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OUTPATIENT GUIDANCE FOR TREATMENT OF COVID-19 IN ADULTS AND CHILDREN

These are interim treatment recommendations based on best available evidence at this time. Recommendations may be modified based on resource availability, testing recommendations, and future published data.

Clinical symptoms range from uncomplicated upper respiratory tract viral infection to pneumonia, acute respiratory distress syndrome (ARDS), sepsis, and septic shock.

Testing:

See link to current COVID-19 testing recommendations: Send testing for COVID-19

Treatment:

1. Supportive care:

   Supportive care is the mainstay of treatment for non-hospitalized patients.

2. Monoclonal antibody infusion:

   The FDA has issued an emergency use authorization (EUA) for bamlanivimab + etesevimab, and casirivimab + imdevimab (Regeneron's antibody cocktail) for non-hospitalized adults and adolescents (12-17 years old) with mild to moderate symptoms of COVID-19 with risk factors for progression to severe disease (see **Michigan Medicine Eligibility Criteria**). These are monoclonal antibodies that have been developed to bind to the spike protein of SARS-CoV-2 and block the virus from invading human cells. Preliminary research suggests that it may reduce the chances that high-risk patients with mild to moderate COVID-19 will develop severe disease that requires a visit to the emergency department and/or hospitalization.

   We have received a limited supply of these monoclonal antibodies, and are actively screening non-admitted potentially eligible candidates with risk factors for progression to severe disease, with a new positive PCR test for SARS-CoV-2 through:

   - Michigan Medicine (including ambulatory testing and ED testing of patients discharged home)
   - MLabs (including UHS and OHS, or community partners)
   - Michigan Medicine patients tested at an outside lab who have the PCR uploaded to MiChart with an "Outside Reported COVID-19 Pos Status" order

   The goal is to give the medication as early in the course of disease as possible. The criteria utilized to identify patients with risk factors for severe disease have been approved by the Scarce Resource Allocation Committee, and will be re-evaluated based on drug supply and infusion capacity. ***Clinicians do not need to contact anyone directly to procure this medication for their patient, but should upload their patients result using the "Outside Reported COVID-19 POS Status" order if their test was completed through an outside lab.*** If a patient is eligible and supply available, the patient will be contacted to discuss further, and proceed with scheduling the infusion. Primary care physicians will be notified if their patient is contacted to discuss the infusion.

   It is a one-hour IV infusion, and requires an hour of observation afterwards. Rarely, patients could experience an allergic reaction or an infusion-related reaction during the infusion (~2% in the BLAZE-1 study).
   The most common reported symptoms after the infusion are nausea, diarrhea, dizziness, vomiting, myalgias, headache, and malaise. These symptoms did not occur more frequently in patients receiving the monoclonal antibody infusion when compared to the placebo group. Thus, for the majority of patients such symptoms are more likely to be related to COVID-19 rather than the infusion. Patients receiving a monoclonal antibody infusion are also still at risk for progression to severe disease. Therefore, a patient complaining of worsening shortness of breath in the few days following the infusion could be experiencing COVID-19 progression OR a delayed reaction to the infusion. Irrespective of the underlying cause, they should be evaluated urgently. Patients without shortness of breath or other concerns requiring emergent evaluation in the ED can be managed with supportive care (i.e., ibuprofen, acetaminophen, fluids, anti-emetics, loperamide).

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Michigan Medicine Monoclonal Antibody Eligibility Criteria*
Patients with mild or moderate COVID-19 who meet criteria #1-4 **AND** *either* criteria #5 **OR** criteria #6 1. Outpatient 2. No requirement for supplemental oxygen (or no increase from baseline supplemental oxygen) 3. Symptoms ≤10 days 4. Not received convalescent plasma 5. Adult ≥18 years old and ≥40 kg **AND** one of the following: a) BMI ≥35 b) Age ≥65 c) Age ≥55 **AND** i) Chronic respiratory disease (e.g., COPD, Asthma, Bronchiectasis, CF, ILD) ii) Cardiovascular disease (e.g., HTN, valvular disease, CVA, PAD, CHF) d) Diabetes e) CKD (stage III, IV, or end stage CKD-GFR <15 or dialysis) f) Immunosuppressed: congenital or acquired immunodeficiency, SOT, active malignancy receiving chemotherapy, BMT, or autoimmune diseases requiring immunosuppressive therapy 6. Pediatric patient 12-17 years old weighing ≥40 kg **AND** one of the following: a) BMI ≥97% for age on CDC growth chart b) Immunosuppressed: congenital or acquired immunodeficiency, SOT, active hematologic malignancy receiving chemotherapy, or BMT

*Criteria apply to all bamlanivimab + etesevimab, and casirivimab + imdevimab products

References:

- Chen P, Nirula A, Heller B, et al. SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19 [published online ahead of print, 2020 Oct 28]. N Engl J Med. 2020 Oct 28;NEJMoa2029849.
- Casirivimab + Imdevimab EUA: https://www.fda.gov/media/143892/download, accessed 11/22/20
- Bamlanivimab + etesevimab EUA: https://www.covid19.lilly.com/bam-ete, accessed 3/15/21

Antimicrobial Subcommittee Approval: N/A	Originated: 03/2020
P&T Approval: N/A	Last Revised: 04/2021

Revision History:

12/2/20: Added MAB EUA information
12/11/20: Added information on common side effects of MAB therapy
1/8/21: Added MAB eligibility criteria
1/13/21: Added cardiovascular disease criteria
3/15/21: Added bamlanivimab + etesevimab information
4/7/21: Removed bamlanivimab monotherapy reference, adjusted eligiblility criteria