Monoclonal Antibodies for the Treatment of COVID-19

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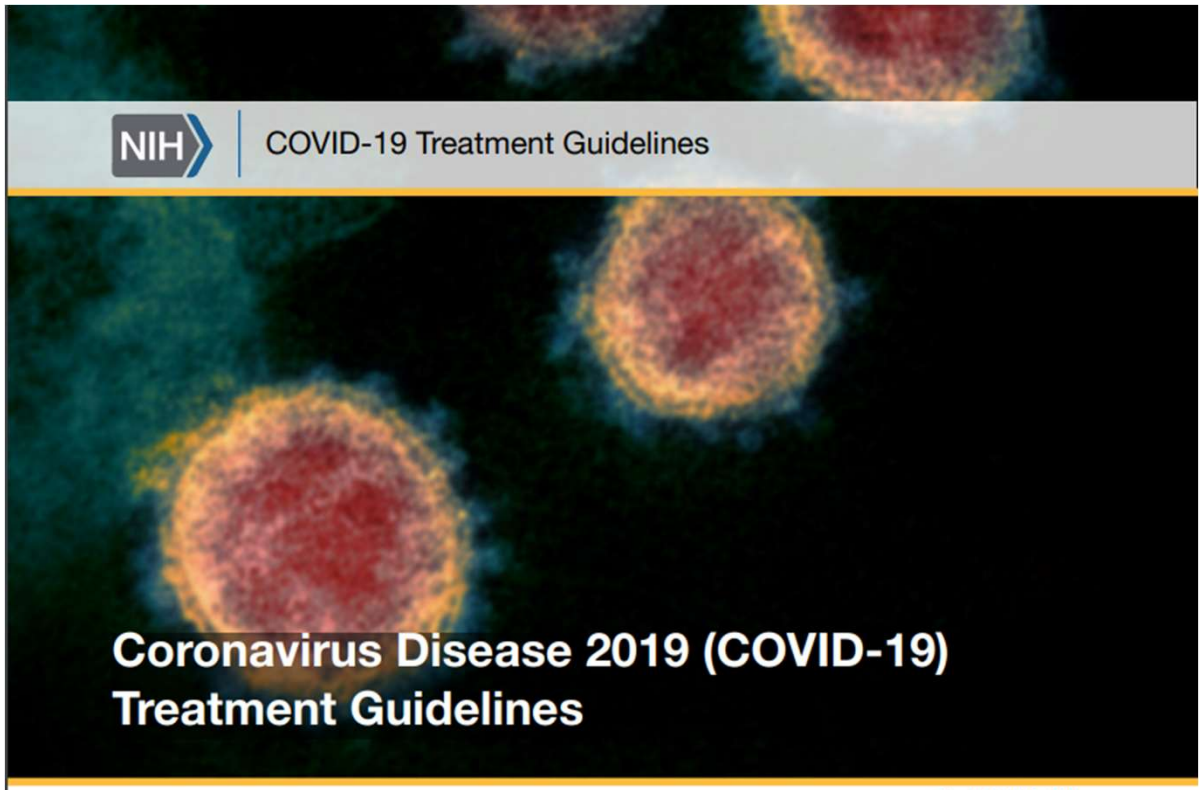
Long Term Care Facilities and Assisted Living Facilities Partners Call

September 16th, 2021

Disclaimer

Please use original source recommendations/guidelines as well as individual health practitioner clinical assessment for patient care. This presentation is not meant to be all-encompassing and more recent clinical guidelines may exist at the time of your review of this presentation. References cited in this presentation were accessed on 9/15/2021.

Treatment for COVID-19



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Hospitalized Adult Treatment for COVID-19

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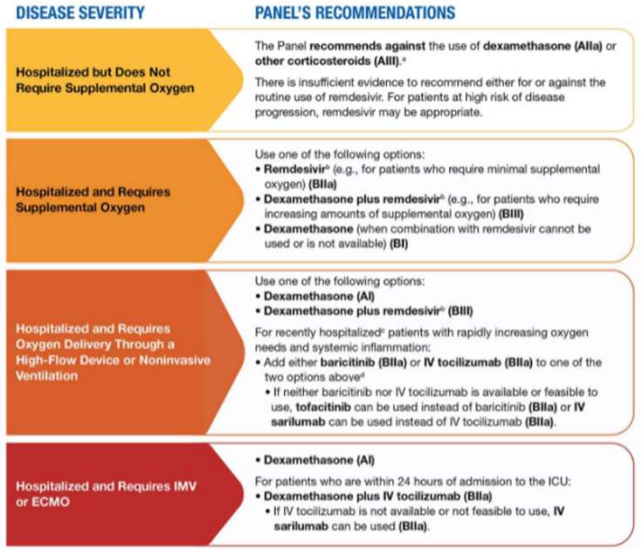
Therapeutic Management of Hospitalized Adults With COVID-19

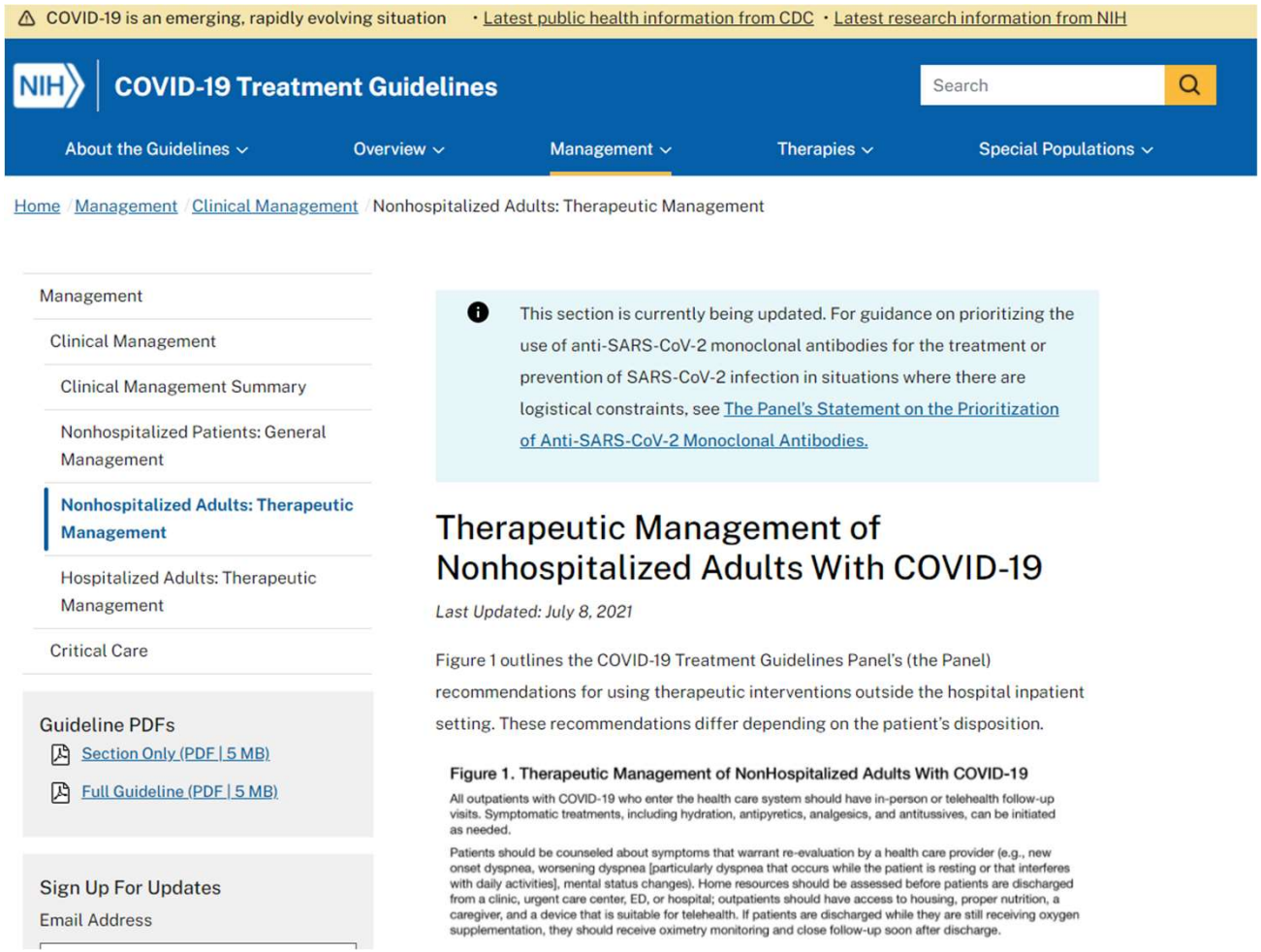
Last Updated: August 25, 2021

Figure 2. Therapeutic Management of Hospitalized Adults With COVID-19 Based on Disease Severity



https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/hospitalized-adults--therapeutic-management/

Non-Hospitalized Adult Treatment for COVID-19



https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/nonhospitalized-adults--therapeutic-management/

General Principles of Treatment for COVID-19

Treatments are based upon the general pathogenesis of COVID-19

- In the early clinical course, the disease is driven by replication of SARS-CoV-2 virus.
  - Therapies that directly target the virus may have greatest effect.
- Later in the clinical course, the disease is driven by dysregulation of the immune and inflammatory response to SARS-CoV-2 virus that leads to tissue damage.
  - Immunosuppressive/anti-inflammatory therapies may be more beneficial in later states of disease.

https://files.covid19treatmentguidelines.nih.gov/guidelines/section/section_121.pdf

Non-Hospitalized Adult Treatment for COVID-19

Figure 1. Therapeutic Management of NonHospitalized Adults with COVID-19

All outpatients with COVID-19 who enter the health care system should have in-person or telehealth follow-up visits. Symptomatic treatments, including hydration, antipyretics, analgesics, and antitussives, can be initiated as needed.

Patients should be counseled about symptoms that warrant re-evaluation by a health care provider (e.g., new onset dyspnea, worsening dyspnea [particularly dyspnea that occurs while the patient is resting or that interferes with daily activities], mental status changes). Home resources should be assessed before patients are discharged from a clinic, urgent care center, ED, or hospital; outpatients should have access to housing, proper nutrition, a caregiver, and a device that is suitable for telehealth. If patients are discharged while they are still receiving oxygen supplementation, they should receive oximetry monitoring and close follow-up soon after discharge.

PATIENT DISPOSITION	PANEL'S RECOMMENDATIONS
Not Requiring Hospitalization or Supplemental Oxygen, As Determined by a Health Care Provider in ED or an In-Person or Telehealth Visit	Anti-SARS-CoV-2 monoclonal antibody products are recommended for outpatients with mild to moderate COVID-19 who are at high risk of disease progression, as defined by the EUA criteria (treatments are listed in alphabetical order):[a] • **Casirivimab plus imdevimab**; *or* • **Sotrovimab** At this time, the Panel **recommends against** the use of **bamlanivimab plus etesevimab** in these patients due to an increase in the proportion of potentially resistant variants **(AIII)**.[a] See text for details. The Panel **recommends against** the use of **dexamethasone** or **other systemic glucocorticoids** in the absence of another indication **(AIII)**.[b]
Discharged From Hospital Inpatient Setting in Stable Condition and Does Not Require Supplemental Oxygen	The Panel **recommends against** continuing the use of **remdesivir (AIIa)**, **dexamethasone (AIIa)**, or **baricitinib (AIIa)** after hospital discharge.
Discharged From Hospital Inpatient Setting and Requires Supplemental Oxygen *For those who are stable enough for discharge but who still require oxygen*[c]	There is insufficient evidence to recommend either for or against the continued use of remdesivir, dexamethasone, and/or baricitinib. Review the text below when considering the use of any of these agents after hospital discharge.
Discharged From ED Despite New or Increasing Need for Supplemental Oxygen *When hospital resources are limited, inpatient admission is not possible, and close follow-up is ensured*[d]	The Panel recommends using **dexamethasone** 6 mg PO once daily for the duration of supplemental oxygen (dexamethasone use should not exceed 10 days) with careful monitoring for adverse events **(BIII)**. There is insufficient evidence to recommend either for or against the use of remdesivir. When considering the use of remdesivir, review the text below for further discussion. The Panel **recommends against** the use of **baricitinib** in this setting, except in a clinical trial **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/nonhospitalized-adults--therapeutic-management/

Therapeutic Management of Non-Hospitalized Adults with COVID-19

- Not all persons will seek care from the healthcare system.
- NIH Guidelines recommend all patients seeking care should have an **in-person** visit or **telehealth** visit.
  - Symptomatic treatment –rest, hydration, antipyretics, analgesics, antitussives
  - Assessment for worrisome symptoms – dyspnea (shortness of breath), mental status changes, low oxygen, etc.
  - If stable, assessment of home resources including housing situation, nutrition, caregiver availability, device for telehealth visits, oximetry monitoring, ability for close follow-up, etc.

https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/nonhospitalized-adults--therapeutic-management/

Therapeutic Management of Non-Hospitalized Adults with COVID-19

- Pharmacologic Treatment –
  - **Monoclonal antibodies** are recommended for outpatients with mild to moderate COVID-19 who are at high risk of disease progression, as defined by FDA EUA criteria and FDA Fact Sheet for each formulation.
  - Recommendation against the use of dexamethasone or other systemic glucocorticoids for non-hospitalized patients who do not require supplemental oxygen in the absence of another indication.
  - **Dexamethasone** is recommended is specific settings where inpatient admission is not performed, when a patient has close monitoring and the patient has a new or increasing use of supplemental oxygen.

https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/nonhospitalized-adults--therapeutic-management/

What are Monoclonal Antibodies?

- They are similar to antibodies that your body makes to fight viruses, however are made in labs of pharmaceutical companies.
- Unlike polyclonal antibodies that target multiple antigens, monoclonal antibodies are copies of antibodies that target specific proteins.
- Monoclonal antibodies used to treat COVID-19 are targeted to bind to the spike protein, and block the virus from entering the body's cells.
- When the virus cannot enter cells, they cannot make copies of themselves and limits the further spread of the virus within the body.
- If a person is already sick, it means monoclonal antibodies can help prevent severe symptoms that result in hospitalization and death.

https://www.webmd.com/vaccines/covid-19-vaccine/news/20210826/monoclonal-antibodies-vs-vaccines-vs-covid-19

FDA Emergency Use Authorization for Regen-COV (casirivimab and imdevimab)

U.S. FOOD & DRUG ADMINISTRATION

September 9, 2021

Regeneron Pharmaceuticals, Inc.
Attention: Yunji Kim, PharmD
Director, Regulatory Affairs
777 Old Saw Mill River Road
Tarrytown, NY 10591

RE: Emergency Use Authorization 091

Dear Dr. Kim:

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes coronavirus disease 2019 (COVID-19).[1] On the basis of such determination, the Secretary of HHS on March 27, 2020, declared that circumstances exist justifying the authorization of emergency use of drugs and biological products during the COVID-19 pandemic, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 360bbb-3), subject to terms of any authorization issued under that section.[2]

On November 21, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for emergency use of REGEN-COV (casirivimab and imdevimab, administered together)[3] for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progressing to severe COVID-19 and/or hospitalization. Casirivimab and imdevimab are recombinant human IgG1 monoclonal antibodies that target the receptor binding domain of the spike protein of SARS-CoV-2. They are investigational drugs and are not approved for any indication.

https://www.fda.gov/media/145610/download

FDA Emergency Use Authorization for Regen-COV (casirivimab and imdevimab)

- **Treatment** of Mild to Moderate COVID-19 in adults and children (12 years of age and older with weight of at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, who are at High Risk for progression to severe COVID-19, including hospitalization or death

OR

- **Post-Exposure Prophylaxis** of COVID-19 for individuals who are at risk for progression to severe COVID-19, including hospitalization or death.
  - Persons not fully vaccinated or who are not expected to mount an adequate immune response
  - Exposed to individual with COVID-19 consistent with CDC criteria for close contact or are at high risk of exposure to an individual infected with SARS-CoV-2 because of occurrence of SARS-CoV-2 infection in other individuals in the same **institutional setting**.

https://www.fda.gov/media/145610/download

FDA Emergency Use Authorization for Regen-COV (casirivimab and imdevimab)

- Method of administration may be through:

IV Administration

or

Subcutaneous Injection

https://www.fda.gov/media/145610/download

FDA Emergency Use Authorization for Regen-COV (casirivimab and imdevimab)

Criteria for Identifying High Risk Individuals

The following medical conditions or other factors may place adults and pediatric patients (age 12-17 years and weighing at least 40 kg) at higher risk for progression to severe COVID-19:

- Older age (for example, age ≥65 years of age)
- Obesity or being overweight (for example, BMI >25 kg/m^2, or if age 12-17, have BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm)
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)
- Sickle cell disease
- Neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital anomalies)
- Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19))

Other medical conditions or factors (for example, race or ethnicity) may also place individual patients at high risk for progression to severe COVID-19 and authorization of REGEN-COV under the EUA is not limited to the medical conditions or factors listed above. For additional information on medical conditions and factors associated with increased risk for progression to severe COVID, see the CDC website: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html. Healthcare providers should consider the benefit-risk for an individual patient.

https://www.fda.gov/media/145610/download

FDA Emergency Use Authorization for Bamlanivimab/Etesevimab

FACT SHEET FOR HEALTH CARE PROVIDERS
EMERGENCY USE AUTHORIZATION (EUA) OF BAMLANIVIMAB AND ETESEVIMAB

AUTHORIZED USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to permit the emergency use of the unapproved products bamlanivimab and etesevimab administered together for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

LIMITATIONS OF AUTHORIZED USE

Combined Frequency of Variants Resistant to Bamlanivimab and Etesevimab

- Bamlanivimab and etesevimab are not authorized for use in states, territories, and US jurisdictions in which the combined frequency of variants resistant to bamlanivimab and etesevimab exceeds 5%.[1]
  - A list of states, territories, and US jurisdictions in which bamlanivimab and etesevimab are and are not currently authorized is available on the following FDA website: https://www.fda.gov/media/151719/download

Use in Patients Who Are Hospitalized or Who Require Oxygen Due to COVID-19

- Bamlanivimab and etesevimab are not authorized for use in patients:
  - who are hospitalized due to COVID-19, OR
  - who require oxygen therapy due to COVID-19, OR
  - who require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
- Treatment with bamlanivimab and etesevimab has not been studied in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab and etesevimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

https://www.fda.gov/media/145802/download

FDA Emergency Use Authorization for Bamlanivimab/Etesevimab

- Must be administered by Intravenous (IV) infusion only
- Indicated for non-hospitalized, non-oxygen requiring adults and children older than 12 years of age who weigh at least 40 kg who are at higher risk for progression to severe COVID-19
- Limited for use in geographic areas where frequency of variants resistant to bamlanivimab/etesevimab does not exceed 5%.
  - Also not indicated for persons who have recent travel or close contact with an infected individual from an area where the frequency of resistant variants exceeds 5%.

FDA Emergency Use Authorization for Bamlanivimab/Etesevimab

The following medical conditions or other factors may place adults and pediatric patients (12 years of age and older weighing at least 40 kg) at higher risk for progression to severe COVID-19:

- Older age (for example age ≥65 years of age)
- Obesity or being overweight (for example, adults with BMI >25 kg/m^2, or if age 12-17, have BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm)
- Pregnancy
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or immunosuppressive treatment
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate-to-severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)
- Sickle cell disease
- Neurodevelopmental disorders (for example, cerebral palsy) or other conditions that confer medical complexity (for example, genetic or metabolic syndromes and severe congenital anomalies)
- Having a medical-related technological dependence (for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19))

Other medical conditions or factors (for example, race or ethnicity) may also place individual patients at high risk for progression to severe COVID-19 and authorization of bamlanivimab and etesevimab under the EUA is not limited to the medical conditions or factors listed above. For additional information on medical conditions

https://www.fda.gov/media/145802/download

FDA List of States for Bamlanivimab/Etesevimab are Authorized as of 9/8/21

Bamlanivimab and Etesevimab Authorized States, Territories, and U.S. Jurisdictions

Document Date: September 8, 2021

Bamlanivimab and etesevimab, administered together, are not authorized for use in states, territories, and U.S. jurisdictions in which the most recently published combined frequency of variants resistant to bamlanivimab and etesevimab exceeds 5%.

Based on the most currently available data, bamlanivimab and etesevimab are now authorized in all U.S. states, territories, and jurisdictions as listed in Table 1.

FDA determines the list of authorized states, territories and U.S. jurisdictions considering current variant frequency data, trends in variant frequency over time, the precision of the estimates and information regarding emerging variants of concern. FDA will update the list of states, territories, and U.S. jurisdictions in which bamlanivimab and etesevimab administered together are authorized as new data and information becomes available. Health care providers should refer to this webpage regularly for updates.

Health care providers should review a patient's travel and contact history within two weeks prior to infection. People who have traveled to, resided in, or had close contact with an infected individual from an area where the frequency of resistant variants to bamlanivimab and etesevimab exceeds 5% should not receive bamlanivimab and etesevimab.

Health care providers should also refer to Section 15 of the Fact Sheet for Health Care Providers for further details regarding specific variants and resistance.

Table 1: States, Territories, and U.S. Jurisdictions in which Bamlanivimab and Etesevimab Are Currently Authorized for Use

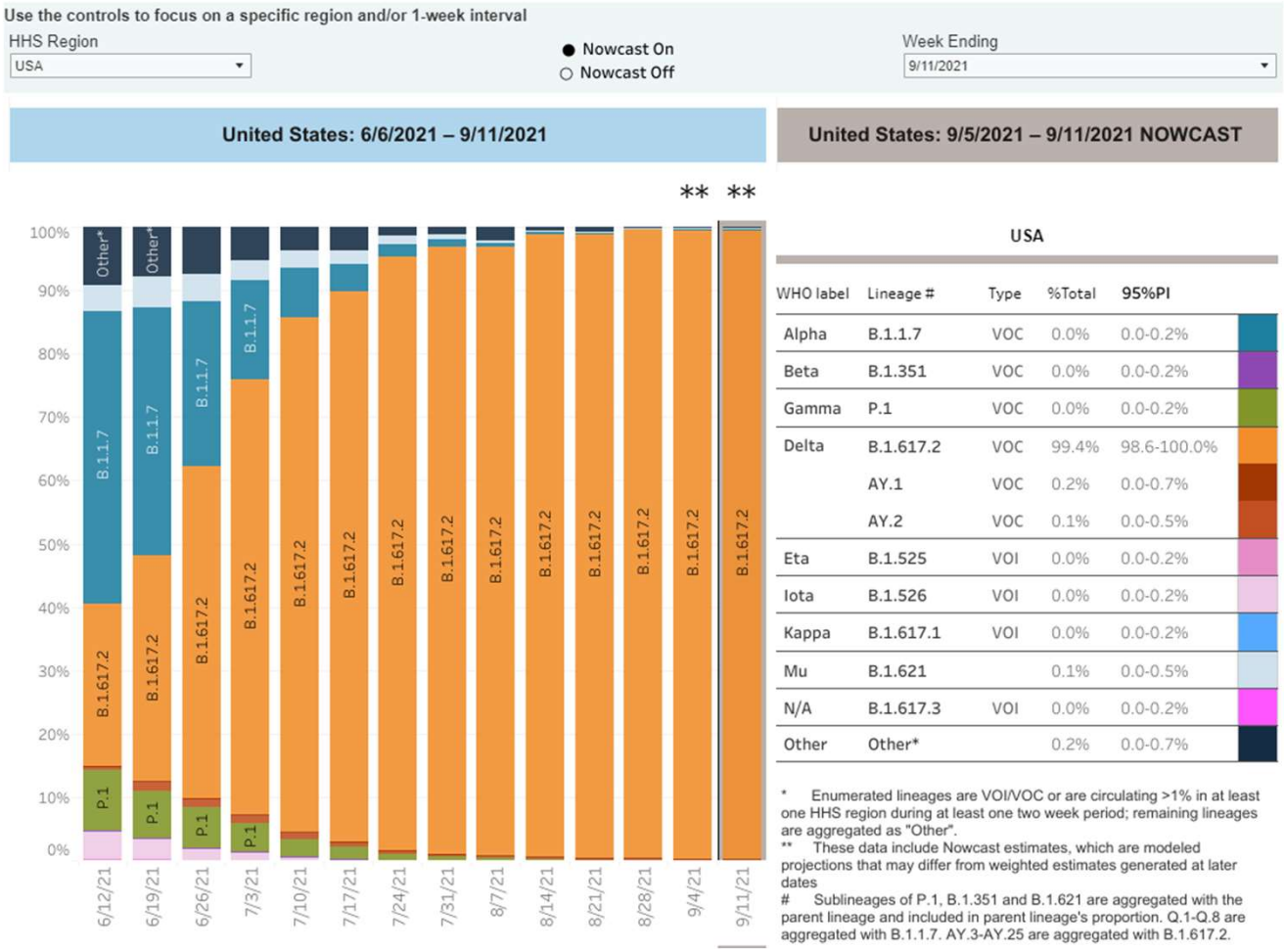
Alabama
Alaska
American Samoa
Arizona
Arkansas
California
Colorado
Commonwealth of the Northern Mariana Islands
Connecticut
Delaware

Nevada
New Hampshire
New Jersey
New Mexico
New York

https://www.fda.gov/media/151719/download

(Full list of states not included in graphic shown)

Variant Distributions within United States



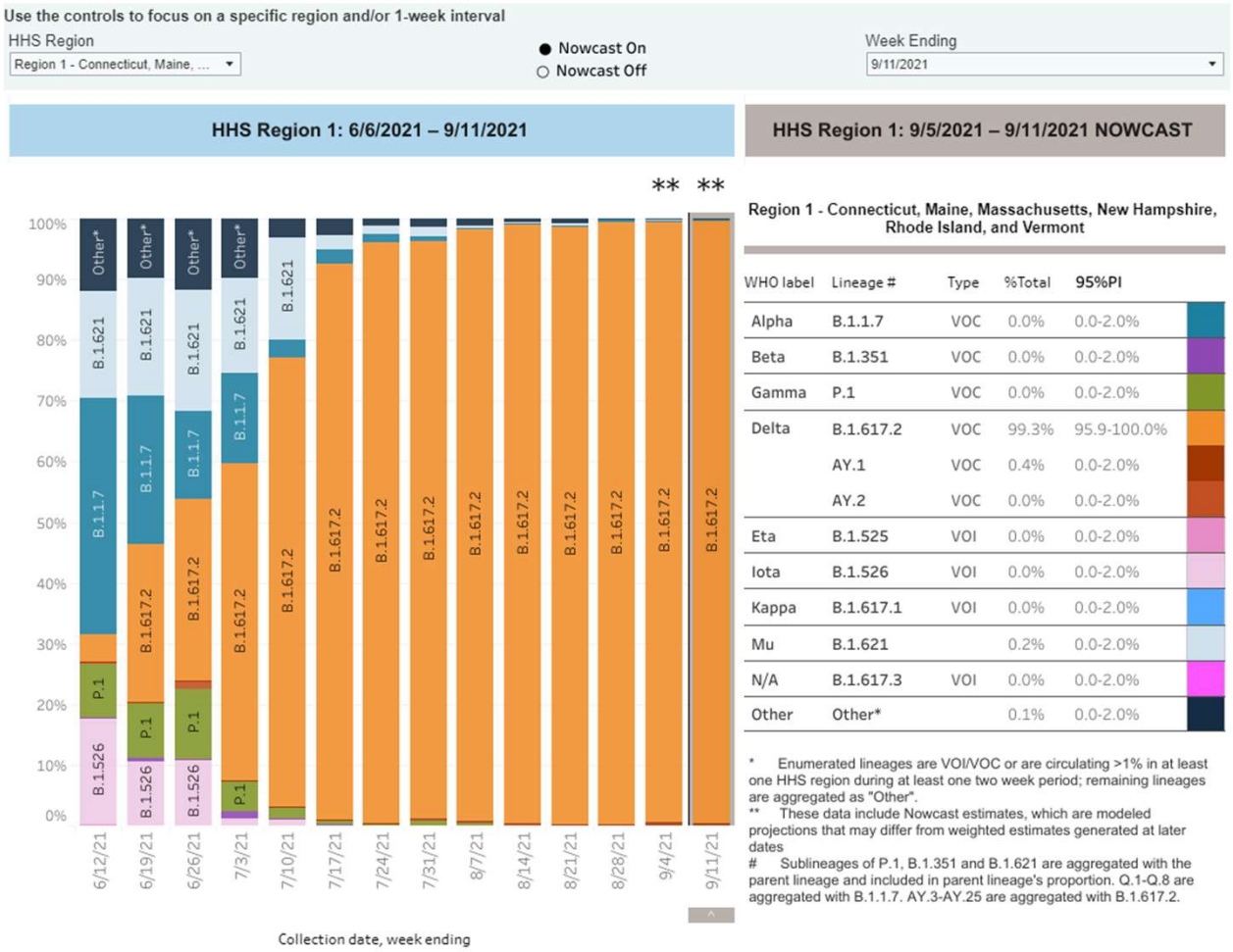
USA

WHO label	Lineage #	Type	%Total	95%PI
Alpha	B.1.1.7	VOC	0.0%	0.0-0.2%
Beta	B.1.351	VOC	0.0%	0.0-0.2%
Gamma	P.1	VOC	0.0%	0.0-0.2%
Delta	B.1.617.2	VOC	99.4%	98.6-100.0%
	AY.1	VOC	0.2%	0.0-0.7%
	AY.2	VOC	0.1%	0.0-0.5%
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%
Mu	B.1.621		0.1%	0.0-0.5%
N/A	B.1.617.3	VOI	0.0%	0.0-0.2%
Other	Other*		0.2%	0.0-0.7%

* 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, B.1.351 and B.1.621 are aggregated with the parent lineage and included in parent lineage's proportion. Q.1-Q.8 are aggregated with B.1.1.7. AY.3-AY.25 are aggregated with B.1.617.2.

Source: Centers for Disease Control and Prevention

Variants Distribution within the Northeast



Region 1 - Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont

WHO label	Lineage #	Type	%Total	95%PI
Alpha	B.1.1.7	VOC	0.0%	0.0-2.0%
Beta	B.1.351	VOC	0.0%	0.0-2.0%
Gamma	P.1	VOC	0.0%	0.0-2.0%
Delta	B.1.617.2	VOC	99.3%	95.9-100.0%
	AY.1	VOC	0.4%	0.0-2.0%
	AY.2	VOC	0.0%	0.0-2.0%
Eta	B.1.525	VOI	0.0%	0.0-2.0%
Iota	B.1.526	VOI	0.0%	0.0-2.0%
Kappa	B.1.617.1	VOI	0.0%	0.0-2.0%
Mu	B.1.621		0.2%	0.0-2.0%
N/A	B.1.617.3	VOI	0.0%	0.0-2.0%
Other	Other*		0.1%	0.0-2.0%

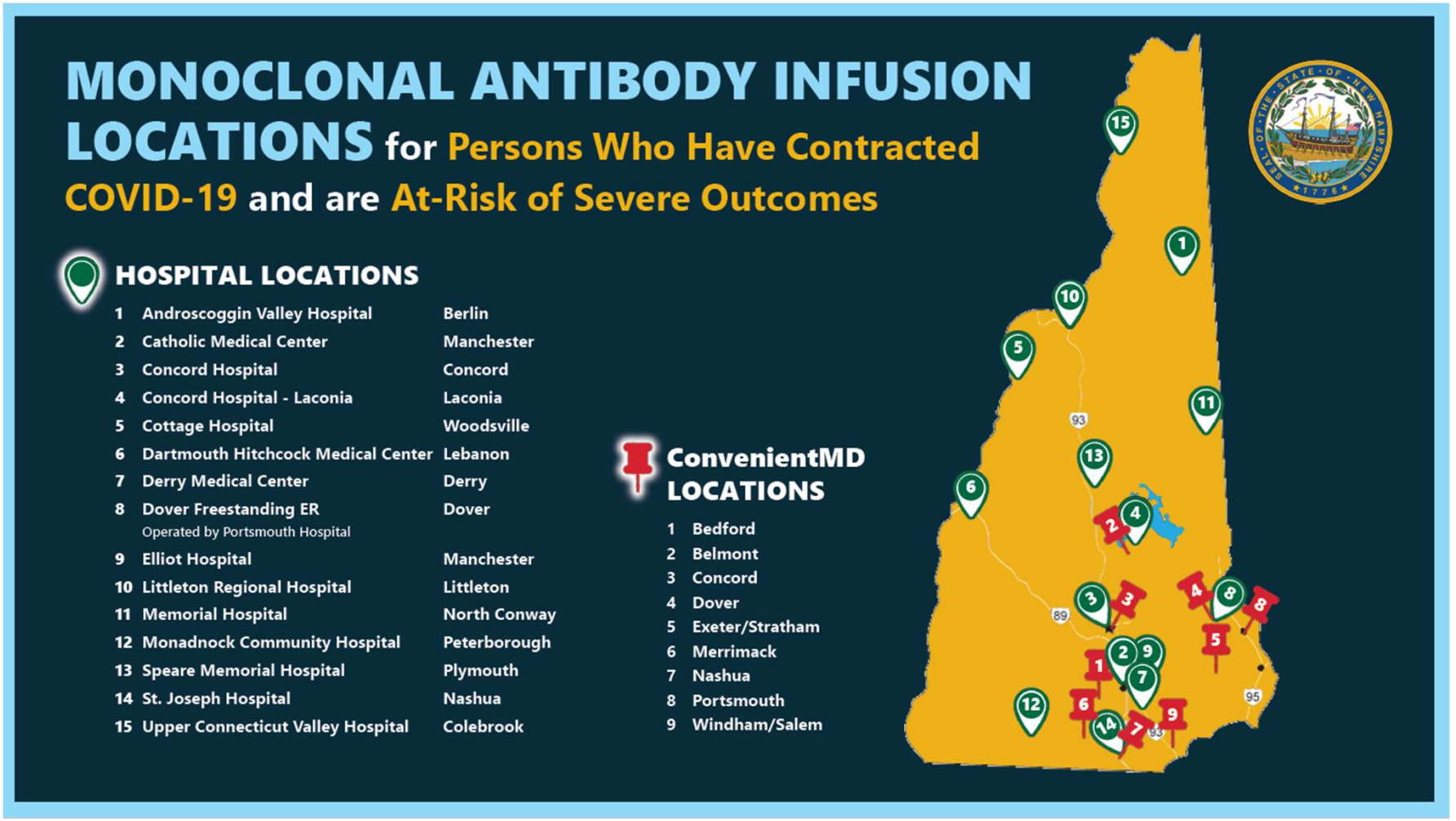
* Enumerated lineages are VOI/VOC or are circulating >1% in at least one HHS region during at least one two week period; remaining lineages are aggregated as "Other".

** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates

Sublineages of P.1, B.1.351 and B.1.621 are aggregated with the parent lineage and included in parent lineage's proportion. Q.1-Q.8 are aggregated with B.1.1.7. AY.3-AY.25 are aggregated with B.1.617.2.

Source: Centers for Disease Control and Prevention

Outpatient Locations for Monoclonal Antibodies



https://www.dhhs.nh.gov/dphs/cdcs/covid19/documents/monoclonal-antibody-map.pdf

Pharmacies with mAB that service Skilled Nursing Facilities

Omnicare of New Hampshire
Health Direct
Northeast Pharmacy Services
Pharmerica

Thank you for all of your work and service!