



Mount Sinai Health System Adult Treatment Guidance for SARS-CoV-2 Infection (COVID-19)¹

Illness Severity ¹	Current Potential Therapy Options	Notes
Asymptomatic	Supportive care	In both inpatients and outpatients , corticosteroids are not recommended.
Symptomatic not requiring supplemental oxygen (> 94% on room air)	<p>Supportive care</p> <p>Outpatient: SARS-CoV-2 specific monoclonal antibody therapy is available for patients at high risk of progression to severe COVID-19 – referral can be made through e-mailing covidtherapeuticreferrals@mountsinai.org or calling 212-824-8390.</p> <p>Mount Sinai South Nassau in Long Island also provides SARS-CoV-2 specific monoclonal antibody therapy. Referrals for patients at high risk of progression to severe COVID-19 can be referred to the MSSN Outpatient Infusion Center at 516-632-4998.</p> <p>Inpatient: Inpatients not hospitalized for COVID-19 but who develop mild to moderate COVID-19 while hospitalized and who are at risk for progression to severe COVID-19 can be considered for EUA SARS-CoV-2 specific monoclonal antibody therapies if not requiring supplemental oxygen. Infectious diseases consultation and site-specific designee approval is required.</p> <p>Please see below for details regarding post-exposure prophylaxis.</p>	<p>In both inpatients and outpatients, corticosteroids are not recommended.</p> <p>Emergency use authorization (EUA) monoclonal antibody therapies:</p> <p>Casirivimab/imdevimab² The FDA issued an EUA on November 21, 2020, for casirivimab/imdevimab, a dual monoclonal SARS-CoV2 antibody cocktail, for select non-hospitalized patients 12 years of age or older (≥ 40kg) with a laboratory-confirmed COVID-19 (i.e., direct SARS-CoV2 viral test), symptom onset within 10 days and risk factors for progression to severe COVID-19.</p> <p>An update to the EUA was released on July 30, 2021, to include the use of casirivimab/imdevimab for post-exposure prophylaxis. Please see below for details.</p>
Hospitalized requiring low-flow nasal cannula (SpO ₂ ≤ 94% on RA)	<p>Supportive care</p> <p>Consider:</p> <ul style="list-style-type: none"> • SARS-CoV-2 specific antibody therapy* • Dexamethasone • Remdesivir <p>In addition to remdesivir, anticoagulation, and dexamethasone consider referring for enrollment in available Clinical Trials.</p>	<p><u>Remdesivir — requires ID consultation and is non-formulary</u> Remdesivir is not recommended in patients with an ALT > 5 times with upper limit of normal. Remdesivir was FDA-approved for the treatment of COVID-19 on October 22, 2020 in hospitalized patients 12 years of age and older weighing at least 40 kg.</p> <p><u>Convalescent plasma³⁻⁷ — requires ID consultation</u> On August 23, 2020, the FDA issued an EUA for the use of convalescent plasma (CP) in hospitalized patients and updated the EUA to only include high-titer CP on February 4, 2021. The Mount Sinai Health System has a protocol in place for the</p>

	<p>*Not inclusive of EUA casirivimab/imdevimab</p>	<p>administration of high-titer convalescent plasma in select immunocompromised individuals with ID physician approval. In patients with evidence of SARS-CoV-2 antibodies, SARS-CoV-2 antibody therapy is not recommended.</p> <p><u>Dexamethasone 6 mg IV/PO once daily for up to 10 days</u> Patients with symptom duration of < 7 days have not demonstrated benefit from dexamethasone. Dexamethasone should not be continued after discharge unless patient has a history of being on chronic steroid therapy.</p>
<p>Hospitalized requiring non-rebreather, high flow nasal cannula, or non-invasive ventilation (i.e., BiPAP)</p>	<p>Supportive care</p> <p>Recommended:</p> <ul style="list-style-type: none"> • SARS-CoV-2 antibody therapy* • Dexamethasone • Remdesivir • Baricitinib or tocilizumab <p>In addition to remdesivir, anticoagulation, antibody therapy, and dexamethasone consider referring for enrollment in available Clinical Trials.</p> <p>*Not inclusive of EUA casirivimab/imdevimab</p>	<p>See above</p> <p><u>Baricitinib requires non-formulary ID and Critical Care approval</u> On November 19, 2020, the FDA issued an EUA for the use of baricitinib for COVID-19. This EUA was updated on July 28, 2021. Due to the national shortage of tocilizumab, oral baricitinib can be considered in combination with dexamethasone in select patients within 5 days of hospital admission <i>and</i> within 24 hours of rapid progression to high-flow nasal cannula and non-invasive ventilation.</p> <p><u>Tocilizumab requires non-formulary ID and Critical Care approval</u> On June 24, 2021, the FDA issued an EUA for the use of tocilizumab for select patients with COVID-19. A single-dose of tocilizumab, an IL-6-receptor antagonist, can be considered in combination with dexamethasone in select patients within 5 days of hospital admission <i>and</i> within 24 hours of rapid progression to high-flow nasal cannula, non-invasive ventilation, or mechanical ventilation.</p> <p>Currently, tocilizumab is on national shortage. There is a limited supply of tocilizumab available for the treatment of COVID-19 and baricitinib may be considered.</p>
<p>Hospitalized requiring mechanical ventilation or ECMO</p>	<p>Supportive care</p> <p>Consider</p> <ul style="list-style-type: none"> • Dexamethasone • Tocilizumab <p>In addition to anticoagulation and dexamethasone consider referring for enrollment in available Clinical Trials.</p>	<p>Remdesivir is not recommended. See above.</p>

Recommendations for POST-EXPOSURE PROPHYLAXIS:

On July 30, 2021, the FDA expanded the EUA for [casirivimab/imdevimab](#) to include **post-exposure prophylaxis**⁸ in patients exposed to COVID-19 in the past 7 days who are age 12 years or older (weighing ≥ 40 kg) who are at [high risk for progression to severe COVID-19](#) including hospitalization and death AND are

- Not [fully vaccinated](#)
- Or are not expected to mount an adequate response to COVID-19 vaccination despite completion of an authorized vaccine series including those taking immunosuppressive medications (e.g., rituximab, mycophenolate, azathioprine, anti-CD20 monoclonal antibodies, BTK inhibitors) and those with immunocompromising conditions (e.g., solid organ transplantation, hematopoietic stem cell transplantation, hematologic malignancies, current chemotherapy).

Exposure includes a household contact or close contact as defined by the CDC (within 6 feet for a cumulative ≥15 minutes during a 24-hour period including 2 days prior to symptom onset or if asymptomatic, 2 days prior to the positive test).

Casirivimab/imdevimab cannot be used for pre-exposure prophylaxis or as a substitute for COVID-19 vaccination.

Outpatient Referrals:

SARS-CoV-2 specific [monoclonal antibody therapy](#) is available for treatment and post-exposure prophylaxis for patients at high risk of progression to severe COVID-19 – referral can be made through e-mailing covidtherapeuticreferrals@mountsinai.org or calling 212-824-8390.

Mount Sinai South Nassau in Long Island also provides SARS-CoV-2 specific monoclonal antibody therapy for treatment and post-exposure prophylaxis. Referrals for patients at high risk of progression to severe COVID-19 can be referred to the MSSN Outpatient Infusion Center at 516-632-4998.

Inpatient Referrals:

Should be discussed with Infectious Diseases consultation and may require site-specific approval.

- The following must be documented in the medical record prior to prescribing: The patient/caregiver has received the appropriate fact sheet and that the patient has been informed of potential alternatives, and that casirivimab/imdevimab is not FDA-approved but is authorized for use under an EUA.
- A [monoclonal antibody consent form](#) will need to be completed.
- **If the patient receives SARS-CoV-2 specific monoclonal antibody therapy, receipt of EUA COVID-19 vaccination including additional doses of vaccine, if partially vaccinated, will be delayed for 90 days.**

Dosing currently available at MSHS:

600 mg of casirivimab with 600 mg of imdevimab x 1 dose infused over 20 minutes to 1 hour

600 mg of casirivimab with 600 mg of imdevimab by subcutaneous injection in 4 equally divided doses (2.5 mL per syringe)

Caution:

Monitor for infusion reactions and/or anaphylaxis for 1 hour after administration

Adverse events should be reported to FDA [Medwatch](#).

Medications used for TREATMENT of COVID-19:

Anticoagulation [The Mount Sinai Health System COVID-19 Anticoagulation Protocol](#)

Baricitinib (Olumiant®)

On November 19, 2020, a EUA was issued for the combination of baricitinib, a JAK inhibitor, with remdesivir for the treatment of COVID-19 in hospitalized patients requiring supplemental oxygen age 2 and older based on data from ACTT-2.⁹ Patients treated with the combination had a median time to recovery of 1 day less compared to those treated with remdesivir alone. In a subsequent analysis, a day 29 mortality benefit was noted in patients who at baseline required low-flow or high flow oxygen, or non-invasive ventilation. The EUA for baricitinib was updated on July 28, 2021 to authorize the use of baricitinib without remdesivir based on data from the COV-BARRIER trial.¹⁰ In this phase III trial there was not a statistically significant difference in disease progression, however, a survival benefit was demonstrated in patients receiving baricitinib compared to placebo. The majority of patients in both arms received concomitant corticosteroids and primarily dexamethasone. Currently, use of baricitinib for the treatment of COVID-19 always requires ID consultation and non-formulary approval.

In the setting of a national shortage of tocilizumab, consider oral baricitinib in combination with dexamethasone (as outlined above), in patients within 5 days of hospital admission **and** within 24 hours of rapidly escalating oxygen requirements (e.g., requiring HFNC, BiPAP). Site designated ID and Critical Care approval is required.

- Exclusions from initiation of baricitinib include those with a GFR < 15 mL/min or requiring renal replacement therapy, those with an absolute neutrophil count < 500, those with an absolute lymphocyte count of < 200, and ALT or AST > 5 times the upper limit of normal.
- Use of baricitinib and other immunosuppressants or immunomodulatory agents including corticosteroids may place the patient at higher risk for bacterial, viral, and fungal infections including opportunistic infections. In patients on concomitant immunosuppressants or immunomodulators (e.g., organ transplant or hematopoietic stem cell transplant), discuss use of baricitinib with primary attending physician.
- The use of baricitinib in a pregnant person must be discussed with maternal fetal medicine.

Discussion regarding off-label use must be documented in the EMR. A copy of the patient or caregiver [fact sheet](#) must be given to patient or caregiver.

Dosing:

Patients age 9 years of age and older:

GFR ≥ 60 mL/min the dose is 4 mg daily by mouth for 14 days or until hospital discharge, whichever is sooner

GFR 30- < 60 mL/min the dose is 2 mg daily by mouth for 14 days or until hospital discharge, whichever is sooner

For GFR 15- <30 mL/min the dose is 1 mg daily for 14 days or until hospital discharge, whichever is sooner

Caution:

- Due to potential increased risk for infectious complications, the combination of tocilizumab and baricitinib is not recommended

Casirivimab/Imdevimab (REGEN-COV™)²

The FDA issued an EUA for outpatient infusion of casirivimab/imdevimab on November 21, 2020 for the treatment of mild-moderate COVID-19. The EUA was expanded to include post-exposure prophylaxis for patients at high risk for progression to severe COVID-19 on July 30, 2021. Casirivimab/imdevimab is a monoclonal antibody cocktail targeting the spike protein of SARS-CoV2. Benefit has not been observed in patients who require oxygen or who are hospitalized. Casirivimab/imdevimab therapy is not considered standard of care and is not to be used for pre-exposure prophylaxis or as a substitute for recommending COVID-19 vaccination.

Treatment (please refer previous page for post-exposure prophylaxis):

- Patients 12 years or older (and over 40 kg) referred for casirivimab/imdevimab must have a documented direct SARS-CoV2 viral test (antigen or PCR), symptoms of COVID-19 for ≤ 10 days and be at high risk for progressing to severe COVID-19. These high-risk conditions are described in the [fact sheet for health care providers](#).

- The following must be documented in the medical record prior to prescribing casirivimab/imdevimab: the patient/caregiver has received the appropriate fact sheet and that the patient has been informed of potential alternatives, and that casirivimab/imdevimab is not FDA-approved but is authorized for use under an EUA.
- A [monoclonal antibody consent form](#) will need to be completed.
- If the patient receives SARS-CoV-2 specific monoclonal antibody therapy, receipt of EUA COVID-19 vaccination including additional doses of vaccine, if partially vaccinated, will be delayed for 90 days.

Dosing:

600 mg of casirivimab with 600 mg of imdevimab x 1 dose infused over 20 minutes to 1 hour

Caution:

Monitor for infusion reactions and/or anaphylaxis for 1 hour after infusion

- Adverse events should be reported to FDA [Medwatch](#).

Dexamethasone¹¹⁻¹³

- Dexamethasone is recommended in patients with confirmed COVID-19 who require supplemental oxygen including those who require mechanical ventilation. Corticosteroid use has not been found to be beneficial in patients who do not require respiratory support and use in this population could be potentially harmful.
- The benefit of dexamethasone was observed in patients > 7 days out from symptom onset.
- Corticosteroids prescribed *specifically for the treatment COVID-19* should not be continued after 10 days or discharge whichever is earlier.
- Oral or inhaled corticosteroids prescribed prior to the diagnosis of COVID-19 for an underlying condition should not be discontinued.

Dosing:

Dexamethasone 6 mg PO or IV q 24 hours for up to 10 days

Alternative corticosteroids (dose equivalent to dexamethasone): Methylprednisolone 32 mg IV q 24 hours, Hydrocortisone 160 mg, or Prednisone 40 mg PO q 24 hours for up to 10 days

In the setting of escalating acuity, escalating dosing of corticosteroids, including stress-dose steroids, may be recommended in consultation with critical care. In a prospective meta-analysis of 7 trials, administration of corticosteroids was associated with lower all-cause mortality with the greatest benefit in those not receiving vasoactive medications. There was no evidence of mortality benefit when comparing high-dose and low-dose corticosteroids.¹³⁻¹⁵

Caution:

- Monitor for hyperglycemia, psychiatric effects, and secondary infections.

Remdesivir (Veklury®)^{16,17}

Remdesivir was FDA-approved for the treatment of COVID-19 on October 22, 2020 in hospitalized patients 12 years of age and older weighing at least 40 kg. The Adaptive COVID-19 Treatment Trial (ACTT-1) is a randomized placebo-controlled trial. In this trial hospitalized patients with lab-confirmed COVID-19 on low-flow oxygen had shorter median symptom duration (10 versus 15 days) and improved 29-day survival (HR for death 0.3). The trial was not powered to evaluate for differences in recovery time or mortality in patients receiving non-invasive ventilation. The WHO SOLIDARITY study combined data from four trials including ACTT-1. In the analysis, low and high flow oxygen were combined and did not demonstrate a mortality benefit.

- Exclusions for initiation and continuation of remdesivir include ALT > 5 times the upper limit of normal and those patients mechanically ventilated or requiring extracorporeal membrane oxygenation (ECMO).
- Consult Infectious Diseases for consideration for remdesivir therapy. Remdesivir is non-formulary and requires ID approval.

- Use of remdesivir in pediatric patients (< 12 years of age) and patients weighing < 40 kg would be considered off-label use of remdesivir. Use of the lyophilized powder for hospitalized pediatric patients weighing ≥ 3.5 kg is available under an emergency use authorization. Due to the lack of data in adults <40 kg, using the EUA to document the off-label use is recommended at this time.

Dosing:

Patients ≥ 40 kg: 200 mg IV on day 1 then 24 hours later start 100 mg IV q 24h for 4 days for a total duration of 5 days¹⁸ or until hospital discharge, whichever is sooner. Patients should not remain hospitalized solely to complete course of remdesivir if discharge is appropriate. Dose adjustment for renal replacement therapy recommended.

Caution:

- Hepatic function tests should be checked prior to initiating remdesivir and daily. Elevation in transaminases have been observed in clinical trials including in both healthy volunteers and patients with COVID-19.
- Remdesivir should be discontinued if ALT > 5 times the upper limit of normal or if there is signs and symptoms of liver inflammation (e.g., increased bilirubin, alkaline phosphatase, or INR).
- Adverse events should be reported to FDA [Medwatch](#).

Sotrovimab¹⁹

The FDA issued an EUA for outpatient infusion of sotrovimab on May 26, 2021 for the treatment of mild-moderate COVID-19. Sotrovimab is a monoclonal antibody targeting the spike protein of SARS-CoV2. Benefit has not been observed in patients who require oxygen or who are hospitalized. Sotrovimab therapy is not considered standard of care.

- Patients 12 years or older (and over 40 kg) referred for sotrovimab must have a documented direct SARS-CoV2 viral test (antigen or PCR), symptoms of COVID-19 for ≤ 10 days and be at high risk for progressing to severe COVID-19. These high-risk conditions are described in the [fact sheet for health care providers](#).
- The following must be documented in the medical record prior to prescribing sotrovimab: the patient/caregiver has received the appropriate fact sheet and that the patient has been informed of potential alternatives, and that sotrovimab is not FDA-approved but is authorized for use under an EUA.
- A [monoclonal antibody consent form](#) will need to be completed.
- **If the patient receives SARS-CoV-2 specific monoclonal antibody therapy, receipt of EUA COVID-19 vaccination including additional doses of vaccine, if partially vaccinated, will be delayed for 90 days.**

Dosing:

500 mg of sotrovimab x 1 dose infused over 30 minutes

Caution:

Monitor for infusion reactions and/or anaphylaxis for 1 hour after infusion

- Adverse events should be reported to FDA [Medwatch](#).

Tocilizumab (Actemra[®])²⁰⁻²⁷

The role of IL-6 antagonists (e.g., tocilizumab, siltuxumab, sarilumab) for the treatment of COVID-19 remains under review. On June 24, 2021, the FDA issued an EUA for the use of tocilizumab in select hospitalized patients age 2 years or older with COVID-19. A recent prospective meta-analysis of 27 trials noted a 28-day mortality benefit with the use of IL-6 antagonists with concomitant corticosteroids.

Consider a single dose of tocilizumab in combination with dexamethasone (as outlined above), in patients within 5 days of hospital admission **and** within 24 hours of rapidly escalating oxygen requirements (e.g., requiring HFNC, BiPAP, or mechanical ventilation with a FiO₂ >40%) with a recent CRP of ≥75. Site designated ID and Critical Care approval is required. **Due to a national shortage of tocilizumab, baricitinib may be considered (see above).**

- Exclusions from initiation of tocilizumab include ALT or AST > 5 times the upper limit of normal, thrombocytopenia (platelets < 50,000), and neutrophil count < 1,000.
- Use of tocilizumab and other immunosuppressants or immunomodulatory agents including corticosteroids may place the patient at higher risk for bacterial, viral, and fungal infections including opportunistic infections. In patients on concomitant immunosuppressants or immunomodulators (e.g., organ transplant or hematopoietic stem cell transplant), discuss use of tocilizumab with primary attending physician.
- The use of tocilizumab in a pregnant person must be discussed with maternal fetal medicine.

A [monoclonal antibody consent form](#) will need to be completed and discussion regarding off-label use must be documented in the EMR. A copy of the patient or caregiver [fact sheet](#) must be given to patient or caregiver.

Dosing:

Patients ≥ 30 kg: 8 mg/kg (actual body weight) IV x single dose (maximum dose: 800 mg)

Caution:

- Interaction: Tocilizumab may reduce levels of apixaban and rivaroxaban but does NOT interfere with enoxaparin or heparin
- Associated with lower gastrointestinal perforations in patients on concomitant steroids (> 10 mg prednisone daily or equivalent), NSAIDS, and/or methotrexate and in patients with diverticulitis
- Due to potential increased risk for infectious complications, the combination of tocilizumab and baricitinib is not recommended

Medications not currently recommended for the treatment of SARS-CoV2 (COVID-19), please consult Infectious Diseases:

ACE inhibitors and ARBs²⁸	Patients prescribed ACE inhibitors and ARBs for preexisting conditions should be continued on their ACE inhibitor and ARB therapy. Currently, there is no scientific or clinical evidence that taking ACE inhibitors or ARBs increases the risk of acquiring COVID-19 or that use may increase the severity of illness for those acquiring infections.
Azithromycin²⁹	Azithromycin with or without hydroxychloroquine is NOT recommended for the treatment of COVID-19.
Bamlanivimab and Bamlanivimab/Etesevimab³⁰⁻³²	The FDA issued an emergency use authorization (EUA) for outpatient infusion of bamlanivimab on November 9, 2020 and for bamlanivimab/etesevimab on February 9, 2021. Bamlanivimab is a monoclonal antibody targeting the spike protein of SARS-CoV-2 and bamlanivimab/etesevimab is a dual monoclonal antibody cocktail also targeting the spike protein. Due to increasing recovery of variants of interest and variants of concern (e.g., P.1) with decreased susceptibility to bamlanivimab, neither bamlanivimab nor bamlanivimab/etesevimab are recommended.
Colchicine³³	Use of colchicine for the treatment of COVID-19 is currently not recommended for ambulatory patients outside of a clinical trial. Inpatient use of colchicine specifically for the treatment of COVID-19 is not recommended. Patients prescribed colchicine for gout should complete their limited course of colchicine.
Famotidine³⁴	Use of H2 blockers or proton pump inhibitors specifically for the treatment of COVID-19 is not recommended.
Fluvoxamine^{35,36}	Limited published data exist for the use of fluvoxamine, a selective serotonin-uptake inhibitor, for the treatment of COVID-19. Fluvoxamine is currently not recommended for the treatment of COVID-19 for ambulatory or hospitalized patients outside of a clinical trial.
Hydroxychloroquine^{29,37-40}	Hydroxychloroquine is NOT recommended for prophylaxis or treatment of COVID-19. Co-administration of remdesivir and hydroxychloroquine or may result in reduced antiviral activity of remdesivir. ⁴¹ Patients prescribed hydroxychloroquine for preexisting rheumatologic conditions should be continued on their current dose.
Interferons⁴²	Data specific to SARS CoV-2 are lacking. Interferon is currently not recommended for the treatment of COVID-19. Clinical trials are ongoing.
Ivermectin⁴³⁻⁴⁷	<i>In vitro</i> studies demonstrate ivermectin inhibits SARS-CoV-2 replication and suggest the dosing required would be above what is recommended by the FDA for parasitic infections. Observational studies and small clinical trials evaluating the use of ivermectin for COVID-19 have been published or are available in pre-print. Most patients included in these reports are prescribed ivermectin early in diagnosis and/or hospitalization and variable comparators are used to determine outcomes including mortality. Regimens are variable in dose and duration. Randomized controlled trials evaluating the potential role of ivermectin are limited especially in hospitalized patients with severe or critical disease. Use of ivermectin for the treatment or prophylaxis of COVID-19 is currently considered unlabeled use and is not recommended outside of a clinical trial. If disseminated strongyloidiasis is being considered, ivermectin remains the treatment of choice and requires ID approval. ^{48,49}
IVIG	Use of IVIG for COVID-19 is not recommended outside of use for MIS-C and MIS-A.
Lopinavir/ritonavir (Kaletra)^{50,51}	Lopinavir/ritonavir is not recommended for the treatment of COVID-19.
Nitazoxanide⁵²	Displays inhibitory activity against the SARS-CoV-2 <i>in vitro</i> . Nitazoxanide is currently not recommended for the treatment of COVID-19 for ambulatory or hospitalized patients with COVID-19.
Oseltamivir	SARS-CoV-2 does not use neuraminidase as part of the viral replication cycle therefore neuraminidase inhibitors are not likely to provide therapeutic value.

Ribavirin	There are insufficient data to recommend the use of ribavirin for the treatment of COVID-19.
Tofacitinib⁵³	<p>Tofacitinib⁵³ is another JAK inhibitor that has been evaluated in clinical trials for the treatment of COVID-19 in hospitalized patients. The STOP-COVID-19 investigators recently published a multicenter study (n=289) conducted in Brazil that demonstrated lower 28-day mortality from respiratory failure in patients receiving tofacitinib versus placebo when offered within 72 hours of hospitalization in patients not requiring noninvasive and invasive mechanical ventilation and ECMO. Use of tofacitinib for the off-label treatment of COVID-19 always requires ID consultation and non-formulary approval.</p> <p>The use of combinations of IL-6 antagonists with JAK inhibitors for the treatment of COVID-19 is not recommended due to the potential risk of infectious complications.</p>
Zinc⁵⁴	There are insufficient data to recommend the use of for the treatment of COVID-19.

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