Novel Therapeutics Update

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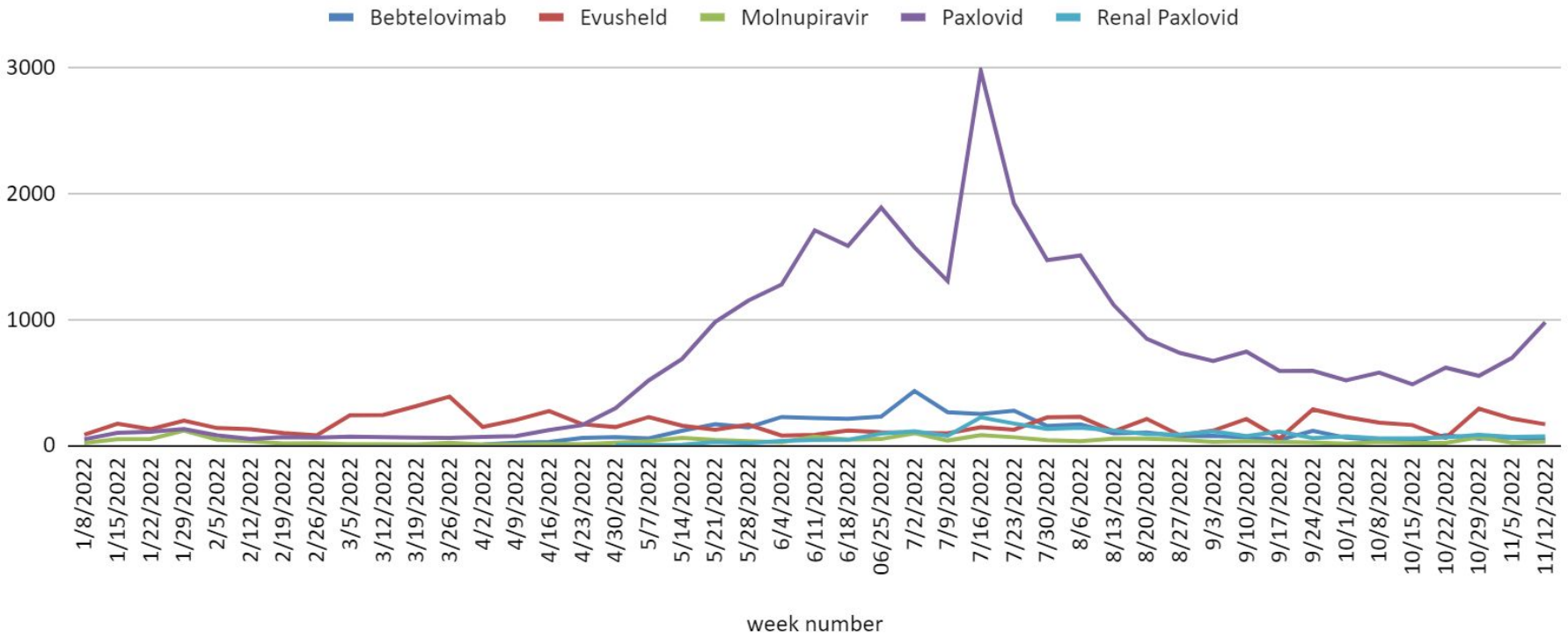
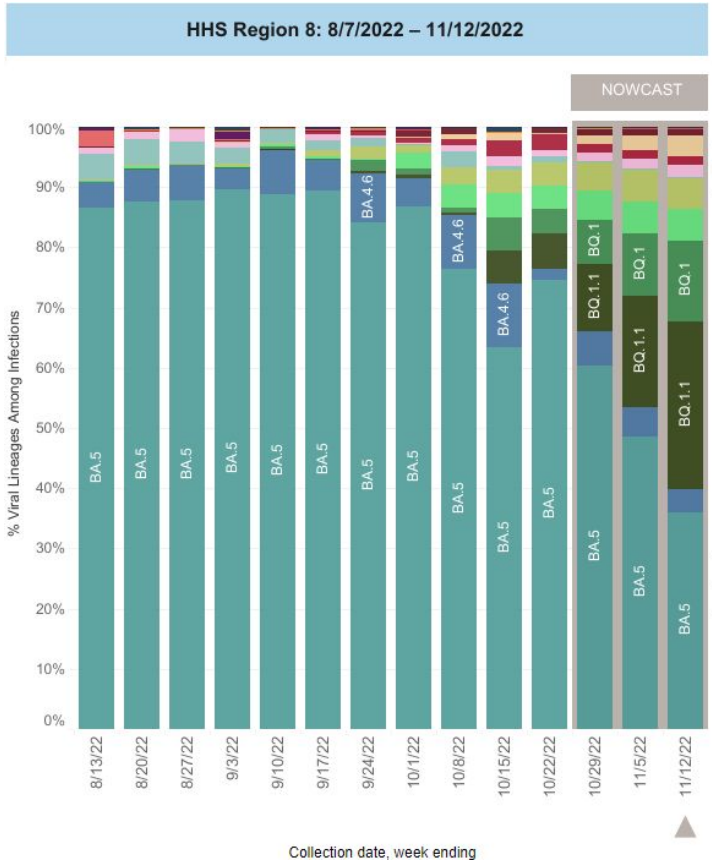
Bebtelovimab, Evusheld, Molnupiravir, Paxlovid and Renal Paxlovid



In state therapeutic availability

	Admin 11-6 to 11-12	Total Administered	Available
Paxlovid	978	31777	13893
Renal Paxlovid	70	2163	1541
Evusheld	165	7400	1682
Molnupiravir	27	1495	14287



HHS Region 8: 11/6/2022 – 11/12/2022 NOWCAST

Region 8 - Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	BA.5	VOC	36.1%	28.3-44.6%
	BQ.1.1	VOC	27.9%	15.6-44.2%
	BQ.1	VOC	13.4%	5.9-26.7%
	BA.5.2.6	VOC	5.3%	3.1-8.9%
	BF.7	VOC	5.2%	3.3-8.0%
	BA.4.6	VOC	3.7%	2.9-4.8%
	BN.1	VOC	3.6%	0.8-11.6%
	BA.2	VOC	2.0%	0.5-6.9%
	BA.2.75	VOC	1.3%	0.7-2.4%
	BA.2.75.2	VOC	1.2%	0.7-2.0%
	BA.4	VOC	0.1%	0.1-0.1%
	BA.1.1	VOC	0.1%	0.0-0.3%
	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*		0.1%	0.0-0.2%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.

** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates

\# BA.1, BA.3 and their sublineages (except BA.1.1 and its sublineages) are aggregated with B.1.1.529. Except BA.2.12.1, BA.2.75, BA.2.75.2, BN.1 and their sublineages, BA.2 sublineages are aggregated with BA.2. Except BA.4.6, sublineages of BA.4 are aggregated to BA.4. Except BF.7, BA.5.2.6, BQ.1 and BQ.1.1, sublineages of BA.5 are aggregated to BA.5. For all the lineages listed in the above table, their sublineages are aggregated to the listed parental lineages respectively. Previously, BN.1 was aggregated with BA.2.75. Lineages BA.2.75.2, BN.1, BA.4.6, BF.7, BA.5.2.6 and BQ.1.1 contain the spike substitution R346T.

Region 8 Variant Levels

Efficacy of COVID-19 Therapeutics against Variants

Evusheld (Psv & live virus)

Lineage with Spike Protein Substitution	Country First Identified	WHO Nomenclature	Key Substitutions Tested	Fold Reduction in Susceptibility* (Pseudotyped VLPs[1])	Fold Reduction in Susceptibility* (Authentic virus[1])
BA.1	Botswana	Omicron (BA.1)	G339D+S371L+S373P+ S375F+K417N+N440K+ G446S+S477N+T478K+ E484A+Q493R+G496S+ Q489R+N501Y+Y505H	132- to 183-fold[a]	12- to 30-fold
BA.1.1	Multiple country origin	Omicron (BA.1.1) [+R346K]	G339D+R346K+S371L+ S373P+S375F+K417N+ N440K+G446S+S477N+ T478K +E484A+Q493R +G496S+Q489R+N501Y+ Y505H	424-fold	176-fold
BA.2.7.5	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
BA.4	Multiple country origin	Omicron (BA.4)	G339D+S371F+S373P+ S375F+T376A+D405N+ R408S+K417N+N440K+ L452R+S477N+T478K+ E484A+F486V+Q498R+ N501Y+Y505H	33- to 65-fold	ND
BA.4.6	United States	Omicron (BA.4.6)	G339D+R346T+S371F+ S373P+S375F+T376A+ D405N+R408S+K417N+ N440K+L452R+S477N+ T478K+E484A+F486V+ Q498R+N501Y+Y505H	>1000-fold[b]	ND
BA.5	Multiple country origin	Omicron (BA.5)	G339D+S371F+S373P+ S375F+T376A+D405N+ R408S+K417N+N440K+ L452R+S477N+T478K+ E484A+F486V+Q498R+ N501Y+Y505H	33- to 65-fold	2.8- to 16-fold

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

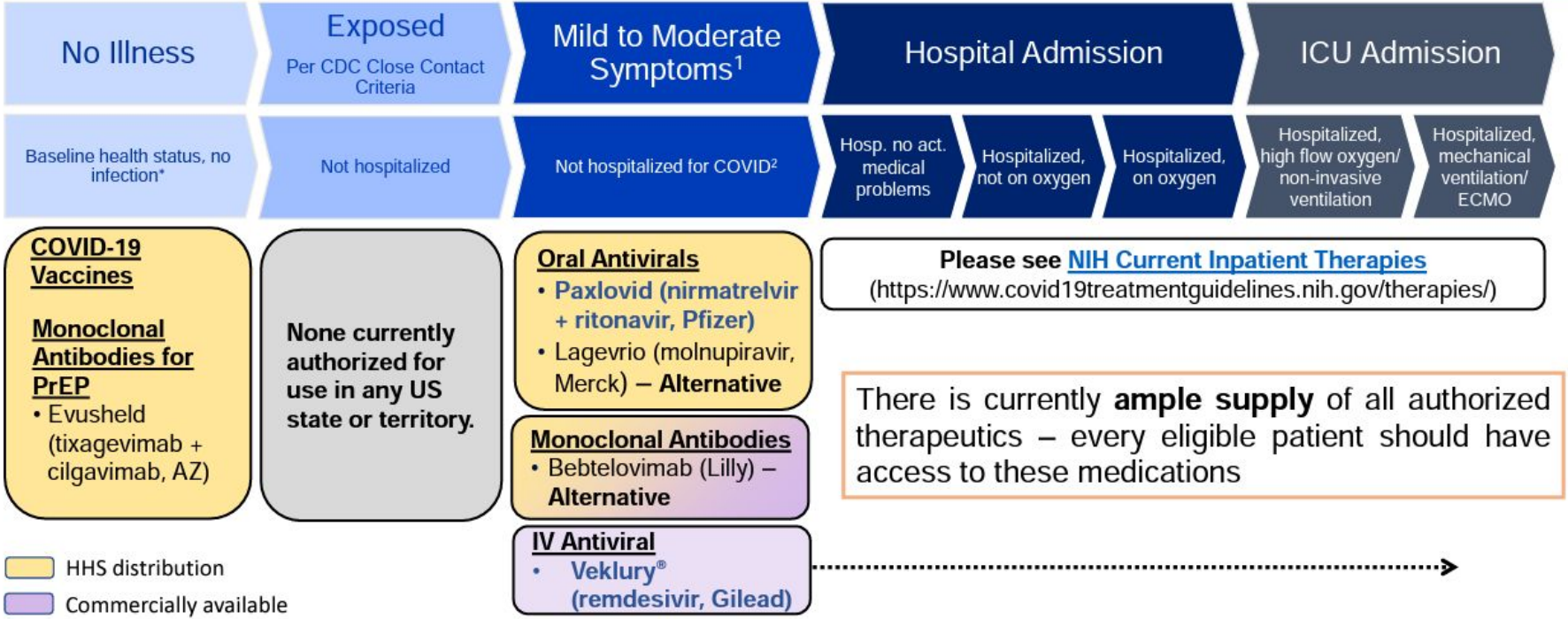
Bebtelovimab (Psv)

Lineage with Spike Protein Substitution	Country First Identified	WHO Nomenclature	Key Substitutions Tested[a]	Fold Reduction in Susceptibility
BA.2.12.1	USA	Omicron [BA.2+L452Q]	BA.2 + L452Q	No change[b]
BA.2.75	India	Omicron [BA.2+D339H, G446S, N460K, R493Q (reversion)]	BA.2 + D339H + G446S + N460K + R493Q (reversion)	No change[b]
BA.2.75.2	India	Omicron [BA.2.75+R346T+F486S]	BA.2.75 + R346T + F486S	No change[b]
BA.4/BA.5	South Africa	Omicron [BA.4/BA.5]	G339D + S371F + S373P + S375F + T376A + D405N + R408S + K417N +	No change[b]
			N440K + L452R + S477N + T478K + E484A + F486V + Q498R + N501Y + Y505H	
BA.4.6/BF.7	USA/Belgium	Omicron [BA.4+R346T]	BA.4 + R346T	No change[b]
BQ.1	Nigeria	Omicron [BA.5+K444T+N460K]	BA.5 + K444T + N460K	>672[d]
BQ.1.1	Multiple	Omicron [BA.5+R346T+K444T+N460K]	BA.5 + R346T + K444T + N460K	>672[d]

- Bebtelovimab Fact Sheet Updated to show lack of neutralization against BQ.1 and BQ.1.1 variants
- Preliminary reports showing **retained activity against BA.4/5 for Veklury[1,2] and oral antivirals (Paxlovid and Lagevrio)**[2]

1. https://www.gilead.com/news-and-press/company-statements/veklury-remdesivir-demonstrates-continued-in-vitro-antiviral-activity-against-omicron-subvariants
2. https://www.nejm.org/doi/full/10.1056/NEJMc2207519

Summary of COVID-19 Preventative Agents & Treatments



[1]COVID19 Convalescent Plasma has EUA for 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

COVID19 Convalescent Plasma EUA

- **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.**

- FDA has issued an EUA to permit the emergency use of the unapproved product, **COVID19 convalescent plasma with high titers** 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 is needed.

- COVID19 convalescent plasma is **not authorized to treat immunocompetent patients** with COVID19

Activity against emerging variants and recommendations

- **Paxlovid /Molnupiravir /Remdesivir expected to retain activity against all circulating variants** based on preliminary data & sequence analysis; additional data pending

- **Evusheld** loses neutralization against BA.4.6 (confirmed) & potentially also against BF.7, BA.2.75.2 & BQ* subvariants (preliminary); retains activity against BA.5, BA.2, BA.2.75*, BA.4 (confirmed)
  - Breakthrough infections are possible, **Advise patients to have a treatment plan in place and to seek timely medical attention if symptoms occur**
  - The FDA recommends continued use of Evusheld in the immunocompromised
  - COVID19 Convalescent Plasma has EUA for treatment of immunocompromised patients

- **Bebtelovimab** loses neutralization against BQ.1 and BQ.1.1 (confirmed); retains activity against BA.5, BA.4.6, BA.2.75, BA.4, BA.5, BF.7, BA.2.75.2 (confirmed); likely against BN.1 (preliminary)
  - Bebtelovimab is **not authorized for treatment of mild-to-moderate COVID-19 in geographic regions where infection is likely to have been caused by a non-susceptible SARS-CoV-2 variant** based on available information including variant susceptibility to this drug and regional variant frequency. **We expect to cross this threshold before the end of November.**

- mAbs currently not authorized for use (Regen-COV, bam/ete, sotrovimab) are routinely tested against emerging variants.