

# 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



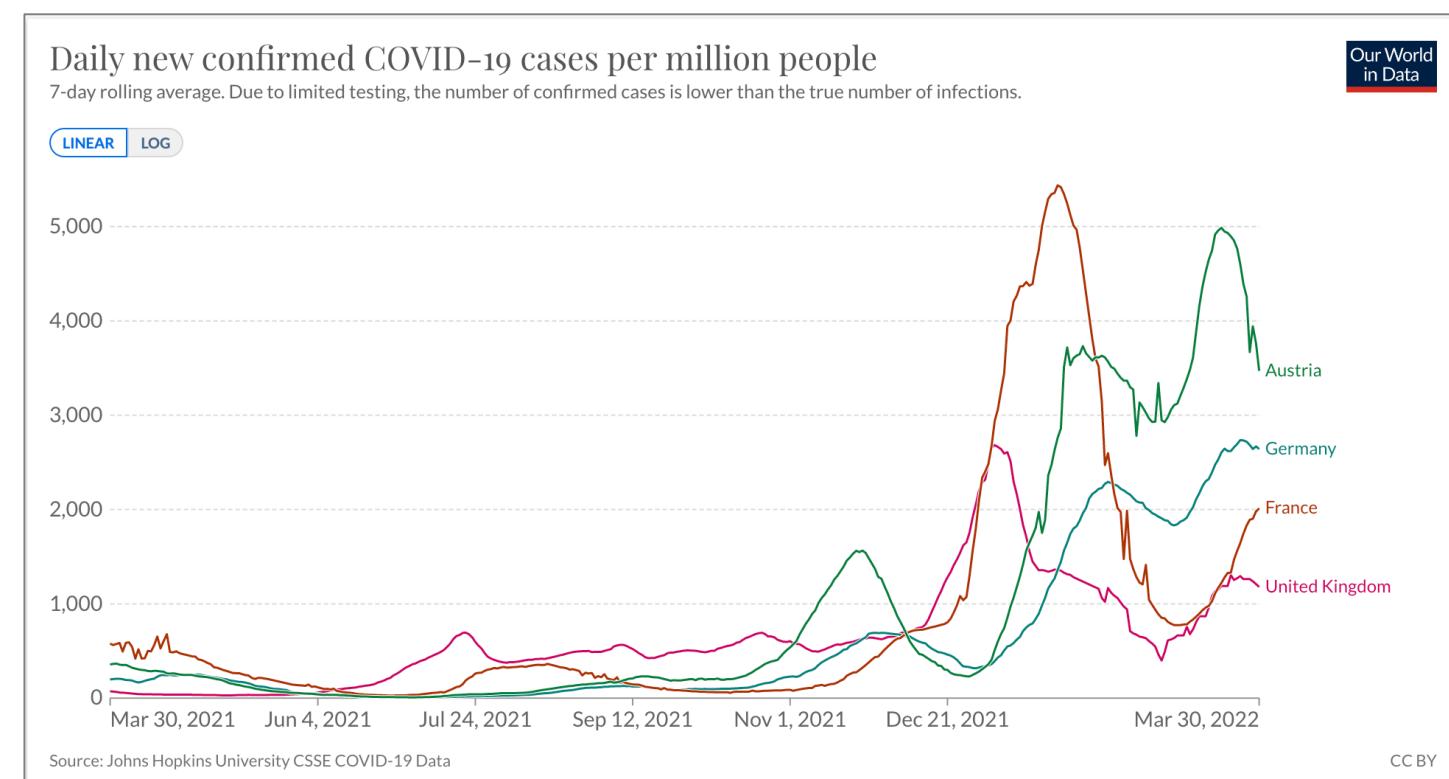
↓ 8/100K

wpost.com

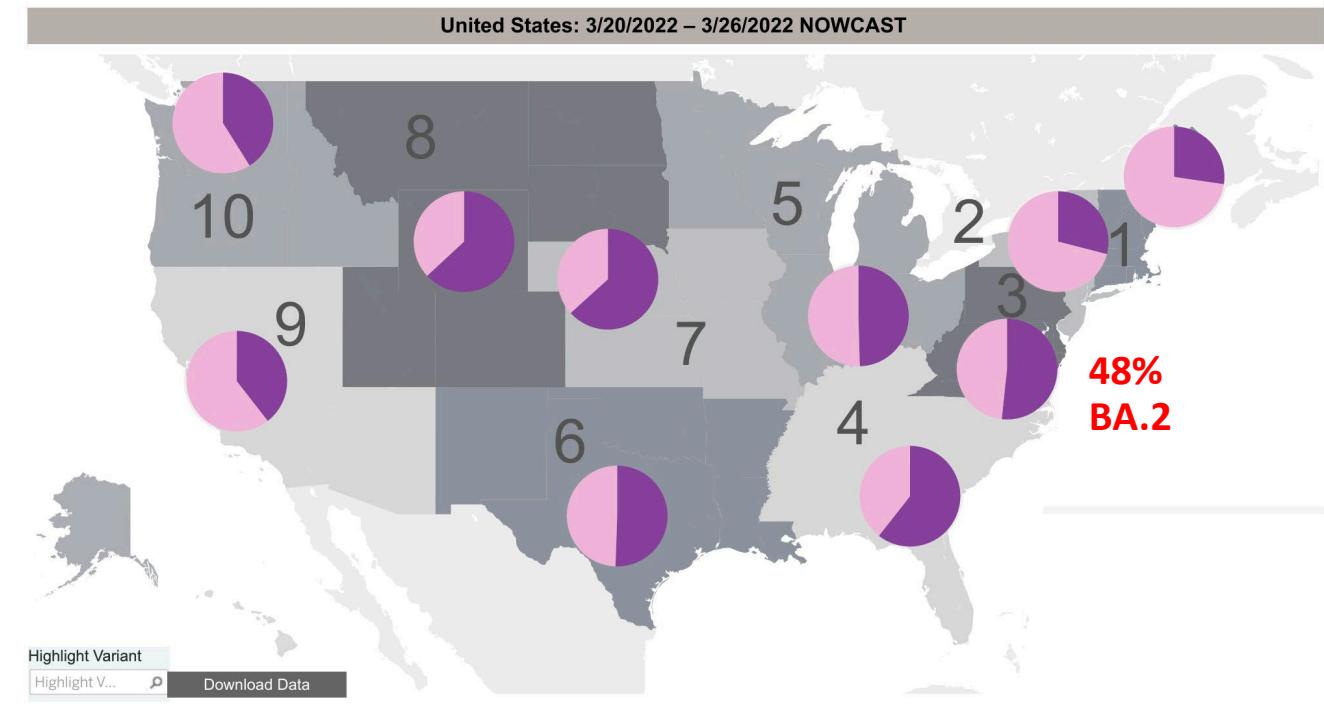
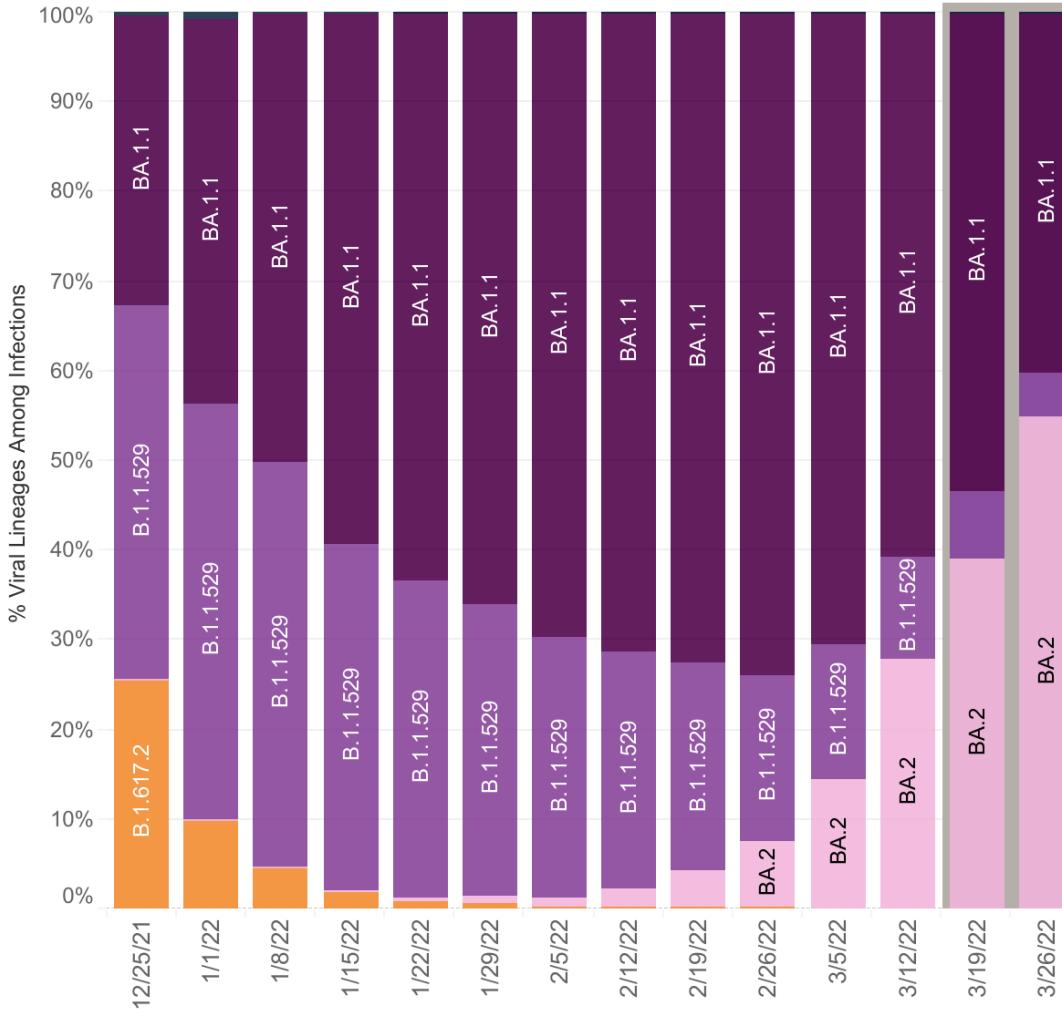
The Omicron variant has three lineages (=sub-variants), known as BA.1, BA.2, and BA.3. There have been few cases of BA.3.

# 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.

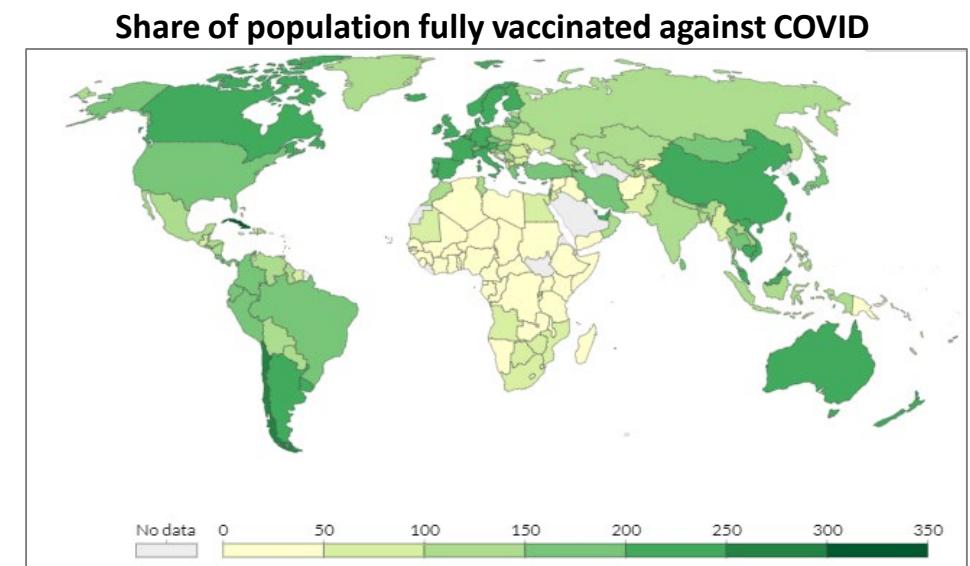
Our World  
in Data



# 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**



# 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  $\geq 12$  ( $\geq 40$  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

<u>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)</u>	<u>Group B: At-risk individuals to be prioritized in the context of supply constraints</u>
<ul style="list-style-type: none"><li>▪ Age <math>\geq</math>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 <math>\geq</math>30</b>), or if age 12-17, have BMI <math>\geq</math>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 <math>\geq</math>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., <math>\geq</math>20mg prednisone per day), methotrexate, TNF-<math>\alpha</math> 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  
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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

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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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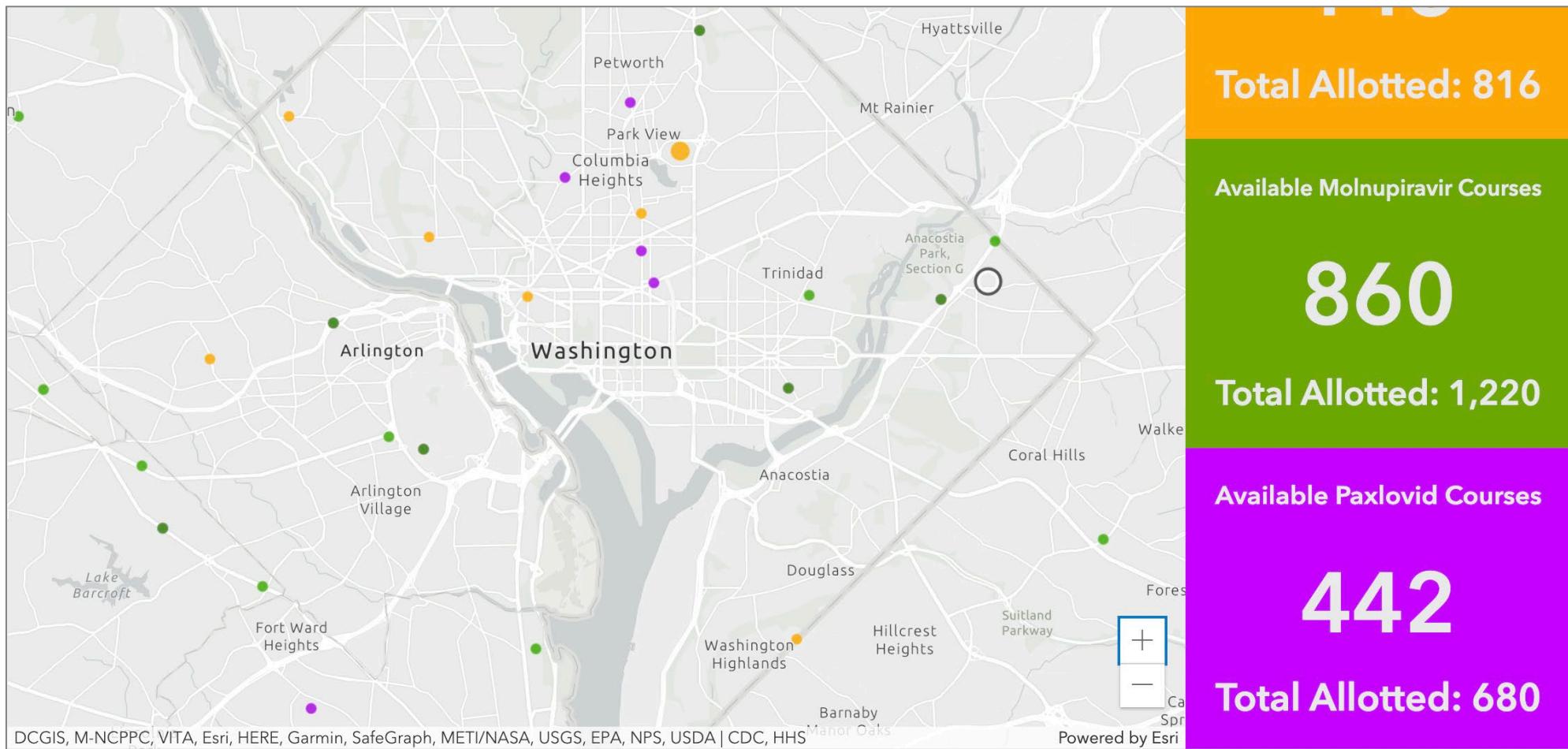
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SAFEWAY PHARMACY	6500 PINEY BRANCH RD NW		Washington	District of Col...	DC	20012	00069-1085-30	Paxlovid	16	POINT (-77.0...	1306882188	244112887
SAFEWAY PHARMACY	1747 COLUMBIA RD NW		Washington	District of Col...	DC	20009	00069-1085-30	Paxlovid	8	POINT (-77.0...	1215973094	244112887
SAFEWAY PHARMACY	1100 4TH ST SW STE 150		Washington	District of Col...	DC	20024	00069-1085-30	Paxlovid	20	POINT (-77.0...	1154645224	244112887
Giant Food Store # 384	1535 ALABAMA AVENUE S.E.		Washington	District of Col...	DC	20032	00069-1085-30	Paxlovid	59	POINT (-76.9...	1265625867	245515224
SAFEWAY PHARMACY	415 14TH ST. SE		Washington	District of Col...	DC	20003	00069-1085-30	Paxlovid	15	POINT (-76.9...	1033155635	244112887
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SAFEWAY PHARMACY	490 L ST NW		Washington	District of Col...	DC	20001	00069-1085-30	Paxlovid	31	POINT (-77.0...	1114174471	244112887
CVS Store #01340	845 BLADENSBURG RD., N.E.	CVS Pharmacy	Washington	District of Col...	DC	20002	00069-1085-30	Paxlovid	19	POINT (-76.9...	1861596835	242515351
CVS Store #01842	1275 PENNSYLVANIA AVENUE ...	CVS Pharmacy	Washington	District of Col...	DC	20004	00069-1085-30	Paxlovid	17	POINT (-77.0...	1760586739	245734408
Fort Totten DC	100 Gallatin St NE		Washington	District of Col...	DC	20011	00069-1085-30	Paxlovid	158	POINT (-77.0...		252876782
CVS Store #07074	2240 M ST NW	CVS Pharmacy	Washington	District of Col...	DC	20037	00069-1085-30	Paxlovid	16	POINT (-77.0...	1104920172	245734408
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Giant Food Store # 378	1345 PARK ROAD, NW		Washington	District of Col...	DC	20010	00069-1085-30	Paxlovid	38	POINT (-77.0...	1538192885	245515224
CVS Store #01347	6 DUPONT CIRCLE NW	CVS Pharmacy	Washington	District of Col...	DC	20036	00069-1085-30	Paxlovid	12	POINT (-77.0...	1114022944	245734408
CVS Store #02174	4555 WISCONSIN AVENUE, NW	CVS Pharmacy	Washington	District of Col...	DC	20016	00069-1085-30	Paxlovid	12	POINT (-77.0...	1023112091	245734408
CVS Store #10685	675 K STREET NW	CVS Pharmacy	Washington	District of Col...	DC	20001	00069-1085-30	Paxlovid	19	POINT (-77.0...	1083087621	245734408
SAFEWAY PHARMACY	2845 ALABAMA AVE SE		Washington	District of Col...	DC	20020	00069-1085-30	Paxlovid	36	POINT (-76.9...	1366488991	244112887
CVS Store #02204	4859 MACARTHUR BOULEVAR...	CVS Pharmacy	Washington	District of Col...	DC	20007	00069-1085-30	Paxlovid	19	POINT (-77.0...	1114021185	245734408
SAFeway PHARMACY	5545 Connecticut Ave Nw		Washington	District of Col	DC	20015	00069-1085-30	Paxlovid	33	POINT (-77.0...	127557907	244112887

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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 (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?

	<b>S gene target*</b>	<b>Sotrovimab</b>	<b>Bebtelovimab</b>	<b>REGEN-COV</b>	<b>Evusheld</b>	<b>Paxlovid</b>
<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