Utah Crisis Standards of Care Monoclonal Antibody Allocation Guidelines

Feb 3, 2021

Produced in cooperation with

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About the Guidelines

The purpose of this document is to guide the allocation of monoclonal antibody therapies while they are a scarce patient care resource, and after being issued an Emergency Use Authorization (EUA) by the US FDA. Ongoing studies suggest that these therapies may be effective in reducing viral load, symptoms, and the risk of hospitalization in patients recently diagnosed with mild to moderate Covid-19. Current available but scarce therapies include bamlanivimab and casirivimab/imdevimab.

The FDA determines allocation of scarce therapies by state based on confirmed hospitalizations and confirmed cases (7-day averages). A committee process to determine ethical allocation frameworks within states is recommended by the U.S. Department of Health and Human Services. The Scarce Medications Allocation Subcommittee of the Utah Crisis Standards of Care Workgroup has developed additional criteria beyond the EUA to ensure that the drug is prescribed fairly and to patients who are most likely to benefit from it. This subcommittee consists of physicians trained in critical care, infectious disease, pediatrics, and internal medicine; hospital pharmacists, and experts in allocation frameworks and ethics. The foundation of our approach to crisis standards of care is that allocation decisions must be based on criteria that ensure that every patient has equitable access to any care from which they might benefit. This protocol meets the CSC ethical goals of fairness, duty to care, transparency, consistency, proportionality, and accountability.

Application of these guidelines will require and depend on physician judgment at the point of patient care. This document will be updated as needed.

Scope of this Document

Where: These triage guidelines apply to all healthcare professionals, clinics, facilities and patients in the state of Utah. Monoclonal antibody therapies may only be administered in settings in which health care providers have immediate access to medications to treat a severe infusion reaction, such as anaphylaxis, and the ability to activate the emergency medical system (EMS), as necessary.

When: This guideline is in effect while therapies are in limited supply, as determined by the Utah Crisis Standards of Care Scarce Medications Subcommittee. The initial projected supply could only treat about 2% of all cases over one month. The health systems have agreed to administer these therapies according to the criteria set forth in this state guideline. We rely on each system's antimicrobial stewardship programs to encourage and verify adherence to the guideline. Monoclonal antibody therapies should be given as soon as possible after a positive direct SARSCoV-2 viral test and within 7 days of symptom onset. Patients receiving monoclonal antibody therapy should consider waiting 90 days before receiving SARS-CoV vaccine.

Pediatric Patient Selection Criteria (age < 18 yo)

Children must meet ALL Inclusion Criteria:

- Between 12 years and 18 years of age
- At least 88 pounds (40 kg)
- Laboratory-confirmed COVID-19 (PCR or Antigen)
- Symptomatic, with no more than 7 days from symptom onset
- NOT being admitted or already admitted to an acute care hospital for COVID 19 specifically, or COVID related complications
- NOT pregnant
- **Must have B-cell immunodeficiency** [primary or acquired (e.g. rituximab therapy, certain types of cancer treatment that are B-cell depleting therapies)]

If your child meets the criteria above and you are interested in COVID-19 monoclonal antibody therapy, please talk with your child's specialist physician (e.g. rheumatologist, immunologist, or oncologist). If your child's provider determines that your child meets the eligibility criteria, the provider should send an email regarding eligible pediatric patients to: Pediatric.MonoclonalAntibodies@imail.org

Pediatric Criteria Rationale:

Children have a lower risk of hospitalization from COVID-19 infection than adults and therefore are less likely to benefit from monoclonal antibody therapy. Studies using COVID-19 monoclonal antibody therapy have NOT included children so it is unclear if children would benefit from the drug. In addition to the uncertainty of benefit, although rare, there is a risk of anaphylaxis and infusion related reaction with the administration of the COVID-19 antibody therapy. We do not have enough information to know if the potential benefits of this therapy in children outweigh the risks.

A serious effect of COVID-19 in children is multisystem inflammatory syndrome in children (MIS-C). This is a condition where multiple organs such as the heart, lungs, brain, kidneys, skin, eyes, and gastrointestinal system become inflamed. Although we do not fully understand what causes this, antibodies to COVID-19 are found in the blood of most children with MIS-C. We do NOT know the effect of COVID-19 monoclonal antibody therapy on risk of MIS-C.

Given that children are less likely to benefit from COVID-19 monoclonal antibody than adults (even adolescents with high-risk conditions), the unknown benefit and the lack of safety information for this drug in children, monoclonal antibody therapy should be considered experimental and should only be considered for children at highest risk of serious complication.

Adult Patient Selection Criteria

Adults must meet ALL Inclusion Criteria:

- Adult ≥ 18 yo
- Laboratory-confirmed COVID-19 (PCR or Antigen)
- Symptomatic, with no more than 7 days from symptom onset
- Utah COVID-19 Risk Score* *greater than threshold listed on the Utah Novel Therapeutics site: https://coronavirus.utah.gov/noveltherapeutics*
- NO new hypoxemia (SpO2<90% on room air or receiving new/increased supplemental oxygen)
- NOT being admitted or already admitted to an acute care hospital for COVID-19 specifically, or COVID-19 related complications*
- NOT pregnant (inadequate safety data)

* Monoclonal antibodies should NOT be used in patients hospitalized for COVID or COVID related issues because trials have shown that they are not useful for patients hospitalized for COVID. We realize though that there may be rare circumstances where a patient may be admitted for non-COVID reasons, and incidentally is found to have acute COVID with mild symptoms developing within prior 7 days but no new hypoxia, and is at high risk of developing severe disease according to the Risk Score, in whom treatment with monoclonal antibodies may be justifiable.

Utah COVID-19 Risk Score

Demographic Risk Factors	**Points**
Male	**1**
Age	**0.5 for every decade:** 18-20=**1**, 21-30=**1.5**, 31-40=**2**, 41-50=**2.5**, 51-60=**3**, 61-70=**3.5**, 71-80=**4**, 81-90=**4.5**, 91-100=**5**, >100=**5.5**
Non-White race or Hispanic/Latinx ethnicity	**2**
Highest-Risk Comorbidities	
Diabetes mellitus	**2**
Severely immunocompromised	**2**
Obesity (BMI>30)	**2**
Other High-Risk Comorbidities	
Hypertension	**1**
Coronary artery disease	**1**
Cardiac arrhythmia	**1**
Congestive heart failure	**1**
Chronic kidney disease	**1**
Chronic pulmonary disease	**1**
Chronic liver disease	**1**
Cerebrovascular disease	**1**
Chronic neurologic disease	**1**
Symptom Risk Factor	
New shortness of breath	**1**
Total	

Adult Risk Score Rationale: The EUA clinical criteria identify a larger eligible population, comprising more than 27% of positive patients in Utah. However, because the currently available supply of monoclonal antibody therapies is sufficient to treat only 2% of positive cases, an accurate and flexible method is needed to prioritize limited drug to patients at highest risk of hospitalization who are most likely to benefit.

Tool Development: Risk factors for hospitalization and mortality are now well-recognized and include age, cumulative comorbidities, male gender, shortness of breath, and importantly, but for reasons not well-understood, non-white race/ethnicity. In order to identify a model that would perform well in our state, the committee validated a modified version of a published risk stratification tool in a population of >22,000 consecutive Utahns with COVID-19. The test performance of the tool is reported below.

Utah COVID-19 Risk Score Threshold: The threshold above which patients are eligible for treatment with monoclonal antibody therapies will be determined based on supply of the therapy relative to patient demand. We will strive to maximize its effectiveness in the community, while ensuring fair and equitable allocation. The initial threshold chosen was a score greater than 8. Because of increased drug availability, the threshold was later changed to 7. Please see the Utah Novel Therapeutics site (https://coronavirus.utah.gov/noveltherapeutics) for the current threshold.

Patient Features/Comorbidity Definitions: Please see the Appendix for definitions for each patient feature and comorbidity. To ensure recommended use of this scarce resource, providers must verify patient eligibility, including adherence to the definitions, prior to ordering treatment.

Ethical Justification for Using Race/Ethnicity in Patient Selection: COVID-19 has had a disproportionate impact on low income communities and certain racial/ ethnic minorities in the United States. Equity calls attention to the systematic differences in health outcomes and opportunities to be healthy that adversely affect socially discounted and/or marginalized groups. For Covid-19, these inequities may arise from higher burdens of preexisting comorbid disease, poor health care access, or not having the option for social distancing due to living in densely populated neighborhoods or households. There are also more economically disadvantaged individuals working essential jobs during the pandemic, and many are unable to perform job functions from the safety of their home. This puts them at greater risk of interacting with others who may transmit Covid-19. Public health interventions may be used to attempt to mitigate these disparities in Covid-19 by recognizing the structural inequities that underlie them. One way to do this is to include race/ethnicity in the patient selection criteria.

Risk Score Accuracy:

Derivation Cohort, n=16,030				Validation Cohort, n=5976			
Hospitalization		28-day Mortality		Hospitalization		28-day Mortality	
AUROC	95% CI	AUROC	95% CI	AUROC	95% CI	AUROC	95% CI
0.82	0.81-0.84	0.91	0.83-0.94	0.8	0.78-0.82	0.8	0.69-0.9

Point Threshold	Sensitivity	Specificity	PPV	NPV	% of Positives
3	95.0%	28.5%	7.5%	98.9%	72.8%
4	89.1%	45.7%	9.3%	98.5%	56.3%
5	80.6%	62.8%	12.1%	98.1%	39.8%
6	71.1%	76.2%	16.6%	97.5%	26.7%
7	60.9%	84.1%	20.6%	97.0%	18.7%
8	51.4%	89.2%	24.4%	96.4%	13.4%
9	41.4%	92.8%	28.2%	95.9%	9.4%
10	32.3%	95.2%	31.7%	95.4%	6.5%
11	25.0%	97.0%	36.1%	94.9%	4.4%
12	17.4%	98.1%	38.5%	94.6%	2.9%

Health System Distribution

State Unified Command will allocate drug to health systems in proportion to weekly infusion appointment capacity. Each system has agreed to follow this guidance but will have flexibility to determine internal operations for accepting referrals, verifying eligibility, managing appointments, writing orders, managing pharmacy distribution and follow up. Systems will redistribute drug within and between systems on an as needed basis with the goal of fair and equitable delivery to patients.

Connecting Eligible Patients with Treatment

Go to the UDOH Novel Therapeutics site (Link to website) for updated delivery locations. Patient eligibility must be confirmed by the ordering provider by calculating the presenting patient's risk score with reference to comorbidity definitions listed in the appendix.

Within the constraints of scarce medication delivery, maintaining equitable access to this and other drugs is top priority to the committee. Patients access care in many ways. To that end we recommend a layered approach to outreach and referral. Where available, prospective screening for eligible patients at the time of test notification is ideal, but logistically challenging. We will work with test providers in the state to include links on test result notifications directing patients to testing locations as well as signage at testing locations. Emergency departments, urgent care and primary care clinics are also important outreach venues where information on drug availability should be posted. We will work with health systems to educate providers on this new resource, eligibility criteria and referral pathways. Finally, community outreach groups may be best positioned to raise awareness in disadvantaged populations.

Appendix – Patient Features/Comorbidity Definitions

Feature	Detailed Definition
Male gender	Does the patient identify as "male?" Male gender is associated with increased risk of severe COVID-19 for reasons that are not fully understood; non-binary and transgender patients may choose to answer this question with that background information.
Non-white race or Hispanic/Latinx ethnicity	Does the patient identify as *either* a race other than "White" or as Hispanic/Latinx?
Shortness of Breath	Applies to patients with symptomatic COVID-19 who are experiencing shortness of breath *beyond their usual baseline*.
Diabetes mellitus	Diagnosed with type I, type II or gestational diabetes by a physician. Pre-diabetes does not qualify.
High Blood Pressure	Diagnosed with high blood pressure by a physician, whether on medications or not.
Cardiovascular Disease	Has the patient had a heart attack or been diagnosed with cardiovascular disease by a physician?
Cardiac Arrhythmia	Has the patient been diagnosed with a supraventricular or ventricular arrhythmia by a physician? Premature ventricular contractions (PVCs) do not qualify.
Chronic Lung Disease	Has the patient been diagnosed with COPD, emphysema, asthma or other less common chronic pulmonary diseases by a physician?
Chronic Kidney Disease	Has the patient been diagnosed with Chronic Kidney Disease Stage III or worse?
Congestive Heart Failure	Has the patient been diagnosed with any type of heart failure (reduced or preserved ejection fraction) or cardiomyopathy by a physician?
Chronic Liver Disease	Has the patient been diagnosed with a chronic liver disease, such as cirrhosis of any stage, non-alcoholic steatohepatitis (fatty liver), chronic viral hepatitis, or other less common disorder by a physician?
Obesity	Does the patient currently have a body mass index of >30 https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm
Severely Immunocompromised	Does the patient have any of the following immunocompromised features: Recipient of a solid organ or hematopoietic (bone marrow) transplant; taking immunosuppressive drugs including calcineurin inhibitors, anti-proliferative agents like mycophenolate or azathioprine, TNF-alpha or other drugs used for autoimmune conditions or systemic steroids of more than 20mg prednisone-equivalent per day for more than 4 weeks; HIV with AIDS; Receiving active chemotherapy; B cell immunodeficiency such as common variable immunodeficiency.
Cerebrovascular disease	Has the patient had a stroke or transient ischemic attack?
Neurological Disease	Has the patient been diagnosed with a systemic neurologic disease such as multiple sclerosis, Parkinson's disease, dementia and other neurodegenerative conditions, myasthenia gravis, or other less common conditions by a physician? Migraines, local neuropathies, and fibromyalgia do not qualify.