster:
https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html

Ventilation
Spend time outside and improve indoor air quality at home by opening windows and using adequate filtration.

Masks
Masks are recommended for those at high risk when COVID-19 community levels are medium and for everyone when levels are high. Learn more:
https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/about-face-coverings.html

COVID-19 Therapeutics Landscape

Summary of COVID-19 Preventative Agents & Treatments



COVID-19 Vaccines

Monoclonal Antibodies for PrEP

- Evusheld (tixagevimab + cilgavimab, AZ)

None currently authorized for use in any US state or territory.

Oral Antivirals

- **Paxlovid (nirmatrelvir + ritonavir, Pfizer)**

Oral Antivirals

- Lagevrio (molnupiravir, Merck) – **Alternative**

IV Antiviral

- **Veklury® (remdesivir, Gilead)**

Please see NIH Current Inpatient Therapies* (https://www.covid19treatmentguidelines.nih.gov/therapies/)

There is currently **ample supply** of COVID-19 therapeutics – every eligible patient should have access to these medications

*As hospitalizations increase, please be sure to check latest updates on inpatient care

HHS distribution

Commercially available

[1] Convalescent Plasma EUA https://www.fda.gov/media/141478/download
Convalescent plasma is authorized for specific immunocompromised patients.

[2] Refer to individual product Fact Sheets for authorization details

Therapeutic Management of Nonhospitalized Adults With COVID-19
Therapeutic Management of Hospitalized Adults With COVID-19

Estimated Prevalence of COVID-19 Variants Nationally

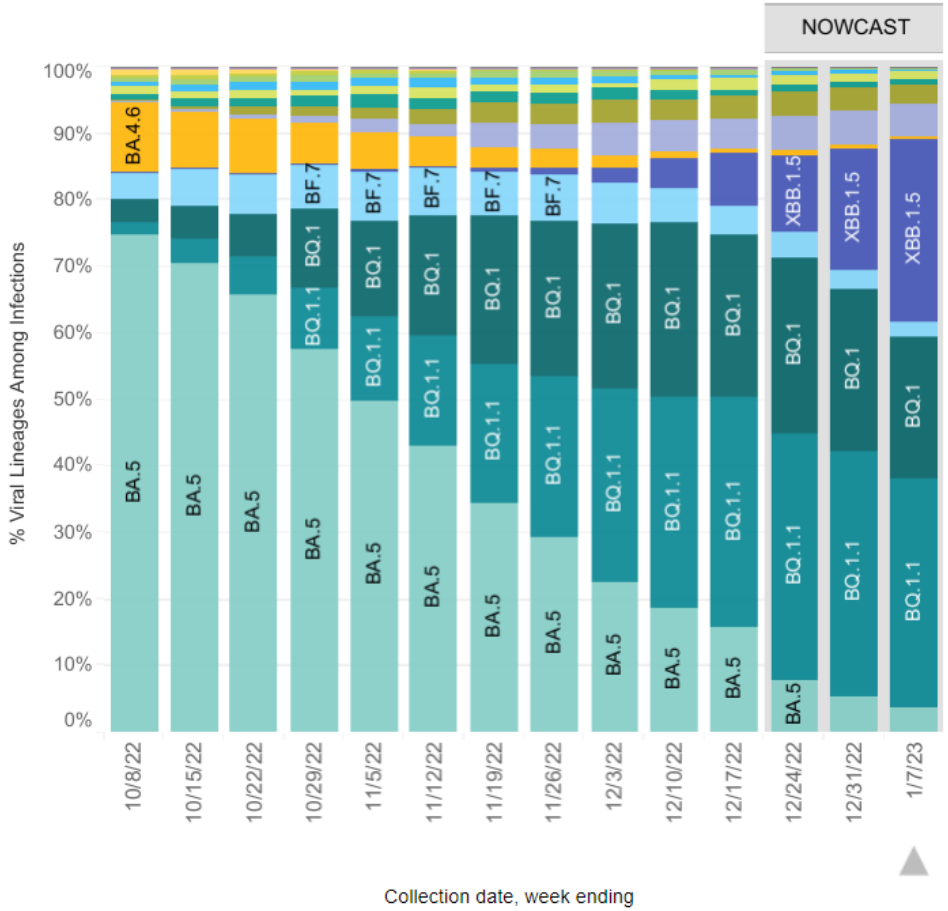
- XBB.1.5 now being monitored separately from XBB
- **XBB.1.5**+BQ.1.1+BQ.1+XBB +BF.7+ BA.5.2.6+BA.4.6+ BF.11+ BA.2.75.2 = ~92% (likely Evusheld resistant)
- BQ.1.1+BQ.1+XBB+BF.7+ BA.5.2.6+BA.4.6+BF.11+ BA.2.75.2 = ~64% (confirmed Evusheld resistant)

United States: 1/1/2023 – 1/7/2023 NOWCAST

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BQ.1.1	VOC	34.4%	26.7-43.0%
	XBB.1.5	VOC	27.6%	14.0-46.5%
	BQ.1	VOC	21.4%	16.1-27.7%
	XBB	VOC	4.9%	4.0-6.1%
	BA.5	VOC	3.7%	2.7-5.0%
	BN.1	VOC	3.0%	2.1-4.1%
	BF.7	VOC	2.2%	1.6-3.0%
	BA.2.75	VOC	1.3%	0.9-2.0%
	BA.5.2.6	VOC	0.7%	0.5-0.9%
	BA.2	VOC	0.3%	0.2-0.5%
	BF.11	VOC	0.3%	0.2-0.4%
	BA.4.6	VOC	0.2%	0.2-0.3%
	BA.2.75.2	VOC	0.1%	0.1-0.1%
	BA.4	VOC	0.0%	0.0-0.0%
	BA.1.1	VOC	0.0%	0.0-0.0%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.2.12.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.1%

United States: 10/2/2022 – 1/7/2023



https://covid.cdc.gov/covid-data-tracker/#variant-proportions

*BA.2.75 includes some lineages with R346T in combination with other mutations making some portion resistant to Evusheld

Therapeutics Activity Against Emerging Variants

- Evusheld ~92% projected resistance nationally (*additional data pending)*
  - Breakthrough infections are possible**, advise patients to have a treatment plan in place and to seek timely medical attention if symptoms occur**
  - This is important messaging to both patients that received Evusheld previously and patients getting first dose
- mAbs currently not authorized for use (Regen-COV, bam/ete, sotrovimab, bebtelovimab) are routinely tested against emerging variants
- Paxlovid/Lagevrio/Veklury are expected to retain activity against all circulating variants based on preliminary data & sequence analysis
  - additional data is pending

https://www.fda.gov/media/154701/download

Product Specific Information Sheets

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**

Continue to monitor our ASPR webpage found here, https://aspr.hhs.gov/COVID-19/Therapeutics/Products/Pages/product-resources.aspx

- **New Lagevrio Information Sheet**
  - Quick reference document for health care providers
  - Highlights patient eligibility and effectiveness information

- This Paxlovid information sheet summarizes current information about **Paxlovid** and offers resources about other COVID-19 therapeutics.
- Veklury information sheet coming soon!

COVID-19 Therapeutics Locator – How to find specific medications

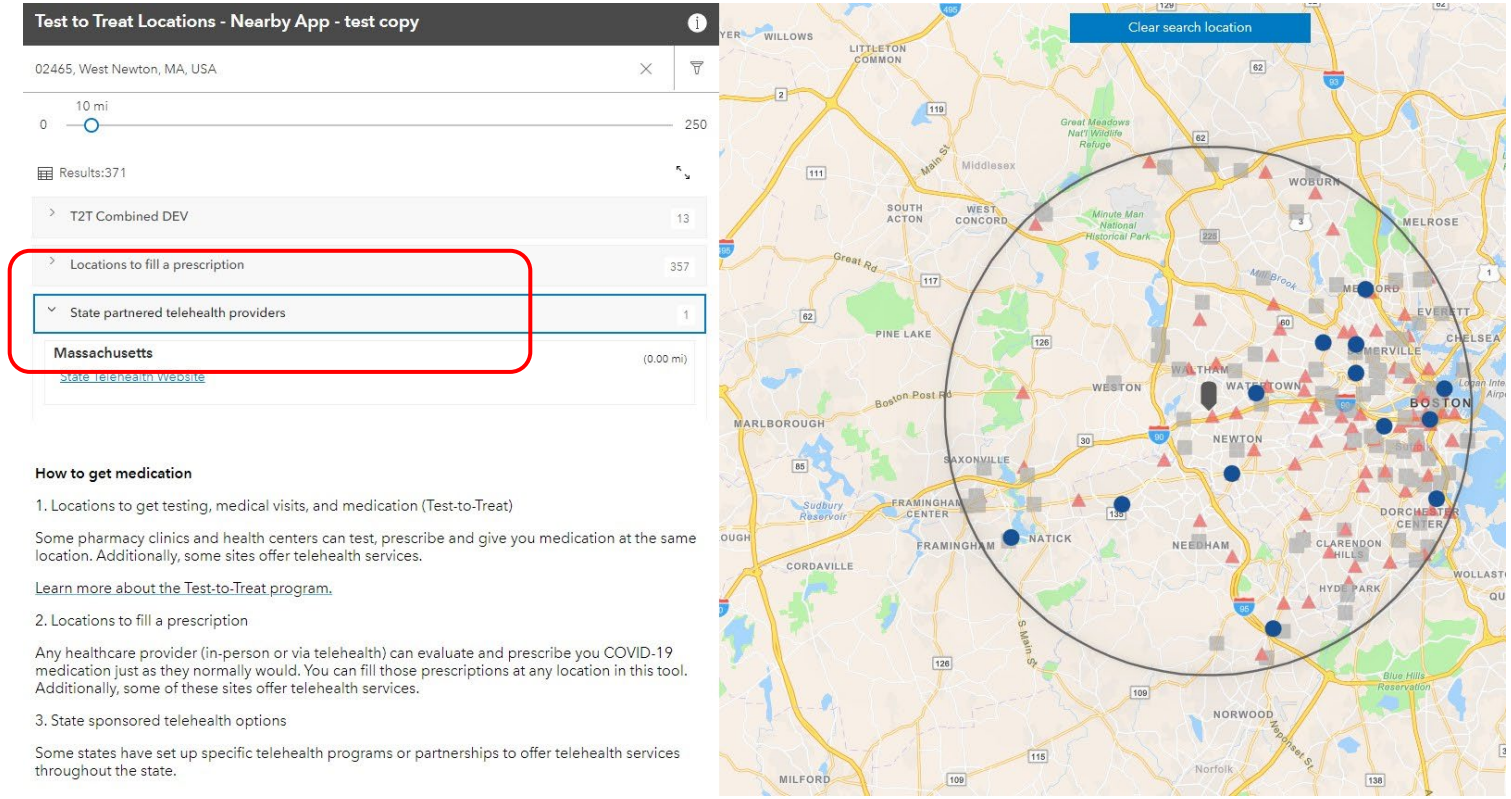
Search by therapy and by zip code to find potential locations

Paxlovid and renal Paxlovid are currently available at 36,947 and 28,628 locations, respectively. They can be found using the COVID-19 Therapeutics Locator or the Test to Treat site locator

Test-to-Treat Locator Updates

- States/Jurisdictions can add their **state-sponsored telehealth programs to the Test-to-Treat locator**.
  - The telehealth program information will appear as the third dropdown option in the menu on the left side of the locator when a user enters an address or zip code in a state with a program.

- **Home delivery** of oral antivirals is **now available** as an opt-in for display on the Test-to-Treat locator.
  - Central partners can leverage the Provider Metadata Management (PMM) tool in Tiberius to update their programs and provide any relevant website links.



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US Senior Medical Director, HQ PAXLOVID Team Lead
Pfizer Medical Affairs

PAXLOVID™ nirmatrelvir tablets; ritonavir tablets

COVID-19 Therapeutics Clinical Update

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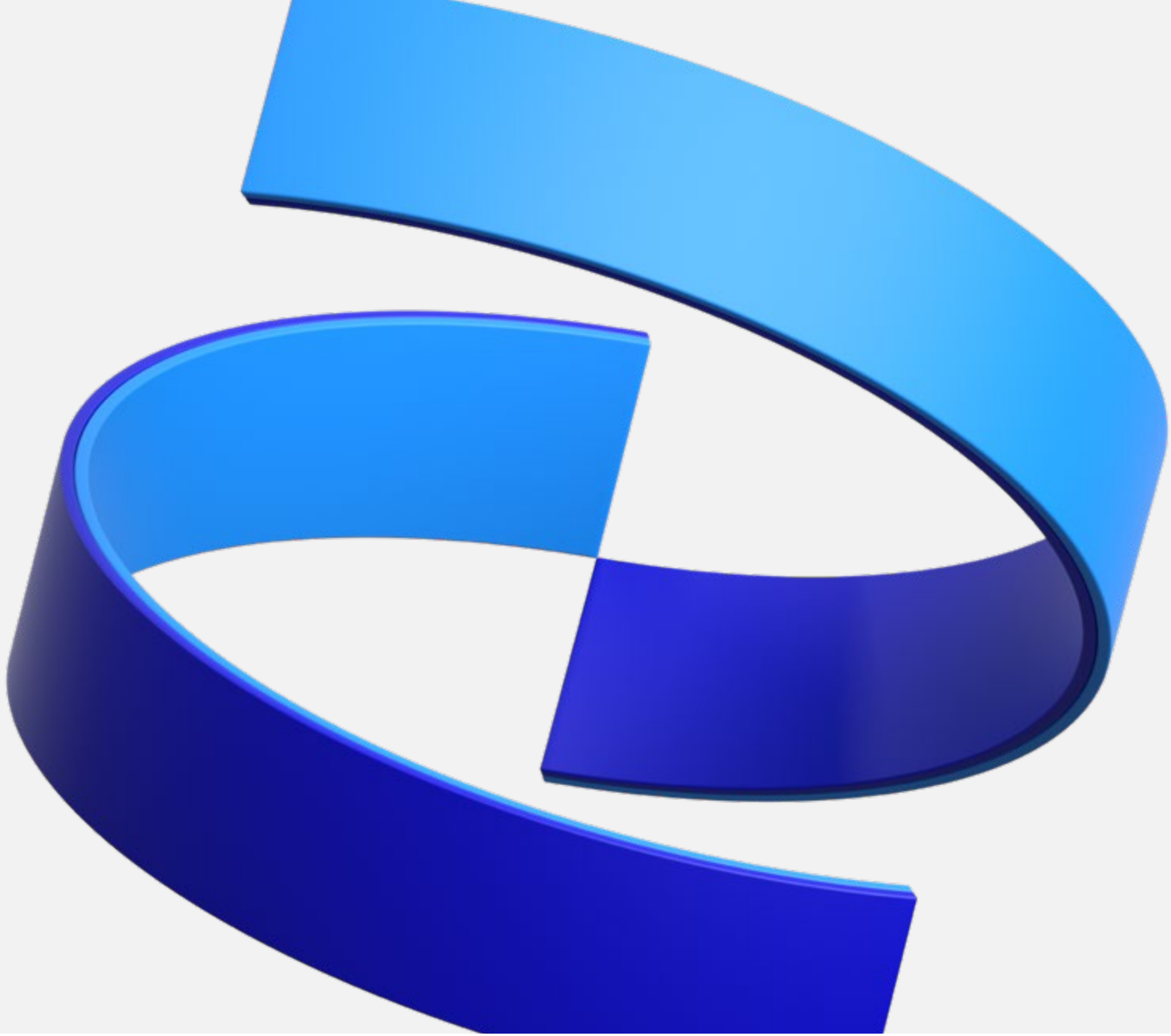
Pfizer Medical Affairs
January 6, 2023



Pfizer Medical Affairs

PAXLOVID (nirmatrelvir tablets; ritonavir tablets) Emergency Use Authorization[1,2]

- PAXLOVID has not been approved, but has been authorized for emergency use by FDA under an EUA, for the treatment of mild-to-moderate COVID-19 in adult 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

- The emergency use of PAXLOVID is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization revoked sooner

EUA, Emergency Use Authorization; FDA, Food and Drug Administration.

Food and Drug Administration. Letter of Authorization for PAXLOVID. October 27, 2022. Accessed December 28, 2022. https://www.fda.gov/media/155049/download

Outline

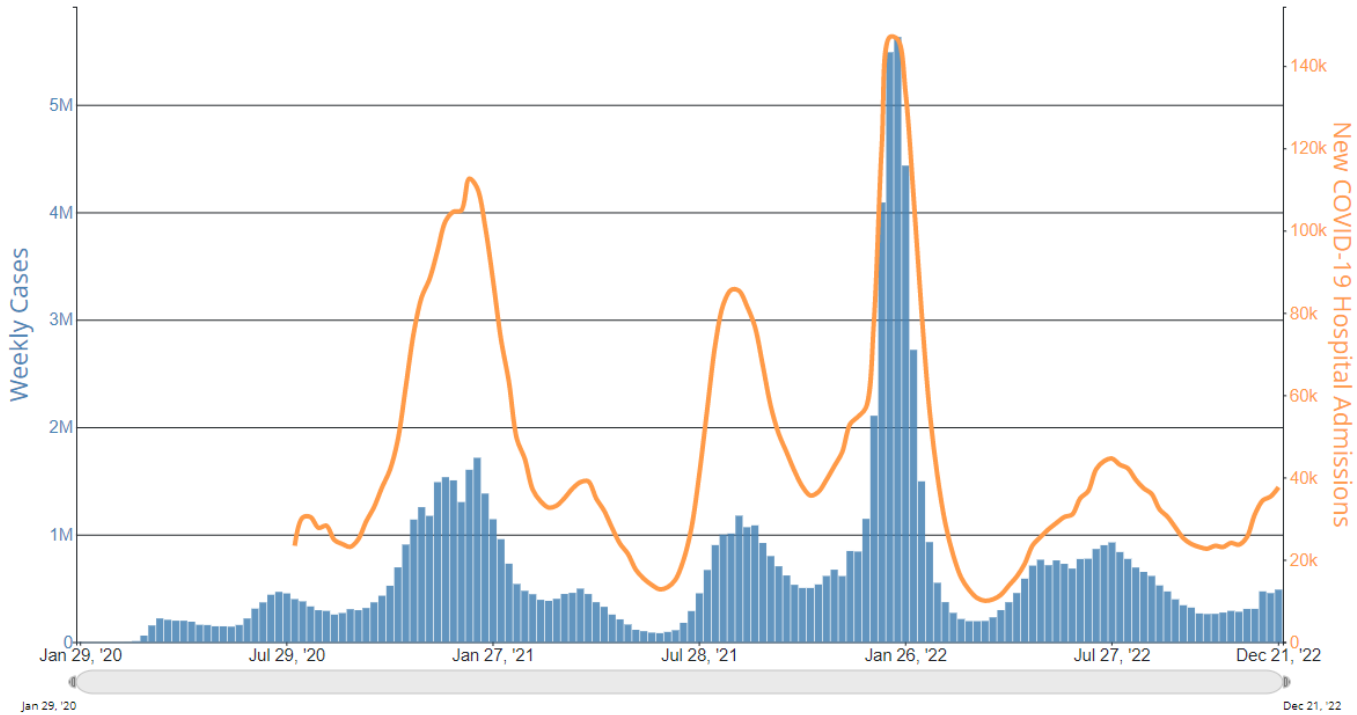
- Identifying Patients at High Risk of Progression to Severe Illness
- MOA; Circulating Variants
- EPIC-HR - Updates
- Drug Interaction Management Resources
- Viral Rebound
- Real World Evidence
- Summary

COVID-19 Cases and Hospitalizations - Weekly Trends

In the US, as of December 23, 2022

- **100,216,983** total recorded cases
- **1,086,197** total deaths
- **487,367** new cases (weekly total)
- **33,406** current hospitalized patients
- **5,374** new hospital admissions (daily average)
- Total Updated Booster Doses (People 5+): **45,675,842**

Weekly Trends in Number of Cases and Number of New Patients Admitted to Hospital with Confirmed COVID-19 Per Week in the US Reported to the CDC



CDC, Centers for Disease Control and Prevention.
Centers for Disease Control and Prevention. COVID Data Tracker. December 23, 2022. Accessed December 27, 2022. https://covid.cdc.gov/covid-data-tracker.

Pfizer Medical Affairs

Nirmatrelvir; ritonavir is an investigational treatment and has not been approved or licensed by the U.S. Food and Drug Administration (FDA), but has been authorized for emergency use by FDA under an Emergency Use Authorization (EUA). It has not been found safe or effective for any use. All data are preliminary and subject to change.

Patients Who May Be at High Risk for Progression to Severe COVID-19

Summary of high-risk factors for progression to severe COVID-19

Age ≥50 years

Age is the **strongest risk factor** for severe COVID-19 outcomes

*Risk of COVID-19-related deaths among people aged **50–64 years** is*

25x ***higher*** *than those aged **18-29 years***

Risk of severe outcomes is increased in people of all ages with certain underlying medical conditions and in people who are ≥50 years, with risk increasing substantially at ages ≥65 years

Underlying Conditions

Patients with **certain underlying medical conditions are at high risk for severe COVID-19**

Risk

Risk of progression increases with increasing number of underlying conditions, as do poorer outcomes

Conditions

Race and Ethnicity

People from **certain racial and ethnic minority groups are more likely to experience severe COVID-19** at younger ages

***Barriers** to accessing healthcare support **are more common** in certain ethnic and racial groups*

yrs, years.

Centers for Disease Control and Prevention. Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Professionals. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html (Accessed December 2022).

People Aged ≥50 Years Are at Increased Risk for Severe COVID-19 Outcomes, with Risk Increasing Substantially in People Aged ≥65 Years[1]

Age Group Rate Ratios Compared to Ages 18 to 29 Years*[2]

	0-4 years old	5-17 years old	18-29 years old	30-39 years old	40-49 years old	50-64 years old	65-74 years old	75-84 years old	85+ years old
Cases	1x	1x	Reference	1x	1x	1x	1x	1x	1x
Hospitalization	1x	<1x	Reference	2x	2x	3x	5x	8x	15x
Death	<1x	<1x	Reference	4x	10x	25x	60x	140x	340x

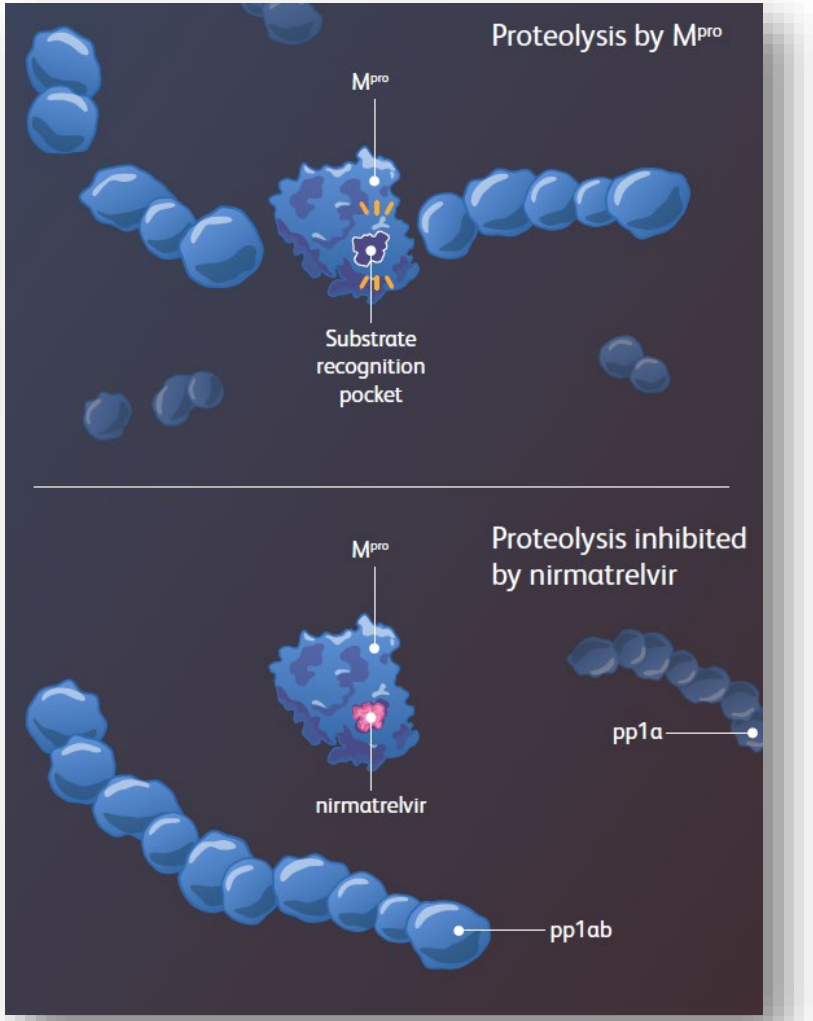
*All rates are relative to the 18 to 29 years age group. This group was selected as the reference group because it has accounted for the largest cumulative number of COVID-19 cases compared to other age groups. Sample interpretation: Compared with ages 18 to 29 years, the rate of death is four times higher in ages 30 to 39 years, and 330 times higher in those who are ages 85 years and older. (In the table, a rate of 1x indicates no difference compared to the 18 to 29 years age group).

1. Centers for Disease Control and Prevention. Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Professionals. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html (Accessed December 2022); 2. Centers for Disease Control and Prevention. Risk for COVID-19 Infection, Hospitalization, and Death By Age Group. Available at: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-age.html (Accessed December 2022).

Nirmatrelvir; Ritonavir - Mechanism of Action

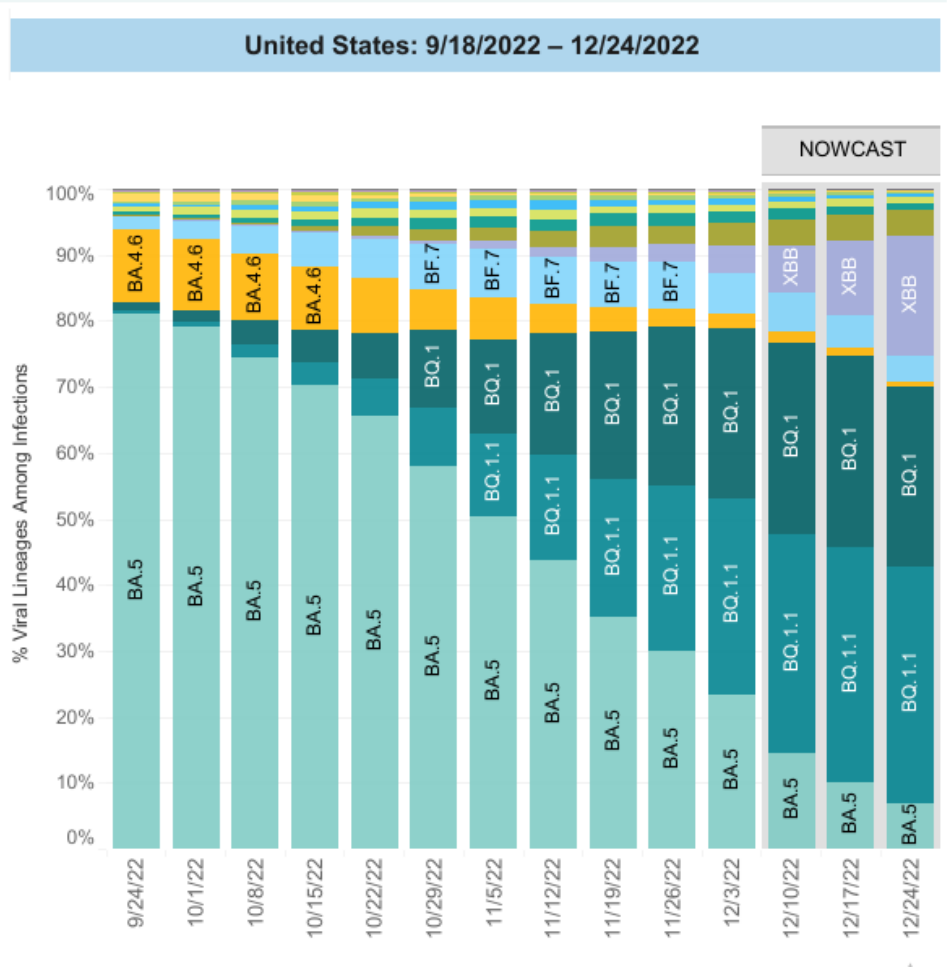
- **Nirmatrelvir** is a peptidomimetic inhibitor of the SARS-CoV-2 main protease (Mpro)[1]
- Inhibition of SARS-CoV-2 Mpro renders it incapable of processing polyprotein precursors, preventing viral replication [1]
- The M^{pro} recognition sequence is unique: no known human homolog[2]
- M^{pro} active site is highly conserved in coronaviruses[2]

- **Ritonavir** is an HIV-1 protease inhibitor but is not active against SARS-CoV-2 Mpro [1]
- Ritonavir inhibits the CYP3A-mediated metabolism of nirmatrelvir → increased plasma concentrations of nirmatrelvir[1]



1. Fact sheet for healthcare providers: Emergency use authorization for PAXLOVID; 2. Mahgoub RE, Mohamed FE, Alzyoud L, Ali BR, Ferreira J, Rabeh WM, AlNeyadi SS, Atatreh N, Ghattas MA. The Discovery of Small Allosteric and Active Site Inhibitors of the SARS-CoV-2 Main Protease via Structure-Based Virtual Screening and Biological Evaluation. Molecules. 2022; 27(19):6710. https://doi.org/10.3390/molecules27196710

Variants of Concern in the US



Microbiology (12.4): addition of Omicron subvariants, *in vivo*, and resistance data 09/2022

Antiviral Activity

Nirmatrelvir exhibited antiviral activity against SARS-CoV-2 (USA-WA1/2020 isolate) infection of differentiated normal human bronchial epithelial (dNHBE) cells with EC_{50} and EC_{90} values of 62 nM and 181 nM, respectively, after 3 days of drug exposure.

Nirmatrelvir had similar cell culture antiviral activity (EC_{50} values ≤3-fold relative to USA-WA1/2020) against SARS-CoV-2 isolates belonging to the Alpha (B.1.1.7), Gamma (P.1), Delta (B.1.617.2), Lambda (C.37), Mu (B.1.621), and Omicron (B.1.1.529/BA.1, BA.2, BA.2.12.1, and BA.4) variants. The Beta (B.1.351) variant was the least susceptible tested variant with approximately 3.7-fold reduced susceptibility relative to the USA-WA1/2020 isolate.

Based on GISAID* sequence analysis, the **active site and Mpro in general is conserved in all the lineages**: BQ.1, BQ.1.1, XBB, XBB.1.5 and also BJ.1, BM.1.1.1, BA.2.75.2, BF.7, and BA.4.6).

Fact sheet for healthcare providers: Emergency use authorization for PAXLOVID; https://covid.cdc.gov/covid-data-tracker/#variant-proportions; Accessed January 5, 2023; *GISAID (Global Initiative on Sharing Avian Influenza Data) https://gisaid.org/ Accessed January 5, 2023.

Pfizer Medical Affairs

EPIC-HR (Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients): Final Analysis of Efficacy Outcomes

EPIC-HR: Pivotal phase 2/3 study that evaluated the safety and efficacy of nirmatrelvir; ritonavir in non-hospitalized adult patients with mild-to-moderate COVID-19 at high risk for progression to severe disease

- **Primary endpoint**: The final analysis showed an **86% reduction in risk of COVID-19-related hospitalization or death** from any cause compared to placebo in patients treated within 5 days of symptom onset[1-3]
- **Secondary endpoint**: The final analysis showed an **89% reduction in risk of COVID-19-related hospitalization or death** from any cause compared to placebo in patients treated within 3 days of symptom onset[1,4]
- In the overall study population through Day 28, no deaths were reported in patients who received nirmatrelvir; ritonavir compared to 12 (1.2%) deaths in patients who received placebo[1,2]

Patients With COVID-19-Related Hospitalization or Death From Any Cause Through Day 28[1]

	Nirmatrelvir; ritonavir	Placebo	*P* value
Primary endpoint Treatment within 5 days of symptom onset	5/697 (0.7%) hospitalized with no deaths	44/682 (6.5%) hospitalized with 9 subsequent deaths	<0.0001
Secondary endpoint Treatment within 3 days of symptom onset	8/1039 (0.8%) hospitalized with no deaths	66/1046 (6.3%) hospitalized with 12 subsequent deaths	<0.0001

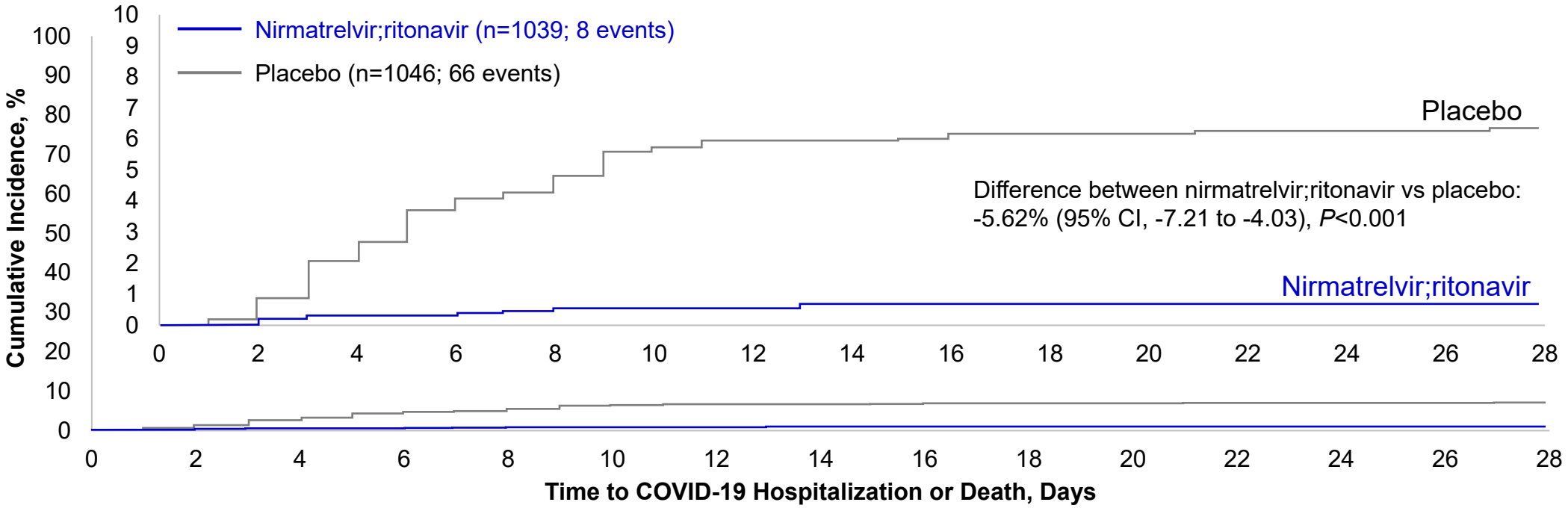
EPIC-HR included 2246 symptomatic, unvaccinated, outpatient, adults at high risk for progression to severe COVID-19 within 5 days after symptom onset, who were randomized to nirmatrelvir; ritonavir (300 mg; 100 mg) or placebo every 12 hours for 5 days.

EPIC-HR, Evaluation of Protease Inhibition for COVID-19 in High-Risk Patients.

1. Food and Drug Administration. Fact sheet for healthcare providers: emergency use authorization for PAXLOVID. September 26, 2022. Accessed December 2, 2022. https://www.fda.gov/media/155050/download; 2. PAXLOVID Data on File, Pfizer. 3. Hammond J, et al. Effect of nirmatrelvir/ritonavir versus placebo on COVID-19–related hospitalizations and other medical visits. Oral presentation at: IDWeek 2022; October 222; Washington, DC. 4. Hammond J, et al. *N Engl J Med.* 2022;386(15):1397-1408. doi: 10.1056/NEJMoa2118542.

EPIC-HR: Primary Endpoint Analysis in Patients Treated with Nirmatrelvir; Ritonavir ≤5 Days After Symptom Onset

COVID-19–Related Hospitalization or Death From Any Cause Through Day 28*



Number at Risk

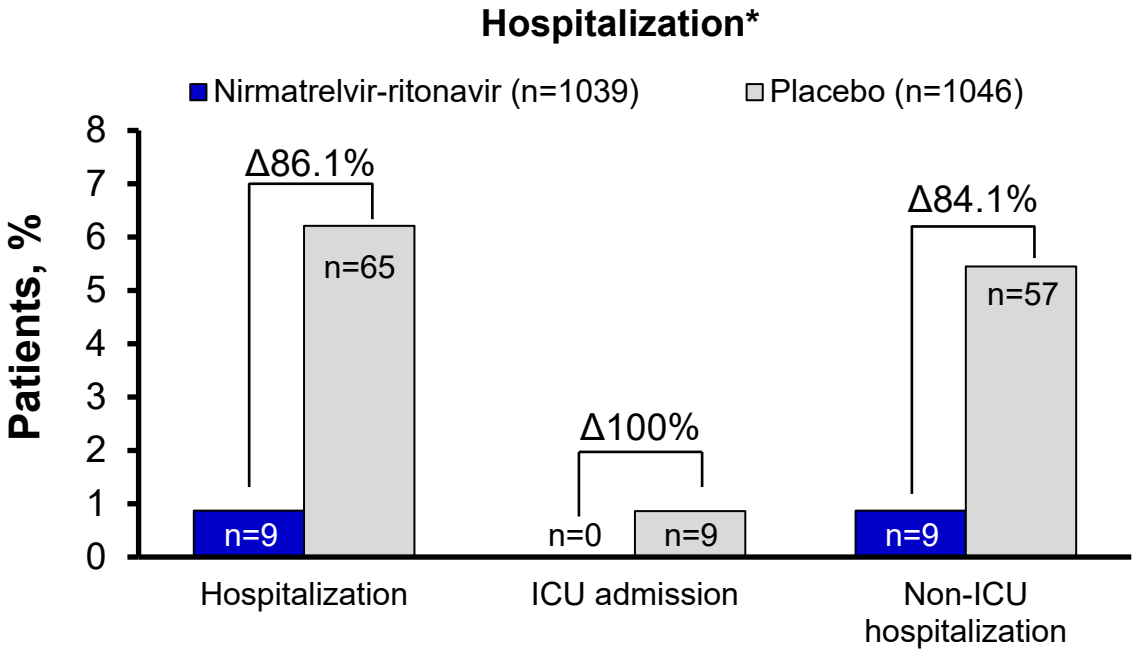
NMV-r	1039	1034	1023	1013	1007	1004	1002	1000	997	995	993	993	993	993	992
Placebo	1046	1042	1015	990	977	963	959	959	955	953	951	948	948	948	945

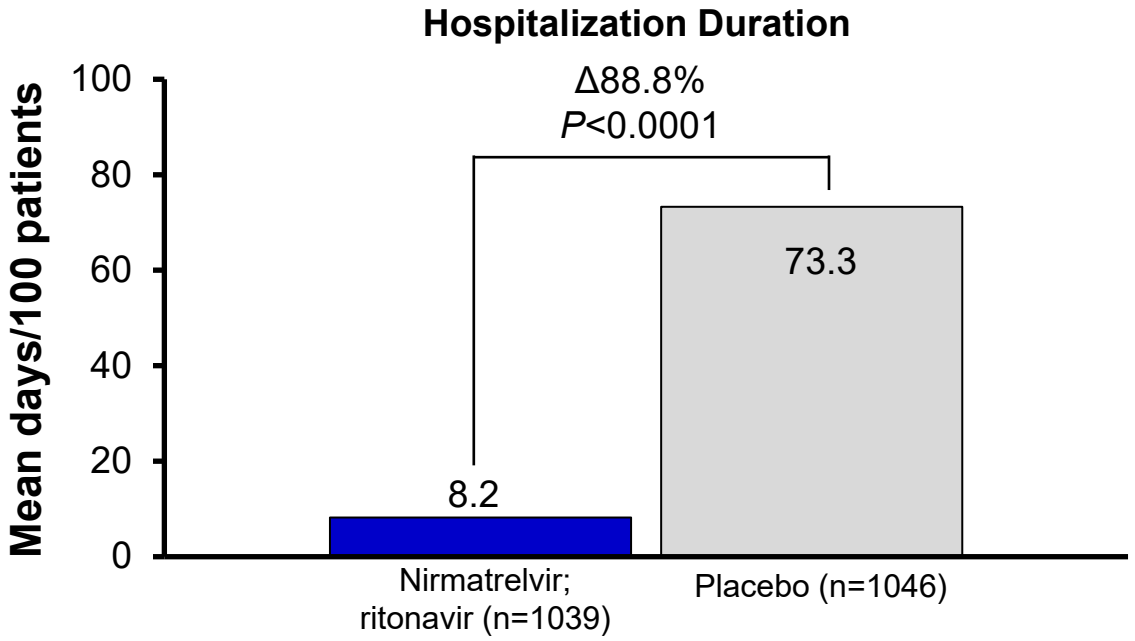
CI, confidence interval; NMV-r, nirmatrelvir;ritonavir.

Hammond J, et al, *N Engl J Med*. 2022;386(15):1397-1408. doi: 10.1056/NEJMoa2118542.

Pfizer Medical Affairs

COVID-19–Related Hospitalization (mITT1)



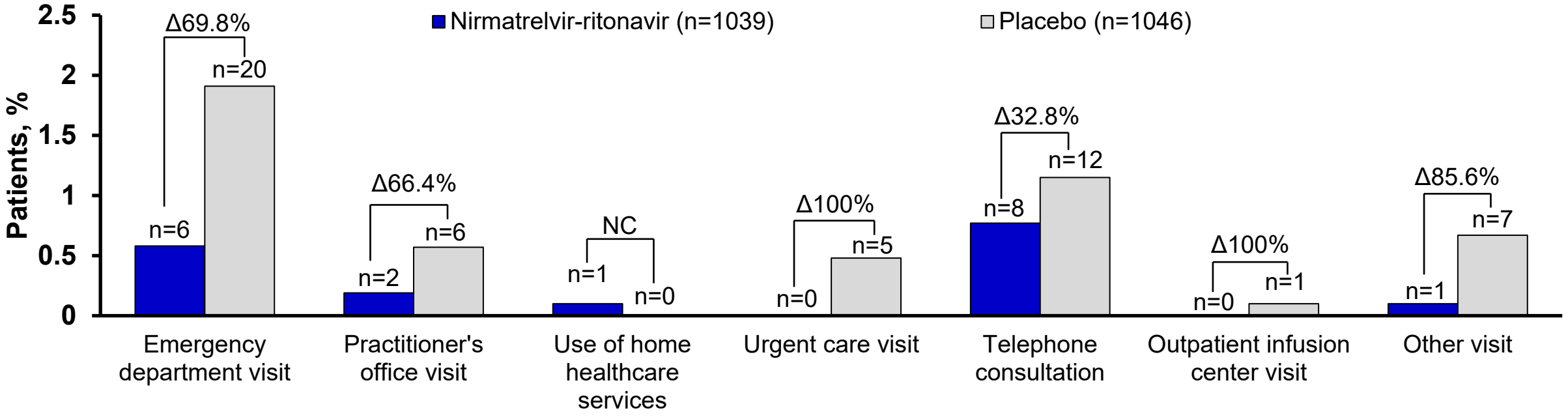


- Fewer hospitalizations were reported among those who received nirmatrelvir; ritonavir compared with placebo
  - No patients in the nirmatrelvir; ritonavir group and 9 patients in the placebo group were admitted to the ICU
  - Mean days of hospitalization per 100 patients was significantly reduced among nirmatrelvir; ritonavir treated patients
- Among hospitalized participants with known discharge status, 100% of those who received nirmatrelvir; ritonavir were discharged to home self-care vs 52.9% of those receiving placebo

*Not limited through Day 28.
Δ, percentage reduction with nirmatrelvir;ritonavir compared with placebo; ICU, intensive care unit; mITT1, modified intent-to-treat 1.
Hammond J et al; Presented at: IDWeek 2022; October 19–23, 2022; Washington, DC, USA; Pfizer, Data on File.

Pfizer Medical Affairs

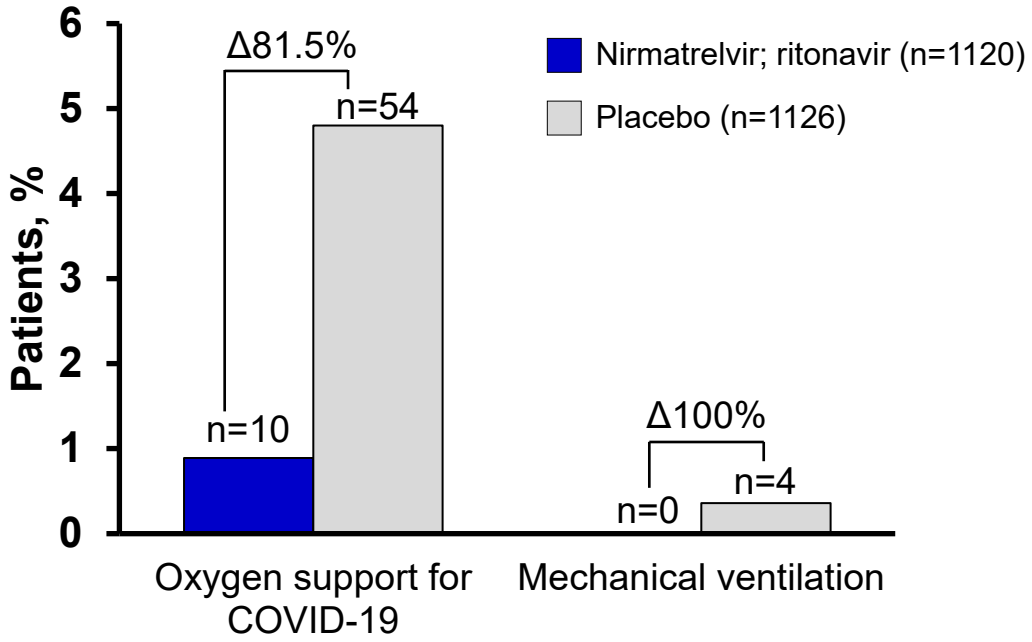
Other COVID-19–Related Medical Visits (mITT1)*



- Through Day 34, fewer patients in the nirmatrelvir; ritonavir group reported COVID-19–related medical visits compared to placebo
  - 2.2% (23/1039) of patients treated with nirmatrelvir; ritonavir and 8.1% (85/1046) of patients who received placebo reported any COVID-19–related medical visit, corresponding to a 73% RRR (*P*<0.0001) with treatment

*Not limited through Day 28.
Δ, percentage reduction with nirmatrelvir;ritonavir compared with placebo; ICU, intensive care unit; mITT1, modified intent-to-treat 1; RRR, relative risk reduction.
Hammond J et al; Presented at: IDWeek 2022; October 19–23, 2022; Washington, DC, USA; Pfizer, Data on File.

Patients Who Received Oxygen Supplementation for COVID-19



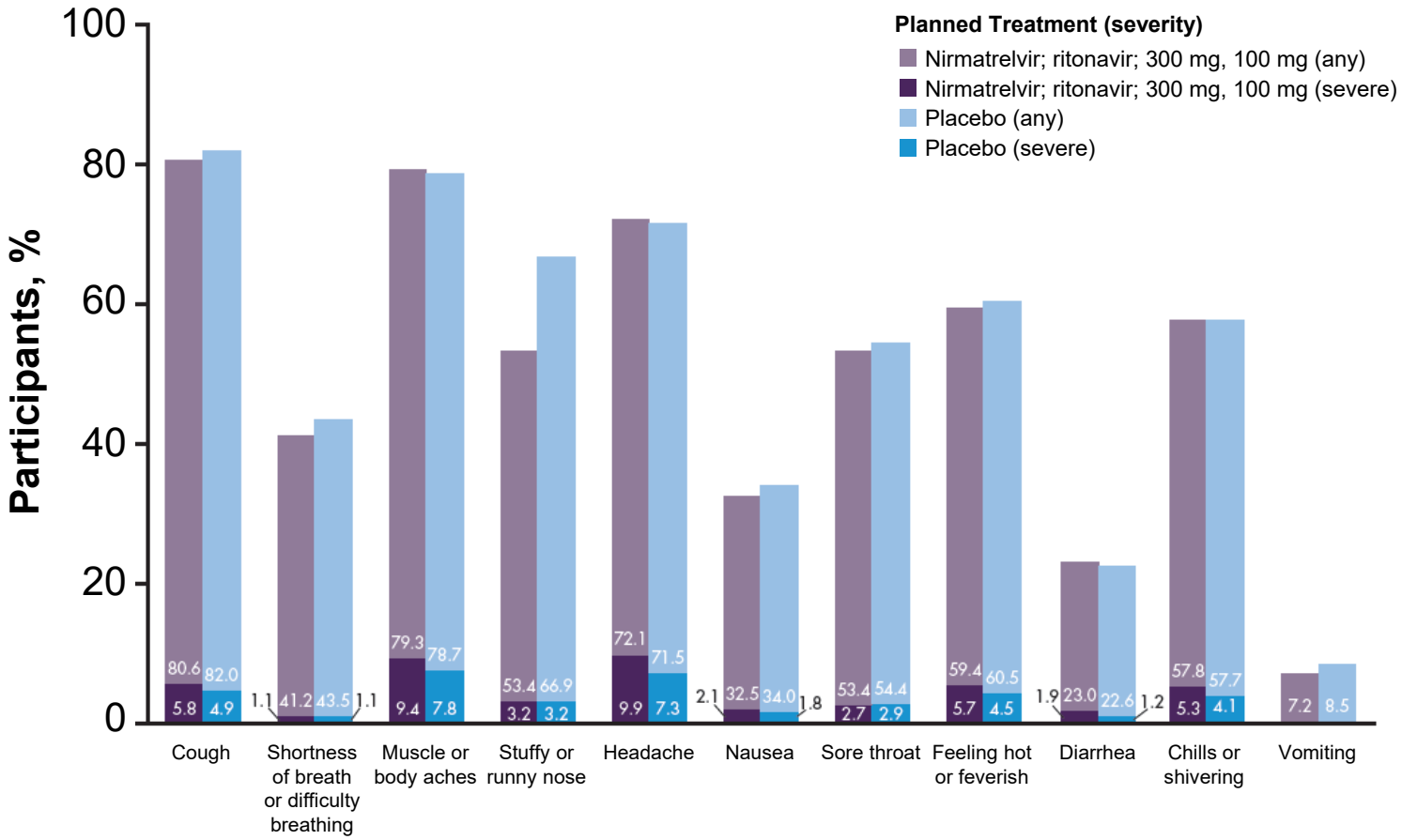
- 81.5% RRR in requirement for oxygen support for COVID-19
- None of the patients in the nirmatrelvir; ritonavir group vs 4 patients in the placebo group received mechanical ventilation

*Not limited through Day 28.
Δ, percentage reduction with nirmatrelvir;ritonavir compared with placebo; RRR, relative risk reduction.
Hammond J et al; Presented at: IDWeek 2022; October 19–23, 2022; Washington, DC, USA; Pfizer, Data on File.

Pfizer Medical Affairs

EPIC-HR Secondary Endpoint: Alleviation and Resolution of Targeted Symptoms

Cough, headache, and muscle or body aches were the most common symptoms at baseline, with headache and muscle or body aches being the most common severe symptoms.



- Patients logged the presence and severity on 3- or 4-point scales of 15 prespecified COVID-19 signs/symptoms from Day 1 (before dose) through Day 28 using an electronic handheld device

Hammond J et al; Poster presentation at: IDWeek 2022; October 19–23, 2022; Washington, DC, USA; Pfizer, Data on File.

Pfizer Medical Affairs

Nirmatrelvir; ritonavir is an investigational treatment and has not been approved or licensed by the U.S. Food and Drug Administration (FDA), but has been authorized for emergency use by FDA under an Emergency Use Authorization (EUA). It has not been found safe or effective for any use. All data are preliminary and subject to change.

EPIC-HR Secondary Endpoint: Alleviation and Resolution of Targeted Symptoms

- Patients logged the presence and severity on 3- or 4-point scales of the 15 prespecified COVID-19 signs/symptoms at approximately the same time daily from Day 1 (before dose) through Day 28 using an electronic handheld device

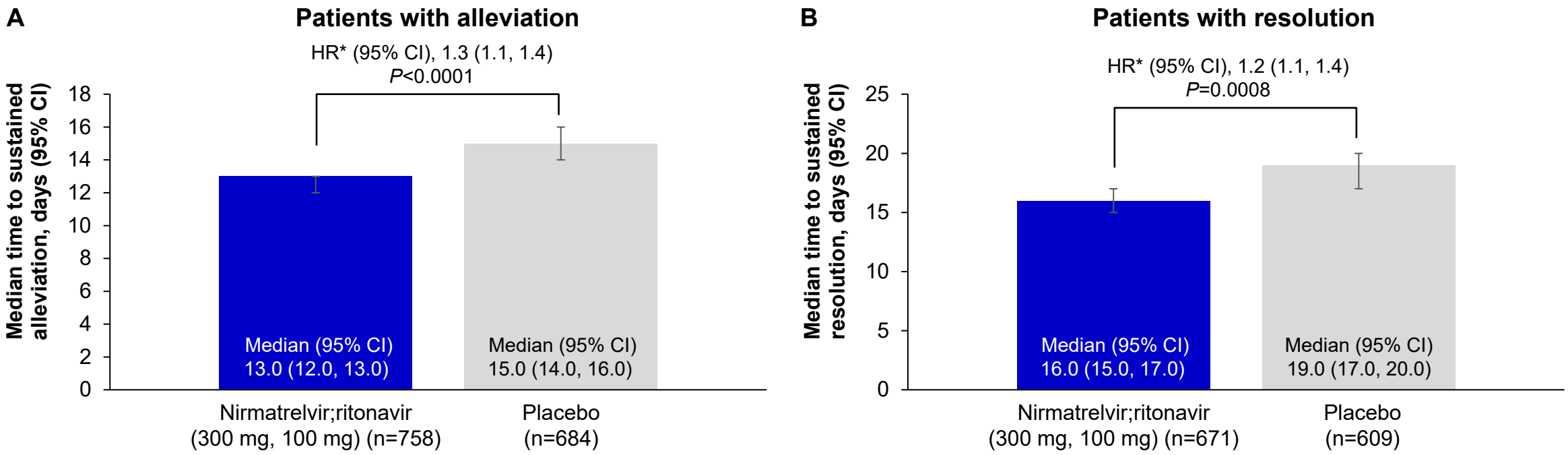
Description of Sustained Alleviation and Sustained Resolution of All Targeted COVID-19 Signs/Symptoms.

Outcome	Definition
Sustained alleviation	• The event occurring on the first of 4 consecutive days when all symptoms scored as moderate or severe at study entry were scored as mild or absent AND all symptoms scored mild or absent at study entry were scored as absent • The first day of the 4 consecutive-day period was considered the First Event Date
Sustained resolution	• The event occurring when all targeted symptoms were scored as absent for 4 consecutive days • The first day of the 4 consecutive-day period was considered the First Event Date

Hammond J et al; Poster presentation at: IDWeek 2022; October 19–23, 2022; Washington, DC, USA; Pfizer, Data on File.

Results: Treatment with Nirmatrelvir; Ritonavir Resulted in an Improvement in Time to Symptom Alleviation and Resolution Relative to Placebo

Nirmatrelvir; ritonavir treatment resulted in a (A) 2-day improvement in time to symptom alleviation vs placebo (*P*<0.0001) and (B) 3-day improvement in time to symptom resolution vs placebo (*P*=0.0008) in the mITT1 analysis set.



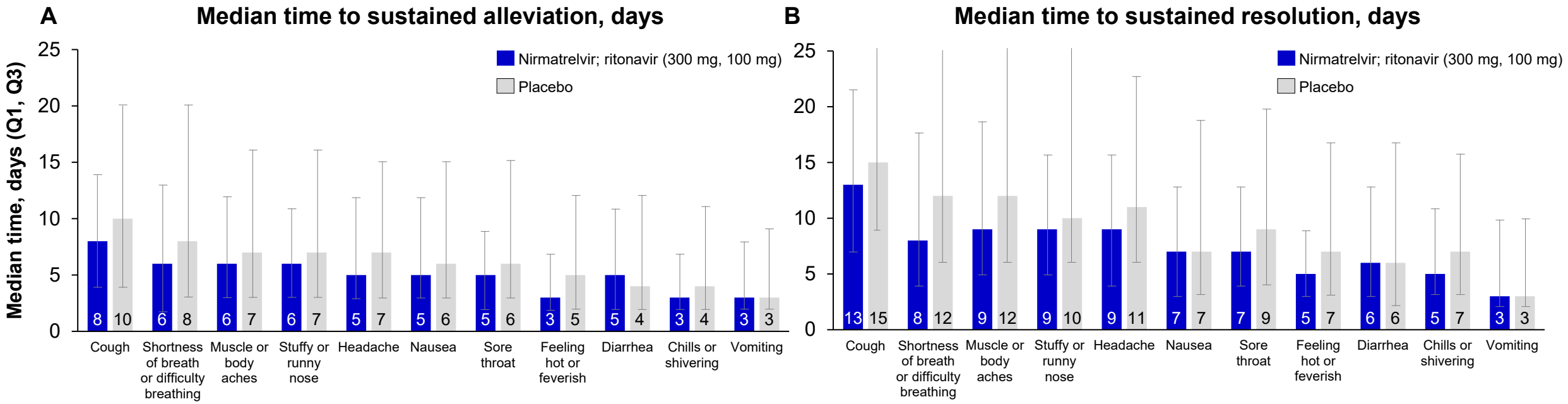
Median time, days (Q1, Q3):	13.0 (8.0, 22.0)	15.0 (9.0, >25.0)	16.0 (10.0, >25.0)	19.0 (11.0, >25.0)

*HR for nirmatrelvir;ritonavir treatment vs placebo.
CI, confidence internal; HR, hazard ratio; mITT1, modified intent-to-treat 1; Q1, first quartile; Q3, third quartile.
Hammond J et al; Poster presentation at: IDWeek 2022; October 19–23, 2022; Washington, DC, USA; Pfizer, Data on File.

Pfizer Medical Affairs

Results: Treatment with Nirmatrelvir; Ritonavir Resulted in an Improvement in Time to Symptom Alleviation and Resolution Relative to Placebo (cont'd)

Nirmatrelvir; ritonavir treatment resulted in faster (A) alleviation and (B) resolution of all individual symptoms vs placebo with the exception of GI-related symptoms (mITT1 analysis set).



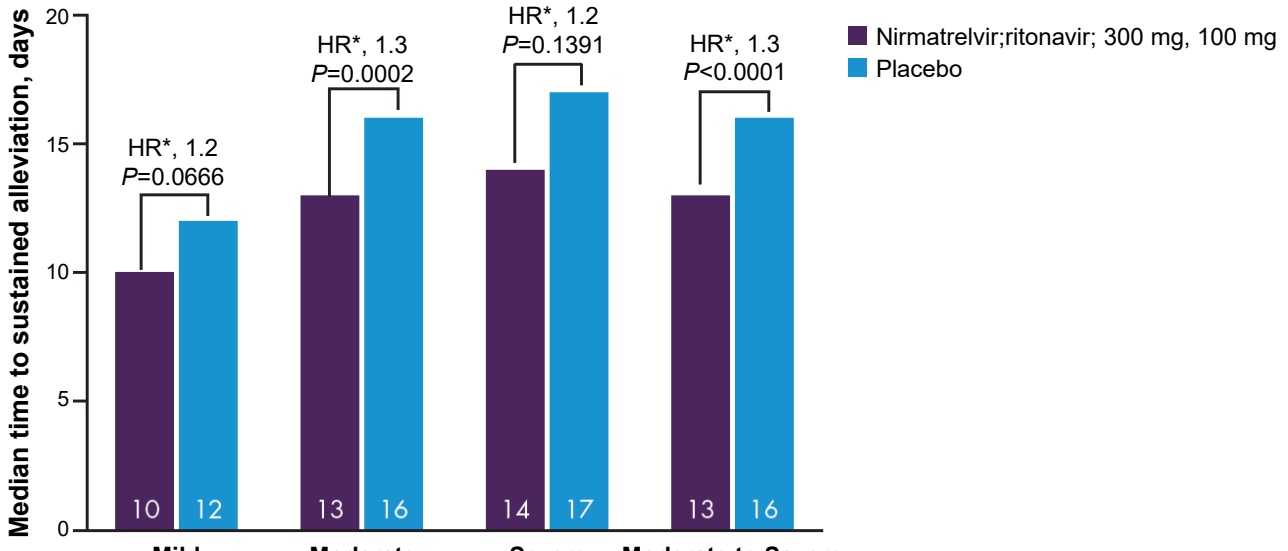
GI, gastrointestinal; mITT1, modified intent-to-treat 1; Q1, first quartile; Q3, third quartile.

Hammond J et al; Poster presentation at: IDWeek 2022; October 19–23, 2022; Washington, DC, USA; Pfizer, Data on File.

Pfizer Medical Affairs

Results: Treatment with Nirmatrelvir; Ritonavir Resulted in an Improvement in Time to Symptom Alleviation and Resolution Relative to Placebo (cont'd)

Patients treated with nirmatrelvir; ritonavir achieved sustained alleviation of COVID-19 symptoms regardless of baseline symptom severity (mITT1 analysis set)



No. of patients	238	264	515	546	213	189	728	735
No. reporting alleviation through Day 28	194	197	136	192	144	111	523	465

- The median times to sustained alleviation were shorter for patients treated with nirmatrelvir; ritonavir compared with placebo, regardless of baseline severity
  - Among the patients who had moderate-to-severe symptoms at baseline (nirmatrelvir; ritonavir, n=728; placebo, n=735), the median time to sustained alleviation was significantly shorter with nirmatrelvir; ritonavir (13 days) vs placebo (16 days; *P*<0.0001)

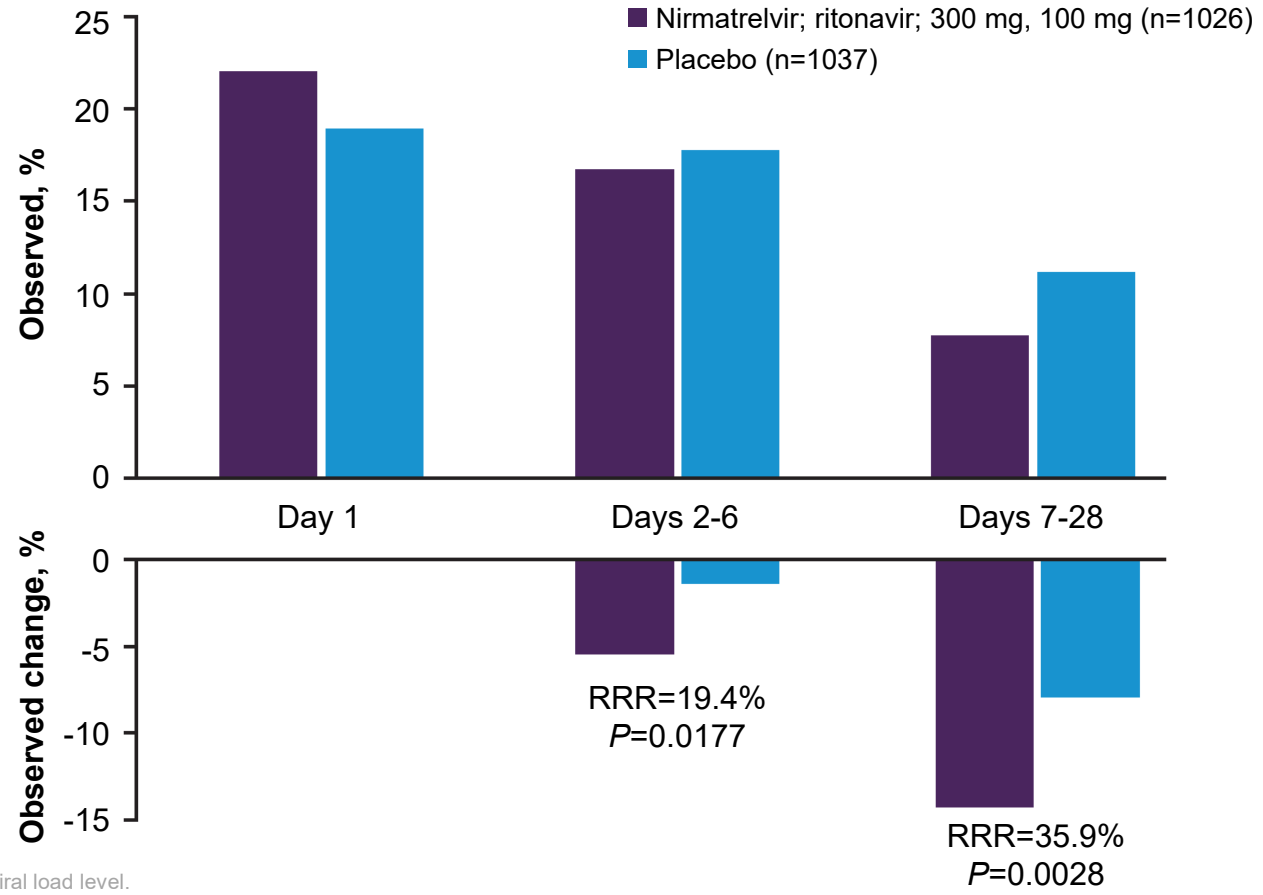
*HR for nirmatrelvir;ritonavir treatment vs placebo.
HR, hazard ratio; mITT1, modified intent-to-treat 1.
Hammond J et al; Poster presentation at: IDWeek 2022; October 19–23, 2022; Washington, DC, USA; Pfizer, Data on File.

Pfizer Medical Affairs

Results: Treatment with Nirmatrelvir; Ritonavir Resulted in an Improvement in Time to Symptom Alleviation and Resolution Relative to Placebo (cont'd)

- The **proportion of patients with severe signs/symptoms** in the nirmatrelvir; ritonavir group compared with placebo group was substantially higher at baseline but significantly lower after treatment and during the follow-up period (Day 7 to Day 28), indicating that nirmatrelvir; ritonavir significantly reduced symptom severity through Day 28

Treatment with nirmatrelvir;ritonavir significantly reduced the percentage of patients with severe signs or symptoms from Days 2-6 and Days 7-28 relative to placebo (mITT1 analysis set).



RRR to placebo estimated as DID using a GEE model adjusting for days since symptom onset, serology status, and viral load level.
DID, Different-In-Difference; GEE, Generalized Estimating Equations; mITT1, modified intent-to-treat 1; RRR, relative risk reduction.

EPIC-HR: Final Analysis of Safety Outcomes

Summary of Treatment-Emergent Adverse Events[1,2]

	Nirmatrelvir-ritonavir	Placebo
N	1109	1115
Patients with adverse events (any)	251 (23%)	266 (24%)
Serious adverse events	18 (1.6%)	74 (6.6%)
Adverse events leading to discontinuation of treatment	23 (2.1%)	47 (4.2%)

The majority of treatment-emergent adverse events were mild in severity

1. Hammond J, et al. *N Engl J Med*. 2022;386(15):1397-1408. doi: 10.1056/NEJMoa2118542. 2. Food and Drug Administration. Fact sheet for healthcare providers: Emergency use authorization for PAXLOVID.

Safety: Post-Authorization Experience

The following adverse reactions have been identified during post-authorization use of PAXLOVID. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- *Immune System Disorders:* Anaphylaxis, hypersensitivity reactions *[see Warnings and Precautions (5.2)]*
- *Gastrointestinal Disorders:* Abdominal pain, nausea
- *General Disorders and Administration Site Conditions:* Malaise

Fact sheet for healthcare providers: Emergency use authorization for PAXLOVID.

Dosage and Administration

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:

300 mg; 100 mg Dose Pack

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).

150 mg; 100 mg Dose Pack

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

- PAXLOVID is not recommended in patients with severe renal impairment (<30 mL/min) as the appropriate dose has not been determined.
- PAXLOVID is not recommended in patients with severe hepatic impairment (Child-Pugh Class C) as no pharmacokinetic or safety data is available in subjects with severe hepatic impairment.

Fact sheet for healthcare providers: Emergency use authorization for PAXLOVID.
*eGFR=estimated glomerular filtration rate based on the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) formula

Resources to Help Identify and Manage Drug-Drug Interactions with PAXLOVID (nirmatrelvir tablets; ritonavir tablets)

Pfizer Medical Resources

- Fact Sheet for Healthcare Providers
- PAXLOVID Medical Information Page, which includes a drug interaction tool
- Potentially Significant Drug Interactions, Including Contraindicated Drugs Resource

Third-party Resources

- NIH Guideline on Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications
- The University of Liverpool COVID-19 Drug Interactions website

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Information on 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 and/or Day 14 in a subset of PAXLOVID and placebo recipients in EPIC-HR, irrespective of COVID-19 symptoms. The frequency of detection of post-treatment viral RNA rebound varied according to analysis parameters but was generally similar among PAXLOVID and placebo recipients, regardless of the rebound definition used. A similar or smaller percentage of placebo recipients compared to PAXLOVID recipients had nasopharyngeal viral RNA results < lower limit of quantitation (LLOQ) at all study timepoints in both the treatment and post-treatment periods.
- Post-treatment viral RNA rebound was not associated with the primary clinical outcome of COVID-19-related hospitalization or death from any cause through Day 28 following the single 5-day course of PAXLOVID treatment. Post-treatment viral RNA rebound also was not associated with drug resistance as measured by Mpro sequencing. The clinical relevance of post-treatment increases in viral RNA following PAXLOVID or placebo treatment is unknown.

*EPIC-HR included 2246 symptomatic, unvaccinated, outpatient, adults at high risk for progression to severe COVID-19 within 5 days after symptom onset, who were randomized to nirmatrelvir;ritonavir (300 mg; 100 mg) or placebo every 12 hours for 5 days.
EUA, Emergency Use Authorization; M^{pro}, main protease.
Food and Drug Administration. Fact sheet for healthcare providers: emergency use authorization for PAXLOVID. September 26, 2022. Accessed December 2, 2022. https://www.fda.gov/media/155050/download.

COVID-19 Rebound Management: CDC and NIH Guidance

CDC Health Advisory[1]

- A brief resurgence of symptoms may be part of the natural course of SARS-CoV-2 infection in some individuals and unrelated to treatment with nirmatrelvir;ritonavir or vaccination status
- Limited data from case reports indicate that patients treated with nirmatrelvir;ritonavir who experienced COVID-19 rebound have had mild symptoms, and no cases of severe disease have been reported
- In cases of suspected COVID-19 rebound, there is currently no evidence that additional treatments with nirmatrelvir;ritonavir or other anti-SARS-CoV-2 therapies are needed
- Early treatment with nirmatrelvir;ritonavir is recommended for mild-to-moderate COVID-19 in individuals at high risk for progression to severe disease
- Regardless of prior treatment with an antiviral agent and/or previous isolation following initial infection, individuals experiencing COVID-19 rebound should adhere to CDC recommendations regarding isolation of infected patients
- Individuals experiencing a resurgence of COVID-19 symptoms or a new positive COVID-19 test after a previous negative test should restart isolation for a minimum of 5 days

NIH Guidelines[2]

- To date, the return of COVID-19 symptoms following treatment with nirmatrelvir;ritonavir has not been associated with progression to severe disease
- Concerns pertaining to recurrence of COVID-19 symptoms following treatment should not be a reason to avoid the use of nirmatrelvir;ritonavir
- The current Emergency Use Authorization does not permit longer treatment courses of nirmatrelvir;ritonavir
- There are insufficient data available on the efficacy of administering a second course of nirmatrelvir;ritonavir

CDC, Centers for Disease Control; NIH, National Institutes of Health.

1. Centers for Disease Control and Prevention. COVID-19 Rebound After Paxlovid Treatment. CDCHAN-00467. May 24, 2022. Accessed November 29, 2022. https://emergency.cdc.gov/han/2022/han00467.asp. 2. National Institutes of Health. COVID-19 Treatment Guidelines: Ritonavir-Boosted Nirmatrelvir (Paxlovid). September 26, 2022. Accessed November 29, 2022. https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ritonavir-boosted-nirmatrelvir--paxlovid-/#:~:text=Viral%20rebound%20and%20the%20recurrence%20of%20COVID%2D19%20symptoms%20can,treatment%20with%20ritonavir%2Dboosted%20nirmatrelvir.&text=The%20EPIC%2DHR%20trial%20demonstrated,progressing%20to%20severe%20COVID%2D19.

Real World Effectiveness – Published US Data;
Pfizer-Sponsored Pre-Print Data *as of Dec 12, 2022*

Nirmatrelvir Plus Ritonavir for Early COVID-19 in a Large U.S. Health System Dryden-Peterson S, et al. Annals of Internal Medicine 2022. doi/10.7326/M22-2141.	• Health system across Massachusetts and New Hampshire • January 1 to May 15, 2022	• Non-hospitalized patients ≥50 yrs old with COVID-19 (N=30,322) • 6036 patients were prescribed nirmatrelvir-ritonavir
Oral Nirmatrelvir and Ritonavir in Nonhospitalized Vaccinated Patients With Coronavirus Disease 2019 (COVID-19) Ganatra S, et al. *Clin Infect Dis*. 2022; doi:10.1093/cid/ciac673.	• TriNetX research network • December 1, 2021 to April 18, 2022	• Non-hospitalized, vaccinated patients ≥18 years old with COVID-19 (N=2,260) • 1130 received nirmatrelvir-ritonavir
COVID-19 Therapeutics and Outcomes Among Solid Organ Transplant Recipients During the Omicron BA.1 Era Hedvat J, et al. *Am J Transplant*. 2022; doi:10.1111/ajt.17140.	• New York-Presbyterian Hospital health system • December 16, 2021 to January 19, 2022	• Solid organ transplant patients with asymptomatic, mild, or moderate COVID-19 (N=154; Range of age = 37 - 68 years)
Hospitalization and Emergency Department Encounters for COVID-19 After Paxlovid Treatment — California, December 2021–May 2022 Malden DE, et al. *MMWR Morb Mortal Wkly Rep*. 2022;71:830-833	• Kaiser Permanente Southern California healthcare system • December 31, 2021 to May 26, 2022	• Non-hospitalized patients ≥12 years old who received nirmatrelvir-ritonavir (N=5,287)
Effectiveness of Nirmatrelvir-Ritonavir Against Hospital Admission: A Matched Cohort Study in a Large US Healthcare System Lewnard JA, et al. *medRxiv*. 2022; doi: 10.1101/2022.10.02.22280623.	• Kaiser Permanente Southern California healthcare system • December 31, 2021 to July 29, 2022	• Non-hospitalized patients ≥12 years old with COVID-19 (N=25,039) • 4329 individuals received nirmatrelvir-ritonavir

Paxlovid Associated with Decreased Hospitalization Rate Among Adults with COVID-19 — United States, April–September 2022 Shah MM, et al. *MMWR Morb Mortal Wkly Rep*. 2022;71(48):1531-1537.	• Cosmos data set containing information from U.S. health systems • April 1 to August 31, 2022	• Patients with COVID-19 aged ≥18 years (N=699,848) • 198,927 (28.4%) were prescribed nirmatrelvir-ritonavir within 5 days of COVID-19 diagnosis
Tolerance and Clinical Outcomes of COVID-19 Antiviral Therapy in Long-Term Care Residents Vuppalanchi S, et al. *J Am Geriatr Soc*. 2022;70(10):3033-3035.	• 26 long-term care facilities in Indiana • January 5 to February 18, 2022	• Long-term care facility residents with COVID-19 who were eligible for oral antiviral therapy (N=125) • Residents' ages ranged from 46 to 99 yrs (median = 81 yrs) and 85% were aged ≥65 yrs
Comparable Outcomes for Bebtelovimab and Ritonavir-Boosted Nirmatrelvir Treatment in High-Risk Patients With Coronavirus Disease-2019 During Severe Acute Respiratory Syndrome Coronavirus 2 BA.2 Omicron Epoch Razonable RR, et al. *J Infect Dis*. 2022;226:1683-1687.	• Mayo Clinic healthcare delivery network in the U.S. • March 20 to June 14, 2022	• High-risk patients aged ≥18 years with mild-to-moderate COVID-19 (N=3,607) • 774 received nirmatrelvir-ritonavir
Real-World Effectiveness of Nirmatrelvir/Ritonavir in Preventing Hospitalization Among Patients With COVID-19 at High Risk for Severe Disease in the United States: A Nationwide Population-Based Cohort Study Zhou X, et al. *medRxiv*. 2022; doi:10.1101/2022.09.13.22279908.	• US Optum COVID-19 Electronic Health Record dataset • December 22, 2021 to June 8, 2022	• Patients ≥12 years old with a positive SARS-CoV-2 test or COVID-19 diagnosis who did (n=2808) or did not (n=10,849) receive nirmatrelvir-ritonavir (after propensity score matching)

Retrospective Study of the Effectiveness of Nirmatrelvir-Ritonavir Against Hospitalization in adult COVID-19 patients

Nirmatrelvir-ritonavir was associated with a 51% lower hospitalization rate in adult COVID-19 patients

Population

- Non-hospitalized adults with COVID-19 aged ≥50 years or ≥18 years with an underlying health condition (N=699,848), of whom:
  - 15% had documentation of previous infection
  - 68.8% of patients were confirmed to have received ≥2 COVID-19 mRNA vaccine
  - 92.4% had ≥1 underlying condition
- 28.4% (198,927) of eligible patients received a nirmatrelvir-ritonavir prescription within 5 days of a COVID-19 diagnosis

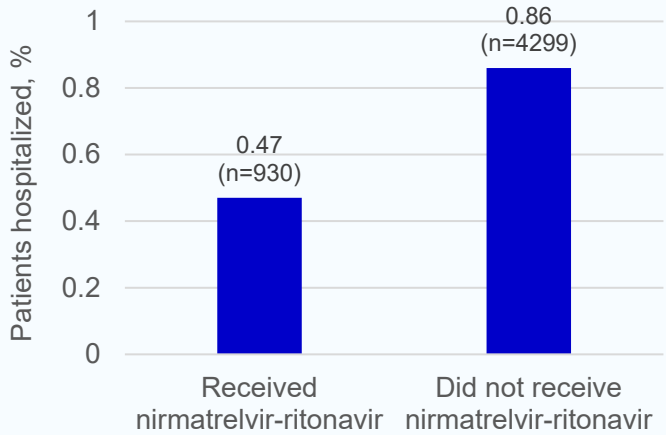
Study design

- Large retrospective study of Cosmos, an electronic health record data set in the US of infections diagnosed between April 1 – August 31, 2022 (different Omicron variants in circulation)
- Primary outcome was to assess the association between receiving a prescription for nirmatrelvir-ritonavir and hospitalization with a COVID-19 diagnosis in the following 30 days

Findings

- 5229 (0.75%) persons were hospitalized. Of these:
  - 3311 (63.3%) of hospitalizations occurred among persons aged ≥65 years
  - 930 (17.8%) received nirmatrelvir-ritonavir during the five days after diagnosis
  - 211 deaths were reported (0.01% vs 0.04% mortality in patients who did vs did not receive nirmatrelvir-ritonavir)
- Nirmatrelvir-ritonavir receipt was associated with a lower rate of all-cause hospitalization (aHR, 0.49; 95% CI, 0.46-0.53) and ARI-associated hospitalization (aHR, 0.48; 95% CI, 0.45-0.51)

Hospitalization in patients who did or did not receive nirmatrelvir-ritonavir treatment



Author conclusions

- Among U.S. adults diagnosed with COVID-19, including those with previous infection or vaccination, patients who were prescribed nirmatrelvir-ritonavir within five days of diagnosis had a 51% lower hospitalization rate within 30 days after diagnosis than those who were not prescribed nirmatrelvir-ritonavir

aHR, adjusted hazard ratio; ARI, acute respiratory illness; CI, confidence interval; mRNA, messenger ribonucleic acid.

Shah MM, et al. *Morb Mortal Wkly Rep.* 2022;71:1531–7.

Pfizer Medical Affairs

Pfizer Medical Portal for Online Educational Resources

https://pfizermedical.pfizerpro.com/infectious-disease

Select the therapeutic area

Pfizer. Pfizer Medical. Available at: https://pfizermedical.pfizerpro.com/infectious-disease. (Accessed December 2022).

Pfizer Medical Affairs

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Summary

1. Patients are at **high risk for progression to severe illness**, which includes hospitalization or death, if ≥ 50 years of age, have certain underlying medical conditions, or belong to certain racial and ethnic minority groups.
2. PAXLOVID is authorized for the treatment of **mild-to-moderate** COVID-19 in adult and pediatric patients (12 years of age and older weighing at least 88 pounds) who are at **high risk for progression to severe COVID-19**, including hospitalization or death
3. Additionally to significantly reduced COVID-19–related hospitalizations and all-cause mortality, treatment with PAXLOVID was associated with **reduced COVID-19–related healthcare utilization** compared to placebo in unvaccinated patients at high risk of progression to severe COVID-19; and with **improvement in time to symptom alleviation and resolution**
4. **RWE supports the efficacy and safety of PAXLOVID** in patients who are at high risk, irrespective of vaccination status
5. Useful resources to help manage drug interactions with PAXLOVID include the Fact Sheet for Healthcare Providers; the PAXLOVID Medical Information Page, which includes a drug interaction tool; the Potentially Significant Drug Interactions, Including Contraindicated Drugs Resource; NIH Guideline on Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications; and The University of Liverpool COVID-19 Drug Interactions website

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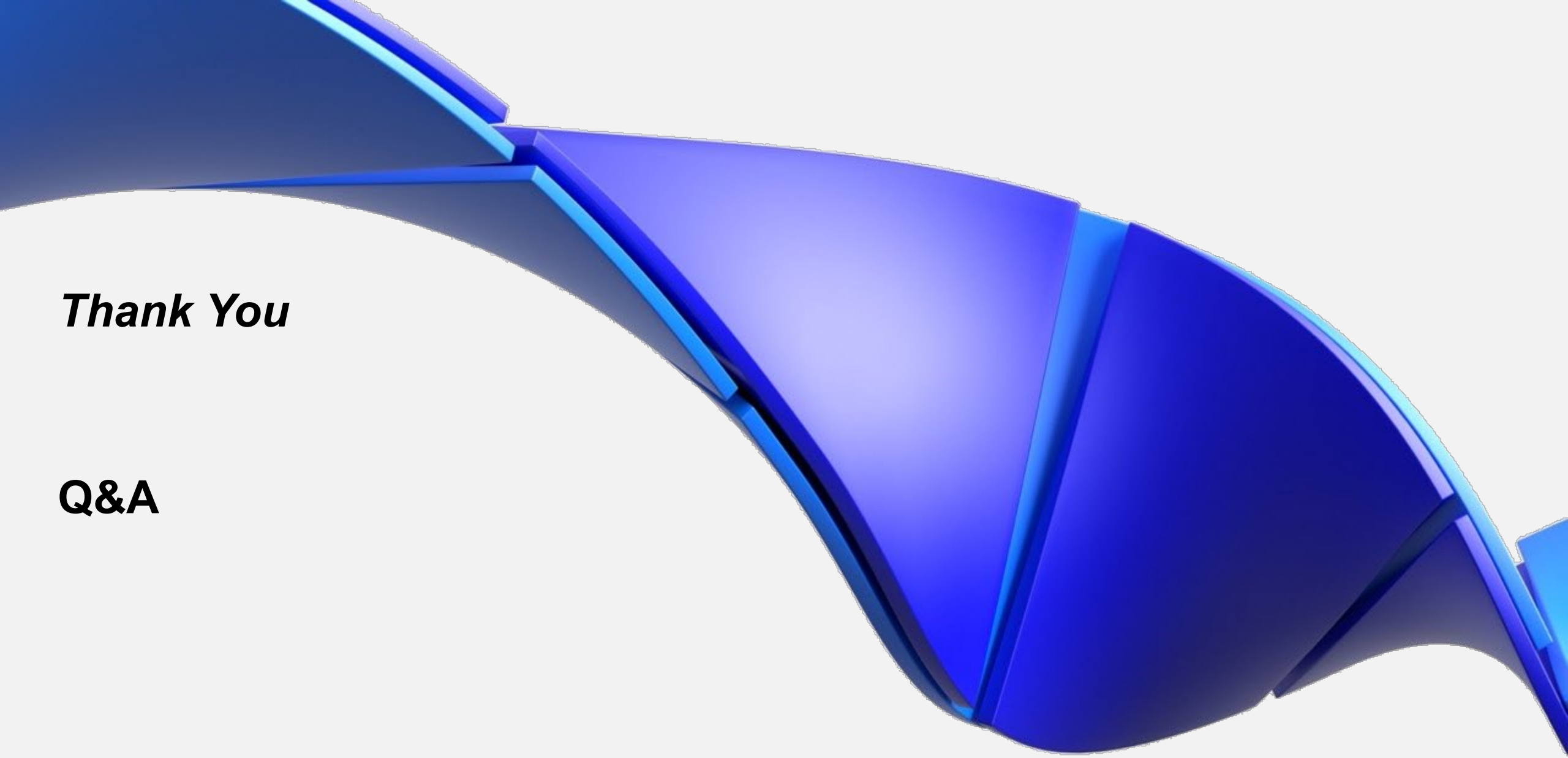

Thank You

Q&A

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Case Scenarios

To Prescribe or Not to Prescribe (Scenario 1)

- 54-year-old female, BMI 36
- h/o hypercholesterolemia and diet-controlled diabetes mellitus – on atorvastatin
- Feels a little fatigued with a mild sore throat for the last day or so - COVID positive (tested at home)

To Prescribe or Not to Prescribe (Scenario 2)

- 68-year-old male with HTN, diabetes, atrial fibrillation, and chronic kidney disease……estimated CrCl = 36
- Meds: Metformin, Furosemide, Amiodarone, Losartan
- Rapid Covid antigen test positive
- 3 days of low-grade fever, sore throat and cough
- Vaccinated, boosted x 3, and just received bivalent covid booster about a week ago

To Prescribe or Not to Prescribe (Scenario 3)

- 52 y/o male with HTN, history of lung transplant for pulmonary fibrosis Medications include tacrolimus

- Vaccinated and boosted x 3 (received covalent booster), received most recent dose of Evusheld 60 days ago

- Has had 2 days of sore throat, low grade fever, runny nose. Covid antigen test +

Q&A and Discussion

Recurring Stakeholder Meetings

- **Office Call Session: HHS/ASPR Distribution and Administration of COVID-19 Therapeutics**
  - Wednesdays (3:30-4:00PM ET); Next Session – January 11
- **Stakeholder Meeting: State/Territorial Health Officials + Nat'l Heath Care & Med Orgs/Associations**
  - Wednesdays (2:00-3:00PM ET); Next Meeting – January 11
- **Stakeholder Meeting: Federal Retail Pharmacy Therapeutics Program (FRPTP) Participants**
  - Monthly on Tuesdays (12:00-12:30PM ET); Next Session – January 17
- **Federal COVID-19 Therapeutics Clinical Rounds**
  - Every other Friday (12:00-1:00PM ET); Next Session – January 20
- **Office Call Session: Health Partner Ordering Portal (HPOP)**
  - Every three weeks/Thursday (4:00-5:00PM ET); Next Session – January 26

Weekly Engagement Opportunities with Federal Team
Questions? Email: COVID19Therapeutics@hhs.gov

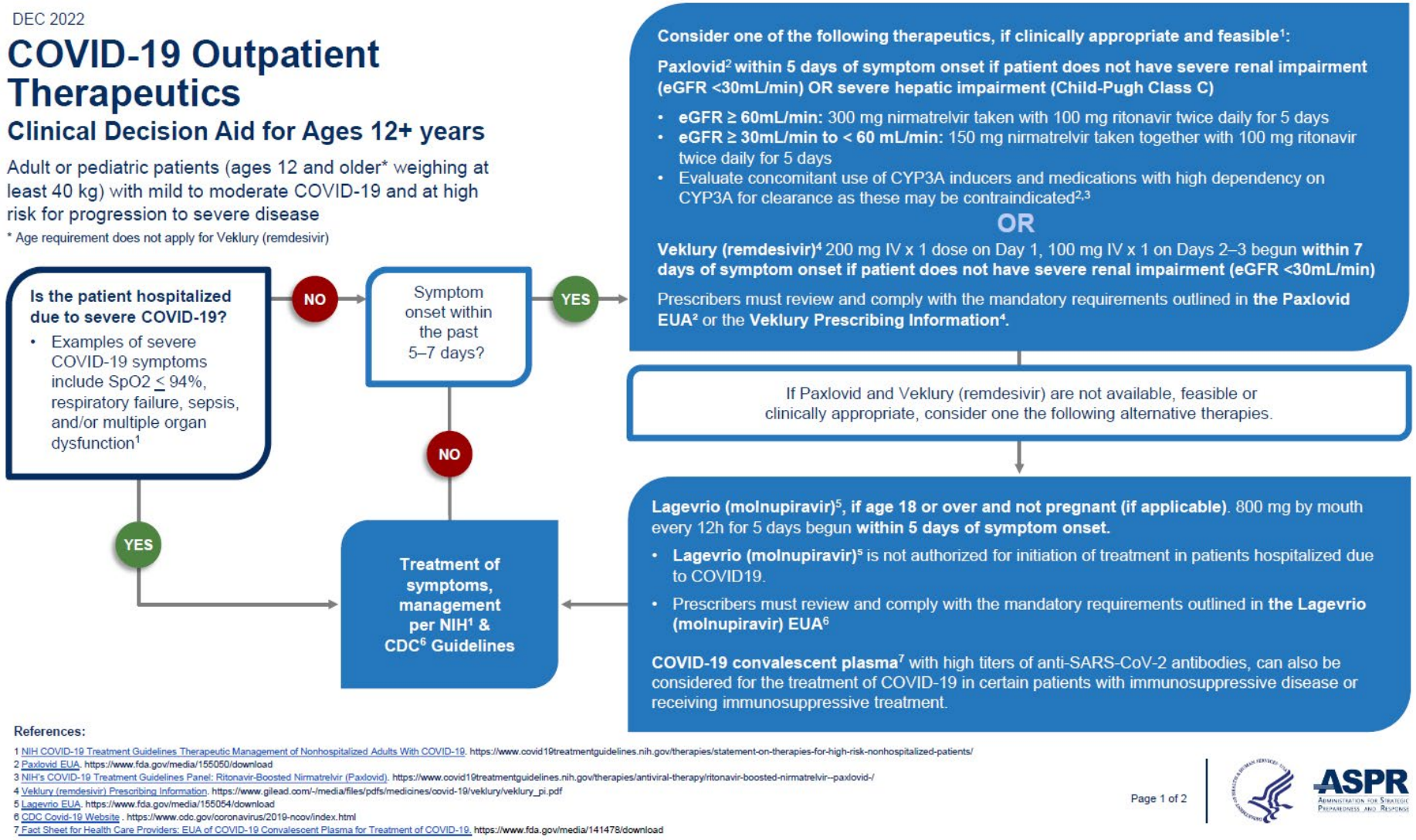
THANK YOU

Email:
COVID19Therapeutics@hhs.gov

Website:
aspr.hhs.gov

COVID-19 Therapeutics Resources

Updated Resources: Clinical Decision Aid



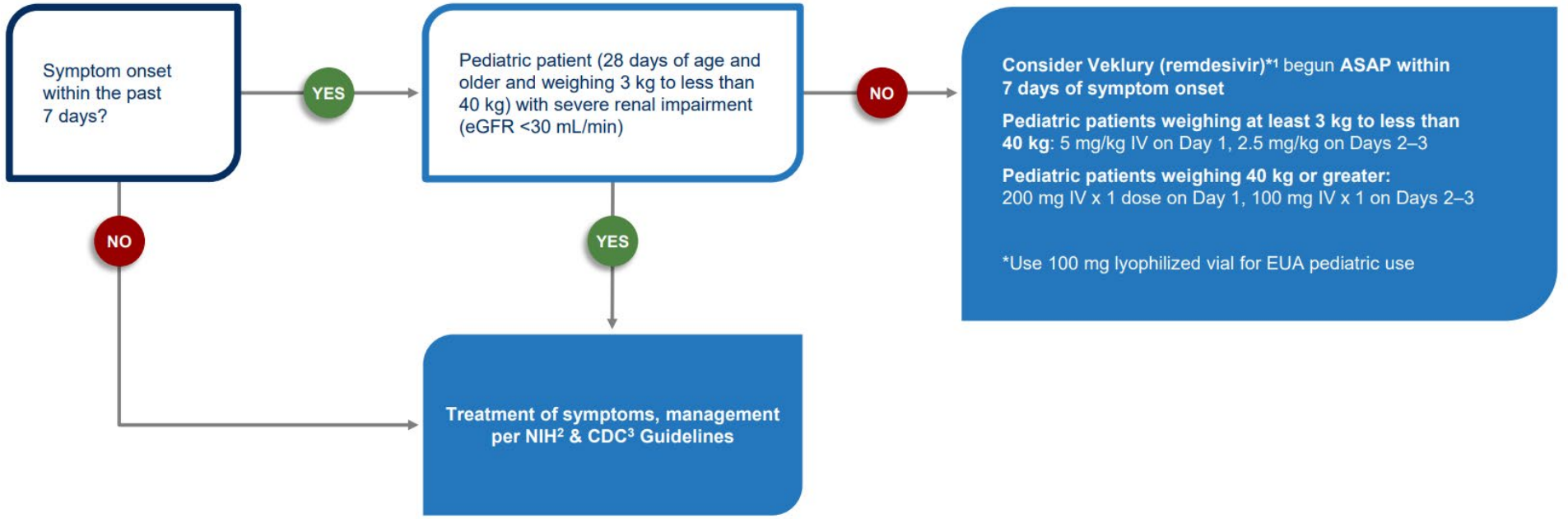
aspr.hhs.gov/COVID-19/Therapeutics/Documents/COVID-Therapeutics-Decision-Aid.pdf

Updated Resource: Clinical Decision Aid (pg 2/2)

DEC 2022

COVID-19 Outpatient Therapeutics

Clinical Decision Aid: Pediatric patients 28 days of age and older weighing 3 kg to less than 40 kg with mild to moderate COVID-19 and at high risk for progression to severe disease



Reference:

1 Veklury Prescribing Information:https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf
2 NIH COVID-19 Treatment Guidelines Therapeutic Management of Nonhospitalized Adults With COVID-19. https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-therapies-for-high-risk-nonhospitalized-patients/
3 CDC Covid-19 Website . https://www.cdc.gov/coronavirus/2019-ncov/index.html

aspr.hhs.gov/COVID-19/Therapeutics/Documents/COVID-Therapeutics-Decision-Aid.pdf

NEW!: Bebtelovimab not currently authorized for emergency use in U.S.

- **Nov. 30, 2022** - U.S. Food and Drug Administration announced bebtelovimab not currently authorized for emergency use in U.S.; it is not expected to neutralize Omicron subvariants BQ.1 and BQ.1.1., according to data included in the Health Care Provider Fact Sheet.
- Given the likelihood that infection is likely to be caused by a non-susceptible variant, and consistent with the terms and conditions of the Letter of Authorization**, bebtelovimab is not currently authorized for emergency use in any U.S. region at this time.**
- Eli Lilly and its authorized distributors have paused commercial distribution of bebtelovimab until further notice by the Agency. Additionally, the Administration for Strategic Preparedness and Response (ASPR) has paused the fulfillment of any pending requests under its Bebtelovimab Product Replacement Initiative.
- The U.S. Government recommends all product be retained in the event that SARS-CoV-2 variants susceptible to bebtelovimab, which are currently circulating at lower prevalence, become more prevalent in the future in the United States. Retained product must be appropriately held in accordance with storage conditions detailed in the authorized Fact Sheet for Health Care Providers and the Letter of Authorization for bebtelovimab.
- Reporting cadence for bebtelovimab is now weekly on Thursdays by 11:59 PM.

Tools to Assist in COVID-19 Outpatient Therapeutic Selection

As variant prevalence changes and new therapeutics become available, there are tools and resources available to assist in clinical decision-making for prescribers.

- Clinical Decision Aid: https://aspr.hhs.gov/COVID-19/Therapeutics/Documents/COVID-Therapeutics-Decision-Aid.pdf
- Side-by-Side Overview of Outpatient Therapeutics: https://aspr.hhs.gov/COVID-19/Therapeutics/Documents/side-by-side-overview.pdf
- NIH Therapeutic Management of Nonhospitalized Adults With COVID-19: https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/nonhospitalized-adults--therapeutic-management/
- NIH COVID-19 Treatment Guidelines Homepage: https://www.covid19treatmentguidelines.nih.gov/therapies/
  - NIH's COVID-19 Treatment Guidelines /What's new: https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/whats-new/
  - CDC Underlying Medical Conditions Associated with Higher Risk for Severe COVID-19: Information for Healthcare Professionals: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html
- CDC COVID Data Tracker:
  - The CDC monitors and publishes variant information on the CDC Covid-19 Data Tracker (https://covid.cdc.gov/covid-data-tracker/#variant-proportions)
  - Information on variants of concern are updated in Section 15 of FDA fact sheets.

COVID-19 Convalescent Plasma (CCP) Resources

- Emergency Use Authorization of COVID-19 Convalescent Plasma
  https://www.fda.gov/media/141478/download
- Implementation of an Outpatient Covid-19 Convalescent Plasma Administration Program
  https://onlinelibrary.wiley.com/doi/full/10.1111/trf.16871
- Early Outpatient Treatment for COVID-19 with Convalescent Plasma- NEJM
  https://www.nejm.org/doi/full/10.1056/NEJMoa2119657
- New COVID-19 Treatments Add-On Payment (NCTAP) | CMS
  https://www.cms.gov/medicare/covid-19/new-covid-19-treatments-add-payment-nctap
  - ICD-10-PCS Code: XW13325, XW14325 (*Only applies to inpatient use)*
- Addendum A and Addendum B Updates | CMS
  https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalOutpatientPPS/Addendum-A-and-Addendum-B-Updates
  - APC Code: 9540 / HCPCS Code: C9507 (*Only applies to outpatient use*)

COVID-19 Convalescent Plasma EUA

- FDA issued an EUA to permit the emergency use of the unapproved product, **COVID-19 convalescent plasma with high titers** of anti-SARS-CoV-2 antibodies, for the **treatment of COVID-19 in patients with immunosuppressive disease or receiving immunosuppressive treatment**, in either the outpatient or inpatient setting.
- Given that the clinical evidence in patients with immunosuppressive disease or receiving immunosuppressive treatment remains limited, **data from additional randomized, controlled trials are needed**.
- COVID-19 convalescent plasma is **not authorized to treat immunocompetent patients** with COVID-19
- FDA has authorized other treatments for emergency use for the treatment of COVID-19 in adults and pediatric patients in the outpatient setting. These products have more consistently demonstrated clinical benefit in this population, and do not carry some of the risks associated with transfusion of blood components.

Reminder: Evusheld Fact Sheet Update (variant data)

Lineage with Spike Protein Substitution	Country First Identified	WHO Nomenclature	Key Substitutions Tested	Fold Reduction in Susceptibility* (Pseudotyped VLPs†)	Fold Reduction in Susceptibility* (Authentic virus‡)
BN.1	Multiple country origin	Omicron (BN.1)	G339D+R346T+K356T+ S371F+S373P+S375F+ D405N+ R408S+ K417N+N440K+G446S+ N460K+S477N+T478K+ E484A+F490S+ Q493R+Q498R+Y505H	68-fold	ND
BQ.1	Nigeria	Omicron (BQ.1)	BA.5+K444T+N460K	>2000-fold[P]	ND
BQ.1.1	Multiple country origin	Omicron (BQ.1.1)	BA.5+R346T+K444T+ N460K	>2000-fold[P]	ND
XBB	Multiple country origin	Omicron (XBB)	G339H+R346T+L368I+ S371F+S373P+S375F+ T376A+D405N+R408S+ K417N+N440K+V445P+ G446S+N460K+S477N+ T478K+ E484A+F486S+ F490S+Q498R+N501Y+ Y505H	>1400-fold[P]	ND
BA.2	Multiple country origin	Omicron (BA.2)	G339D+S371F+S373P+ S375F+T376A+D405N+ R408S+K417N+N440K+ S477N+T478K+E484A+ Q493R+Q498R+N501Y+ Y505H	No Change[§]	5.4-fold
BA.2.75	India	Omicron (BA.2.75)	G339H+S371F+S373P+ S375F+T376A+D405N+ R408S+K417N+N440K+ G446S+N460K+S477N+ T478K+E484A+Q498R+ N501Y+ Y505H	2.4- to 15-fold	ND
BF.11	Multiple country origin	Omicron (BF.11)	G339D+R346T+S371F+ S373P+ S375F+T376A+ D405N+R408S+K417N+ N440K+L452R+S477N+ T478K+E484A+F486V+ Q498R+N501Y+Y505H	>500-fold	ND
BA.5.2.6	Multiple country origin	Omicron (BA.5.2.6)	G339D+R346T+S371F+ S373P+S375F+T376A+ D405N+R408S+K417N+ N440K+L452R+S477N+ T478K+E484A+F486V+ Q498R+N501Y+Y505H	>500-fold	ND
BF.7	United States/Belgium	Omicron (BF.7)	BA.4+R346T	>5000-fold[P]	ND

- Evusheld ~93% projected resistance nationally
- Breakthrough infections are possible**, advise patients to have a treatment plan in place and to seek timely medical attention if symptoms occur**
  - This is important messaging to both patients that received Evusheld previously and patients getting first dose

- NIH Guidelines update (Dec 1) notes the prevalence of Omicron subvariants that are resistant to Evusheld is rapidly increasing. However, Evusheld is the only agent FDA authorized for SARS-CoV-2 PrEP in people who are not expected to mount an adequate immune response to COVID-19 vaccination or those with contraindications for COVID-19 vaccines. Therefore, the **Panel continues to recommend the use of tixagevimab plus cilgavimab** as PrEP for eligible individuals. This **recommendation may change if the prevalence of resistant subvariants increases**.

https://www.fda.gov/media/154701/download

Correction: Additional Shelf-Life Extension for Evusheld

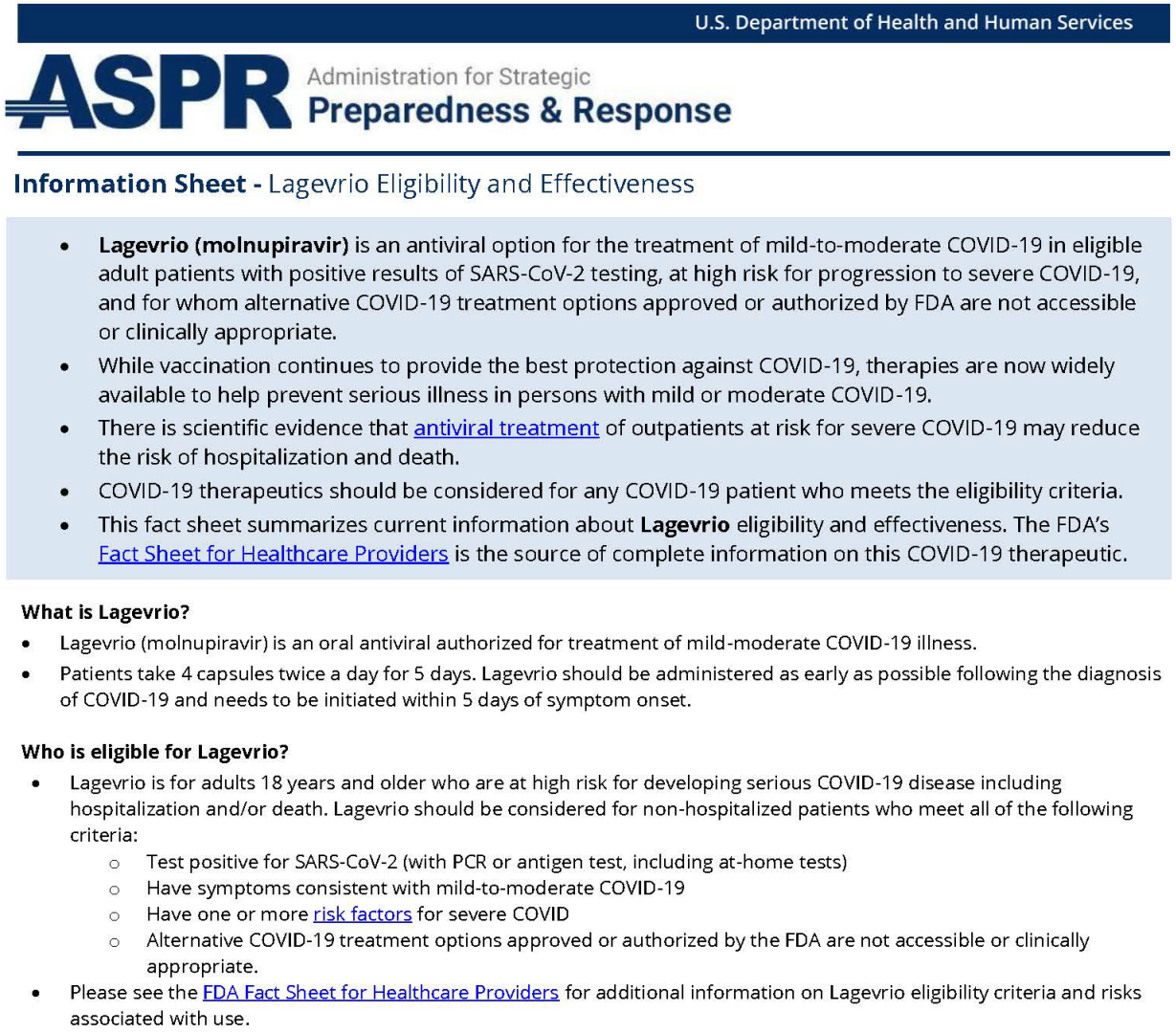
- **December 5, 2022** – FDA authorized an additional extension to the shelf-life from 18 or 24 months **to 30 months for all lots of Evusheld** (tixagevimab co-packaged with cilgavimab)
  - As a result of this extension to all Evusheld product, **there are currently no expired Evusheld lots** and therefore no returns or on-site destruction of uncompromised product is allowable.
- This extension applies to all unopened vials of Evusheld that have been held in accordance with storage conditions detailed in the authorized Fact Sheet for Health Care Providers and the Letter of Authorization for Emergency Use Authorization (EUA) 104 for Evusheld.
- Visit ASPR's website to learn more and review the table with co-pack lot numbers, labelled co-pack expiration dates, and the extended co-pack expiration dates.

Related Resources: Evusheld

Additional Evusheld Prescribing Resources

- FDA Evusheld Fact Sheet for Providers
- FDA Evusheld Fact Sheet for Patients
- Evusheld Patient, Parent and Caregiver Guide
- Evusheld Product Information

New Resource: Lagevrio Information Sheet



U.S. Department of Health and Human Services

ASPR Administration for Strategic Preparedness & Response

Information Sheet - Lagevrio Eligibility and Effectiveness

- **Lagevrio (molnupiravir)** is an antiviral option for the treatment of mild-to-moderate COVID-19 in eligible adult patients with positive results of SARS-CoV-2 testing, at high risk for progression to severe COVID-19, and for whom alternative COVID-19 treatment options approved or authorized by FDA are not accessible or clinically appropriate.
- While vaccination continues to provide the best protection against COVID-19, therapies are now widely available to help prevent serious illness in persons with mild or moderate COVID-19.
- There is scientific evidence that antiviral treatment of outpatients at risk for severe COVID-19 may reduce the risk of hospitalization and death.
- COVID-19 therapeutics should be considered for any COVID-19 patient who meets the eligibility criteria.
- This fact sheet summarizes current information about **Lagevrio** eligibility and effectiveness. The FDA's Fact Sheet for Healthcare Providers is the source of complete information on this COVID-19 therapeutic.

What is Lagevrio?

- Lagevrio (molnupiravir) is an oral antiviral authorized for treatment of mild-moderate COVID-19 illness.
- Patients take 4 capsules twice a day for 5 days. Lagevrio should be administered as early as possible following the diagnosis of COVID-19 and needs to be initiated within 5 days of symptom onset.

Who is eligible for Lagevrio?

- Lagevrio is for adults 18 years and older who are at high risk for developing serious COVID-19 disease including hospitalization and/or death. Lagevrio should be considered for non-hospitalized patients who meet all of the following criteria:
  - Test positive for SARS-CoV-2 (with PCR or antigen test, including at-home tests)
  - Have symptoms consistent with mild-to-moderate COVID-19
  - Have one or more risk factors for severe COVID
  - Alternative COVID-19 treatment options approved or authorized by the FDA are not accessible or clinically appropriate.
- Please see the FDA Fact Sheet for Healthcare Providers for additional information on Lagevrio eligibility criteria and risks associated with use.

- **New Lagevrio Information Sheet**
  - Quick reference one page document for health care providers
  - Highlights patient eligibility and effectiveness information

- **Information Sheet for Providers – Paxlovid**
  - Updated version coming soon

Lagevrio – Recent Analysis of EHR Evidence

- Epic analysis of over 1.6 million COVID-19 cases compared patients treated with Paxlovid or Lagevrio to those who did not receive a COVID-19 outpatient therapeutic[1]
  - **21,615 Lagevrio** treatments and 191,848 Paxlovid patients
  - 50.4 % of patients treated with Lagevrio were 65 or older
    - Lagevrio is an important option for this population
  - 39.1% of patients treated with Paxlovid were 65 or older
  - **Significant reduction in rates of hospitalization (1.86% vs. 3%) and death (0.2% vs 0.42%) in patients age 65 and older treated with Lagevrio compared to those not treated with Lagevrio or Paxlovid**
    - *Improvements across age groups, most significant in age 65+*

[1]https://epicresearch.org/articles/lagevrio-significantly-reduces-covid-19-hospitalization-and-death

Related Resources: Lagevrio (molnupiravir)

Additional Lagevrio Prescribing Resources

- FDA Lagevrio Fact Sheet for Providers
- FDA Lagevrio Fact Sheet for Patients
- NIH COVID-19 Treatment Guidelines – Lagevrio (molnupiravir)
- Lagevrio (molnupiravir) Product Information

Reminder: Paxlovid Access

- **November 14, 2022** - In our continued efforts to increase oral antiviral dispensing in vulnerable areas, an extension of the enhanced distribution initiative was launched to pre-position Paxlovid at new sites, with a focus on areas of higher 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 to better prepare for winter cases
  - Emails were sent to nearly 50,000 provider sites to invite a one-time distribution request of 20 courses of Paxlovid
    - Targeted outreach to sites in counties/parishes with higher SVI or sites with no previous dispensing
    - Emails were sent Monday, November 14
- Paxlovid supply used for this effort is separate from jurisdictional thresholds

Paxlovid (nirmatrelvir and ritonavir) Effectiveness

Real-world studies have consistently demonstrated that Paxlovid is effective in preventing hospitalizations and deaths.

- Study of 2,504 patients over 65 treated with Paxlovid in Israel (Arbel et al. 2022).
  - **67% reduction in hospitalizations and 81% reduction in deaths compared to the untreated.**
- Study of 6,036 patients over 50 treated with Paxlovid in MA (Dryden-Peterson et al. 2022).
  - **45% reduction in hospitalization and greater reductions for obese or unvaccinated patients.**
- Study of 5,663 adult outpatients treated with Paxlovid during a BA.2 wave in Hong Kong (Wong et al. 2022).
  - **31% reduction in hospitalization and 75% reduction in death compared to non-users.**
- Study of 890 adult inpatients treated with Paxlovid during a BA.2 wave in Hong Kong (Wong et al. 2022).
  - **43% reduction in disease progression and 66% reduction in death compared to non-users.**

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)

Related Resources: Paxlovid

Additional Paxlovid Prescribing Resources

- New! HHS Information Sheet for Providers – Paxlovid
- FDA Paxlovid Patient Eligibility Screening Checklist for Providers
- University of Liverpool COVID-19 Drug Interactions
- FDA PAXLOVID Patient Eligibility Screening Checklist Tool for Prescribers
- Pfizer
- NIH COVID-19 Treatment Guidelines - Ritonavir-Boosted Nirmatrelvir (Paxlovid)
- CDC/IDSA COVID-19 Clinician Call: All About Paxlovid; Plus Variants Update
- Paxlovid Potential Drug-Drug Interactions Resource (Pfizer)

Veklury (remdesivir) Product Information

- Prescribing Information & FDA Fact Sheets
  - Veklury (remdesivir) Prescribing Information: https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_pi.pdf
  - Veklury Patient Information: https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury_patient_pi.pdf
- Manufacturer's Resources:
  - Website for Healthcare Providers: https://www.vekluryhcp.com/
  - Website for Patients: https://www.veklury.com/
- Safety Reporting:
  - FDA MedWatch: https://www.accessdata.fda.gov/scripts/medwatch/index.cfm
  - Safety Reporting Email: Safety_fc@gilead.com

Veklury (remdesivir) – Outpatient Use

- FDA **approved** expanded use of Veklury (remdesivir) to certain **non-hospitalized** adults and pediatric patients for treatment of mild-to-moderate COVID-19 disease (Jan 21, 2022), including:
  - Adults and pediatric patients 28 days of age and older and weighing at least 3 kg with positive results of direct SARS-CoV-2 viral testing, **AND**
  - Who are not hospitalized and have mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death
- Veklury (remdesivir) should be initiated as soon as possible and **within 7 days** of symptom onset.
  - recommended total duration of treatment for non-hospitalized patients is 3 days
- Sites are encouraged to offer outpatient Veklury, especially in collaboration with tertiary centers treating patients (e.g., transplant centers, oncology, etc) or other patients for whom Paxlovid may not be clinically appropriate (including vulnerable pediatric patients)

FDA Takes Actions to Expand Use of Treatment for Outpatients with Mild-to-Moderate COVID-19: https://www.fda.gov/news-events/press-announcements/fda-takes-actions-expand-use-treatment-outpatients-mild-moderate-covid-19
Veklury (remdesivir) Prescribing Information: https://www.gilead.com/-/media/files/pdfs/medicines/COVID-19/veklury/veklury_pi.pdf

Veklury (remdesivir) Supply Overview

- Gilead has been meeting real-time global demand for Veklury since October 2020.
- Gilead fully anticipates an ability to continue to meet patient demand for Veklury in both hospital and non-hospital settings.
- The Veklury non-hospital distribution network now includes both AmerisourceBergen Specialty Division and Cardinal Specialty.
  - Non-hospital entities that can attest to the proper administration of Veklury in accordance with the label can order Veklury for outpatient use.
  - Veklury is not available in retail pharmacies.
- Hospitals should continue ordering Veklury through AmerisourceBergen Specialty Division, Cardinal Specialty, and McKesson Plasma & Biologics.

Related Resources: Veklury (remdesivir)

Additional Veklury (remdesivir) Prescribing Resources

- Prescribing Information & FDA Fact Sheets
  - Veklury (remdesivir) Prescribing Information
  - Veklury Patient Information
- Manufacturer's Resources:
  - Website for Healthcare Providers
  - Website for Patients
  - Veklury Product Information
- Additional Resources:
  - NIH's COVID-19 Treatment Guidelines Therapeutic Management of Nonhospitalized Adults With COVID-19
  - FDA MedWatch
  - Safety Reporting Email

Related Resources: Telehealth

Helpful Information and Resources

- Telehealth resources website
- Telehealth resources for healthcare providers
- Health equity in telehealth
- Office for the Advancement of Telehealth
- Telehealth Resource Centers for technical assistance, webinars, and training
- Health Centers Program
- Health Center Finder

Related Resources: Long Covid

Helpful Information and Resources

- Biden–Harris Administration Releases Two New Reports on Long COVID to Support Patients and Further Research
- Addressing the Long-term Effects of COVID-19
- Long COVID Research, Services, And Supports: A Call To Action
- CDC Long COVID

Related Resources

Helpful Information and Resources

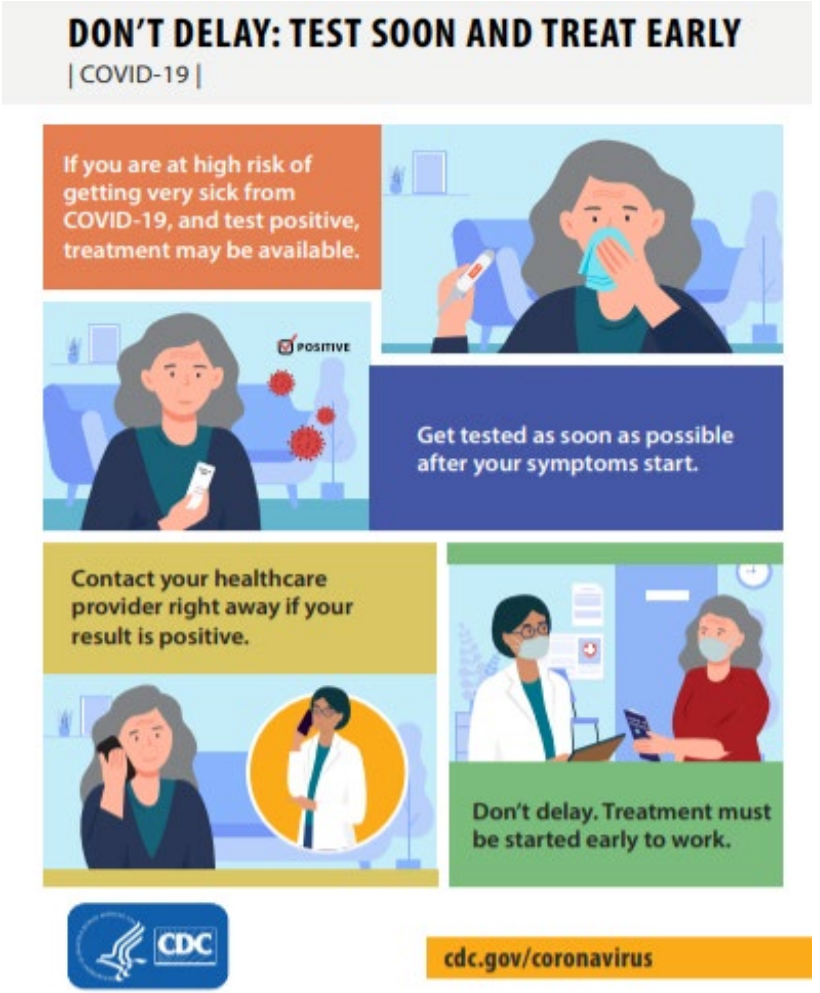
- HHS Therapeutics Homepage
- Product Expiration Date Extensions
- Test to Treat Initiative webpage and Fact Sheet
- Test to Treat Site Locator and Digital Tool Kit
- General Therapeutics Locator
- HHS Clinical Implementation Guide
- Outpatient Therapeutics Decision Aid
- Side-by-Side Overview of Outpatient Therapeutics
- ASPR Regional Emergency Coordinators
- CMS reimbursement information for mAbs
- CMS reimbursement information for oral antivirals

Disparities in Access to COVID-19 Treatments and Care

- Key Considerations (NIH Guidelines update Dec 1)
  - The Panel recommends that health care providers, health care systems, and payers **ensure equitable access to high-quality care and treatment for all patients,** regardless of race, ethnic identity, or other minoritized identity or social status (AIII).
  - Promoting equitable care for these groups must include considering the full range of medical, demographic, and social factors that may negatively impact health outcomes.
  - Supporting equitable access to high-quality care and treatment for all groups is now an imperative for all Joint Commission-accredited health care organizations, as well as a priority for the CDC and other public health agencies.
- MMWR Oct 28: Data from 41 US healthcare systems revealed disparities in dispensing rates for ritonavir-boosted nirmatrelvir (Paxlovid) and molnupiravir (Lagevrio)
  - During the period when the use of outpatient COVID-19 medication was increasing substantially, **treatment with Paxlovid was 35.8% lower among Black/African American patients and 29.9% lower among Hispanic patients** than among White patients.
  - **Despite a greater number of dispensing sites higher social vulnerability neighborhoods, oral antivirals were prescribed at a lower rate for patients with COVID-19** who were living in these areas than in lower social vulnerability.
- Disparities may not be limited to outpatient settings. One retrospective cohort study of veterans hospitalized with COVID-19 reported that Black veterans had lower odds of receiving COVID-19–specific treatments, including systemic steroids, remdesivir, and immunomodulators, than White veterans. www.ncbi.nlm.nih.gov/pubmed/36282499; covid19treatmentguidelines.nih.gov/overview/overview-of-covid-19/

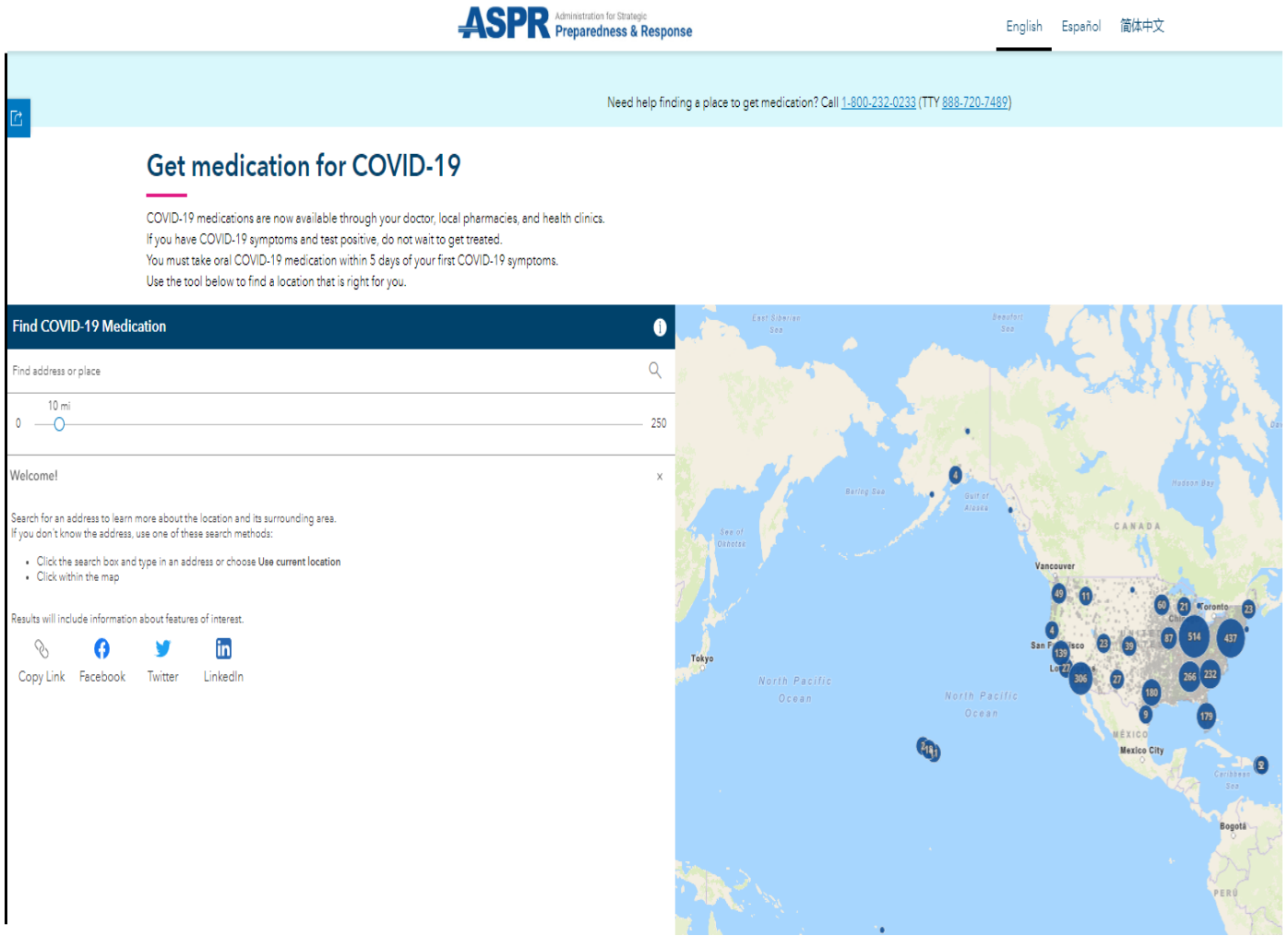
Test to Treat: About the Program

- Overall goal of Test to Treat program is to increase access to COVID-19 oral therapeutics, **particularly for individuals who don't have ready access to a health care provider**
- COVID-19 treatments delivered as part of Test to Treat Program (Paxlovid and Lagevrio) must be taken within 5 days of initial COVID-19 symptoms.
  - Helps close gap between positive COVID-19 test and receiving treatment for those eligible
- Builds upon existing distribution of oral antivirals we are already making available at no cost to thousands of locations nationwide.
- More than 2500 Test to Treat sites across country; more than 40,000 total locations with oral antivirals
- An individual's healthcare providers remain the first option for care; Test to Treat sites are one additional access point.



Test to Treat Locator

- Test to Treat site locator launched on 3/30.
- Identifies all Test to Treat program sites and all sites to fill an existing prescription.
  - Increasing visibility of telehealth options on locator.
- Call center also available: 1-800-232-0233 (TTY 1-888-720-7489) to get help in English, Spanish, and more than 150 other languages—8 AM to 12 midnight ET, 7 days a week.
- Disability Information and Access Line (DIAL) also available to specifically help those with disabilities access services.
  - 1-888-677-1199, Monday to Friday from 9 AM to 8 PM ET or email DIAL@usaginganddisability.org.

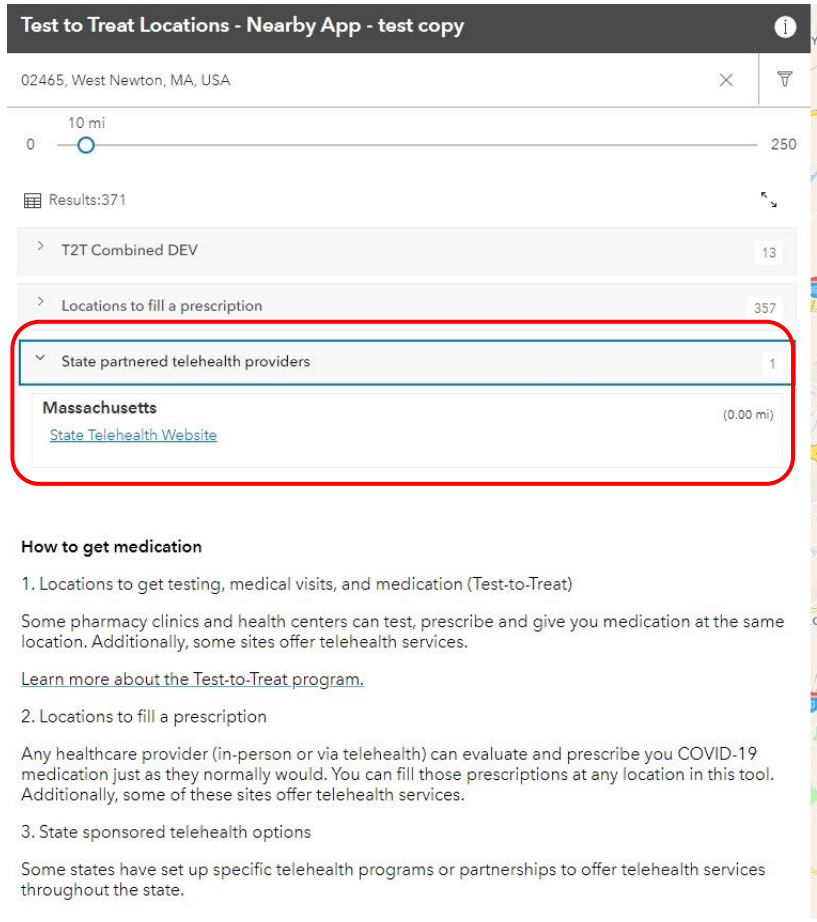


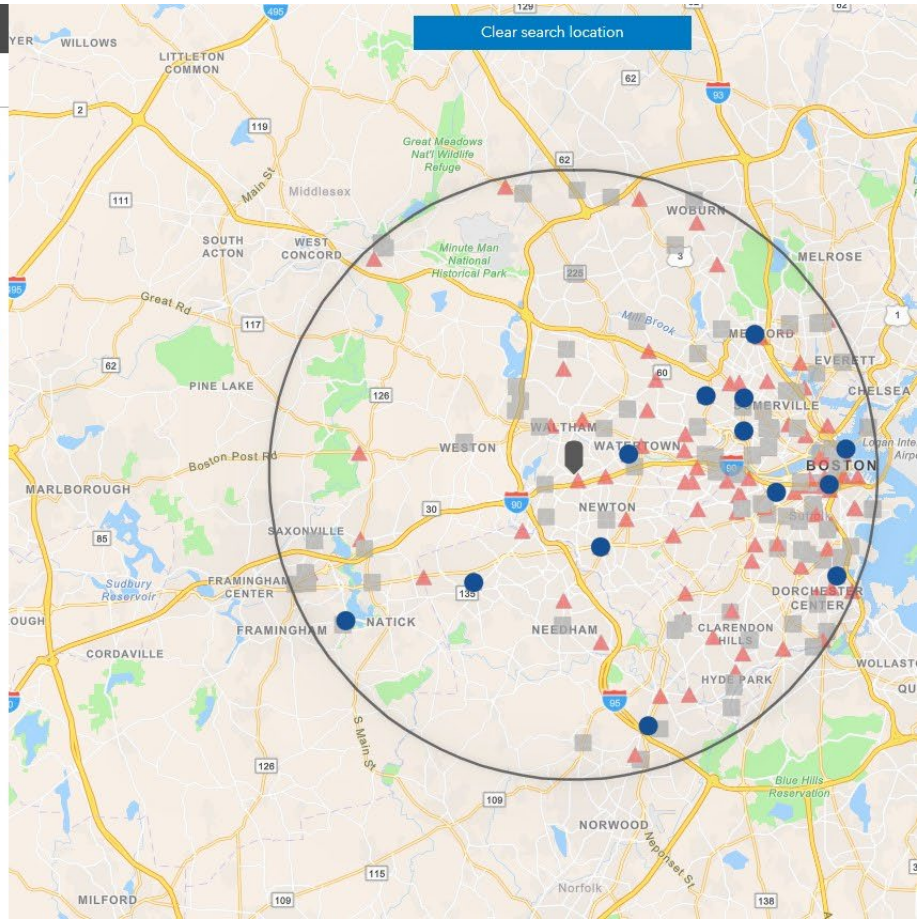
https://covid-19-test-to-treat-locator-dhhs.hub.arcgis.com/

State-Sponsored Telehealth on the Test to Treat Locator

1. States/Jurisdictions can add their state-sponsored telehealth programs to the Test to Treat locator. When a user left-hand enters an address or zip code in a state that has a telehealth program it will appear as a third dropdown menu on the side of the locator.

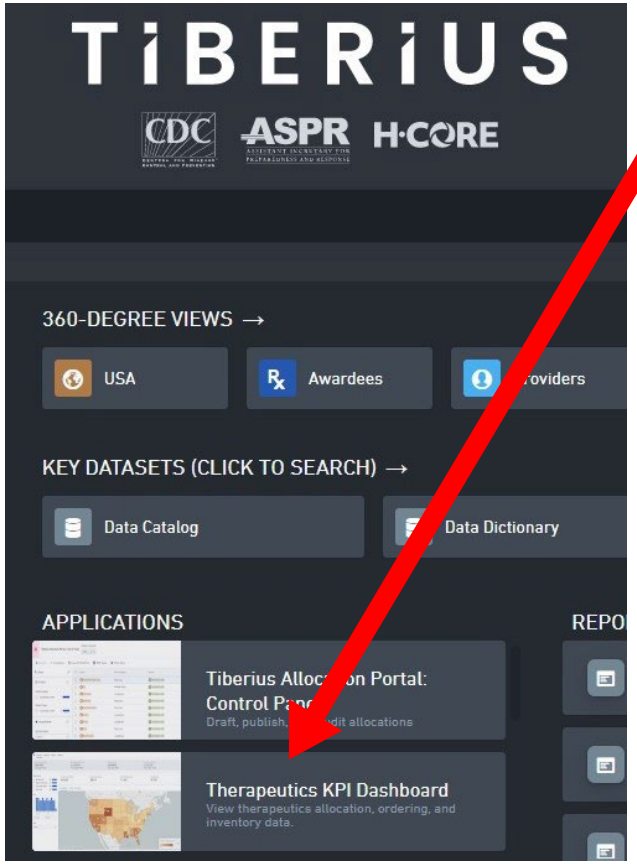
1



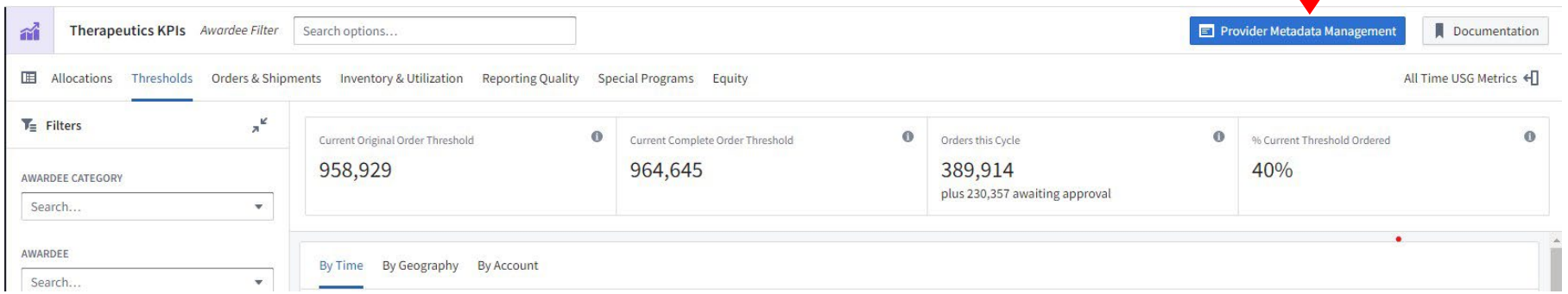


Adding State-Sponsored Telehealth Using the Tiberius PMM Tool

States/Jurisdictions can add their state-sponsored telehealth program, to be reflected on the Test to Treat locator, using the Tiberius Provider Metadata Management (PMM) tool. States/Jurisdictions can also use this portal to keep their program's information up-to-date.



2. States/Jurisdictions need to log in to Tiberius and go to the KPI Dashboard.
3. Once in the KPI Dashboard, the link for Provider Metadata Management (PMM) tool is in the upper right corner of the dashboard. Click on this link.



Using the Tiberius PMM Tool: To Add State Telehealth

4. In the PMM tool go to the “Telehealth” tab.

5. State users will only see their state in this dropdown menu. Regional users will see the States/Jurisdictions within their region.

6. States can add their telehealth provider name, URL, and a phone number. <u>If there is no phone number just leave it blank</u>. States can add up to 5 providers if needed.

7. If a state needs to delete a provider, they can select it from their provider list and delete.