Utah Crisis Standards of Care Scarce COVID Therapeutics Allocation Guidelines

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Produced in cooperation with

UHA UTAH HOSPITAL ASSOCIATION

UTAH DEPARTMENT OF HEALTH

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V23 Updates

-Removed paxlovid from eligibility determination using the Utah COVID-19 Risk Score, as this product is not in scarcity in Utah at this time.
-Extended the days since symptom onset to 10 days in Utah COVID-19 Risk Score.
-Restored automatic eligibility for residents of congregate settings, such as skilled nursing facilities, correctional facilities, or the like. This is detailed under the "Where" section of this guidance.

About the Guidelines

The purpose of this document is to guide the allocation of COVID therapies while they are a scarce patient care resource, and after being issued an Emergency Use Authorization (EUA), with updates, by the US FDA. Ongoing studies suggest that monoclonal antibodies and some novel oral medications are effective in reducing viral load, symptoms, and the risk of hospitalization in patients recently diagnosed with mild to moderate COVID-19 and in preventing infection in high-risk individuals who have had a direct exposure to someone with COVID-19. This document will continue to be updated as needed.

A committee process to determine ethical allocation frameworks within states is recommended by the U.S. Department of Health and Human Services. The development of crisis standards of care and other resource scarcity guidance is also a performance measure for the Hospital Preparedness Program cooperative agreement awarded to states. The Scarce Medications Allocation Subcommittee of the Utah Crisis Standards of Care Workgroup has developed additional criteria beyond the EUA to ensure that scarce products are prescribed 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.

This committee is acutely aware of the pressure that COVID is placing on our hospitals, caregivers, and society. We are very supportive of expanding eligibility to all patients that might benefit, as outlined in the EUA. However, we continue to deliver these therapies primarily within existing and already stressed healthcare systems, and drug supplies and healthcare capacity are limited.

Scope of this Document

Why: Monoclonal antibodies are effective at reducing viral levels, attenuating progression of disease and preventing hospitalization or death when administered to high-risk patients early in their symptom course. However, during surge phases of the current pandemic, FDA EUA criteria identify an eligible population that exceeds maximum statewide capacity and supply to provide monoclonal antibody infusions and treatments. To equitably prioritize limited drug to patients at highest risk of hospitalization who are most likely to benefit, an accurate risk-assessment tool was developed using Utah data. Depending on community transmission levels, treatment capacity, and product supply statewide, eligibility thresholds can be adjusted to allow dynamic demand-capacity matching. As infusion capacity and available drug supply increases, the eligibility criteria will be expanded to provide access to a larger group of progressively lower-risk patients. Utah's 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.

As of August 2021, given COVID-19 vaccination provides strong protection against severe disease and need for hospitalization, we recommend targeting scarce therapies to patients with COVID-19 who are either not previously fully vaccinated or those who remain at high risk for hospitalization or death despite vaccination.

The rationale for this decision is based on the following factors:

1) Capacity to provide these therapies remains limited compared to the number of new COVID-19 cases occurring daily.
2) The primary objective of these therapies is to prevent hospitalization and death.
3) Risk of hospitalization and mortality is dramatically decreased in fully vaccinated individuals with breakthrough COVID-19. Vaccinated patients who are ultimately admitted tend to be immunocompromised and those with advanced age and multiple medical comorbidities, with an average COVID Risk Score of 9. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8261136)
4) The committee regularly reviews published literature and local data from UDOH and Utah healthcare systems to inform decision making about risks for hospitalization and characteristics of patients currently requiring hospitalization, ventilation, or dying from COVID-19. For this update, data from more than one hundred eighty-eight thousand Utahns with test-positive COVID-19 was analyzed and reviewed by this committee. As with prior analyses, these data again show significantly higher risk of hospitalization in those not fully vaccinated, patients with a greater combination of age and number of comorbidities, those experiencing shortness of breath and among patients who identify with certain race and ethnicity groups.
5) Clinical trial data confirms that compared to the very strong benefit in unvaccinated, the effectiveness of these therapies in fully vaccinated individuals may be much lower.

Where: These eligibility guidelines apply to all healthcare professionals, clinics, facilities and patients in the state of Utah EXCEPT those in long term care facilities, skilled nursing facilities, correctional facilities and other similar congregate facilities. Patients in these facilities have increased risk of infection due to cohabitation and shared caregivers, have higher risk of hospitalization, and can often be treated simultaneously through our outreach teams. Providers should apply the EUA criteria and coordinate with UDOH Healthcare Associations Infections team to schedule treatments. 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.

Within the constraints of scarce medication delivery, maintaining equitable access 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 eligibility assessment 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 new resources, eligibility criteria, and referral pathways. Finally, community outreach groups may be best positioned to raise awareness in underserved populations.

When: Monoclonal antibodies should be given as soon as possible after a positive direct SARS-CoV-2 viral test; within 10 days of symptom onset for monoclonal antibodies. Patients receiving monoclonal antibody therapy should consider waiting 90 days before receiving SARS-CoV vaccine.

What: Due to increased incidence of Omicron which has greater resistance to monoclonal antibody monotherapies, as of Dec 29, 2021 and in alignment with HHS guidance, we currently recommend exclusive use of sotrovimab. The two monoclonal products we previously offered (casirivimab/imdevimab (Regeneron) and bamlanivimab/etesevimab (Eli Lilly) have no neutralizing activity against the Omicron variant. Paxlovid has also received an FDA EUA and is effective against Omicron. Importantly, this committee does NOT endorse routine or widespread use of the other currently available oral therapy, molnupiravir, because of very limited efficacy as well as safety concerns. Please see the Utah COVID-19 Treatments site (https://coronavirus.utah.gov/treatments/) for the current recommended therapies.

Post-Exposure Prevention

With the dominance of the Omicron variant, and extreme scarcity of effective therapies, we no longer recommend the use of these therapies for post-exposure prevention. The FDA EUA for sotrovimab excludes post-exposure prophylaxis from eligible use of this product.

Connecting Eligible Patients with Treatment

For adult patients age 18 years or greater, go to the UDOH COVID-19 Treatments site (https://coronavirus.utah.gov/treatments/) 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. The Utah COVID-19 Risk Score calculator is located in the Novel Therapeutics section of the webpage - https://coronavirus.utah.gov/noveltherapeutics/

For pediatric patients from 12 years of age but less than age 18 years, 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 (using the under 16 or 16 and over cut points), the provider should send an email regarding eligible pediatric patients to: Pediatric.MonoclonalAntibodies@imail.org

Patient < 16 yo Selection Criteria

Children must meet ALL Inclusion Criteria:

- Must be at least 12 years and up to and including 15 years of age
- At least 88 pounds (40 kg)
- Test confirmed COVID-19 (PCR or Antigen; home or lab)
- Symptomatic, with no more than 10 days from symptom onset
- NOT being admitted or already admitted to an acute care hospital for COVID-19 specifically, or for COVID related complications
- **Must have one of the following risk factors for severe disease:**
    - Recipients of CAR-T therapy (2 years)
    - Recipient of allogeneic stem cell transplant (2 years or receiving immunosuppressants)
    - Recipient of B-cell depleting therapy within 6 months (e.g. rituximab, ocrelizumab, ofatamumab, alemtuzumab)
    - Patient with severe primary humoral immunodeficiency

Pediatric Criteria Rationale: 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. Our hospitalization data supports the use of monoclonal antibodies only in the groups of patients listed above.

Patient ≥ 16 yo Selection Criteria

Age ≥ 16 yo must meet ALL Inclusion Criteria:

- Test confirmed COVID-19 (PCR or Antigen; home or lab)
- Symptomatic, with no more than 10 days from symptom onset
- 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 for COVID-19 related complications[1]

IF meeting above inclusion criteria AND severely immunocompromised[2] then patient is eligible, regardless of vaccination status.

IF meeting above inclusion criteria AND NOT severely immunocompromised, determine eligibility based on COVID-19 vaccination status[3] and other factors:

- IF NOT fully vaccinated AND Age 75 or greater, the patient is eligible.
- IF NOT fully vaccinated AND Pregnant[4], the patient must have a Utah COVID-19 Risk Score greater than 3.5 (=4 or more).
- IF NOT fully vaccinated, the patient must have a Utah COVID-19 Risk Score greater than 5.5 (=6 or more).
- IF fully vaccinated, the patient must have a Utah COVID-19 Risk Score greater than 7.5 (=8 or more).

Utah COVID-19 Risk Score

Demographic Risk Factors	Points
Age	**0.5 for every decade:** 16-20=**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**
Highest-Risk Comorbidities	
Diabetes mellitus	**2**
Obesity (BMI>30 kg/m²)	**2**
Other High-Risk Comorbidities	
Active Cancer	**1**
Other immunosuppressive therapies and conditions	**1**
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	

1. Monoclonal outpatient treatment 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. There may be 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 10 days but no new hypoxia, and is at moderate to high risk of developing severe disease according to the Risk Score, in whom treatment with these therapies may be justifiable.

2. Severely Immunocompromised includes:

- Patients who are within 1 year of receiving B-cell depleting therapies (e.g., rituximab, ocrelizumab, ofatumumab, alemtuzumab, etc.)
- Chimeric antigen receptor T cell recipients (CAR-T cell therapy)
- Hematopoietic cell transplant recipients
- Patients with hematologic malignancies who are on active therapy
- Solid-organ transplant on anti-rejection drugs
- Patients with humoral or combined immunodeficiencies
- Patients with untreated HIV who have a CD4 T lymphocyte cell count <200 cells/mm^3
- Patients with autoimmune or inflammatory diseases on the following therapies: [anti-proliferatives: (azathioprine, mycophenylate)], calcineurin inhibitors (tacrolimus, cyclosporine, etc), CTLA-4 inhibitors (abatacept), JAK inhibitors (upicitinib, baracitinib, ruloxitinib, tofacitinib, etc)

The following immunosuppressive drugs do NOT automatically qualify a patient (see Appendix):

- Methotrexate, hydroxychloroquine, leflunomide, chronic steroids
- TNF inhibitors (etanercept, infliximab, adaliumuab, cetrolizumab, golimumab)
- IL 12/23 Inhibitor (ustikinumab. guselkumab)
- IL-17 -Inhibitor (secukinumab, ixekizumab)
- IL-1 Inibitor (anakinra, canakinumab, rilonacept)
- Hormone therapy for breast or prostate cancer (tamoxifen, raloxifene, leuprolide, anastrozole, letrozole)
- Integrin inhibitors (Vedolizumab, Natalizumab)
- Immunotherapy (pembrolizumab, ipilimumab, nivolumab, atezolizumab, avelumab, durvalumab, cemiplimab)
- Myelosuppressive chemotherapy for solid tumor malignancy

Patients with active malignancies or use of immunosuppressive treatments for an autoimmune or inflammatory condition not meeting the severely immunocompromised definition are assigned points per the risk score.

3. Fully vaccinated is defined as having one dose of the Johnson and Johnson vaccine, or 2 doses of an mRNA vaccine (Pfizer or Moderna), and 2 weeks or more have passed since the final dose in the series.

4. We strongly recommend that COVID therapies be prioritized for pregnant patients, given their greater risk for progression to severe COVID-19 disease and adverse pregnancy-specific outcomes. Pregnant patients were not included in the clinical trials for monoclonal antibodies. FDA emergency use authorization for these therapies recommends that patients and providers consider the possible benefits and risks of treatment.

Utah COVID-19 Risk Score Threshold: As novel therapeutics for COVID-19 have emerged, strategies that focus treatment on patients whose clinical and demographic features place them at highest risk of developing severe disease and poor outcomes have proven effective in optimizing

clinical efficacy and minimizing harm. In the case of mAbs, a risk-targeted approach has been very successful in delivering infusions to patients who are most likely to derive the greatest clinical benefit. The threshold above which patients are eligible for treatment with federally-allocated therapies is determined based on supply of the therapy relative to patient demand. When necessitated by scarcity of these resources, the goal of this prioritization framework is to maximize its effectiveness in the community, while ensuring fair and equitable allocation. As of August 2021, given COVID-19 vaccination provides strong protection against severe disease and need for hospitalization, we recommend targeting therapies to patients with COVID-19 who are either not previously fully vaccinated or those whom are at greatest risk despite full vaccination. To ensure recommended use of this scarce resource, providers must verify patient eligibility, including adherence to the definitions, prior to ordering treatment.

Appendix – Patient Features/Comorbidity Definitions

Feature	Detailed Definition
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	Adapted from the NIH Guidelines for Prioritization of COVID-19 Therapeutics: • Patients who are within 1 year of receiving B-cell depleting therapies (e.g., rituximab, ocrelizumab, ofatumumab, alemtuzumab, etc.) • Chimeric antigen receptor T cell recipients (CAR-T cell therapy) • Hematopoietic cell transplant recipients • Patients with hematologic malignancies who are on active therapy • Solid-organ transplant on anti-rejection drugs • Patients with humoral or combined immunodeficiencies • Patients with untreated HIV who have a CD4 T lymphocyte cell count <200 cells/mm^3 • Patients with autoimmune or inflammatory diseases on the following therapies: [anti-proliferatives: (azathioprine, mycophenylate)], calcineurin inhibitors (tacrolimus, cyclosporine, etc), CTLA-4 inhibitors (abatacept), JAK inhibitors (upicitinib, baracitinib, ruloxitinib, tofacitinib, etc)

Other immunosuppressive therapies	These drugs and conditions are also immunosuppressive but the degree of risk for severe disease or death in COVID-19 is not as high as the *severe* immunocompromised conditions defined by the NIH prioritization guidelines (see above). • Methotrexate, hydroxychloroquine, leflunomide, chronic corticosteroids • TNF inhibitors (etanercept, infliximab, adaliumuab, cetrolizumab, golimumab) • IL 12/23 Inhibitor (ustikinumab. guselkumab) • IL-17 -Inhibitor (secukinumab, ixekizumab) • IL-1 Inibitor (anakinra, canakinumab, rilonacept) • Integrin inhibitors (Vedolizumab, Natalizumab**)** • Immunotherapy (pembrolizumab, ipilimumab, nivolumab, atezolizumab, avelumab, durvalumab, cemiplimab) • Myelosuppressive chemotherapy for solid tumor malignancy • Asplenia and functional asplenia (sickle cell disease)
Active Cancer	Cancer not in remission, independent of treatment
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.