Monoclonal Antibodies: Updates from the Federal COVID Response
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
7. 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 Sotrovimab 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 co-formulated 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
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 bamlanivimab/etesevimab (administered together) and REGEN-COV for additional information
- Healthcare providers should consider the benefit-risk for an individual patient

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

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 The Lilly Return Goods Procedure, detailed guidance can be found at: https://www.lillytrade.com/
  - 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

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 states**\(^1\)

- 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

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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**

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**REGEN-COV fact sheet**

**bamlanivimab / etesevimab fact sheet**

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

<table>
<thead>
<tr>
<th>Lineage with Spike Protein Substitution</th>
<th>Key Substitutions Tested</th>
<th>Fold Reduction in Susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.1.1.7 (UK origin)</td>
<td>N501Y</td>
<td>no change</td>
</tr>
<tr>
<td>B.1.351 (South Africa origin)</td>
<td>K417N, E484K, N501Y</td>
<td>no change</td>
</tr>
<tr>
<td>P.1 (Brazil origin)</td>
<td>K417T + E484K</td>
<td>no change</td>
</tr>
<tr>
<td>B.1.427/B.1.429 (California origin)</td>
<td>L452R</td>
<td>no change</td>
</tr>
<tr>
<td>B.1.526 (New York origin)</td>
<td>E484K</td>
<td>no change</td>
</tr>
<tr>
<td>B.1.617.1/B.1.617.3 (India origin)</td>
<td>L452R + E484Q</td>
<td>no change</td>
</tr>
<tr>
<td>B.1.617.2 (India origin)</td>
<td>L452R + K478T</td>
<td>no change</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Lineage with Spike Protein Substitution</th>
<th>Key Substitutions Tested</th>
<th>Fold Reduction in Susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.1.1.7 (UK origin)</td>
<td>N501Y</td>
<td>no change</td>
</tr>
<tr>
<td>B.1.351 (South Africa origin)</td>
<td>K417N + E484K + N501Y</td>
<td>215</td>
</tr>
<tr>
<td>P.1 (Brazil origin)</td>
<td>K417T + E484K + N501Y</td>
<td>47</td>
</tr>
<tr>
<td>B.1.427/B.1.429 (California origin)</td>
<td>L452R</td>
<td>9</td>
</tr>
<tr>
<td>B.1.526 (New York origin)</td>
<td>E484K</td>
<td>31</td>
</tr>
</tbody>
</table>

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1. FDA factsheets: https://www.fda.gov/media/145611/download; https://www.fda.gov/media/145802/download
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
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

<table>
<thead>
<tr>
<th>State</th>
<th>B.1.1.7</th>
<th>B.1.351</th>
<th>B.1.427 / B.1.429</th>
<th>P.1</th>
<th>Other lineages</th>
<th>Total Available Sequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arizona</td>
<td>67.8%</td>
<td>0.7%</td>
<td>4.2%</td>
<td>9.0%</td>
<td>18.3%</td>
<td>600</td>
</tr>
<tr>
<td>California</td>
<td>58.1%</td>
<td>1.0%</td>
<td>5.1%</td>
<td>9.5%</td>
<td>26.3%</td>
<td>4,060</td>
</tr>
<tr>
<td>Colorado</td>
<td>79.0%</td>
<td>0.5%</td>
<td>2.5%</td>
<td>2.2%</td>
<td>15.8%</td>
<td>2,312</td>
</tr>
<tr>
<td>Connecticut</td>
<td>53.9%</td>
<td>0.7%</td>
<td>0.8%</td>
<td>4.1%</td>
<td>40.8%</td>
<td>714</td>
</tr>
<tr>
<td>Florida</td>
<td>67.4%</td>
<td>0.3%</td>
<td>0.9%</td>
<td>10.4%</td>
<td>21.0%</td>
<td>5,281</td>
</tr>
<tr>
<td>Georgia</td>
<td>80.0%</td>
<td>1.5%</td>
<td>0.3%</td>
<td>5.2%</td>
<td>13.1%</td>
<td>950</td>
</tr>
<tr>
<td>Illinois</td>
<td>61.1%</td>
<td>1.0%</td>
<td>1.1%</td>
<td>22.6%</td>
<td>14.3%</td>
<td>2,598</td>
</tr>
<tr>
<td>Indiana</td>
<td>73.6%</td>
<td>0.5%</td>
<td>0.7%</td>
<td>12.2%</td>
<td>13.1%</td>
<td>1,347</td>
</tr>
<tr>
<td>Kentucky</td>
<td>78.2%</td>
<td>0.6%</td>
<td>3.3%</td>
<td>5.3%</td>
<td>15.9%</td>
<td>358</td>
</tr>
<tr>
<td>Maine</td>
<td>36.1%</td>
<td>1.2%</td>
<td>3.7%</td>
<td>57.0%</td>
<td>326</td>
<td></td>
</tr>
<tr>
<td>Maryland</td>
<td>75.8%</td>
<td>1.2%</td>
<td>0.3%</td>
<td>1.2%</td>
<td>21.6%</td>
<td>781</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>52.1%</td>
<td>0.1%</td>
<td>0.7%</td>
<td>13.0%</td>
<td>34.1%</td>
<td>5,145</td>
</tr>
<tr>
<td>Michigan</td>
<td>81.5%</td>
<td>0.5%</td>
<td>1.0%</td>
<td>3.0%</td>
<td>14.1%</td>
<td>1,984</td>
</tr>
<tr>
<td>Minnesota</td>
<td>80.6%</td>
<td>0.7%</td>
<td>3.5%</td>
<td>3.2%</td>
<td>12.0%</td>
<td>4,296</td>
</tr>
<tr>
<td>Missouri</td>
<td>79.2%</td>
<td>0.5%</td>
<td>0.8%</td>
<td>7.2%</td>
<td>12.3%</td>
<td>390</td>
</tr>
<tr>
<td>New Hampshire</td>
<td>54.4%</td>
<td>0.4%</td>
<td>6.7%</td>
<td>36.6%</td>
<td>555</td>
<td></td>
</tr>
<tr>
<td>New Jersey</td>
<td>53.8%</td>
<td>0.1%</td>
<td>0.5%</td>
<td>5.0%</td>
<td>40.7%</td>
<td>1,468</td>
</tr>
<tr>
<td>New Mexico</td>
<td>73.3%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New York</td>
<td>57.8%</td>
<td>1.7%</td>
<td>0.7%</td>
<td>7.1%</td>
<td>32.9%</td>
<td>1,032</td>
</tr>
<tr>
<td>North Carolina</td>
<td>68.0%</td>
<td>0.6%</td>
<td>0.2%</td>
<td>2.9%</td>
<td>28.0%</td>
<td>1,681</td>
</tr>
<tr>
<td>Ohio</td>
<td>79.7%</td>
<td>0.6%</td>
<td>0.2%</td>
<td>5.7%</td>
<td>13.7%</td>
<td>839</td>
</tr>
<tr>
<td>Oregon</td>
<td>49.5%</td>
<td>2.2%</td>
<td>9.5%</td>
<td>10.8%</td>
<td>28.1%</td>
<td>548</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>68.8%</td>
<td>0.5%</td>
<td>0.4%</td>
<td>1.8%</td>
<td>26.5%</td>
<td>2,772</td>
</tr>
<tr>
<td>Rhode Island</td>
<td>45.4%</td>
<td>0.5%</td>
<td>0.8%</td>
<td>10.0%</td>
<td>43.4%</td>
<td>791</td>
</tr>
<tr>
<td>Tennessee</td>
<td>86.0%</td>
<td>0.5%</td>
<td>0.5%</td>
<td>5.7%</td>
<td>7.3%</td>
<td>757</td>
</tr>
<tr>
<td>Texas</td>
<td>74.1%</td>
<td>0.2%</td>
<td>1.0%</td>
<td>6.1%</td>
<td>18.6%</td>
<td>3,092</td>
</tr>
<tr>
<td>Vermont</td>
<td>68.4%</td>
<td>0.4%</td>
<td>1.3%</td>
<td>7.0%</td>
<td>29.3%</td>
<td>450</td>
</tr>
<tr>
<td>Virginia</td>
<td>75.5%</td>
<td>1.2%</td>
<td>3.5%</td>
<td>37.5%</td>
<td>695</td>
<td></td>
</tr>
<tr>
<td>Washington</td>
<td>63.4%</td>
<td>2.0%</td>
<td>9.7%</td>
<td>10.5%</td>
<td>14.5%</td>
<td>1,741</td>
</tr>
<tr>
<td>West Virginia</td>
<td>61.4%</td>
<td>0.1%</td>
<td>0.5%</td>
<td>37.9%</td>
<td>736</td>
<td></td>
</tr>
<tr>
<td>Wisconsin</td>
<td>61.1%</td>
<td>0.6%</td>
<td>2.8%</td>
<td>1.0%</td>
<td>26.4%</td>
<td>633</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>State</th>
<th>B.1.1.7</th>
<th>B.1.351</th>
<th>B.1.427/ B.1.429</th>
<th>P.1</th>
<th>Other lineages</th>
<th>Total available sequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZ</td>
<td>67.8%</td>
<td>0.7%</td>
<td>4.2%</td>
<td>9.0%</td>
<td>18.3%</td>
<td>600</td>
</tr>
<tr>
<td>RI</td>
<td>45.4%</td>
<td>0.5%</td>
<td>0.8%</td>
<td>10.0%</td>
<td>43.4%</td>
<td>791</td>
</tr>
</tbody>
</table>
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
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.
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
  - Meeting ID: 160 432 9034
  - Passcode: 897674

Weekly Stakeholder Update Calls

- **Next call:** Wed, June 16, 3.15-4:00PM EST
- Send email to [ASPRstakeholder@hhs.gov](mailto:ASPRstakeholder@hhs.gov) for inclusion

Contact the Federal COVID-19 Response Team:
[COVID19Therapeutics@hhs.gov](mailto: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/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
Helpful information and resources (II/II)

Informational resources:

- HHS Website: [https://combatcovid.hhs.gov/](https://combatcovid.hhs.gov/)
- HHS/ASPR Website: [https://www.phe.gov](https://www.phe.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](https://combatcovid.hhs.gov/hcp/resources)
- Updated information sheets and resources for providers in English and Spanish [https://combatcovid.hhs.gov/hcp/resources](https://combatcovid.hhs.gov/hcp/resources)
Thank you!