



Update: Distribution and Administration of COVID-19 Therapeutics

AUGUST 25, 2021

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 distribution and utilization
- 2 Instructions for the administration of sotrovimab
- 3 In the spotlight. Extension of shelf-life for bam product
- 4 Reminder: National bam/ete and ete alone shipment pause
- In the spotlight: tocilizumab and baricitinib
- 6 Update on COVID-19 variants of concern
- Reminder: REGEN-COV post-exposure prophylaxis EUA
- 8 COVID-19 mAb therapeutics resources
- 9 Reimbursement for subcutaneous admin of mAbs
- 10 Product ordering reminders
- Upcoming webinars and helpful resources
- 12 Discussion / Q&A



Distribution and utilization summary

1.70M Shipped through all Tx programs¹

7,190 Number of sites shipped to¹

736K Total reported usage²

43% % of distributed supply used³

^{1.} Total for entire period 2. Total usage as reported since 12/9 3. Reported through date 8/20 Note: Number of sites, % of total stock on hand and total reported usage is updated weekly Source: ABC Distribution reports, TeleTracking, State Reports

FDA authorizes sotrovimab for treatment of COVID-19

- Effective May 26, 2021, sotrovimab (GSK / Vir Biotechnology) authorized for the treatment of mild to moderate COVID-19
- 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)

General guidelines for sotrovimab dosing, dilution, and administration

PREPARATION

Sotrovimab is supplied in a single-dose vial and must be diluted prior to administration. Sotrovimab injection should be prepared by a qualified healthcare professional using aseptic technique.

- Gather the materials for preparation:
 - Polyvinyl chloride (PVC) or polyolefin (PO), sterile prefilled infusion bag. Choose one of the following sizes: prefilled 50-mL or 100-mL infusion bag containing 0.9% Sodium Chloride Injection, and
 - One vial of sotrovimab (500 mg/8 mL).
- Remove one vial of sotrovimab from refrigerated storage and allow to equilibrate to room temperature, protected from light, for approx. 15 minutes. Inspect the vial of sotrovimab visually for particulate matter and discoloration prior to administration. Should either be observed, the solution must be discarded, and a fresh solution prepared.
 - Sotrovimab is a clear, colorless or yellow to brown solution
- 3 Gently swirl the vial several times before use without creating air bubbles. Do not shake the vial.
- Withdraw 8 mL sotrovimab from one vial and inject into a prefilled infusion bag containing 0.9% Sodium Chloride Injection.
- 5 Discard any product remaining in the vial.
- Prior to the infusion, gently rock the infusion bag back and forth by hand 3 to 5 times. Do not invert the infusion bag. Avoid forming air bubbles.
- This product is preservative-free; therefore, the diluted infusion solution should be administered immediately.
 - If immediate administration is not possible, store the diluted solution of sotrovimab up to 4 hours at room temperature (20°C to 25°C [68°F to 77°F]) or refrigerated up to 24 hours (2°C to 8°C [36°F to 46°F]).

ADMINISTRATION

- A Infuse over 30 minutes
- B Do NOT deliver via IV or IV bolus
- Monitor patient for 60 minutes after infusion

In the spotlight: Extension of shelflife of bamlanivimab

- ➤ FDA and ASPR have announced the authorization of an extension to the shelf-life from 12 months to 18 months for the refrigerated Eli Lilly monoclonal antibody, bamlanivimab.
- ➤ Bamlanivimab is authorized for the treatment of mild to moderate COVID-19 only when administered together with etesevimab.
- Please refer to the following for more information:
 - Shelf-life extension of bamlanivimab
 - Fact Sheet for Health Care Providers and EUA Letter of Authorization

Please contact **COVID19Therapeutics@hhs.gov** with any questions

Reminder | National shipment pause of bam/ete and ete alone due to Beta and Gamma variant prevalence

Presence of variants

- In June, <u>CDC</u> identified upward trends in the frequencies of the Beta variant (B.1.351, first identified in South Africa) and the Gamma variant (P.1, first identified in Brazil) throughout the U.S.
- Results from in vitro studies suggest that:
 - Bam / ete administered together are not active against either Beta or Gamma variants
 - REGEN-COV and sotrovimab are likely to retain activity against Beta and Gamma variants

Impact on providers

- Distribution of bam / ete together and etesevimab alone have been paused on a national basis until further notice
- FDA recommends health care providers use alternative authorized mAb therapies (REGEN-COV OR sotrovimab) until further notice
 - REGEN-COV can be ordered directly from Amerisource Bergen
 - Sotrovimab can be ordered via GlaxoSmithKline's website



In the spotlight: Shortages of tocilizumab and baricitinib

- ➤ Both Actemra (tocilizumab) & Olumiant (baricitinib) have been reported in short supply, with shortages of tocilizumab being more severe
- NIH guidelines for <u>Therapeutic Management of</u> <u>Hospitalized Adults with COVID-19</u>

Hospitalized and Requires
Oxygen Delivery Through a
High-Flow Device or
Noninvasive Ventilation

Use one of the following options:

- Dexamethasoned (AI)
- Dexamethasoned plus remdesivirb,c (BIII)

For patients who were recently hospitalized with rapidly increasing oxygen needs and systemic inflammation:

 Add either baricitinib^{f,g} (Blla) or tocilizumab^{f,h} (Blla) to one of the two options above

Hospitalized and Requires IMV or ECMO

For most patients:

Dexamethasone^{d,i} (Al)

For patients who are within 24 hours of admission to the ICU:

Dexamethasone^{d,i} plus tocilizumab^{f,h} (BIIa)

In the spotlight: Actemra (tocilizumab) IL-6 Inhibitor

- **EUA issued February 2020**. Commercially available for other indications.
 - Hospitalized adults and children ≥ 2 years
 - Receiving systemic corticosteroids & requiring supplemental O2, non-invasive or invasive mechanical ventilation, or ECMO
 - NIH guidelines: Recently hospitalized patients (within 3 days) who require ICU-level care and have increased inflammatory markers (CRP > 75)
- Administration
 - Single 60-minute intravenous infusion
- Dosing
 - Patients < 30kg: 12mg/kg
 - Patients ≥ 30kg: 8mg/kg
- Precautions
 - Should not be administered if patients have any other concurrent infection, including localized infection
- > RECOVERY Trial (RCT of 4116 UK pts)
 - 28-day mortality: 34.9% placebo vs 30.7% Actemra (4.1% risk reduction)
 - Median time to discharge
 - o 19 days with Actemra + usual care
 - > 28 days with usual care alone

In the spotlight: Olumiant (baricitinib) oral Janus kinase(JAK) inhibitor

- **EUA issued November 2020**, updated July 28, 2021. Commercially available for other indications.
 - Hospitalized adults and children ≥ 2 years
 - Receiving systemic corticosteroids and require supplemental oxygen, noninvasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation
 - Update July 2021 no longer requires concurrent administration with remdesivir
 - Not recommended for patients who are on dialysis, have end stage renal disease, or have acute kidney injury
 - Refer to EUA for further dosing adjustments related to GFR, absolute neutrophil count, absolute lymphocyte count, and aminotransferases
 - NIH guidelines: Patients requiring high flow oxygen or non-invasive ventilation
- Administration
 - Oral dosing
- Dosing (treatment for 14 days or until hospital discharge, whichever is first)
 - 9 years of age and older: 4mg once daily
 - Ages 2-9: 2mg once daily
- Precautions
 - There is limited information regarding the use of barcitinib in patients with COVID-19 and concomitant active serious infection
 - Prophylaxis for venous thromboembolism is recommended unless contraindicated
 - Avoid use of live vaccines with baricitinib
- ACTT-2 Study in Hospitalized Adults Diagnosed with COVID-19 Infection
 - Baricitinib + remdesivir: decrease in mortality or progression of oxygen needs in treatment group (23%) compared to placebo+remdesivir (28%)

Links for Additional Information

- > ASHP tocilizumab update
- > IDSA guidelines
- Lilly baricitinib page
- Genentech statement on tocilizumab

CDC variants of concern by state

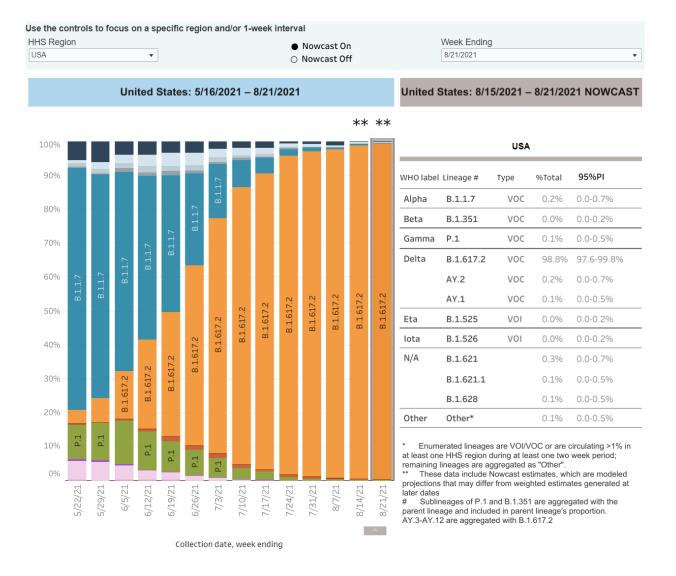
proportions of the most common SARS-CoV-2 lineages circulating in the U.S available from the CDC variant proportions data tracker

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

State	A	B.1.1.7	B.1.351	B.1.617.2	P.1	Other lineages	AY.1	ΔΥ 2	Total Available Sequences
Alabama	Z	3.8%	D.1.551	94.2%	1.0%	0.8%	A1.1	0.2%	1,316
Arizona 2.3%			89.3%	3.5%	3.9%		1.0%	1,049	
Arkansas		2.7%		96.5%	0.3%	0.5%		1.0 /0	656
California		2.1%	0.0%	91.7%	1.5%	2.7%	0.5%	1.5%	22,309
Colorado		3.2%	010,0	93.3%	0.8%	2.2%	0.070	0.4%	2,608
Florida		2.9%	0.0%	91.0%	2.2%	3.6%	0.0%	0.2%	14,079
Georgia		3.3%	01070	92.7%	1.2%	2.3%	0.070	0.6%	3,107
Illinois		2.2%		93.3%	1.5%	2.1%	0.1%	0.9%	1,381
Indiana		1.4%		94.9%	1.4%	1.8%		0.4%	488
Kansas		1.5%		96.7%		1.9%			478
Kentucky		5.0%		87.7%	3.5%	3.5%		0.3%	318
Louisiana		5.7%		92.5%	0.2%	1.5%		0.1%	996
Maryland		5.6%		89.3%	2.1%	2.3%	0.1%	0.7%	829
Massachusetts		0.5%		94.9%	1.6%	3.0%	0.0%		3,147
Michigan		3.9%		91.4%	0.6%	3.3%		0.9%	337
Minnesota		1.4%		94.9%	1.3%	2.2%		0.3%	1,174
Mississippi		3.6%		92.8%	0.2%	3.1%		0.2%	417
Missouri		1.0%		97.3%	0.5%	1.0%		0.3%	1,566
Nevada		2.5%		89.6%	0.8%	2.7%	0.1%	4.2%	1,900
New Jersey		1.8%		93.4%	1.2%	3.3%	0.2%	0.0%	2,429
New York		1.0%		91.9%	1.5%	5.2%	0.2%	0.2%	1,723
North Carolina		2.9%	0.0%	93.8%	0.8%	2.4%	0.1%		3,943
Ohio		4.2%		90.5%	1.4%	3.6%		0.3%	639
Oklahoma		0.9%		96.4%		2.7%			333
Oregon		10.4%		82.8%	2.1%	2.5%		2.1%	517
Pennsylvania		3.4%		92.3%	1.7%	2.5%		0.2%	597
Rhode Island		1.5%		94.4%	0.6%	3.5%			341
South Carolina		4.1%		93.6%	0.4%	1.4%	0.1%	0.5%	806
Tennessee		4.4%		92.3%	0.5%	2.0%	0.1%	0.8%	1,723
Texas		3.5%	0.0%	89.3%	1.6%	4.9%		0.7%	6,923
Utah		2.0%		93.6%	0.7%	3.0%		0.8%	607
Virginia		2.3%		93.3%	1.8%	2.3%	0.1%	0.2%	953
Washington		3.5%		90.2%	2.7%	2.8%	0.5%	0.4%	2,301
Wisconsin		0.8%		95.0%	0.4%	3.5%		0.4%	515

Variant proportions are based on representative CDC sequence data (NS3 + CDC-funded contract sequencing) collected over a 4-week period ending July 31, 2021 for states with at least 300 sequences.

Prevalence of Delta variant nationally



- Delta (B.1.617.2) variant was at 31% nationally as of 6/19 and is 98.8% nationally as of 8/21 (pending data via Nowcast)
- States/territories encouraged to reach out with questions/concerns

CDC variants of concern susceptibility

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

REGEN-COV fact sheet

Table 9: Pseudotyped Virus-Like Particle Neutralization Data for SARS-CoV-2
Variant Substitutions with Casirivimab and Imdevimab Together

Lineage with Spike Protein	Country First	WHO Nomenclature	Key Substitutions Tested	Fold Reduction in
Substitution	Identified	Nomenciature	Testeu	Susceptibility
B.1.1.7	UK	Alpha	N501Y ^a	no change ^e
B.1.351	South	Beta	K417N, E484K,	no change ^e
	Africa		$N501Y^b$	
P.1	Brazil	Gamma	K417T, E484K,	no change ^e
			N501Y ^c	
B.1.427/B.1.429	USA	Epsilon	L452R	no change ^e
	(California)			
B.1.526 ^f	USA (New	Iota	E484K	no change ^e
	York)			
B.1.617.1/B.1.617.3	India	Kappa/no	L452R+E484Q	no change ^e
		designation		
B.1.617.2/AY.3	India	Delta	L452R+T478K	no change ^e
AY.1/AY.2g	India	Delta	K417N, L452R,	no change ^e
		[+K417N]	$T478K^d$	
B.1.621/B.1.621.1	Colombia	No designation	R346K, E484K,	no change ^e
			N501Y	
C.37	Peru	Lambda	L452Q+F490S	no change ^e

Last revised 8/2021

bamlanivimab / etesevimab fact sheet

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 were tested.

Last revised 5/2021

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

^c 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.

7

Reminder: REGEN-COV Emergency Use Authorization (EUA) expanded to include post-exposure prophylaxis

- ➤ As of July 30, 2021, FDA has authorized post-exposure prophylaxis use of the COVID-19 monoclonal antibody therapeutic REGEN-COV (casirivimab and imdevimab)
- REGEN-COV is expected to be effective against circulating variants, including the Delta variant Please refer to the following for more information:
 - FDA fact sheet and EUA Letter of Authorization
 - Regeneron press release
- For additional information and approved materials, including information about ordering, please refer to the <u>REGEN-COV</u> webpage
- Should you have any questions regarding the expanded indication for REGEN-COV, please contact us at COVID19therapeutics@hhs.gov

Reminder: COVID-19 mAb communications toolkit live on phe.gov/mAbs

COVID-19 Monoclonal Antibody Therapeutics Communications Toolkit

Introduction

The all-of-community approach to combating COVID-19 continues. It is more important than ever that clear, accurate, and consistent information is provided to the public regarding prevention and treatment. While vaccines are at the heart of ending the pandemic, COVID-19 treatments known as monoclonal antibodies are also available and have the potential to save lives and relieve burden on our nation's health care system. It is imperative that partners at all levels of government and within the private sector work together to ensure widest dissemination of information regarding these treatments.

This communications toolkit was developed by the Federal COVID-19 Response Team to assist with this priority effort.



What's in the COVID-19 monoclonal antibody communications toolkit?

- About Monoclonal Antibody Treatments Monoclonal Treatment Products
- Locating and Opening Up Treatment Sites
- ▶ Payment and Allocation
- Resources for Treatment Sites Resources for Providers
- Resources for Patients
- Digital Communications Tools
- Additional Resources

Who should use this resource?

- ▶ Health communicators
- Health department officials
- Health care providers
- ▶ Health system administrators
- Monoclonal antibody treatment sites
- ▶ Entities involved with monoclonal antibody distribution and/or administration

developed by the Federal COVID-19 response team and other partners on monoclonal antibody therapeutics.

<u>Communications toolkit</u> provides a series of resources

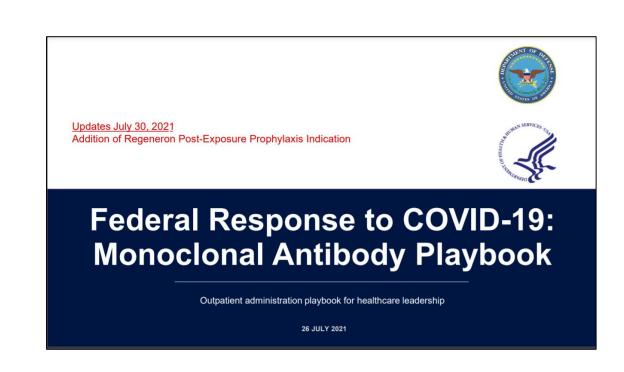
Communications resources include information for:

- Healthcare providers
- Patients
- Digital media tools

Reminder: Revised mAb playbook live on phe.gov

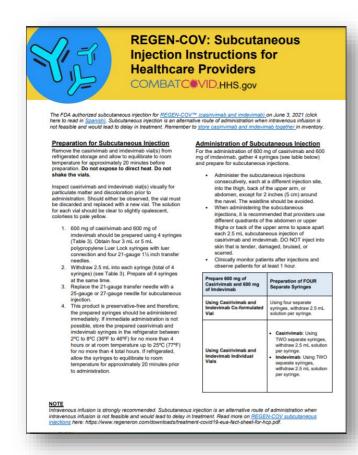
Revised Federal Response to COVID-19:

Monoclonal Antibody Playbook with addition of Regeneron Post-Exposure Prophylaxis indication live on phe.gov.



Please contact **COVID19Therapeutics@hhs.gov** with any questions

Reminder:
Subcutaneous
injection
instructions for
healthcare
providers



On June 3, 2021, the FDA authorized **subcutaneous injection** for REGEN-COV[™] (casirivimab and imdevimab) as an **alternative when IV infusion is not feasible** and would lead to a delay in treatment.

REGEN-COV: Subcutaneous injection instructions for healthcare providers flyer is live on phe.gov.

Reimbursement for subcutaneous administration of mAbs

- ➤ During the COVID-19 public health emergency (PHE), Medicare will cover and pay for mAb product infusions (when furnished consistent with their respective EUAs) the same way it covers and pays for COVID-19 vaccines.
- ➤ Learn more about Medicare's Coverage for Monoclonal Antibody Products to Treat COVID-19
- Learn more about <u>specified subQ or IV</u> <u>reimbursement rates</u> during the public health emergency
- ➤ For guidance on coverage for doctor's office administration see Medicare's Coverage of mAbs to treat COVID-19 infographic



Product ordering reminders

- ➤ HHS/ASPR continues to manage the distribution of mAb products under EUA as stated in the FDA Letters of Authorization
- Please follow regional / state guidelines on products that can be requested via direct ordering for all sites

- Casirivimab/imdevimab supply is currently ample and sites should not be hesitant to request supply
- We recommend that sites use their anticipated two-week utilization as the baseline metric for determining their respective maximum order
- We monitor and review ordering and may contact sites for further information or to adjust order amounts.

Questions regarding ordering process:

- HHS: COVID19Therapeutics@hhs.gov
- Amerisource Bergen (ABC) commercial distributor: <u>C19therapies@amerisourcebergen.com</u>



Upcoming webinars

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

- 1x/week office call sessions
- **Next call:** Thu, August 26, 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, September 1

Contact the Federal COVID-19 Response Team:

COVID19Therapeutics@hhs.gov

Helpful information and resources (I/II)

Product resources:

- HHS Protect Therapeutics Dashboard https://protect.hhs.gov/workspace/module/view/latest/ri.workshop.main.mod ule.084a09b4-bcd0-4a6b-817a-90afb7a3cd1d
- Direct Ordering Link via ABC
 https://app.smartsheet.com/b/form/255d164d67834793b4ab549e160941e8
- Guidance for Returning Product
 - For bam and bam/ete, see <u>The Lilly Return Goods Procedure</u>; detailed guidance can be found at: https://www.lillytrade.com/
 - For REGEN-COV, call 844-734-6643
- Monoclonal Antibody Therapeutics Homepage https://www.phe.gov/mabs
- COVID-19 Monoclonal Antibody Therapeutics Communications Toolkit https://www.phe.gov/mabs-toolkit
- REGEN-COV: Subcutaneous Injection Instructions for Healthcare Providers

https://www.phe.gov/emergency/events/COVID19/therapeutics/Pages/REG EN-COV-Subcutaneous-Injection-Instructions-for-Healthcare-Providers.aspx

Helpful information and resources (II/II)

Informational resources:

- > HHS/ASPR Website (mAbs): phe.gov/mAbs
- > HHS Website: https://combatcovid.hhs.gov/
- > ASPR Regional Teams
 - Consult the ASPR Regional Team in your area 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
- Increased CMS reimbursement rates for mAb administration: https://www.cms.gov/medicare/medicare-part-b-drug-averagesales-price/covid-19-vaccines-and-monoclonal-antibodies





Thank you!