COVID-19 Therapeutics

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Unclassified/For Public Use
These medications are not a substitute for vaccination.

Agenda

- Introduction to COVID Therapeutics
- Pre-Exposure Prophylaxis (PrEP)
- Post-Exposure Prophylaxis
- Treatment
- Administration Considerations
- Resources
- **Q & A / Discussion**

IMPORTANT UPDATES

- FDA Expands Authorization of Two Monoclonal Antibodies for Treatment and Post-Exposure Prevention of COVID-19 to Include Younger Pediatric Patients

- USG to Make Newly Authorized AstraZeneca COVID-19 Therapeutic Available Nationwide

FDA Expands Authorization of Bam/Ete for Treatment and Post-Exposure Prevention of COVID-19 to Include Younger Pediatric Patients

- FDA revised the emergency use authorization (EUA) of bamlanivimab and etesevimab (Eli Lilly and Company)
- Bam/Ete now authorized for the **treatment** of mild to moderate COVID-19 **in all younger pediatric patients**, including newborns, who have a positive COVID-19 test and are at high risk for progression to severe COVID-19, including hospitalization or death
- Revision also authorizes bam/ete for **post-exposure prophylaxis** for prevention of COVID-19 in all pediatric patients, including newborns, at high risk of progression to severe COVID-19, including hospitalization or death
- EUA Details: https://www.fda.gov/media/145802/download
- Federal COVID Response working w Pediatric Organizations on Education and Rollout

Section 1: Overview

Frequently Asked Questions Related to EUA

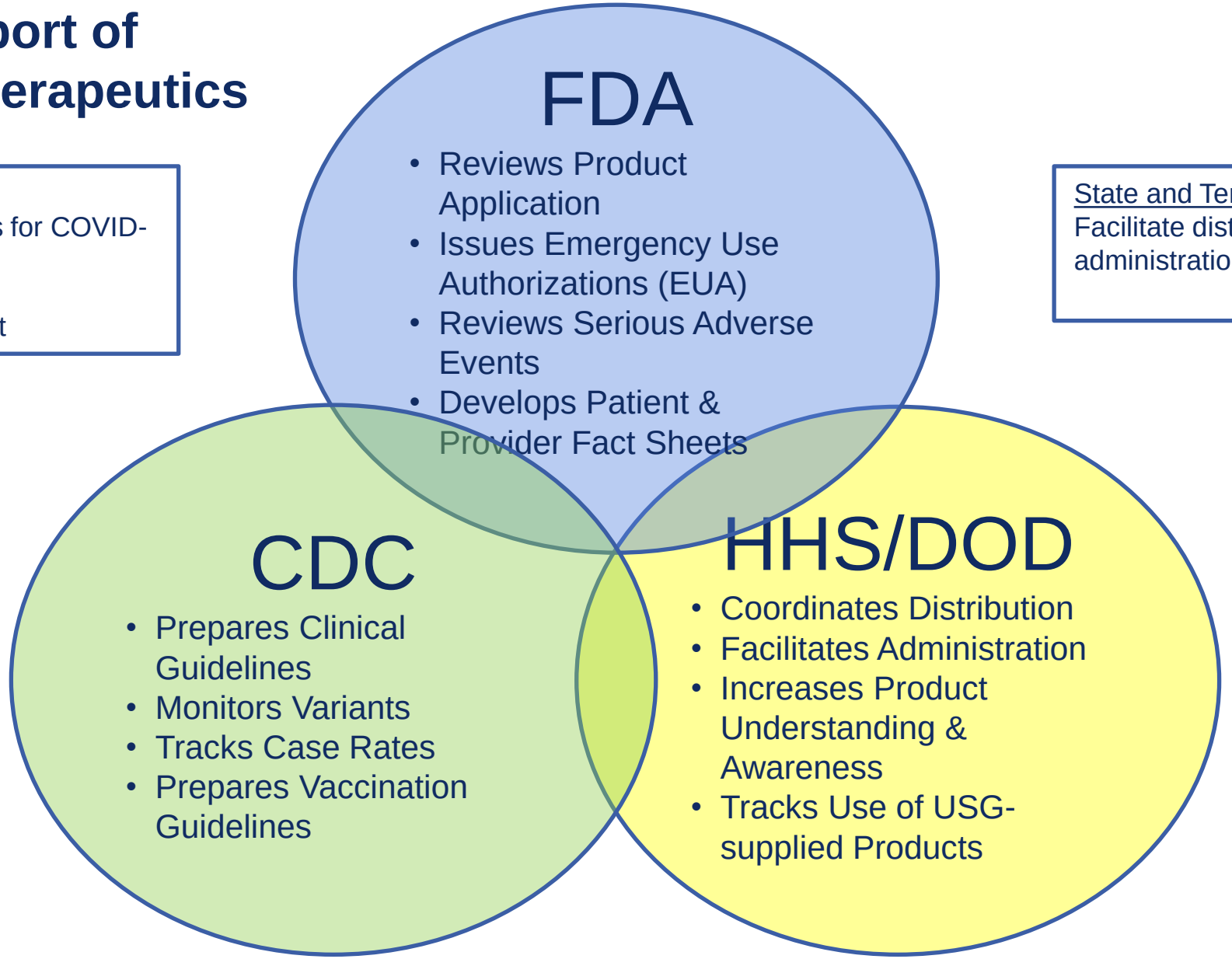
- Products under EUA **must be administered in accordance with the EUA.**
- **A signed consent form is not needed** to administer products under EUA.
- **No clinical data reporting is required** beyond established FDA mechanisms for tracking and reporting serious adverse events.

Current Information on Variants

- Delta
- Omicron

Federal Support of COVID-19 Therapeutics

NIH
Issues clinical guidelines for COVID-19 treatment
CMS/HRSA
Manages reimbursement



State and Territorial Agencies
Facilitate distribution and administration

Principles for USG allocation/ distribution of mAbs

1. Use USG infrastructure, plus:
   - Eli Lilly, Regeneron, GlaxoSmithKline (manufacturers)
   * AmerisourceBergen (distributor)

2. Allocations must ensure both **temporal** and **geographic** equity

3. USG allocates to state and territorial health depts. based on:
   - Confirmed hospitalizations (7-day)
   - Confirmed cases (7-day)

4. **States/territories** distribute to administration sites

5. Admin sites report weekly mAb utilization

6. Manufacturer tracks pharmacovigilance, issues mandatory reports

USG-procured mAbs are provided at no cost

- Administration fees for mAbs may be billed by sites
- CMS reimbursement rates increased:
  - **$450** for most outpatient settings
  - **$750** when administered in patient's home
- Additional information on reimbursement: Monoclonal Antibody COVID-19 Infusion | CMS
- Reimbursement options for uninsured individuals: HRSA

NIH COVID-19 Treatment Guidelines

- The COVID-19 Treatment Guidelines Panel **recommends** using anti-SARS-CoV-2 mAbs for:
  - Treatment of mild to moderate COVID-19
  - Post-exposure prophylaxis (PEP) of SARS-CoV-2 infection in individuals who are at high risk for progression to severe COVID-19
  - … as outlined in the FDA EUAs.
- See individual EUAs for details.

NIH Logistical Constraints

- Where necessary to triage, the NIH suggests:
  - **Prioritize treatment of COVID-19** over PEP of SARS-CoV-2 infection
  - **Prioritize these groups over vaccinated individuals** who are expected to have mounted an adequate immune response:
    - Unvaccinated or incompletely vaccinated, and at high risk of progressing to severe COVID-19
    - Vaccinated but not expected to mount an adequate immune response (e.g., immunocompromised)
- **Use clinical judgment** when prioritizing treatment or PEP
- When there are no logistical constraints for administering therapy, these considerations **should not** limit providing mAbs for SARS-CoV-2

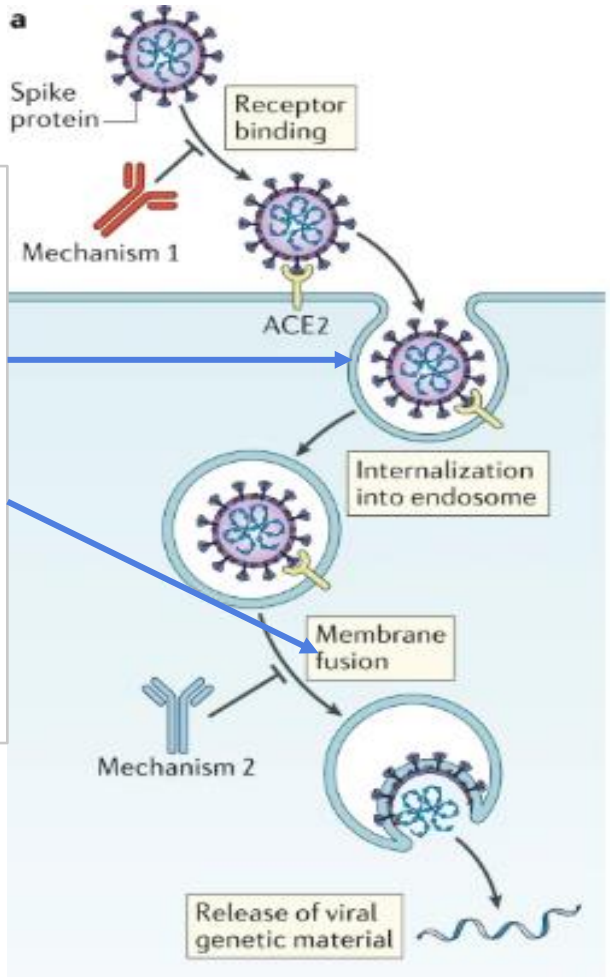
Potential Mechanisms for mAbs' Clinical Effects

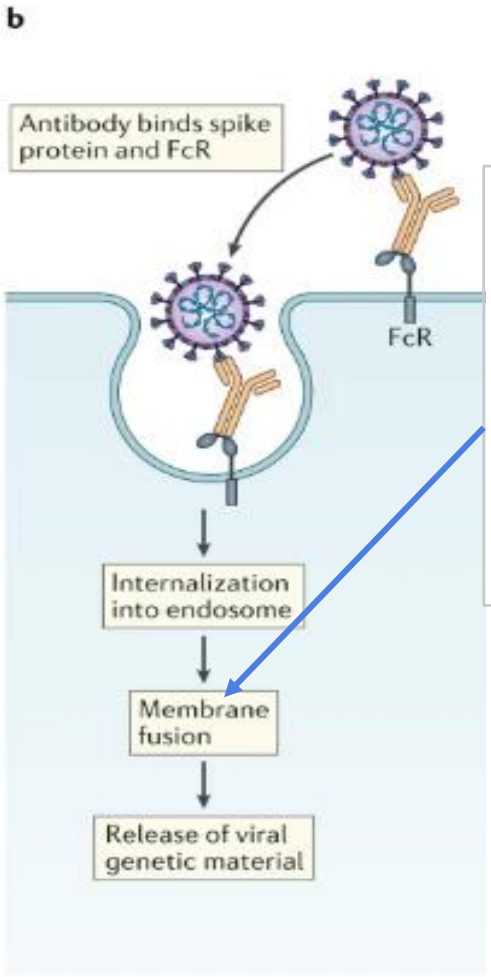
a) Bind to Virus

1) Block cell uptake

2) Block membrane fusion

Impede replication





b) Bind to Virus

3) Deliver to immune cells

Destruction

Source: Nature

Stages of COVID-19 Therapeutics

NIH Guidelines for Hospitalized Adult COVID-19 Patients

Section 2: Pre-exposure Prophylaxis (PrEP)

Summary of COVID-19 Preventative Agents & Therapeutics

PrEP

Monoclonal Antibodies for PrEP

- Evusheld AZD7442 (tixagevimab + cilgavimab)

[1]Use and distribution of bam / ete has resumed nationally as of 09/02/2021, see PHE.gov

PrEP: Clinical Indications

- Evusheld (tixagevimab and cilgavimab) is only authorized for those individuals who are not currently infected with the SARS-CoV-2 virus and who have not recently been exposed to an individual infected with SARS-CoV-2.
- The authorization also requires that individuals either have:
  - Moderate to severely compromised immune systems due to a medical condition or due to taking immunosuppressive medications or treatments and may not mount an adequate immune response to COVID-19 vaccination (examples of such medical conditions or treatments can be found in the fact sheet for health care providers), **or**
  - A history of severe adverse reactions to a COVID-19 vaccine and/or component(s) of those vaccines, therefore vaccination with an available COVID-19 vaccine, according to the approved or authorized schedule, is not recommended.

PrEP: Medication and Administration

- One dose of Evusheld, administered as two separate consecutive intramuscular injections (one injection per monoclonal antibody, given in immediate succession), may be effective for pre-exposure prevention for six months.
- Evusheld is not authorized for individuals for the treatment of COVID-19 or for post-exposure prevention of COVID-19.
- As with any other IM injection, administer with caution to patients with thrombocytopenia or any coagulation disorder

https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-new-long-acting-monoclonal-antibodies-pre-exposure

Section 3: Post-exposure Prophylaxis (PEP)

Summary of COVID-19 Preventative Agents & Therapeutics

PEP

Monoclonal Antibodies for PEP

- Casirivimab + Imdevimab (RGN)
- Bamlanivimab + Etesevimab (Lilly)

[1]Use and distribution of bam / ete has resumed nationally as of 09/02/2021, see PHE.gov

Post Exposure Prophylaxis: Clinical Indications

EUA-authorized mAbs are authorized for PEP of COVID-19 in individuals who are:

- Adult or pediatric (≥ 12 years of age and weighing at least 40kg) patient **at high risk for progressing to severe disease or death (*see high risk criteria) OR***
- Pediatric Patient <40kg (including neonates)*** **at high risk for progressing to severe disease or death (*see high risk criteria) **bamlanivimab/etesevimab only***

AND

- Not fully vaccinated[1] **or** who are not expected to mount an adequate immune response to complete SARS-CoV-2 vaccination (for example, individuals with immunocompromising conditions including those taking immunosuppressive medications[2]) **AND**
  - have been exposed to an individual infected with SARS-CoV-2 consistent with close contact criteria per CDC[3] **OR**
  - **who are at high risk of exposure to an individual infected with SARS-CoV-2** because of occurrence of COVID-19 in other individuals in the same institutional setting (for example, nursing homes, prisons) [*see limitations of authorized use]*

1. CDC's Have You Been Fully Vaccinated? (https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated.html#vaccinated)
2. CDC's Science Brief: COVID-19 Vaccines and Vaccination (https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html)
3. CDC's Quarantine and Isolation (https://www.cdc.gov/coronavirus/2019-ncov/if-you-are-sick/quarantine.html)

RISK FACTORS FOR TREATMENT AND PEP WITH mAbs INCLUDE, BUT ARE NOT LIMITED TO:

- Older age (e.g., ≥ 65 years of age)
- Age <1 year for bam/ete
- Obesity or overweight
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease or hypertension
- Chronic lung diseases
- Sickle cell disease
- Neurodevelopmental disorders
- Medical-related technological dependence

…or Provider Judgment

PEP: Limitations of Authorized Use

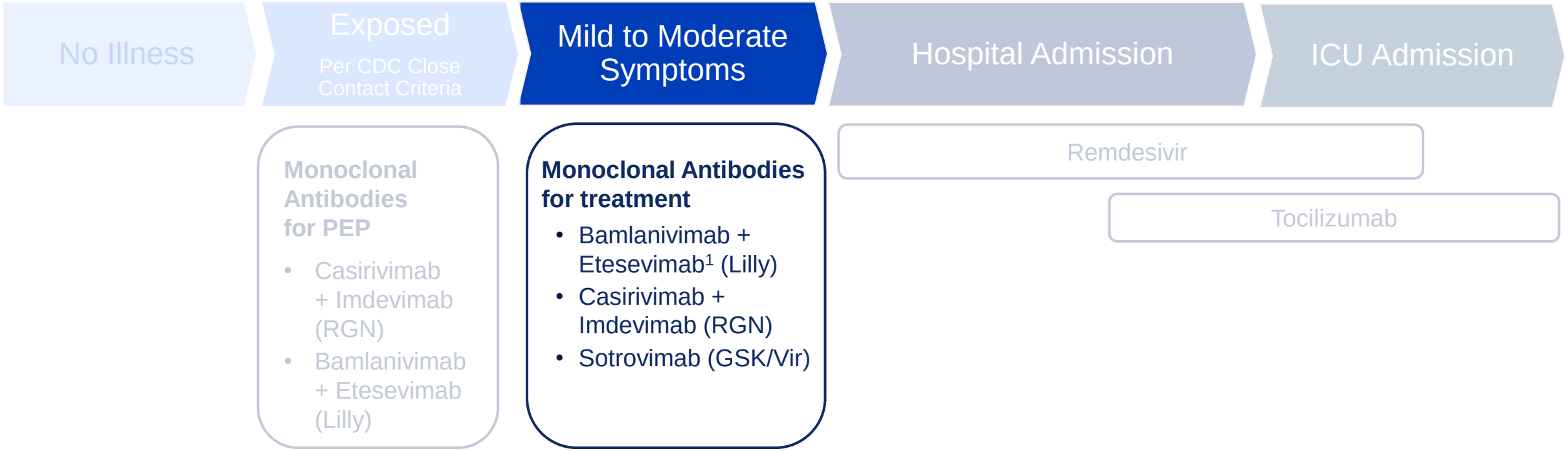
- Post-exposure prophylaxis with bamlanivimab + etesevimab or REGEN-COV (casirivimab + imdevimab) is not a substitute for vaccination against COVID-19.

- Bamlanivimab + etesevimab REGEN-COV (casirivimab + imdevimab) and are not authorized for pre-exposure prophylaxis for prevention of COVID-19

Section 3: Treatments

Summary of COVID-19 Preventative Agents & Therapeutics

Treatment



[1]Use and distribution of bam / ete has resumed nationally as of 09/02/2021, see PHE.gov

Bottom Line: Monoclonal antibody treatment reduces relative risk of hospitalization

- Individuals with **mild to moderate COVID-19 who are at high risk of developing severe disease**
- Likely most effective when **given early in disease course**
- Bamlanivimab + etesevimab[1] and REGEN-COV (casirivimab + imdevimab) **reduce the relative risk of hospitalization by up to 87% in high-risk patients**
- Sotrovimab **reduces relative risk of hospitalization by up to 79% in high-risk patients**

[1]Use and distribution of bam / ete has resumed nationally as of 09/02/2021, see PHE.gov

Therapy: Clinical Indications

- **Mild to moderate COVID-19 cases** early in infection, and...
- Who are at **high risk for progressing to severe COVID-19 and/or hospitalization,** and...
- Who meet the following criteria:
  - Adult or pediatric (≥12 years and weighing at least **40kg**)
  - Pediatric patients (including neonates) ***bamlanivimab/etesevimab only
  - Confirmation via **positive PCR or antigen test**
  - Treatment **as soon as possible** following positive viral test and **within 10 days of symptom onset**
  - Patient symptomatic but **not yet progressed to require hospitalization (2 years of age or older) or oxygen therapy (or increase from baseline chronic oxygen therapy)**

December 8 Update: Pediatric Indications for Bam/Ete

- **Bam/Ete EUA Updates:**
  - Post-Exposure Prophylaxis **AND**
  - Treatment
  - Children down to age newborn
  - Age < 1 year now listed as ***High-Risk Criteria***
  - Admitted Children Less than 2 years old can receive Bam/Ete **In-Patient**
  - Still not able to receive if on supplemental oxygen
  - EUA Details: https://www.fda.gov/media/145802/download
  - Federal COVID Response working w Pediatric Organizations on Education and Roll out

RISK FACTORS FOR TREATMENT AND PEP WITH mAbs INCLUDE, BUT ARE NOT LIMITED TO:

- Older age (e.g., ≥ 65 years of age)
- Age <1 year for bam/ete
- Obesity or overweight
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease or hypertension
- Chronic lung diseases
- Sickle cell disease
- Neurodevelopmental disorders
- Medical-related technological dependence

…or Provider Judgment

Monoclonal Antibody Indications and Routes of Administration

Monoclonal Antibody	PRE-EXPOSURE PROPHYLAXIS (PREP) for eligible individuals	POST-EXPOSURE PROPHYLAXIS (PEP) for individuals who are not fully vaccinated or immunocompromised, with high risk of progression to severe disease	TREATMENT of Mild to Moderate COVID-19 Infection within 10 days of symptom onset in patient with high risk of progression to severe disease
bamlanivimab and etesevimab[1] (Eli Lilly)	**N/A**	**Dose:** bamlanivimab 700mg and etesevimab 1400mg **Route:** Intravenous **Post-administration monitoring:** 60 minutes **Weight-based pediatric (< 40kg) dosing[1]**	**Dose:** bamlanivimab 700mg and etesevimab 1400mg **Route:** Intravenous **Post-administration monitoring:** 60 minutes **Weight-based pediatric (< 40kg) dosing[1]**
casirivimab and imdevimab[2] (REGEN-COV)	**N/A**	**Dose:** casirivimab 600mg and imdevimab 600mg **Route:** Intravenous is preferred route, however subcutaneous injection may be utilized in situations where there would be a delay in intravenous administration **Post-administration monitoring:** 60 minutes	**Dose:** casirivimab 600mg and imdevimab 600mg **Route:** Intravenous or subcutaneous **Post-administration monitoring:** 60 minutes
sotrovimab[3] (Glaxo Smith Kline)	**N/A**	**N/A**	**Dose:** sotrovimab 500mg **Route:** Intravenous **Post-administration monitoring:** 60 minutes
tixagevimab and cilgavimab[4] (AstraZeneca)	**Dose:** tixagevimab 150mg and cilgavimab 150mg **Route:** Intramuscular **Post-administration monitoring:** 60 min	**N/A**	**N/A**

- Refer to product Emergency Use Authorizations for detail on indications and administration
- [1] Fact Sheet for Health Care Providers Emergency Use Authorization of Bamlanivimab and Etesevimab (https://www.fda.gov/media/145802/download)
- [2] Fact Sheet for Health Care Providers Emergency Use Authorization of REGEN-COVTM (casirivimab and imdevimab) (https://www.fda.gov/media/145611/download)
- [3] Fact Sheet for Health Care Providers Emergency Use Authorization of Sotrovimab (https://www.fda.gov/media/149534/download)
- [4]Fact Sheet for Health Care Providers Emergency Use Authorization for Evusheld (tixagevimab co-packaged with cilgavimab (https://www.fda.gov/media/154701/download)

General Guidelines for Bamlanivimab / Etesevimab Dosing & Administration: Pediatric Patients <40kg (including neonates)

Table 2: Recommended Dosing, Preparation and Administration Instructions for Undiluted Bamlanivimab (BAM) and Etesevimab (ETE) for IV Infusion in Pediatric Patients (<18 years and weighing less than 40 kg)

Body Weight	BAM/ETE dose (mg)	Amount of BAM (as mL)[a]	Amount of ETE (as mL)[a]	Maximum Infusion Rate
>20 kg to <40 kg	350 mg / 700 mg	10 mL	20 mL	1.88 mL/min
>12 kg to 20 kg	175 mg / 350 mg	5 mL	10 mL	0.94 mL/min
>11 kg to 12 kg	138 mg / 276 mg	3.9 mL	7.9 mL	0.74 mL/min
>10 kg to 11 kg	126 mg / 252 mg	3.6 mL	7.2 mL	0.68 mL/min
>9 kg to 10 kg	114 mg / 228 mg	3.3 mL	6.5 mL	0.61 mL/min
>8 kg to 9 kg	102 mg / 204 mg	2.9 mL	5.8 mL	0.54 mL/min
>7 kg to 8 kg	90 mg / 180 mg	2.6 mL	5.1 mL	0.48 mL/min
>6 kg to 7 kg	78 mg / 156 mg	2.2 mL	4.5 mL	0.42 mL/min
>5 kg to 6 kg	66 mg / 132 mg	1.9 mL	3.8 mL	0.36 mL/min
>4 kg to 5 kg	54 mg / 108 mg	1.5 mL	3.1 mL	0.29 mL/min
>3 kg to 4 kg	42 mg / 84 mg	1.2 mL	2.4 mL	0.23 mL/min
>2 kg to 3 kg	30 mg / 60 mg	0.9 mL	1.7 mL	0.16 mL/min
>1.5 kg to 2 kg	21 mg / 42 mg	0.6 mL	1.2 mL	0.11 mL/min
1 kg to 1.5 kg	15 mg / 30 mg	0.4 mL	0.9 mL	0.08 mL/min

Fact Sheet for Health Care Providers Emergency Use Authorization of Bamlanivimab and Etesevimab (http://pi.lilly.com/eua/bam-and-ete-eua-factsheet-hcp.pdf)

Section 5: Administration

Administration can occur across a variety of models

Hospitals

Ambulatory centers

Nursing homes

Mobile sites

Home

Information support via PHE.gov/mAbs and CombatCOVID.hhs.gov/
(links to EUA criteria, consolidated playbooks, educational materials)

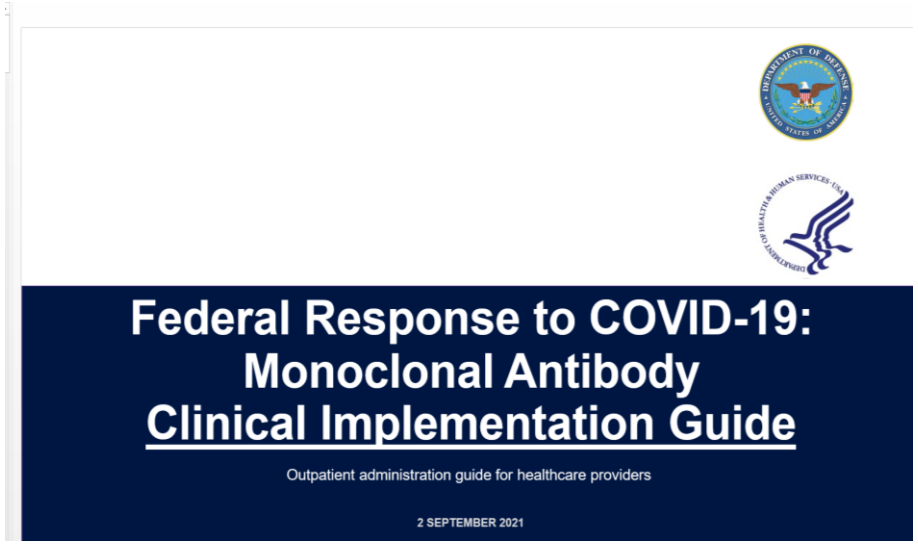
Section 6: Resources

Clinical Implementation Guide

Federal Response to COVID-19: Monoclonal Antibody Clinical Implementation Guide

- Updated periodically with EUA changes
- **PHE.gov/mabs**

Monoclonal antibody side-by-side overview



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

Best Practices and Resources

- USG shares best practices with medical and professional societies
  - Best practices and testimonials: https://combatcovid.hhs.gov/hcp/videos-monoclonal-antibodies

- Additional information and resources: phe.gov/mAbs and CombatCOVID.hhs.gov
  - mAbs calculator for infusion sites to estimate capacity and maximize use of resources: www.PHE.gov/mAbs-calculator
  - Information Toolkit – resources for administration sites, communications and public information officers, providers, patients: https://www.phe.gov/emergency/events/COVID19/therapeutics/Pages/toolkit.aspx\

Asks for Community Leaders and Healthcare Providers

Increase awareness of therapies in your community:

- Share information in local outlets
- Post information (neighborhood apps, social media, etc.): "Monoclonal antibodies are available treatment options"
- Host outreach events

Locate administration sites in your community

Share your experiences:

- Post online (blogs, social media, etc.)
- Share with HHS/ASPR at COVID19Therapeutics@hhs.gov

Weekly Stakeholder Engagements

- **Office Call Sessions: HHS / ASPR Distribution and Administration of COVID-19 Therapeutics – open to all with equity in the process**
  - Tuesdays (2:00 - 2:30PM ET)
  - Thursdays (2:00 - 2:30PM 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)
- **Federal COVID-19 Response: Therapeutics 210 Webinar**
  - Fridays (12:00 - 1:00PM ET)
  - Target audience: new administration sites, health officials
    https://hhsasproea.zoomgov.com/j/1617536991?pwd=NjFMcnJOUENuSFhtRFFtaWltejYzZz09

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

Additional Resources

- Evusheld (AZD7442)
- Bamlanivimab/etesevimab
- REGEN-COV
- Sotrovimab
- COVID-19 Monoclonal Antibody Eligibility: Treatment and Post-Exposure Prophylaxis
- COVID-19 Monoclonal Antibody (mAb) Checklist: Subcutaneous & Intravenous Administration
- EMS Template Protocol for COVID-19 Monoclonal Antibody Administration: Treatment and Post-Exposure Prophylaxis of REGEN-COV (casirivimab and imdevimab)
- REGEN-COV: Subcutaneous Injection Instructions for Healthcare Providers