COVID-19 Therapeutics Bi-Weekly Update
July 25th, 2022

Clinical updates

Efficacy Update: Monoclonal Antibodies

The HHS Office of the Administration for Strategic Preparedness and Response (ASPR) highlighted in a recent discussion the retained efficacy of monoclonal antibodies, EVUSHELD and Bebtelovimab, against the current circulating variants. However, live virus data for BA.4/5 remains pending. For more in depth reporting see the EUA Factsheet EVUSHELD and EUA Factsheet Bebtelovimab.

Efficacy of Evusheld

Lineage	Country 1st Identified	WHO Nomenclature	Key Substitutions Tested	Fold Reduction (Pseudotyped VLPs)	Fold Reduction (Authentic Virus)
BA.1	Botsw ana	Omicron (BA.1)	G339D+S371L+S373P+ S375F+K417N+N440K+ G446S+S477N+T478K + E484A+Q493R+G496S+ Q489R+N501Y+Y505H	132- to 183-fold#	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	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.2.12.1	United States	Omicron (BA.2.12.1)	G339D+ S371F+S373P+S375F+ T376A+D405N+R408S+ K417N+N440K+L452Q+ S477N+T478K+E484A+ Q493R+Q498R+N501Y+ Y505H	5-fold	ND
BA.3	Multiple country origin	Omicron (BA.3)	G339D+S371F+ S373P+S375F+D405N+ K417N+N440K+G446S+ S477N+T478K+E484A+ Q493R+Q498R+N501Y+ Y505H	16-fold	ND
BA.4/5	Multiple country origin	Omicron (BA.4/5)	+G339D+S371F+S373P+ S375F+T376A+D405N+ R408S+K417N+N440K+ L452R+S477N+T478K+ E484A+F486V+Q498R+ N501Y+Y505H	33- to 65-fold	ND

Efficacy of Bebtelovimab

Lineage with Spike Protein Substitution	Country First Identified	WHO Nomenclature	Key Substitutions Tested[a]	Fold Reduction in Susceptibility
B.1.1.529/BA.1	South Africa	Omicron [BA.1]	G339D + S371L + S373P + S375F + K417N + N440K + G446S + S477N + T478K + E484A + Q493R + G496S + Q498R + N501Y + Y505H	No change[b]
BA.1.1	South Africa	Omicron [+R346K]	BA.1 + R346K	No change[b]
BA.2	South Africa	Omicron [BA.2]	G339D + S371F + S373P + S375F + T376A + D405N + R408S + K417N + N440K + S477N + T478K + E484A + Q493R + Q498R + N501Y + Y505H	No change[b]
BA.2.12.1	USA	Omicron [BA.2+L452Q]	BA.2 + L452Q	No change[b]
BA.4/BA.5	South Africa	Omicron [BA.4/BA.5]	G339D + S371F + S373P + S375F + T376A + D405N + R408S + K417N + N440K + L452R + S477N + T478K + E484A + F486V + Q498R + N501Y + Y505H	No change[b]

- Current monoclonal antibody products retain activity against circulating variants
- Live virus data for BA.4/5 is pending

Prescribing Paxlovid: What Pharmacists Need to Know

The process remains very new and adjustments will take time. Main points for pharmacists to consider:

- Kidney and renal function cannot be verified
- Drug-drug interaction(s) must be resolved with modification of another medication
- Patient is not eligible for Paxlovid

The pharmacist should refer the patient to a medical provider for further consultation. For more in depth information, see Fact Sheet for Healthcare Providers: EUA for Paxlovid here.

REMINDER: EVUSHELD Dosing

Please see below for important information on repeat EVUSHELD doses.

Evusheld Fact Sheet Update on Repeat Dosing

- The repeat dosage of EVUSHELD in adults and pediatric individuals (12 years of age and older weighing at least 40 kg) is **300 mg of tixagevimab and 300 mg of cilgavimab** administered every 6 months, refer to Table 1 below. Repeat dosing should be timed from the date of the most recent EVUSHELD dose.

Table 1 Dosage of 300 mg of Tixagevimab and 300 mg of Cilgavimab

EVUSHELD* (tixagevimab co-packaged with cilgavimab)	Antibody dose	Number of vials needed	Volume to withdraw from vial(s)
	tixagevimab 300 mg	2 vials	3 mL
	cilgavimab 300 mg	2 vials	3 mL

* 300 mg of tixagevimab and 300 mg of cilgavimab are to be administered as separate, consecutive intramuscular injections

Table 2 Dosage of 150 mg of Tixagevimab and 150 mg of Cilgavimab

EVUSHELD* (tixagevimab co-packaged with cilgavimab)	Antibody dose	Number of vials needed	Volume to withdraw from vial
	tixagevimab 150 mg	1 vial	1.5 mL
	cilgavimab 150 mg	1 vial	1.5 mL

* 150 mg of tixagevimab and 150 mg of cilgavimab are to be administered as separate, consecutive intramuscular injections

In the News

COVID-19 Public Health Emergency Declaration Renewed

Effective July 15, U.S Health and Human Services Secretary Xavier Becerra renewed the COVID-19 public health emergency declaration to meet the continued needs during the ongoing COVID-19 pandemic. Health care providers and state and territorial health departments need continued flexibility to respond to the pandemic. Renewing the public health emergency declaration ensures these needs are met.

HHS will provide states and territories with no less than 60 days' notice prior to the termination of the public health emergency declaration for COVID-19.

Visit ASPR's website to read the latest information about the COVID-19 public health emergency declaration renewal, and to learn more about public health emergency declarations.

HHS Reorganized to Better Meet Pandemic Needs

It was just announced by US DHHS Secretary O'Connell that Administration for Strategic Preparedness and Response (ASPR), formerly known as the Office of the Assistant Secretary for Preparedness and Response, has undergone some organizational changes.The current statutory authorities and responsibilities of ASPR remain unchanged. Read more of the Washington Post article here.

Changes include:

- New name: Administration for Strategic Preparedness and Response (ASPR)
- Addition of an institutional profile of an "operating division" (OpDiv) who will work alongside other HHS agencies such as the FDA and the CDC.

Process and logistics updates

NEW: Renal Paxlovid-Out of Cycle (OOC) Request

At the current, temporary, supply environment HHS is unable to support any OOC request for Renal Paxlovid. When the supply environment improves we can re-engage with these requests.

As a reminder, when dispensing Paxlovid for the renally impaired and renal packaging is not available, healthcare professionals should complete the following:

- Remove **two** nirmatrelvir tablets from daily blister cards (i.e., **one** of the 150 mg nirmatrelvir tablets from the morning dose and **one** of the 150 mg nirmatrelvir tablets from the evening dose) prior to dispensing
- Notify patients that blister cards have been altered at the pharmacy and counseling patients about renal dosing instructions. Stickers are placed over the area that has been punched out.

AmerisourceBergen has additional stickers for this and sites can place requests directly to them if more stickers are required. In addition, at this time we do not expect the thresholds at the jurisdictional channel to be impacted, and should continue with similar amounts of Renal Paxlovid. If an order fulfillment is delayed, please reach out directly to AmerisourceBergen at c19therapies@amerisourcebergen.com to obtain stickers to implement a renal dose adjustment.

Reminder: Paxlovid Shelf-Life Extension

Lot#	Extended Expiry Date
FL4516, FL4517, FR7229	The initial 3 lots were extended from 7/31 to 10/31/22.
FR9088	4th lot was extended from 8/31 to 11/30/22

EVUSHELD: How to properly report inventory

Reporting is required in HPOP, at a minimum of **twice per week**

To stay consistent with historical reporting, we ask that you continue to report Evusheld inventory and administrations per 300mg units (1 carton)

- Thus, **one patient dose with 600mg should be reported as 2 administrations**!!

- Administrations reporting should **always** be an **even number**
- **2** patients dosed → report in HPOP as **"4"** (2 patients, 4 cartons, 8 vials)
- **6** patients dosed → report in HPOP as **"12"** (6 patients, 12 cartons, 24 vials)

If you have been reporting differently (as 600mg units), please reach out to us at covid19therapeutics@vdh.virginia.gov and we will work with you to correct your reporting.

REMINDER: HPoP Direct Order Temporary Suspension on TUESDAYS

HPoP Direct Ordering will be temporarily suspended **every Tuesday from 12:00-5:00 PM EST** to allow for order processing. This will provide adequate time to verify orders and coordinate redistribution of products between providers. We apologize for any inconvenience that may cause providers. We appreciate your continued work and support in providing COVID-19 therapeutics across the Commonwealth of Virginia. Any questions regarding Direct Ordering should be sent to covid19therapeutics@vdh.virginia.gov.

REMINDER: HPoP Direct Order Request (DOR) Process

VDH hosted a webinar on 6/23 to go over the Direct Order Request (DOR) process. The recording for this webinar can be accessed here. For further instructions on the DOR process, please use the HPoP Job Aid.

REMINDER: Federal Holiday Therapeutics Thresholds and Compliance Reporting

Therapeutic threshold determinations and notifications **will not occur** on the following federal holidays that fall on a Monday: Labor Day 9/5/22, Columbus Day 10/11/22, and Christmas 12/26/22. Deliveries will occur as scheduled on all Fridays **prior** to the corresponding Federal Holiday. If you wish to hold orders on Friday, please contact Amerisource Bergen at C19therapies@amerisourcebergen.com

Provider compliance reporting should occur on Mondays and Thursdays by 11:59 PM EST. However, on these federal holidays that fall on a Monday, the **deadlines will be shifted one day** and should be performed on the **next business day** (Tuesdays 9/6/22, 10/12/22 and 12/27/22) by 11:59 PM EST.

Any questions regarding therapeutics thresholds and notifications or provider reporting compliance should be sent to covid19therapeutics@vdh.virginia.gov.

Allocation data

Total Allocations to Therapeutic Administration Sites (07/07/2022 - 07/20/2022):

Therapeutic (mAB & OAV*)	Central	Eastern	Northern	Northwest	Southwest	Total

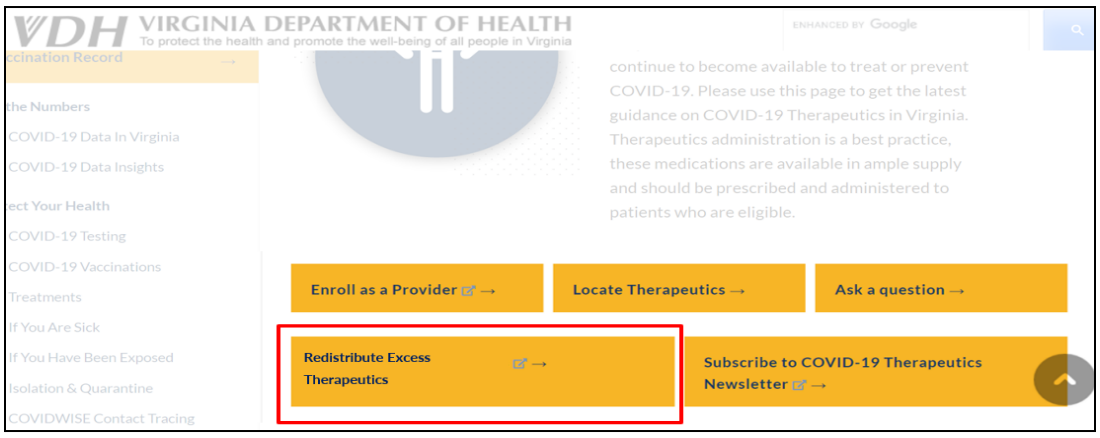
Bebtelovimab	85	270	285	190	320	**1150**
Evusheld	168	96	264	240	48	**816**
Lagevrio (Molnupiravir)	-	-	-	-	72	**72**
Paxlovid	40	140	900	220	100	**1400**
Renal Paxlovid	5	30	100	45	65	**245**

*Oral Antiviral numbers presented do not include those allocated to Community Pharmacy Enhanced Services Network. These Oral Antiviral courses were bulk ordered and distribution to individual site locations is managed by respective Federal Retail Pharmacy Therapeutic Program (FRPTP) partners, VDH does not have visibility of course distribution to each region.
*Please reference the Outpatient Therapeutic Portfolio- Jurisdiction Allocations for more detail.

REMINDER on Redistribution

VDH can redistribute therapeutics within our Commonwealth. Any providers wishing to make their therapeutics available for transfer can do so by clicking the link "Redistribute Excess Therapeutics" on the VDH home page. The VDH Therapeutics team will prioritize these available therapeutics before pulling from federal supplies whenever it is advantageous to do so.

Listen to the Redistribution webinar here. The Redistribution discussion starts at 8:55.



Resources and Tools

CLINICAL REMINDER: What therapeutics are currently authorized?

There are currently 5 therapeutics authorized. **Other therapeutics should not be prescribed or administered at this time.**

Available Therapeutics

	Type	Classification	Use	How is it given?	When is it given?
Prevention	Tixagevimab / cilgavimab (EVUSHELD)	Monoclonal antibody for pre-exposure prophylaxis	• For those NOT infected with COVID-19 • No known exposure to COVID-19 AND • Moderate to severe immune system compromise or who may not mount an adequate immune response to vaccination	By injection into muscle	When NOT currently infected with COVID-19 AND no known recent exposure
Treatment	Bebtelovimab	Monoclonal antibody	For treatment of mild-moderate COVID-19	By infusion into a vein	Within 7 days of symptoms starting
	Remdesivir (Veklury)	IV Antiviral	For treatment of COVID-19 (inpatient or outpatient)	By infusion into a vein	Within 7 days of symptoms starting
	Nirmatrelvir/ritonavir (Paxlovid)	Oral Antiviral	For treatment of mild-moderate COVID-19	By oral tablet	Within 5 days of symptoms starting
	Molnupiravir (Lagevrio)				

These therapeutics are currently **deauthorized by the FDA, and should **not be ordered, dispensed, or administered:**

- REGEN-COV (Casirivimab and Imdevimab)
- Sotrovimab
- Bamlanivimab and Etesevimab (“Bam-ete”)

Link to sign up for the newsletter:

Did your colleague share this newsletter with you, and you’d like to sign up to receive it directly? Do you know of a colleague that would benefit from receiving information on therapeutics from VDH? Click here to sign up!

VDH Therapeutics Website for Healthcare Providers

Check out the VDH Therapeutics webpage here. Reach out to COVID19Therapeutics@vdh.virginia.gov for questions, comments, or feedback on information you’d like to see.

COVID-19 Therapeutics Webinars and Open Forum Calls for Providers

- VDH is continuing to facilitate webinars and open forums monthly.
  See below for links to ***register***!

  July 27 Open Forum: Register here.
  July 27 Pharmacist Webinar for Prescribing Paxlovid: Register here.
  August 10 Healthcare Provider COVID-19 Therapeutics Webinar: Register here.

Other resource links:
VDH: COVID-19 Therapeutics FAQs for Providers
VDH: Guidance on Expiring & Expired Therapeutics
VDH: EVUSHELD Fact Sheet for Providers

VDH: Lagevrio (Molnupiravir) Prescribing Checklist
VDH: Paxlovid Prescribing Checklist
VDH: Paxlovid Prescribing Checklist- Pharmacists
HHS: ASPR Test to Treat Fact Sheet
Find where to access therapeutics here.