

Monoclonal Antibodies: Updates from the Federal COVID Response

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Office of the Assistant Secretary for Preparedness and Response U.S. Department of Health and Human Services

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Agenda

- 1 Update on new COVID-19 mAb authorized (third mAb): Sotrovimab
- 2 Updated Regeneron EUA
- 3 EUA expanded eligibility criteria
- 4 NIH Criteria
- 5 Variants of Concern and impact on mAb utilization
- 6 mAb Administration models
- Outreach Resources and Factsheets for providers
- 8 Helpful Information and Resources

FDA authorizes additional mAb for treatment of COVID-19

As of May 26, 2021

- Sotrovimab (GSK / Vir Biotechnology) authorized for the treatment of mild to moderate COVID-19
- NOT distributed by USG
 - > commercially available therapy
- > Please refer to the following for more information:
 - FDA fact sheet and EUA Letter of authorization
 - FDA press release
 - COMET-ICE clinical trial
- For additional information and approved materials, including information about ordering, please refer to the <u>Sotrovimab</u> webpage

Please contact the GSK COVID Contact Center if you have further questions: 1-866-GSK-COVID (1-866-475-2684)



Updated EUA for REGEN-COV™ (casirivimab and imdevimab)

- ➤ Effective June 3, 2021, the FDA has authorized under emergency use a **lower dose** of REGEN-COV (600mg casirivimab and 600mg imdevimab), which is half the dose originally authorized.
- REGEN-COV should be administered by intravenous (IV) infusion; subcutaneous injections are an alternative when IV infusion is not feasible and would lead to a delay in treatment.
- Additionally, later this month a new presentation of a **single vial** of coformulated product will be available to order via AmerisourceBergen.
 - Single vial represents one full, complete treatment at the lower authorized dose

Please contact Regeneron Medical Affairs with any questions about using **existing** inventory to treat patients at 1-844-734-6643

Updates for sites administering mAbs

- 1 Eligibility criteria for the definition of patients who are high-risk for progressing to severe COVID-19 have been expanded (effective as of May 14, 2021)¹
 - Please see updated FDA factsheets for <u>bamlanivimab/etesevimab</u>
 (administered together) and <u>REGEN-COV</u> for additional information
 - Healthcare providers should consider the benefit-risk for an individual patient
- 2 CMS has increased reimbursement rates for mAb treatment (effective as of May 6, 2021)
 - \$450/reimbursement for mAb administration in most health care settings
 - \$750/reimbursement when administered in the beneficiary's home²
- 3 Information for sites seeking to return EUA product
 - If undamaged product needs to be returned, follow the below instructions:
 - For bam and bam/ete, see <u>The Lilly Return Goods Procedure</u>, detailed guidance can be found at: <u>https://www.lillytrade.com/</u>
 - For REGEN-COV, call 844-734-6643
 - Reconstituted (diluted) product SHOULD NOT be returned and should be treated as waste per your facility's SOP

^{1.} Refer to <u>CDC</u> for additional information for the treatment of mild to moderate COVID-19 in eligible patients. 2. CMS press release: https://www.cms.gov/newsroom/press-releases/cms-increases-medicare-payment-covid-19-monoclonal-antibody-infusions

Shipments of bam/ete and ete alone to 8 states paused due to P.1 and B.1.351 prevalence

- ➤ CDC has identified that the combined frequency of P.1 variant (originally identified in Brazil) and the B.1.351 variant (originally identified in South Africa) is circulating with increasing frequency in 8 states¹
- Results from in vitro studies suggest that:
 - > Bam / ete administered together are not active against either the P.1 or B.1.351 variants
 - > REGEN-COV is likely to retain activity against the P.1 or B.1.351 variants



- Distribution of bam / ete together and etesevimab alone (to pair with existing supply of bamlanivimab) to AZ, CA, FL, IL, IN, MA, OR, WA have been paused
- > FDA recommends that health care providers in these states use REGEN-COV until further notice, which can be ordered directly from Amerisource Bergen

Please contact COVID19Therapeutics@hhs.gov with any questions

^{1. &}lt;a href="https://covid.cdc.gov/covid-data-tracker/?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fcases-updates%2Fvariant-proportions.html#variant-proportions">https://covid.cdc.gov/covid-data-tracker/?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fcases-updates%2Fvariant-proportions.html#variant-proportions

COVID-19 treatment guidelines

- ➤ The NIH has **strongly recommended (Alla)** the following for use in non-hospitalized COVID-19 patients:
 - Casirivimab + imdevimab (Regeneron)
 - Bamlanivimab + etesevimab (Eli Lilly)
- ➤ Updated NIH COVID-19 guidelines can be found at: https://www.covid19treatmentguidelines.nih.gov/statement-on-anti-sars-cov-2-monoclonal-antibodies-eua/

Results from REGEN-COV randomized Ph3 trial | Preprint posted May 21, 2021

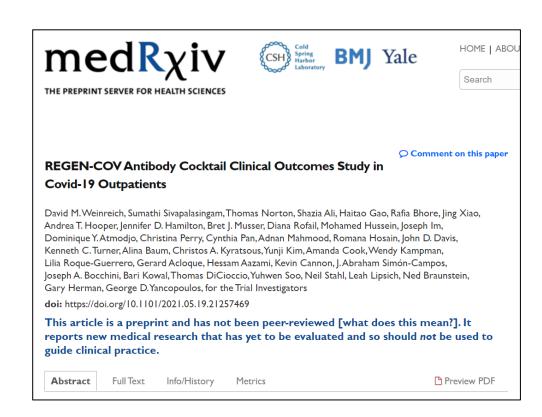
Methodology

- Ph3 randomized clinical trial of COVID-19 outpatients with ≥ 1 risk factors for severe disease (n = 4,057)¹
- ➤ Patients randomized to a single treatment of IV placebo, or various doses of REGEN-COV, and followed for 28 days



Key Findings

- 2400mg and 1200mg doses significantly reduced Covid-19-related hospitalization or all-cause death compared to placebo (71.3% reduction [p<0.0001] and 70.4% reduction [p=0.0024], respectively)
- Median time to resolution of Covid-19 symptoms was
 4 days shorter in both dose arms vs placebo (p<0.0001)
- > Serious adverse events occurred more frequently in the placebo group (4.0%) than in the 1200mg (1.1%) and 2400mg (1.3%) groups



Note: This article is a pre-print and has not been peer-reviewed.

CDC variants of concern susceptibility

Information on variants of concern updated in **Section 15 of FDA fact sheets**

REGEN-COV fact sheet¹

Table 6: Pseudotyped Virus-Like Particle Neutralization Data for SARS-CoV-2 Variant Substitutions with Casirivimab and Imdevimab Together

Lineage with Spike Protein Substitution	Key Substitutions Tested	Fold Reduction in Susceptibility
	NI501379	
B.1.1.7 (UK origin)	N501Y ^a	no changed
B.1.351 (South Africa origin)	K417N, E484K, N501Y ^b	no change ^d
P.1 (Brazil origin)	K417T + E484K ^c	no change ^d
B.1.427/B.1.429 (California origin)	L452R	no changed
B.1.526 (New York origin) ^e	E484K	no changed
B.1.617.1/B.1.617.3 (India origin)	L452R+E484Q	no change ^d
B.1.617.2 (India origin)	L452R+K478T	no changed

bamlanivimab / etesevimab fact sheet¹

Table 3: Pseudotyped Virus-Like Particle Neutralization Data for SARS-CoV-2 Variant Substitutions with Bamlanivimab and Etesevimab Together (1:2 Molar Ratio)

Lineage with Spike Protein Substitution	Key Substitutions Tested ^a	Fold Reduction in Susceptibility
B.1.1.7 (UK origin)	N501Y	no change ^b
B.1.351 (South Africa origin)	K417N + E484K + N501Y	215°
P.1 (Brazil origin)	K417T + E484K + N501Y	>46°
B.1.427/B.1.429 (California origin)	L452R	9 ^d
B.1.526 (New York origin) ^e	E484K	31

For variants with more than one substitution of concern, only the substitution(s) with the greatest impact on activity is(are) listed. For B.1.351, P.1 and B.1.427/B.1.429, spike variants reflective of the consensus sequence for the lineage

b No change: <5-fold reduction in susceptibility.</p>

Bamlanivimab and etesevimab together are unlikely to be active against variants from this lineage. No activity observed at the highest concentration tested for the P.1 variant.

d Etesevimab retains activity against this variant.

e Isolates of the B.1.526 lineage harbor several spike protein amino acid substitutions, and not all isolates contain the E484K substitution (as of February 2021). This assay was conducted using pseudotyped VLPs with the E484K substitution only.

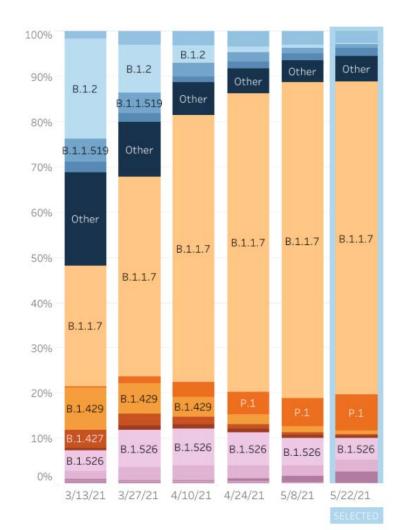


Estimated proportions of SARS-CoV-2 lineages available on CDC

website

Please refer to the following webpage for updated CDC variant proportions:

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



United States: 2/28/2021 - 5/22/2021

CDC variants of concern by state

Estimated biweekly proportions of the most common SARS-CoV-2 lineages circulating in the U.S available from the CDC variant proportions data tracker

Unweighted Proportions of Variants of Concern and Other Lineages by State or Jurisdiction

State 5	B.1.1.7	B.1.351	B.1.427 / B.1.429	P.1	Other lineages	Total Available Sequences
Arizona	67.8%	0.7%	4.2%	9.0%	18.3%	600
California	58.1%	1.0%	5.1%	9.5%	26.3%	4,060
Colorado	79.0%	0.5%	2.5%	2.2%	15.8%	2,312
Connecticut	53.9%	0.7%	0.6%	4.1%	40.8%	714
Florida	67.4%	0.3%	0.9%	10.4%	21.0%	5,281
Georgia	80.0%	1.5%	0.3%	5.2%	13.1%	950
Illinois	61.1%	1.0%	1.1%	22.6%	14.3%	2,598
Indiana	73.6%	0.5%	0.7%	12.2%	13.1%	1,347
Kentucky	78.2%		0.6%	5.3%	15.9%	358
Maine	38.1%		1.2%	3.7%	57.0%	328
Maryland	75.8%	1.2%	0.3%	1.2%	21.6%	781
Massachusetts	52.1%	0.1%	0.7%	13.0%	34.1%	5,145
Michigan	81.5%	0.5%	1.0%	3.0%	14.1%	1,984
Minnesota	80.6%	0.7%	3.5%	3.2%	12.0%	4,286
Missouri	79.2%	0.5%	0.8%	7.2%	12.3%	390
New Hampshire	54.4%		0.4%	6.7%	38.6%	555
New Jersey	53.8%	0.1%	0.5%	5.0%	40.7%	1,468
New Mexico	73.3%		3.3%	1.8%	21.6%	329
New York	57.8%	1.7%	0.7%	7.1%	32.9%	1,032
North Carolina	68.0%	0.8%	0.2%	2.9%	28.0%	1,681
Ohio	79.7%	0.6%	0.2%	5.7%	13.7%	839
Oregon	49.5%	2.2%	9.5%	10.8%	28.1%	548
Pennsylvania	68.8%	0.5%	0.4%	1.8%	28.5%	2,772
Rhode Island	45.4%	0.5%	0.8%	10.0%	43.4%	791
Tennessee	86.0%	0.5%	0.5%	5.7%	7.3%	757
Texas	74.1%	0.2%	1.0%	6.1%	18.6%	3,092
Vermont	68.4%		0.4%	1.3%	29.8%	450
Virginia	75.5%	1.2%	Construction	3.5%	19.9%	695
Washington	63.4%	2.0%	9.7%	10.5%	14.5%	1,741
West Virginia	61.4%	0.1%	(2017) - 30F	0.5%	37.9%	736
Wisconsin	65.1%	0.6%	2.8%	6.0%	25.4%	633

Variant proportions are based on representative CDC sequence data (NS3 + CDC-funded contract sequencing) collected over a 4-week period ending May 22, 2021 for states with at least 300 sequences.



CDC variants of concern by state

- > Detailed unweighted proportions of variants of concern for AZ and RI in the table below
- > Please refer to the CDC variant proportions data tracker for data on other states

State	B.1.1.7	B.1.351	B.1.427/ B.1.429	P.1	Other lineages	Total available sequences
AZ	67.8%	0.7%	4.2%	9.0%	18.3%	600
RI	45.4%	0.5%	0.8%	10.0%	43.4%	791

Administration can occur across a wide variety of models











Hospital

- Hospital-based infusion centers
- Emergency departments
- Converted space within hospital for COVID infusion
- Alternate care sites

Ambulatory center

- Infusion centers
- Urgent care clinics
- Dialysis centers
- Alternate care sites

Nursing homes

- Skilled nursing facilities
- Long-term care facilities

Mobile sites

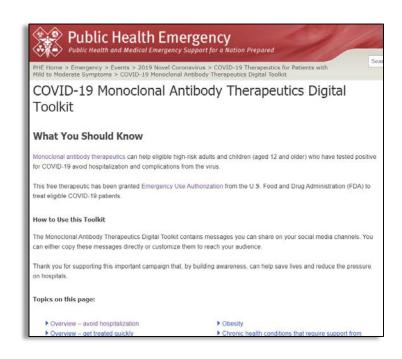
- Bus/trailer
- Other mobile sites

Home

At patient's home

Information support via https://combatcovid.hhs.gov/
Materials include links to EUA criteria, consolidated playbooks & educational materials

In the spotlight: updated mAb Digital Toolkit

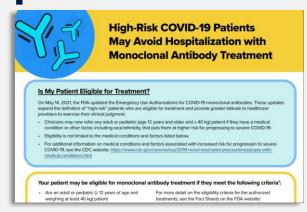


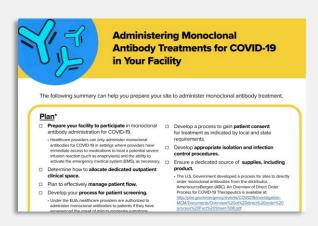


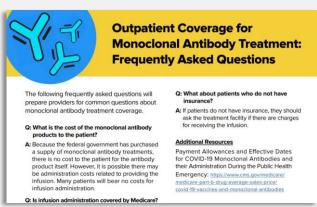
How to Use this Toolkit:

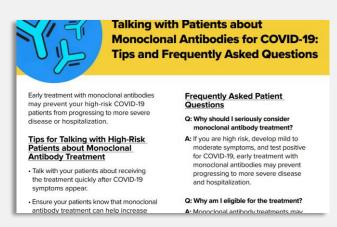
- Monoclonal Antibody Therapeutics Digital Toolkit contains messages you can share on your social media channels
 - Messages available for Twitter, Instagram, and Facebook
- Please either copy these messages directly or customize them to reach your appropriate audience
- > Toolkit available at phe.gov

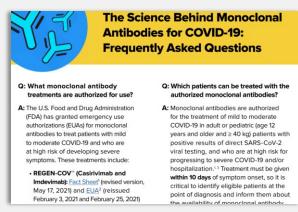
Updated factsheets and resources available for providers

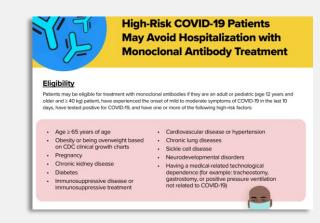












Fact sheets are available in English and Spanish at https://combatcovid.hhs.gov/hcp/resources
Please share with the providers in your network.



Upcoming webinars

Office Call Sessions HHS / ASPR Allocation, Distribution, Administration of COVID-19 Therapeutics

- New update: 1x/week office call sessions
- **Next call:** Thu, June 17, 2:00-2:30PM EST
- Zoom link: https://bit.ly/3rfRv4E
 - Meeting ID: 160 432 9034
 - Passcode: 897674

Weekly Stakeholder Update Calls

- **Next call:** Wed, June 16, 3.15-4:00PM EST
- Send email to <u>ASPRstakeholder@hhs.gov</u> for inclusion

Contact the Federal COVID-19 Response Team:

COVID19Therapeutics@hhs.gov

Helpful information and resources (I/II)

Product resources

- HHSProtect Therapeutics Dashboard https://protect.hhs.gov/workspace/module/view/latest/ri.workshop. main.module.084a09b4-bcd0-4a6b-817a-90afb7a3cd1d
- Direct Ordering Link via ABC https://app.smartsheet.com/b/form/255d164d67834793b4ab549e1 60941e8
- Guidance for Returning Product
 - For bam and bam/ete, see <u>The Lilly Return Goods</u>
 <u>Procedure</u>; detailed guidance can be found at: https://www.lillytrade.com/
 - For REGEN-COV, call 844-734-6643

Helpful information and resources (II/II)

Informational resources:

- ➤ HHS Website: https://combatcovid.hhs.gov/
- > HHS/ASPR Website: https://www.phe.gov
- > ASPR Regional Teams
 - Consult <u>the ASPR Regional Team in your area</u> for questions regarding COVID-19 medical countermeasures
- ASPR TRACIE general hurricane resources
- HRSA Uninsured Program <u>fact sheet</u>
- ▶ Updated information sheets and resources for providers in English and Spanish https://combatcovid.hhs.gov/hcp/resources



Thank you!