STAY SAFE MN

Suggested Criteria for Monoclonal Antibody Treatment of COVID-19 in Children

5/28/2021

Introduction

Since November 2020, the U.S. Food and Drug Administration (FDA) has issued several Emergency Use Authorizations (EUAs) to permit the emergency use of investigational monoclonal antibody (mAb) therapies for the treatment of mild to moderate COVID-19 in adult and pediatric patients. The currently authorized mAbs are:

- Casirivimab/Imdevimab (Regeneron) EUA issued November 21, 2020[1]
- Bamlanivimab/Etesevimab (Eli Lilly) EUA issued February 9, 2021[2]

The patient eligibility criteria listed in the EUA of each of the authorized monoclonal antibody therapies are identical. Each therapy is authorized for use in pediatric patients with positive results from direct SARS-CoV-2 viral testing who are age 12 to 17, weigh at least 40 kg, and are at high risk for progressing to severe COVID-19 and/or hospitalization.

As of May 14, 2021, the FDA has expanded eligibility criteria for mAb treatment.

- Per each EUA, high risk for **all patients older than 12 years** is now defined as meeting at least one of the following criteria: Older age (for example aged 65 years or older).
- Obesity or being overweight (for example, (for example, adults with BMI greater than 25 kg/m2, or if age 12-17, have BMI greater than or equal to 85th percentile for their age and gender based on CDC growth charts.
- Pregnancy.
- Chronic kidney disease.
- Diabetes.
- Immunosuppressive disease or immunosuppressive treatment.

[1] US Food and Drug Administration (FDA). Nov 21, 2020. Letter to Yunji Kim, PharmD, Regeneron Pharmaceuticals, Inc. https://www.fda.gov/media/143891/download

[2] US Food and Drug Administration (FDA). Feb 9, 2021. Letter to Christine Phillips, PhD, RAC, Eli Lilly and Company. https://www.fda.gov/media/145801/download

- 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 abnormalities).
- 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 mAbs under these EUAs 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-19, visit CDC: People with Certain Medical Conditions (www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html). Health care providers should consider the benefit-risk for an individual patient. Efficacy and safety data for the use of these monoclonal antibodies in pediatric patients is currently lacking. Initial guidance from the Pediatric Infectious Diseases Society recommends against their routine use in children and adolescents, while acknowledging that this guidance may be subject to change as more data becomes available. Refer to Initial Guidance on Use of Monoclonal Antibody Therapy for Treatment of Coronavirus Disease 2019 in Children and Adolescents (https://academic.oup.com/jpids/advance-article/doi/10.1093/jpids/piaa175/6060076).

Individual clinicians and institutions may choose to administer these agents on a case-by-case basis to pediatric patients who meet EUA criteria.

The suggested clinical criteria listed below for the use of mAbs in pediatric patients are designed to assist providers with clinical decision-making and was developed by an advisory group consisting of clinicians from Children's Minnesota, Mayo Clinic, and the University of Minnesota, in collaboration with the Minnesota Department of Health. The list does not supersede the current EUA eligibility criteria nor is the use of mAbs in pediatric patients in Minnesota restricted to these clinical criteria only. The list is a resource for providers to help identify patients most at risk for severe disease and hospitalization who may be most likely to benefit from mAb treatment and is based on expert clinical opinion. MDH gratefully acknowledges the assistance of this advisory group in the development of these criteria.

Please note that these are suggested criteria for **pediatric patients only, not adults.**

Fact sheets for providers

The U.S. Food and Drug Administration has issued revised fact sheets for health care providers to include additional information on susceptibility of SARS-CoV-2 variants to each of the mAb currently available. These fact sheets contain full EUA prescribing information, including eligibility criteria, contraindications, dosing and monitoring recommendations, and safety information on adverse reactions and hypersensitivity. These fact sheets are subject to revision as additional data emerges and providers are encouraged to review them for details regarding specific variants and potential resistance that may make the authorized mAb therapies less effective.

- Fact Sheet for Health Care Providers: Emergency Use Authorization for Casirivimab/Imdevimab (www.fda.gov/media/145611/download)

- Fact Sheet for Health Care Providers: Emergency Use Authorization for Bamlanivimab/Etesevimab (www.fda.gov/media/145802/download)

Suggested clinical criteria

Cardiology

- Single ventricle physiology (Fontan physiology or similar and/or presence of protein-losing enteropathy or plastic bronchitis).
- Complex conotruncal disease (interrupted aortic arch, pulmonary atresia, truncus).
- Cardiac failure/transplant (decision-making in conjunction with heart failure/transplant team).
- Pulmonary hypertension on oral or inhaled therapy (decision-making in conjunction with pulmonary and/or pulmonary HTN team).
- Significant secondary immunosuppression due to pharmacologic agents (see Immunology).

Endocrinology

- Obesity (BMI ≥99% percentile).
- Type 1 diabetes mellitus.
- Type 2 diabetes mellitus.
- Significant secondary immunosuppression due to pharmacologic agents (see Immunology).

Gastroenterology

- Significant secondary immunosuppression due to pharmacologic agents (see Immunology).

Hematology/oncology

- Allogeneic stem cell transplant within the previous three months.
- Acute myeloid leukemia (AML) on therapy.
- High risk and relapsed acute lymphocytic leukemia (ALL) on intensive intravenous therapy.
- Sickle cell disease with significant pulmonary disease and/or greater than one hospitalization for confirmed or suspected acute chest episode.
- Significant secondary immunosuppression due to pharmacologic agents (see Immunology).

Immunology

- Primary or secondary cellular (T cell) immunodeficiency.
- HIV infection with history of opportunistic infection or with severe CD4 lymphocytopenia (CD4% <15% if under age 14; CD4 count <200 lymphocytes/mm3 if older than age 14).
- Primary immunodeficiency on immunoglobulin therapy.

- Combined immunodeficiency associated with immune dysregulation, with or without current immunosuppression.
- Significant secondary immunosuppression due to pharmacologic agents:

1. Agents used for malignant conditions and related complications.
    a. Chemotherapeutic agents (e.g., cyclophosphamide, methotrexate, mycophenolate).
    b. Anti–B lymphocyte monoclonal antibodies (e.g., rituximab), or anti-T lymphocyte monoclonal antibodies (e.g., alemtuzumab).
    c. Cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4) inhibitors (e.g., abatacept).
    d. Tumor necrosis factor-alpha (TNF-α) antagonists (e.g., adalimumab, certolizumab, infliximab, etanercept, and golimumab).
    e. Select anti-cytokine antagonists (e.g., tocilizumab, ustekinumab, secukinumab, ixekizumab).*
2. Immunosuppressive agents used for solid organ transplant, and rheumatologic and other autoimmune conditions (e.g., inflammatory bowel disease, hemolytic uremic syndrome).
    a. Conventional immunosuppression: mycophenolate, sirolimus, tacrolimus, azathioprine.**
    b. Anti–B lymphocyte monoclonal antibodies or inhibiting agents (e.g., rituximab or belimumab).
    c. Cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4) inhibitors (e.g., abatacept).
    d. Anti-C5 monoclonal antibody (e.g., eculizumab).
    e. Tumor necrosis factor-alpha (TNF-α) antagonists (e.g., adalimumab, certolizumab, infliximab, etanercept, and golimumab).
    f. Select anti-cytokine antagonists (e.g., tocilizumab, ustekinumab, secukinumab, ixekizumab).*
3. Daily corticosteroid therapy at a dose ≥20 mg of prednisone or equivalent for longer than 14 days.

*Does not include anakinra when used as monotherapy as there is no significant increase in the risk of severe infection. Tocilizumab is included because it can cause neutropenia and generally is associated with more infections.

**Does not include low-dose methotrexate, hydroxychloroquine, colchicine, or leflunomide as used in rheumatic conditions.

Nephrology

- Dialysis (peritoneal or hemodialysis).
- Significant secondary immunosuppression due to pharmacologic agents (see Immunology).

Neurology

- Oxygen- or ventilator-dependent neuromuscular disease.
- Cerebral palsy/spastic quadriplegia.
- Congenital chromosomal abnormality (e.g., trisomy 21, trisomy 18, 22q11del or other chromosome abnormalities, on an individual basis as recommended by a geneticist).
- Mitochondrial disease and other inborn errors of metabolism with risk of metabolic decompensation (e.g., maple syrup urine disease (MSUD), organic acidemias, urea cycle disorders).

- Significant secondary immunosuppression due to pharmacologic agents (see Immunology).

Obstetrics

- Pregnancy

Pulmonology

- Oxygen- or ventilator-dependent chronic lung disease or neuromuscular disease.
- High risk (severe or poorly controlled) asthma.
- History of bronchopulmonary dysplasia with lung function impairment or other fixed obstructive lung disease.
- Cystic fibrosis, primary ciliary dyskinesia, and other causes of bronchiectasis (e.g., primary immunodeficiency).
- Significant secondary immunosuppression due to pharmacologic agents (see Immunology).

Race/Ethnicity

- Black/African American
- Hispanic/Latino
- Asian
- Native Hawaiian or Pacific Islander
- American Indian or Alaskan Native

Rheumatology

- Significant secondary immunosuppression due to pharmacologic agents (see Immunology).

The FDA has provided guidance that other medical conditions or factors may also place individual patients at high risk for progression to severe COVID-19 and authorization of monoclonal antibodies under the EUA is not limited to the medical conditions or factors listed above. Health care providers should consider the benefit-risk for an individual patient.

Advisory Group: Children's Minnesota, Mayo Clinic, University of Minnesota (5/25/21)

Additional resources

- Therapeutic Options for COVID-19 Patients (www.health.state.mn.us/diseases/coronavirus/hcp/therapeutic.html)
- COVID-19 Medication Options (www.health.state.mn.us/diseases/coronavirus/meds.html)

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