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### Covid-19 Clinical Update 3/31/2022

George Washington University

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# Omicron BA.2 and outpatient treatment options for mild-moderate COVID-19

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# Omicron surge in the U.S.

- By the end of March ~40-50% of us will have been infected with Omicron
- Cases are *far* underreported
- A majority of Omicron infections may have been asymptomatic
- Current average daily case rates:



↑ 13/100K



↓ 5/100K



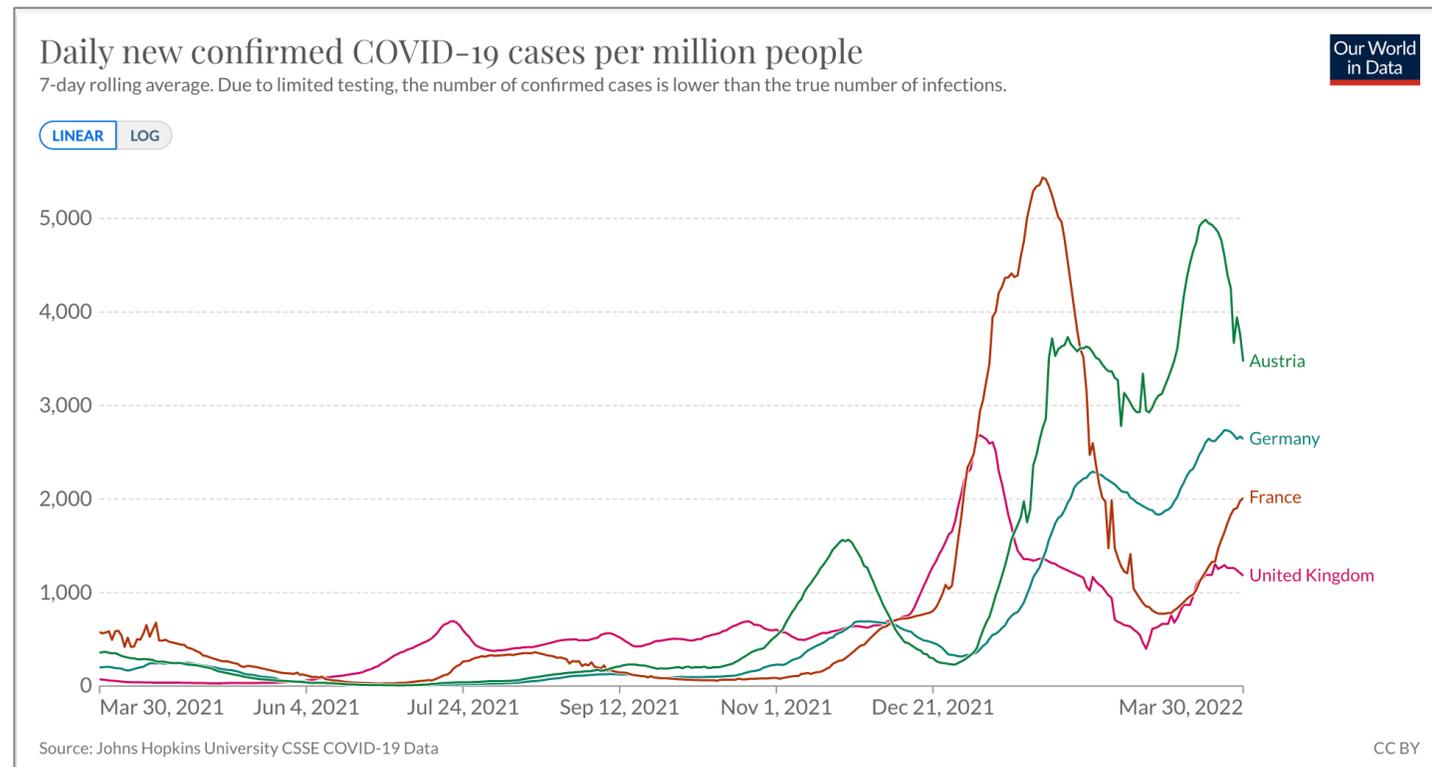
↓ 8/100K

wpost.com

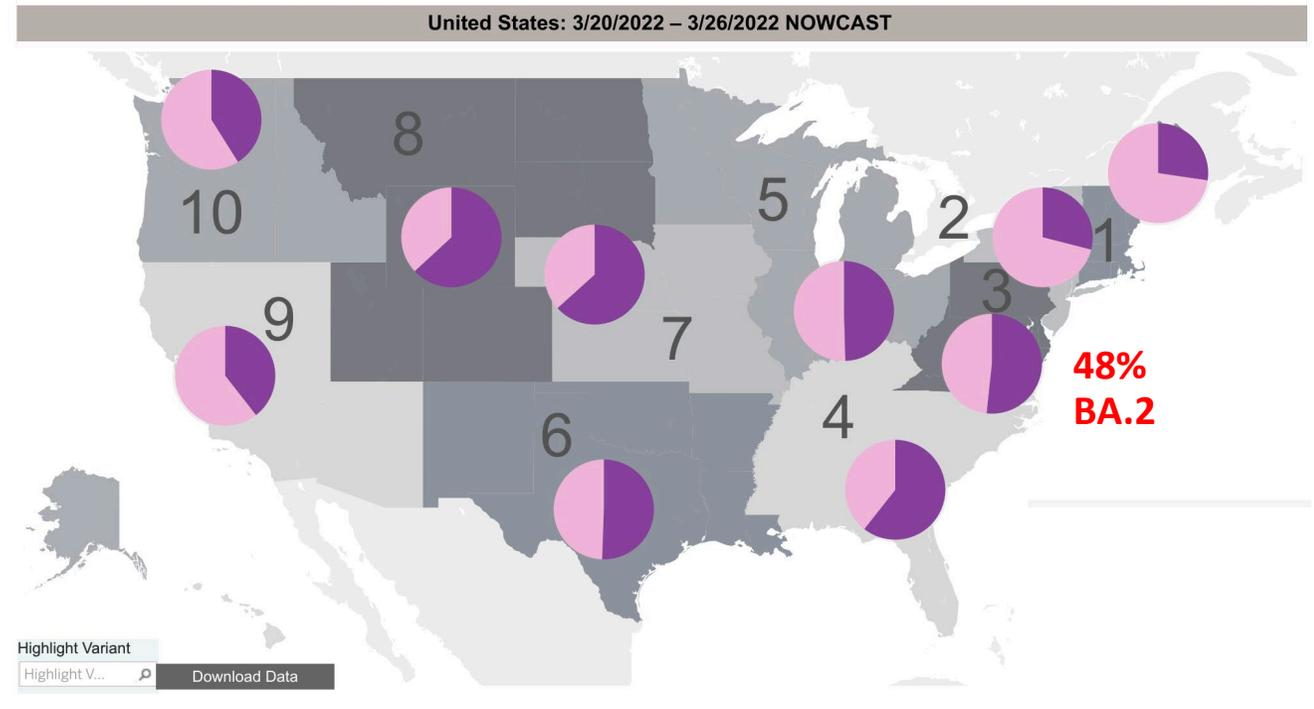
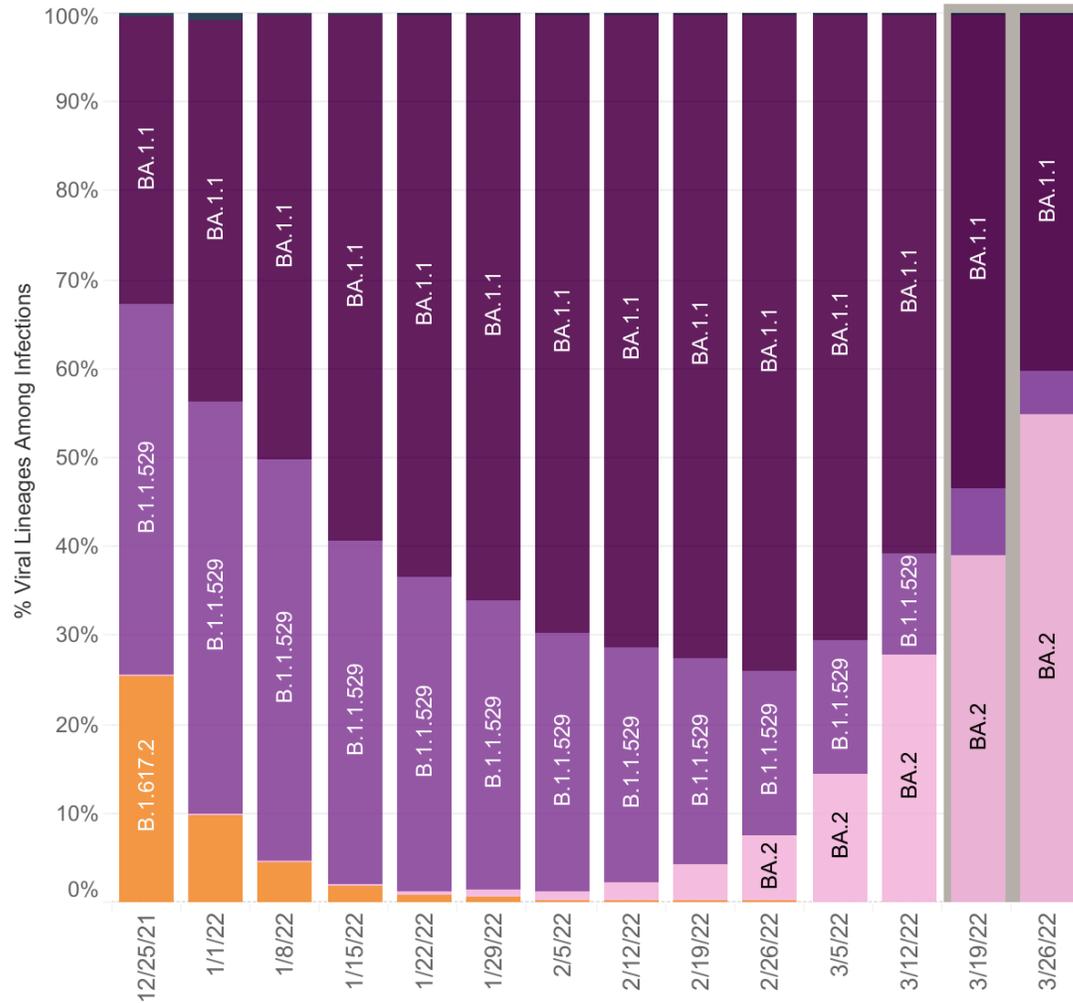
The Omicron variant has three lineages (=sub-variants), known as BA.1, BA.2, and BA.3. There have been few cases of BA.3.

# Omicron outside the U.S.

- Europe: Rise in cases and hospitals with little change in ICU/deaths
- A majority of cases due to Omicron BA.2
  - 25-40% more transmissible than Omicron BA.1
  - The masks are off
  - Immunity from boosters waning
- New Zealand, some E. Asian countries, Hong Kong
- Africa: Few data outside S. Africa



# BA.2 represents an increasing share of Omicron in the U.S.



# U.S. COVID-19 case rate has plateaued at a low level

## Daily new confirmed COVID-19 cases per million people

7-day rolling average. Due to limited testing, the number of confirmed cases is lower than the true number of infections.

Our World  
in Data

LINEAR LOG



Source: Johns Hopkins University CSSE COVID-19 Data

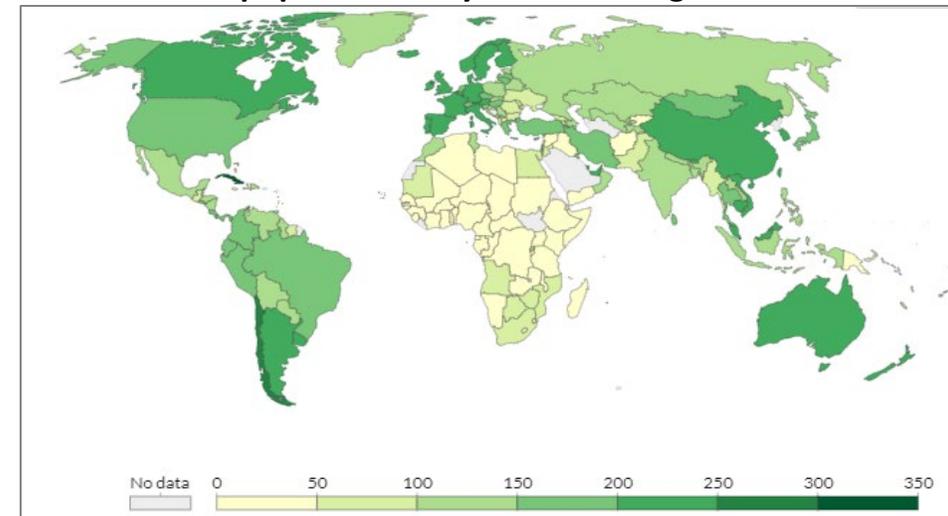
CC BY

# We all want the pandemic to be over

## *But no one can say it is over*

- “Endemic” means: a disease that prevails continually in a region
  - Does not mean it is a less virulent disease or doesn’t make people seriously ill
  - Examples: malaria in Africa, tuberculosis in India, opioid use in the U.S.
- There is no rule that viruses evolve to become more benign
- What is predictable about SARS-CoV-2:  
It’s unpredictable
  - SARS-CoV-2 has shown faster genetic drift than predicted
  - There is a large animal reservoir
  - Nobody can predict when/if a new variant will appear
- **While rates are low we must use the opportunity to prepare for a next wave**

Share of population fully vaccinated against COVID



# Early therapeutics for COVID

- Monoclonal antibodies –
  - Sotrovimab – active against BA.1 but not BA.2
  - Bebtelovimab – active against both BA.1 and BA.2
- Early remdesivir (PINETREE)
- Oral therapeutics:
  - Paxlovid
  - Molnupiravir

# Sotrovimab

- **Not active with BA.2**
  - Was second choice therapy for mild-moderate COVID, at high risk of progressing to severe disease
  - NOT for those hospitalized for COVID-19 or on O<sub>2</sub>
  - Age ≥12 (≥40 kg)
  - Reduces risk of hospitalization or death by 70-85% compared with placebo
  - Administer within 7 days of symptom onset (but as early as possible).
- One 500 mg infusion. Patients must be monitored for 1 hour after infusion.
  - Adverse effects: Almost none. Rash in 2%, diarrhea in 1%. Anaphylaxis rare with mABs.



# Coming soon...Bebtelovimab

- FDA EUA for high-risk, nonhospitalized patients with mild-moderate COVID-19
- ***Predicted activity against BA.1 and BA.2***
- Age  $\geq 12$  ( $\geq 40$  kg) and within 7 days of symptom onset
- No unexpected safety events in Phase 2 studies
- Efficacy studies in progress

# mAb prioritization at GWUH

<b>Group A: Underlying medical conditions that increase risk of severe COVID-19 (in alphabetical order based on <a href="#">evidence-based list</a> from CDC)</b>		<b>Group B: At-risk individuals to be prioritized in the context of supply constraints</b>
<ul style="list-style-type: none"> <li>▪ Age ≥50 years</li> <li>▪ Cancer</li> <li>▪ Cerebrovascular disease</li> <li>▪ Chronic kidney disease</li> <li>▪ Chronic liver disease</li> <li>▪ Down syndrome</li> <li>▪ Diabetes mellitus</li> <li>▪ Heart disease (such as heart failure, coronary artery disease, or cardiomyopathy)</li> <li>▪ Having a medical-related technological dependence (e.g., tracheostomy, gastrostomy)</li> <li>▪ HIV infection</li> <li>▪ Immunocompromising conditions, including solid organ or blood stem cell transplantation, use of corticosteroids or other immunosuppressive medications</li> </ul>	<ul style="list-style-type: none"> <li>▪ Lung disease (such as chronic obstructive pulmonary disease, <b>moderate-to-severe</b> asthma, interstitial lung disease, cystic fibrosis, pulmonary hypertension)</li> <li>▪ Mental health disorders (mood disorders, including depression, and schizophrenia spectrum disorders)</li> <li>▪ Neurologic conditions (such as dementia, cerebral palsy)</li> <li>▪ Obesity (<b>BMI ≥30</b>), or if age 12-17, have BMI ≥85th percentile for age/gender</li> <li>▪ Pregnancy and recent pregnancy</li> <li>▪ Smoking, current</li> <li>▪ Sickle cell disease</li> <li>▪ Tuberculosis</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Age ≥65 years (regardless of underlying conditions)</b></li> <li>▪ <b>Moderately or severely Immunocompromised individuals</b> <ul style="list-style-type: none"> <li>○ On active treatment for solid tumor and hematologic malignancies</li> <li>○ Receipt of solid organ transplant, CAR-T-cell or hematopoietic stem cell transplant</li> <li>○ Advanced or untreated HIV infection</li> <li>○ Use of mTOR inhibitors (e.g., tacrolimus), mycophenolate, high dose corticosteroids (e.g., ≥20mg prednisone per day), methotrexate, TNF-α blockers (e.g., etanercept, infliximab, adalimumab), B-cell-depleting agents (e.g., rituximab, ocrelizumab, ofatumumab)</li> </ul> </li> <li>▪ <b>“Group A” individuals who are unvaccinated or not-fully vaccinated</b></li> </ul>

**Thanks to  
Jose Lucar, M.D.**



[Full guidelines link here](#)  
(CTRL-click)

# Early IV remdesivir – PINETREE trial

- Third choice therapy for mild-moderate COVID, at high risk of progressing to severe disease
  - Approved for outpatients age  $\geq 12$  ( $\geq 40$  kg); EUA for high-risk outpatients  $\geq 3.5$  kg
  - Reduces risk of hospitalization or death by **87%** compared with placebo
  - Administer within 7 days of symptom onset
  - IV remdesivir infusions on three consecutive days
- Adverse effects: nausea, transaminase elevation; rare hypersensitivity
  - The only drug authorized for treatment of  $\leq 12$  yo or  $\leq 40$  kg
  - Works for all variants to date

# Nirmatrelvir/Ritonavir (Paxlovid)

- **First choice therapy** for mild-moderate COVID, at high risk of progressing to severe disease
- Age  $\geq 12$  ( $\geq 40$  kg)
- Reduced the risk of hospitalization or death by **88%** compared to placebo
- Start within 5 days of symptom onset
- Protease inhibitor (Mpro) boosted by ritonavir (CYP3A inhibitor)
- 30 pills over 5 days
- Works for all variants to date
- Adverse effects: dysgeusia, diarrhea, HTN, myalgia

- Long list of drug-drug interactions (CHECK PT MEDS CAREFULLY)
  - CYP3A inducers (rifampin, carbamazepine, phenobarb, phenytoin, St. John's wort)  $\downarrow$  level
  - RTV is CYP3A inhibitor so cannot use with many CYP3A dependent drugs that could have  $\downarrow$  clearance (amiodarone, midazolam)
- GFR  $\geq 30$  only, and dose adjust for 30-60 – a challenge given the drug is supplied in blister packs



Thanks to  
Jose Lucar, M.D.



[GWU guidance link](#)  
(CTRL click)

<https://www.idsociety.org/globalassets/idsa/public-health/covid-19/nirmatrelvir-ritonavir-quick-reference.pdf>

<https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-paxlovid-drug-drug-interactions/>

# Molnupiravir

- Fourth choice therapy for mild-moderate COVID, at high risk of progressing to severe disease
  - Age  $\geq 18$
  - Reduced the risk of hospitalization or death by **30%** compared to placebo
  - Start within 5 days of symptom onset
  - Four 200 mg capsules twice daily x 5 days
  - Mutagenic ribonucleoside polymerase inhibitor
- Potential risks: embryofetal toxicity; impaired bone/cartilage growth; mutagenicity
  - [Theoretical risk of viral mutations → new variants]
  - Contraindicated during pregnancy and lactation
  - Works for all variants to date



# How you can prescribe Paxlovid/molnupiravir

<https://healthdata.gov/Health/COVID-19-Public-Therapeutic-Locator/rxn6-qnx8/data>

An official website of the United States government [Here's how you know](#)

## HealthData.gov

Home Page Browse Support Health Equity DataJam Sign In

### COVID-19 Public Therapeutic Locator

Based on [COVID-19 Public Therapeutic Locator](#)

Locations of publicly available COVID-19 Therapeutics. Dataset only includes locations for Evusheld (monoclonal)

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Store Name	Address	Pharmacy Type	City	State	Zip	Year	Drug	Count	Coordinates	Phone	Website
CVS Store #02378	2226 WISCONSIN AVENUE NW	CVS Pharmacy	Washington	District of Col...	DC	20007	Paxlovid	19	POINT (-77.0...	1487/58454	245/34408
SAFEWAY PHARMACY	6500 PINEY BRANCH RD NW		Washington	District of Col...	DC	20012	Paxlovid	16	POINT (-77.0...	1306882188	244112887
SAFEWAY PHARMACY	1747 COLUMBIA RD NW		Washington	District of Col...	DC	20009	Paxlovid	8	POINT (-77.0...	1215973094	244112887
SAFEWAY PHARMACY	1100 4TH ST SW STE 150		Washington	District of Col...	DC	20024	Paxlovid	20	POINT (-77.0...	1154645224	244112887
Giant Food Store # 384	1535 ALABAMA AVENUE S.E.		Washington	District of Col...	DC	20032	Paxlovid	59	POINT (-76.9...	1265625867	245515224
SAFEWAY PHARMACY	415 14TH ST. SE		Washington	District of Col...	DC	20003	Paxlovid	15	POINT (-76.9...	1033155635	244112887
CVS Store #01337	1403 WISCONSIN AVENUE NW	CVS Pharmacy	Washington	District of Col...	DC	20007	Paxlovid	13	POINT (-77.0...	1407950330	245734408
SAFEWAY PHARMACY	490 L ST NW		Washington	District of Col...	DC	20001	Paxlovid	31	POINT (-77.0...	1114174471	244112887
CVS Store #01340	845 BLADENSBURG RD., N.E.	CVS Pharmacy	Washington	District of Col...	DC	20002	Paxlovid	19	POINT (-76.9...	1861596835	242515351
CVS Store #01842	1275 PENNSYLVANIA AVENUE ...	CVS Pharmacy	Washington	District of Col...	DC	20004	Paxlovid	17	POINT (-77.0...	1760586739	245734408
Fort Totten DC	100 Gallatin St NE		Washington	District of Col...	DC	20011	Paxlovid	158	POINT (-77.0...		252876782
CVS Store #07074	2240 M ST NW	CVS Pharmacy	Washington	District of Col...	DC	20037	Paxlovid	16	POINT (-77.0...	1104920172	245734408
SAFEWAY PHARMACY	3830 GEORGIA AVE NW		Washington	District of Col...	DC	20011	Paxlovid	17	POINT (-77.0...	1316983190	244112887
Giant Food Store # 378	1345 PARK ROAD, NW		Washington	District of Col...	DC	20010	Paxlovid	38	POINT (-77.0...	1538192885	245515224
CVS Store #01347	6 DUPONT CIRCLE NW	CVS Pharmacy	Washington	District of Col...	DC	20036	Paxlovid	12	POINT (-77.0...	1114022944	245734408
CVS Store #02174	4555 WISCONSIN AVENUE, NW	CVS Pharmacy	Washington	District of Col...	DC	20016	Paxlovid	12	POINT (-77.0...	1023112091	245734408
CVS Store #10685	675 K STREET NW	CVS Pharmacy	Washington	District of Col...	DC	20001	Paxlovid	19	POINT (-77.0...	1083087621	245734408
SAFEWAY PHARMACY	2845 ALABAMA AVE SE		Washington	District of Col...	DC	20020	Paxlovid	36	POINT (-76.9...	1366488991	244112887
CVS Store #02204	4859 MACARTHUR BOULEVAR...	CVS Pharmacy	Washington	District of Col...	DC	20007	Paxlovid	19	POINT (-77.0...	1114021185	245734408
SAFEWAY PHARMACY	5545 Connecticut Ave. Nw		Washington	District of Col...	DC	20015	Paxlovid	33	POINT (-77.0...	1275579807	244112887

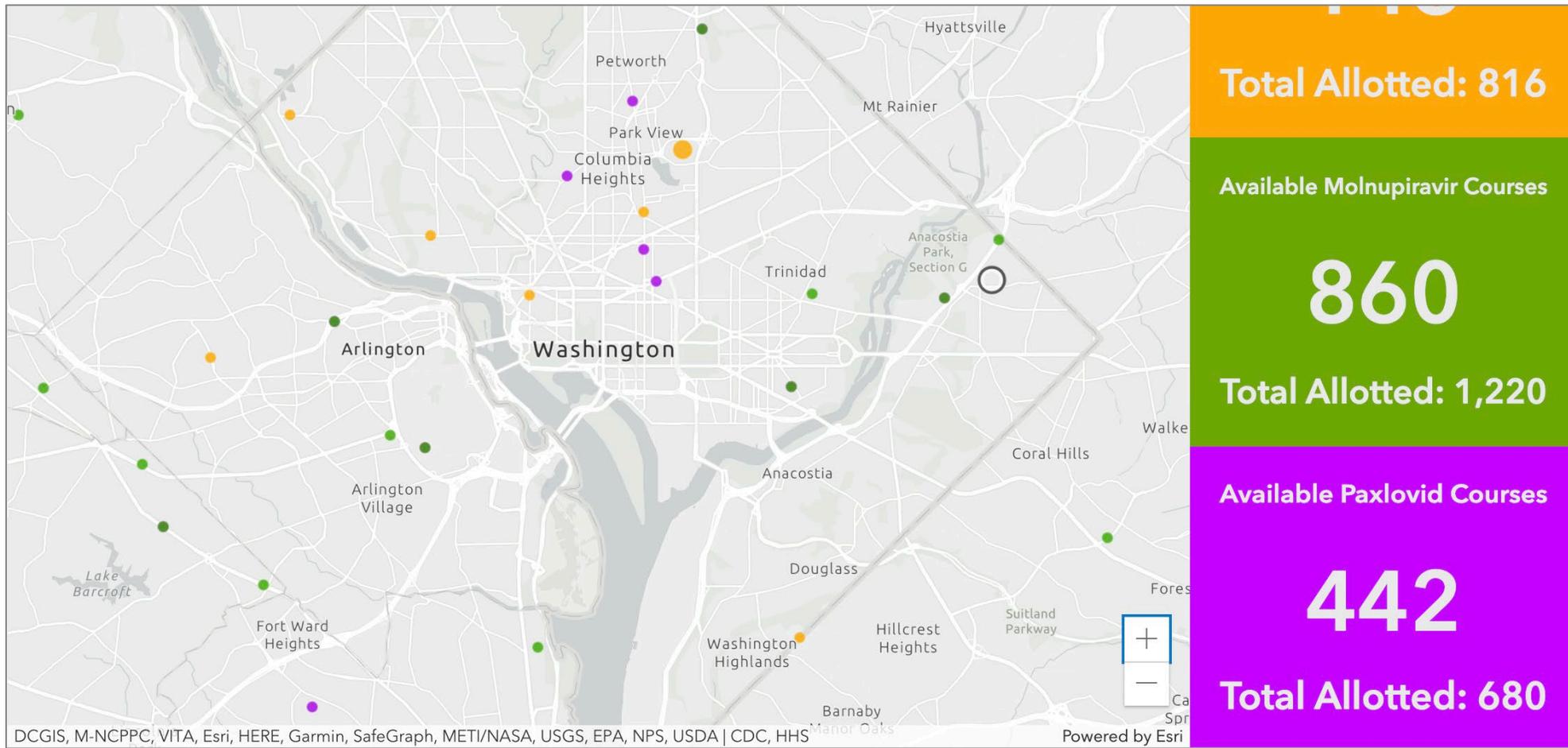
Showing all 51 rows

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# How you can prescribe Paxlovid/molnupiravir

## COVID-19 Therapeutics Locator:

<https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/>



# Recommended COVID therapeutics

Therapeutic	Admin	Efficacy	Advantage	Cautions	NNT
<b>Nirmatrelvir/ ritonavir</b>  <b>(Paxlovid)</b>	Two 150 mg nirmatrelvir tabs + one 100 mg ritonavir tab bid x 5 days	88% RR reduction (hosp/death)	- Oral - Safe in pregnancy	- Drug-drug interactions (ritonavir)	18
<b>Sotrovimab</b>	One-time IV infusion	85% RR reduction (hosp/death)	- Single dose - Safe in pregnancy	- IV with 1 hr observation (IM maybe soon)	17
<b>Remdesivir</b>	IV infusion daily x 3 days	85% RR reduction (hosp/death)	- Studied in pregnancy - Few/no drug interactions, extensive experience	- IV infusion daily x 3 days	22
<b>Molnupiravir</b>	800 mg (four 200 mg capsules) q 12 hours x 5 days	30% RR reduction (hosp/death)	- Oral - Few/no drug interactions	- Modest efficacy - Mutagenicity concerns - Not rec for children/ pregnant	31

# How does the Omicron lineage affect treatment options?

	S gene target*	Sotrovimab	Bebtelovimab	REGEN-COV	Evusheld	Paxlovid
<b>BA.1</b>	negative	Susceptible	Susceptible	NS	Susceptible (high dose)	Susceptible
<b>BA.2</b>	positive	NS	Susceptible	Susceptible <i>in vitro</i>	Susceptible (high dose)	Susceptible

\*PCR identification of lineage