Yale NewHaven Health

TO: **YNHHS MEDICAL STAFF**

FROM: **YNHH ANTIMICROBIAL STEWARDSHIP COMMITTEE**

SUBJECT: **UPDATE TO YNHHS CRITERIA FOR COVID-19 MONOCLONAL ANTIBODY THERAPY**

DATE: **DECEMBER 3, 2021**

Situation:
Over the past few weeks, there has been a marked increase in the number of COVID-19 cases in CT and RI. In parallel, the demand for monoclonal antibody therapy to treat mild to moderate COVID-19 has increased significantly which has impacted our ability to provide timely therapy within the 7-day window from the date of a patient's positive SARS CoV-2 PCR/Ag test.

Background:
Monoclonal antibody therapy for mild to moderate COVID-19 was evaluated in unvaccinated individuals and reduced the risk for hospitalization and death within 29 days of receiving the medication as noted in the table below:[1,2,3]

Therapy	All Cause Hospitalization or Death Through Day 29
Imdevimab-Casirivimab vs. Placebo	7/736 (1.0%) vs. 24/748 (3.2%)
Sotrovimab vs. Placebo	3/291 (1.0%) vs. 21/292 (7%)
Bamlanivimab-Etesevimab vs. Placebo	4/511 (0.8%) vs. 15/258 (5.8%)

The FDA's current Emergency Use Authorization, which delineates the criteria for using monoclonal antibody therapy for COVID-19, does not address COVID-19 vaccination status given the studies' participants were unvaccinated.[4]

However, individuals who mount an effective immune response to COVID-19 vaccination, have a much lower risk of hospitalization then unvaccinated individuals. [5]

COVID-19 vaccine effectiveness* against COVID-19–associated hospitalization among adults without immunocompromising conditions, by vaccine product — 21 hospitals in 18 U.S. states, March–August 2021

Vaccine/Period	Vaccinated patients/Total patients (%)		VE against COVID-19 hospitalization (95% CI)
	Case-patients	Control-patients	
Moderna VE after full vaccination			
Full surveillance period[§]	54/1,517 (3.6)	422/1,321 (31.9)	93 (91–95)
14–120 days after full vaccination	36/1,499 (2.4)	345/1,244 (27.7)	93 (90–95)
>120 days after full vaccination	18/1,481 (1.2)	77/976 (7.9)	92 (87–96)
Pfizer-BioNTech VE after full vaccination			
Full surveillance period	128/1,591 (8.0)	610/1,509 (40.4)	88 (85–91)
14–120 days after full vaccination	65/1,528 (4.3)	495/1,394 (35.5)	91 (88–93)
>120 days after full vaccination	63/1,526 (4.1)	115/1,014 (11.3)	77 (67–84)
Janssen (Johnson & Johnson) VE after full vaccination			
Full surveillance period	37/1,500 (2.5)	76/975 (7.8)	71 (56–81)
>28 days after full vaccination	33/1,496 (2.2)	59/958 (6.2)	68 (49–80)

So, when prioritizing patients for such therapy during a period when our capacity to deliver it in a timely fashion is constrained, vaccination status is an important factor. This approach has been endorsed in the current NIH COVID-19 Treatment Guidelines.[6]

Assessment:
To ensure availability in a timely manner (i.e., within 7 days of a positive SARS CoV-2 PCR/antigen test) for patients at the highest risk from complications from COVID-19, the criteria for the use of monoclonal antibody therapy for mild to moderate COVID-19 need to be revised.

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Recommendations:
EFFECTIVE IMMEDIATELY, the YNHHS clinical criteria for monoclonal antibody therapy have been TEMPORARILY revised to incorporate a patient's prior COVID-19 vaccination status as delineated below.

COVID 19 Vaccination Status	Clinical Criteria for Use for COVID-19 Monoclonal Antibody Therapy
Unvaccinated OR Not Fully Vaccinated*	**1) Patient is ≥ 65 years of age** **OR** **2) Patients (ages 12 to 64) with ANY of the following co-morbidities:** • **Obesity or overweight (BMI > 25 kg/m^2 or age 12-17 or have BMI ≥ 85th percentile for their age & gender based on CDC growth charts)** • **Diabetes mellitus** • **Cardiovascular disease (including hypertension or congenital heart disease)** • **Chronic lung disease (e.g., COPD, moderate to severe asthma, ILD, CF, pulmonary HTN)** • **Chronic kidney disease** • **Immunosuppressive disease or immunosuppressive treatment** • **Pregnancy** • **Cirrhosis** • **Parkinson's disease** • **Sickle cell disease** • **Neurodevelopmental disorders (e.g., cerebral palsy) or other conditions that confer medical complexity (e.g., genetic or metabolic syndromes and congenital abnormalities)** • **Having medical-related technology dependence (e.g., tracheostomy, gastrostomy, or positive pressure ventilation [not related to COVID-19])**

Previously Vaccinated	**Age ≥ 65 years and have NOT received a booster dose of COVID-19 vaccine**
	OR
	Unlikely to mount an effective response to COVID-19 vaccination defined below:
	• **Active hematologic malignancy:**
	  • **Acute leukemia (myeloid or lymphoid)**
	  • **Lymphoblastic lymphoma**
	  • **S/P CAR-T therapy**
	  • **S/P allogeneic or autologous stem cell transplant**

	• **S/P solid organ transplant**
	• **HIV disease AND CD4 count < 200/mm^3**
	• **Sphingosine 1-phosphate modulators (fingolimod, ozanimod and siponimod)**

	Have received/actively receiving any of the following monoclonal antibodies or immunosuppressive therapies during the time frame listed:
	• **Received mycophenolate mofetil (MMF) in the last 6 months**
	• **Received Anti-B cell agents in the last 6 months:**
	  ○ **Rituximab, ofatumumab, obinutuzumab, ocrelizumab, blinatumomab**
	• **Received purine analog therapy in the last 6 months:**
	  ○ **Cladribine**, clofarabine, nelarabine, fludarabine, pentostatin, mercaptopurine****
	• **Alemtuzumab in the last 12 months**

*Fully vaccinated is defined by the CDC as 2 weeks after their 2nd dose of a 2-dose vaccine series (Pfizer, Moderna) or 2 weeks after a single dose vaccine (Janssen-J&J).
** When used at doses for oncologic indications

References:

1. Weinreich DM et al. REGEN-COV Antibody Combination and Outcomes in Outpatients with Covid-19. *NEJM* 2021; NEJMoa2108163.doi: 10.1056/NEJMoa2108163.
2. Gupta A et al. Early Treatment for Covid-19 with SARS-CoV-2 Neutralizing Antibody Sotrovimab. *NEJM* 2021;385:1941-50.
3. Dougan M et al. Bamlanivimab plus Etesevimab in Mild or Moderate Covid-19. *CID* 2021; Oct 28;ciab912.doi: 10.1093/cid/ciab912.
4. Anonymous. Full Emergency Use Authorization (EUA) Prescribing Information for Casirivimab/Imdesivimab. Revised 11/2021.
   Available at: https://www.fda.gov/media/145611/download
5. CDC. Comparative Effectiveness of Moderna, Pfizer-BioNTech, and Janssen (Johnson & Johnson) Vaccines in Preventing COVID-19 Hospitalizations Among Adults Without Immunocompromising Conditions — United States, March–August 2021. *MMWR* 2021;70(38);1337–1343.
6. NIH. Updated COVID-19 Treatment Guidelines Panel's Statement on the Prioritization of Anti-SARS-CoV-2 Monoclonal Antibodies for the Treatment or Prevention of SARS-CoV-2 Infection When There Are Logistical or Supply Constraints. Updated October 27, 2021.
   Available at: https://www.covid19treatmentguidelines.nih.gov/therapies/updated-statement-on-the-prioritization-of-anti-sars-cov-2-mabs/