MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

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. Inhaled corticosteroids:
   Inhaled budesonide (800 mcg BID x14 days) and ciclesonide (320 mcg BID x30 days) have been studied in non-hospitalized adults with mild-moderate symptoms of COVID-19. The results of these studies do not demonstrate a consistent impact of inhaled corticosteroid therapy on time to recovery of COVID-related symptoms. Similarly, inhaled corticosteroid therapy reduced COVID-related emergency-department visits or hospitalizations in some studies but not others. As such, while we do not recommend inhaled corticosteroids as routine therapy, they may be considered on a case-by-case basis given some potential for benefit and a low risk of harm. Studies to date have not identified an optimal product or dose. While short-term inhaled corticosteroid therapy in COVID-19 patients has been shown to be relatively safe in studies to date, budesonide, ciclesonide, and fluticasone are all CYP3A4 substrates, and concomitant administration with potent CYP3A4 inhibitors such as azole antifungals, ritonavir, cobicistat, and clarithromycin (among others) may result in symptoms of corticosteroid excess. Such co-administration is not recommended.

3. Monoclonal antibody infusion:
   Casirivimab + Imdevimab (REGEN-COV) and Bamlanivimab + Etesevimab have been approved by the FDA for emergency use authorization (EUA) for post-exposure prophylaxis in certain individuals with close contact exposures at high risk for progression to severe disease. Please see the Post-exposure prophylaxis guidelines for more information.

   The FDA has issued an EUA for sotrovimab, bamlanivimab + etesevimab, and casirivimab + imdevimab (REGEN-COV) 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. 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.

   To reach the most eligible patients as quickly and efficiently as possible, we 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 who meet the high-risk criteria below but should upload a patient's result using the "Outside Reported COVID-19 POS Status" order if their test was completed through an outside lab.*** If a patient is eligible, the patient will be contacted to discuss further, and proceed with scheduling the infusion based on capacity available. Primary care physicians will be notified if their patient is contacted to discuss the infusion.

The FDA has expanded the EUA criteria outside of those "high-risk" patient populations that have the most data to support use. While the approach will still be to actively seek out those highest risk patients, if a patient does not meet the high-risk criteria defined below but their provider is concerned and determines them to be high-risk (e.g., 49-year-old with BMI of 34), referrals can be placed for evaluation. **By placing a "Referral for COVID-19 Monoclonal Antibody Treatment" order, a referral will go directly to the COVID mAb trained pharmacy team.** Patients will be called, evaluated for eligibility based on symptoms and duration, and will be scheduled as capacity allows. Prioritization will remain for the highest risk patients. This only needs to be done for patients outside of the criteria below.

It is an approximately 30-minute IV infusion, depending on the product, and requires one 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). Casirivimab + Imdevimab may also be given by subcutaneous injection, as an alternative route of therapy. Local injection site reactions occur in 2-4% of patients.

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 most 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).

Michigan Medicine Monoclonal Antibody Eligibility Criteria*

A patient must have had a Michigan Medicine encounter in the last 5 years **OR** be a Michigan Medicine employee **OR** be a University of Michigan student **OR** be a resident of Washtenaw County

Patients with mild or moderate COVID-19 who meet criteria #1-4 **AND** *either* criteria #5, #6, **OR** criteria #7:

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. Not fully vaccinated Adult ≥18 years old and ≥40 kg **AND** one of the following:
   a) BMI ≥35
   b) Age ≥50
   c) Chronic respiratory disease (e.g., COPD, moderate or severe asthma (requires daily inhaled corticosteroid), bronchiectasis, CF, ILD)
   d) Cardiovascular disease (e.g., HTN, valvular disease, CVA, PAD, CHF)
   e) Diabetes
   f) CKD (stage III, IV, or end stage CKD-GFR <15 or dialysis)
   g) Immunosuppressed: congenital or acquired immunodeficiency, SOT, active malignancy receiving chemotherapy, BMT, or autoimmune diseases requiring immunosuppressive therapy
   h) Pregnancy
6. Vaccinated Adult ≥18 years old and ≥40 kg **AND** one of the following:
   a) BMI ≥35
   b) Age ≥65
   c) Chronic respiratory disease (e.g., COPD, moderate or severe asthma (requires daily inhaled corticosteroid), bronchiectasis, CF, ILD)
   d) Immunosuppressed: congenital or acquired immunodeficiency, SOT, active malignancy receiving chemotherapy, BMT, or autoimmune diseases requiring immunosuppressive therapy
   e) Pregnancy
   f) Age ≥50 and one of the following
      i) Diabetes
      ii) CKD (stage III, IV, or end stage CKD-GFR <15 or dialysis)
      iii) Cardiovascular disease (e.g., HTN, valvular disease, CVA, PAD, CHF)
7. Pediatric patient 12-17 years old weighing ≥40 kg **AND** one of the following:
   a) BMI ≥95% for age on CDC growth chart
   b) Immunosuppressed: congenital or acquired immunodeficiency, SOT, active hematologic malignancy receiving chemotherapy, BMT, or autoimmune diseases requiring immunosuppressive therapy
   c) Pregnancy

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

References:

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Antimicrobial Subcommittee Approval: N/A	Originated: 03/2020
P&T Approval: N/A	Last Revised: 10/2021

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
6/7/21: Revised mAb criteria and casirivimab + imdevimab hyperlinks
8/10/21: Revised mAb selection and added post-exposure prophylaxis hyperlink.
10/7/21: Revised mAb criteria
10/14/21: Added inhaled corticosteroid section and added sotrovimab