Update: Distribution and Administration of COVID-19 Therapeutics

SEPTEMBER 1, 2021

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

Agenda

1. Update on distribution and utilization
2. *In the spotlight:* Use and distro of bam/ete resumed in select states
3. Reminder: Extension of shelf-life for bam product
4. Update on COVID-19 variants of concern
5. Reminder: COVID-19 mAb therapeutics resources
6. Reminder: REGEN-COV post-exposure prophylaxis EUA
7. Reminder: Instructions for the administration of sotrovimab
8. Reimbursement for subcutaneous admin of mAbs
9. Upcoming webinars and helpful resources
10. Discussion / Q&A

Distribution and utilization summary

1.92M Shipped through all Tx programs[1]

7,483 Number of sites shipped to[1]

821K Total reported usage[2]

43% % of distributed supply used[3]

1. Total for entire period 2. Total usage as reported since 12/9 3. Reported through date 8/25
Note: Number of sites, % of total stock on hand and total reported usage is updated weekly
Source: ABC Distribution reports, TeleTracking, State Reports

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Distribution and utilization reminders

- HHS/ASPR continues to manage the distribution of mAb products under EUA as stated in the FDA Letters of Authorization
- Please remember that **utilization reporting affects ordering**; We monitor and review ordering and may contact sites for further information or to adjust order amounts.
- If you need help **registering a site to report utilization**, please reach out to hhs-protect@teletracking.com to set up an account

Resumption of use and distro of bamlanivimab and etesevimab (together) in certain states due to Delta variant prevalence

- The CDC has determined that the **frequency of the Delta variant (B.1.617.2**, first identified in India) is increasing throughout the U.S. and **has become the dominant variant in the country.**
- Results from in vitro studies suggest that:
  - Bamlanivimab and etesevimab (together) administered together **are active against the Delta variant** (B.1.617.2)
- Following the shipment pause, effective 08/27/2021, **distribution of bamlanivimab and etesevimab administered together has resumed in certain states, territories, and U.S. jurisdictions** in which recent data shows the combined frequency of variants resistant to bam / ete together is less than or equal to 5%.

- Bam / ete together is currently authorized for use in Colorado, Connecticut, Illinois, Indiana, Iowa, Kansas, Maine, Massachusetts, New Hampshire, Michigan, Minnesota, Missouri, Montana, Nebraska, North Dakota, Ohio, Rhode Island, South Dakota, Utah, Vermont, Wisconsin, and Wyoming, which comprise HHS regions 1, 5, 7, and 8.
- **For more information**
  - EUA Letter of Authorization
  - Bamlanivimab and Etesevimab Authorized States, Territories, and U.S. Jurisdictions
  - FDA Fact Sheet

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

Reminder: Extension of shelf-life 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

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]

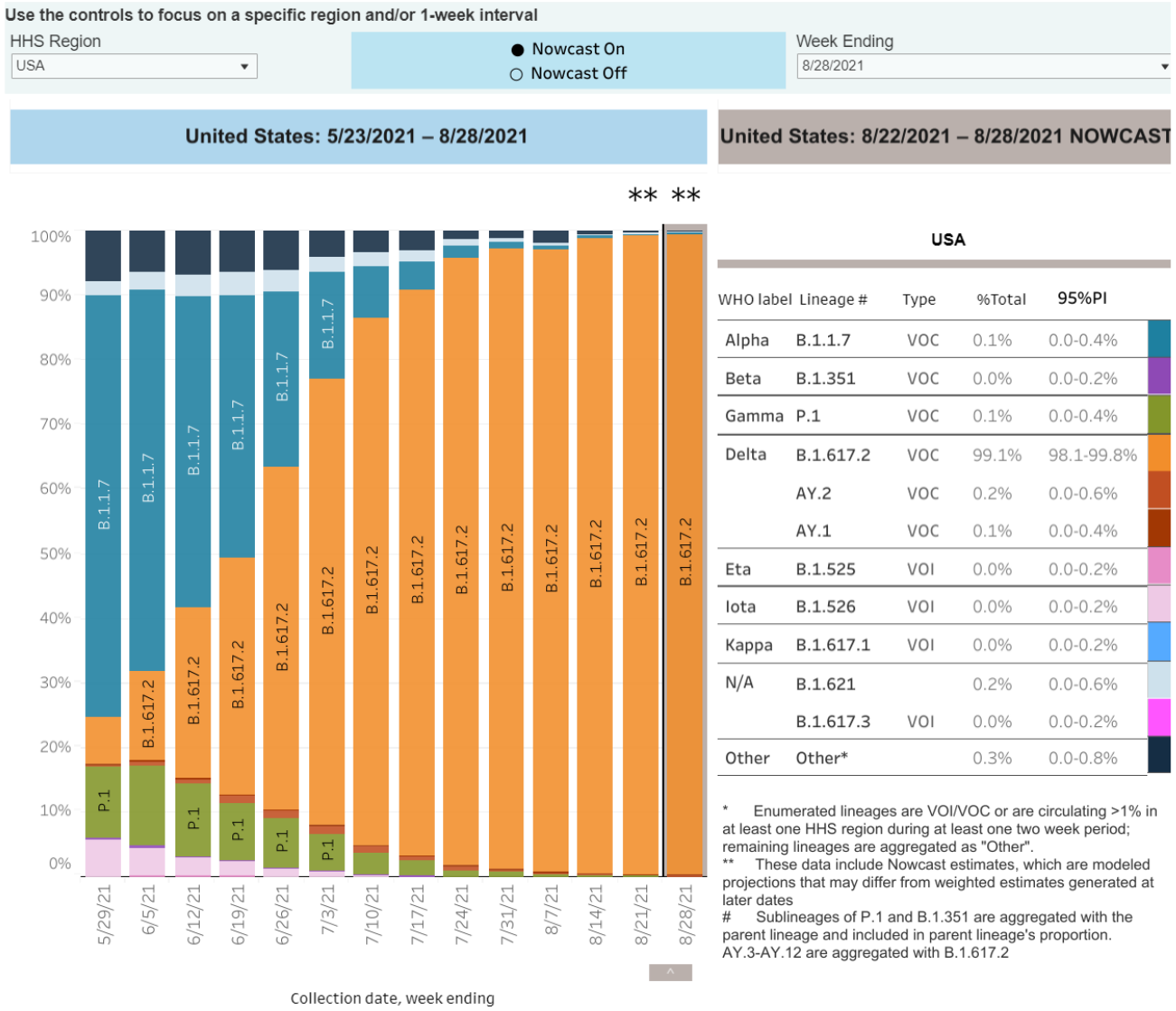
Unweighted Proportions of Variants of Concern and Other Lineages by State or Jurisdiction

State	B.1.1.7	B.1.351	B.1.617.2	P.1	AY.1	AY.2	Other	Total available sequences
Alabama	1.6%		95.0%	0.5%	0.1%	0.1%	2.7%	2,542
Arizona	0.8%		93.8%	1.1%	0.1%	0.3%	3.9%	1,425
Arkansas	0.6%		96.6%	0.2%		0.3%	2.4%	679
California	0.7%	0.0%	94.9%	0.6%	0.6%	0.9%	2.3%	33,472
Colorado	1.2%	0.1%	96.1%	0.2%	0.1%	0.4%	2.0%	2,874
Connecticut	1.2%		95.9%	0.7%		0.2%	2.0%	588
District of Columbia	0.3%		98.9%				0.8%	378
Florida	1.3%	0.0%	92.5%	1.1%	0.0%	0.2%	4.9%	18,661
Georgia	0.9%		95.6%	0.5%	0.0%	0.3%	2.8%	5,584
Illinois	0.8%		95.3%	0.3%	0.1%	0.8%	2.7%	2,156
Indiana	0.7%		96.6%	0.7%		0.3%	1.8%	774
Kansas	0.2%		97.8%				1.9%	464
Kentucky	1.6%		94.0%	0.8%	0.1%	0.2%	3.4%	894
Louisiana	2.1%		92.8%	0.2%		0.1%	4.9%	1,378
Maryland	0.8%		95.9%	0.8%	0.1%	0.2%	2.1%	1,679
Massachusetts	0.1%		96.7%	0.8%	0.2%	0.0%	2.2%	6,492
Michigan	0.4%		96.4%	0.6%		0.4%	2.2%	502
Minnesota	0.2%		97.3%	0.4%		0.2%	1.9%	2,590
Mississippi	0.7%		95.1%	0.3%			3.9%	698
Missouri	0.6%		96.3%	0.3%			2.8%	1,216
Nevada	0.7%		94.2%	0.1%	0.1%	2.2%	2.6%	1,397
New Jersey	0.7%		96.3%	0.3%	0.2%	0.1%	2.4%	3,601
New Mexico	0.9%		94.4%	0.6%			4.1%	467
New York	0.4%		96.8%	0.5%	0.4%	0.1%	1.8%	2,819
North Carolina	0.7%		97.3%	0.3%	0.0%	0.0%	1.6%	7,292
Ohio	1.5%		94.3%	0.7%		0.2%	3.3%	943
Oklahoma			94.3%				5.7%	406
Oregon	3.2%		92.1%	0.9%	0.2%	1.1%	2.5%	984
Pennsylvania	0.6%		97.8%	0.3%	0.1%	0.1%	1.1%	1,263
Rhode Island	0.4%		97.2%	0.2%			2.3%	562
South Carolina	1.0%		96.5%			0.3%	2.2%	1,558
Tennessee	1.1%		94.5%	0.3%	0.1%	0.5%	3.7%	2,743
Texas	1.2%		93.4%	0.6%	0.0%	0.4%	4.3%	9,370
Utah	0.8%		94.2%	0.3%		0.5%	4.3%	650
Vermont	0.3%		98.7%	0.2%			0.8%	595
Virginia	0.7%		97.4%	0.2%	0.1%	0.3%	1.4%	1,979
Washington	0.9%		96.3%	0.7%	0.4%	0.2%	1.4%	3,378
West Virginia	1.2%		96.4%	1.0%		0.2%	1.2%	415
Wisconsin	0.1%		97.0%	0.3%		0.2%	2.5%	1,123

Variant proportions are based on representative CDC sequence data (NS3 + CDC-funded contract sequencing) collected over a 4-week period ending August 14, 2021 for states with at least 300 sequences.

Updated Aug 31, 2021

Prevalence of Delta variant nationally



USA

WHO label	Lineage #	Type	%Total	95%PI
Alpha	B.1.1.7	VOC	0.1%	0.0-0.4%
Beta	B.1.351	VOC	0.0%	0.0-0.2%
Gamma	P.1	VOC	0.1%	0.0-0.4%
Delta	B.1.617.2	VOC	99.1%	98.1-99.8%
	AY.2	VOC	0.2%	0.0-0.6%
	AY.1	VOC	0.1%	0.0-0.4%
Eta	B.1.525	VOI	0.0%	0.0-0.2%
Iota	B.1.526	VOI	0.0%	0.0-0.2%
Kappa	B.1.617.1	VOI	0.0%	0.0-0.2%
N/A	B.1.621		0.2%	0.0-0.6%
	B.1.617.3	VOI	0.0%	0.0-0.2%
Other	Other*		0.3%	0.0-0.8%

* Enumerated lineages are VOI/VOC or are circulating >1% in at least one HHS region during at least one two week period; remaining lineages are aggregated as "Other".
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# Sublineages of P.1 and B.1.351 are aggregated with the parent lineage and included in parent lineage's proportion. AY.3-AY.12 are aggregated with B.1.617.2

- Delta (B.1.617.2) variant was at 31% nationally as of 6/19 and is **99.1% nationally as of 8/28** (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 Substitution	Country First Identified	WHO Nomenclature	Key Substitutions Tested	Fold Reduction in Susceptibility
B.1.1.7	UK	Alpha	N501Y[a]	no change[e]
B.1.351	South Africa	Beta	K417N, E484K, N501Y[b]	no change[e]
P.1	Brazil	Gamma	K417T, E484K, N501Y[c]	no change[e]
B.1.427/B.1.429	USA (California)	Epsilon	L452R	no change[e]
B.1.526[f]	USA (New York)	Iota	E484K	no change[e]
B.1.617.1/B.1.617.3	India	Kappa/no designation	L452R+E484Q	no change[e]
B.1.617.2/AY.3	India	Delta	L452R+T478K	no change[e]
AY.1/AY.2[g]	India	Delta [+K417N]	K417N, L452R, T478K[d]	no change[e]
B.1.621/B.1.621.1	Colombia	No designation	R346K, E484K, N501Y	no change[e]
C.37	Peru	Lambda	L452Q+F490S	no change[e]

Last revised 8/2021

bamlanivimab / etesevimab fact sheet

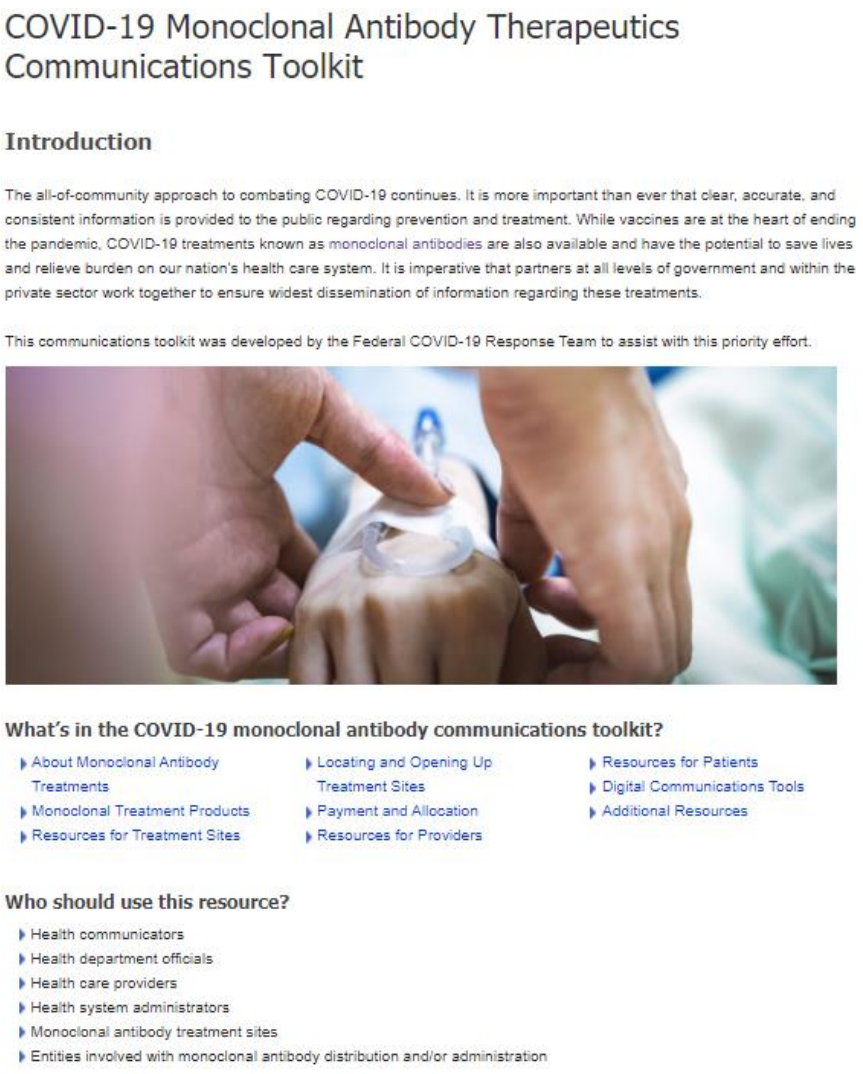
Table 3: Pseudotyped Virus-Like Particle Neutralization Data for SARS-CoV-2 Variant Substitutions with Bamlanivimab and Etesevimab Together (1:2 Molar Ratio)

Lineage with Spike Protein Substitution	Country First Identified	WHO Nomenclature	Key Substitutions Tested[a]	Fold Reduction in Susceptibility
B.1.1.7	UK	Alpha	N501Y	no change[b]
B.1.351	South Africa	Beta	K417N + E484K + N501Y	431[c]
P.1	Brazil	Gamma	K417T + E484K + N501Y	252[c]
B.1.617.2/AY.3	India	Delta	L452R + T478K	no change[b]
AY.1/AY.2 (B.1.617.2 sublineages)	India	Delta [+K417N][d]	L452R + T478K + K417N	1,235[c]
B.1.427/B.1.429	USA (California)	Epsilon	L452R	9[e]
B.1.526[f]	USA (New York)	Iota	E484K	30
B.1.617.1	India	Kappa	L452R + E484Q	6[e]

[a] 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, B.1.427/B.1.429, B.1.526, B.1.617.1, B.1.617.2, and AY.1/AY.2 spike variants reflective of the consensus sequence for the lineage were tested.
[b] No change: <5-fold reduction in susceptibility.
[c] Bamlanivimab and etesevimab together are unlikely to be active against variants from this lineage.
[d] Commonly known as "Delta plus."
[e] Etesevimab retains activity against this variant.
[f] 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).

Last revised 8/2021

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
- Resources for Treatment Sites
- Locating and Opening Up Treatment Sites
- Payment and Allocation
- 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

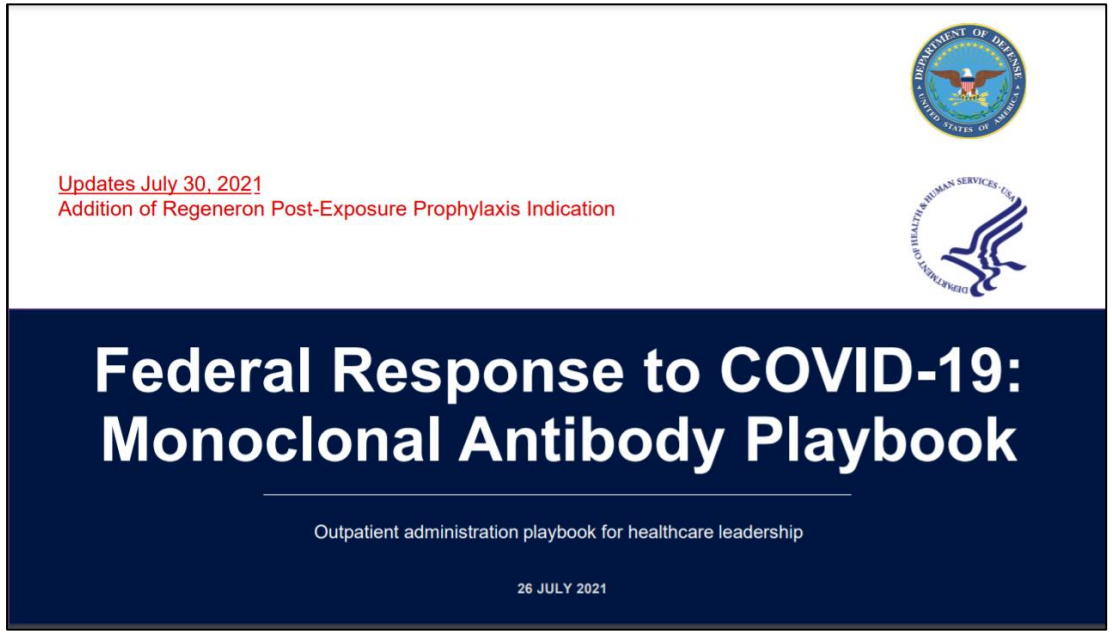
Communications toolkit provides a series of resources developed by the Federal COVID-19 response team and other partners on monoclonal antibody therapeutics.

Communications resources include information for:

- Administration sites
- Healthcare providers
- Patients
- Digital media tools

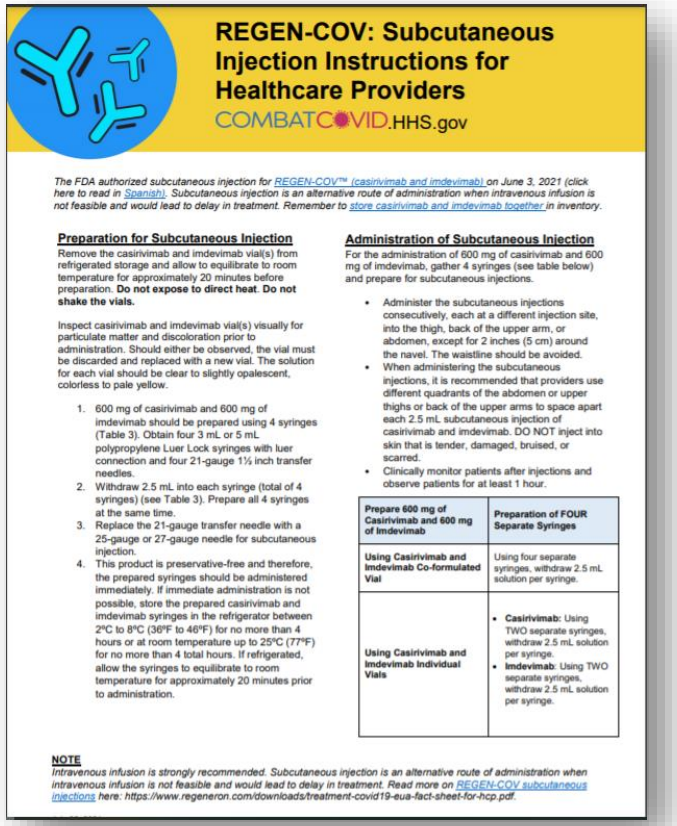
Reminder: Revised mAb playbook live on PHE.gov

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



REGEN-COV: Subcutaneous Injection Instructions for Healthcare Providers

COMBATCOVID.HHS.gov

The FDA authorized subcutaneous injection for REGEN-COV™ (casirivimab and imdevimab) on June 3, 2021 (click here to read in Spanish). Subcutaneous injection is an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment. Remember to store casirivimab and imdevimab together in inventory.

Preparation for Subcutaneous Injection

Remove the casirivimab and imdevimab vial(s) from refrigerated storage and allow to equilibrate to room temperature for approximately 20 minutes before preparation. **Do not expose to direct heat. Do not shake the vials.**

Inspect casirivimab and imdevimab vial(s) visually for particulate matter and discoloration prior to administration. Should either be observed, the vial must be discarded and replaced with a new vial. The solution for each vial should be clear to slightly opalescent, colorless to pale yellow.

1. 600 mg of casirivimab and 600 mg of imdevimab should be prepared using 4 syringes (Table 3). Obtain four 3 mL or 5 mL polypropylene Luer Lock syringes with luer connection and four 21-gauge 1½ inch transfer needles.
2. Withdraw 2.5 mL into each syringe (total of 4 syringes) (see Table 3). Prepare all 4 syringes at the same time.
3. Replace the 21-gauge transfer needle with a 25-gauge or 27-gauge needle for subcutaneous injection.
4. This product is preservative-free and therefore, the prepared syringes should be administered immediately. If immediate administration is not possible, store the prepared casirivimab and imdevimab syringes in the refrigerator between 2ºC to 8ºC (36ºF to 46ºF) for no more than 4 hours or at room temperature up to 25ºC (77ºF) for no more than 4 total hours. If refrigerated, allow the syringes to equilibrate to room temperature for approximately 20 minutes prior to administration.

Administration of Subcutaneous Injection

For the administration of 600 mg of casirivimab and 600 mg of imdevimab, gather 4 syringes (see table below) and prepare for subcutaneous injections.

- Administer the subcutaneous injections consecutively, each at a different injection site, into the thigh, back of the upper arm, or abdomen, except for 2 inches (5 cm) around the navel. The waistline should be avoided.
- When administering the subcutaneous injections, it is recommended that providers use different quadrants of the abdomen or upper thighs or back of the upper arms to space apart each 2.5 mL subcutaneous injection of casirivimab and imdevimab. DO NOT inject into skin that is tender, damaged, bruised, or scarred.
- Clinically monitor patients after injections and observe patients for at least 1 hour.

Prepare 600 mg of Casirivimab and 600 mg of Imdevimab	Preparation of FOUR Separate Syringes
Using Casirivimab and Imdevimab Co-formulated Vial	Using four separate syringes, withdraw 2.5 mL solution per syringe.
Using Casirivimab and Imdevimab Individual Vials	• **Casirivimab:** Using TWO separate syringes, withdraw 2.5 mL solution per syringe. • **Imdevimab:** Using TWO separate syringes, withdraw 2.5 mL solution per syringe.

NOTE

Intravenous infusion is strongly recommended. Subcutaneous injection is an alternative route of administration when intravenous infusion is not feasible and would lead to delay in treatment. Read more on REGEN-COV subcutaneous injections here: https://www.regeneron.com/downloads/treatment-covid19-eua-fact-sheet-for-hcp.pdf.

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.

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 REGEN-COV webpage
- Should you have any questions regarding the expanded indication for REGEN-COV, please contact us at COVID19therapeutics@hhs.gov

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 sotrovimab webpage

Please contact the GSK COVID Contact Center if you have further questions:

1-866-GSK-COVID (1-866-475-2684)

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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.

1. 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).
2. 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.**
4. 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.
6. 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.
7. 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

C. Monitor patient for 60 minutes after infusion

https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Sotrovimab/pdf/SOTROVIMAB-EUA.PDF#nameddest=HCPFS

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 specified subQ or IV reimbursement rates 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

Updated mAbs Weekly Engagements

- **Office Call Sessions**: **HHS / ASPR Distribution and Administration of COVID-19 Therapeutics – call all to open to all with equity in the process**
  - Tuesdays (2:00-3:00PM ET)
  - Thursdays (2:00-3:00PM ET)

- **Stakeholder Call: State, Local, Tribal, and Territorial Health Officials**
  - Wednesdays (2:00-3:00PM ET)

- **Stakeholder Call: National Health Care and Medical Orgs and Associations**
  - Wednesdays (3:15-4:15PM ET)
  - Thursdays (2:00-3:00PM ET)

Please email COVID19Therapeutics@hhs.gov to request Zoom links for these calls

Upcoming webinars

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

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

Weekly Stakeholder Update Calls

- **Next call:** Wed, September 8

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.module.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 The Lilly Return Goods Procedure; 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/REGEN-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** fact sheet
- **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-average-sales-price/covid-19-vaccines-and-monoclonal-antibodies

Thank you!