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

Updated in the setting of Omicron subvariant BA.2

Illness Severity[1]	Current Potential Therapy Options	Notes
Asymptomatic	Supportive care	In both inpatients and outpatients, corticosteroids are not recommended for asymptomatic individuals diagnosed with COVID-19.
Symptomatic not requiring supplemental oxygen (> 94% on room air)	Supportive care **Outpatient**: Paxlovid™ (nirmatrelvir/ritonavir) is preferred for the treatment of COVID-19 in patients at high risk for progression. For oral antivirals, like Paxlovid™, please see details below: • Patient cannot be hospitalized for COVID-19 • Patient must be able to initiate treatment within 5 days of symptom onset • Patient must have a medical condition that increases their risk for severe illness or death from COVID-19 SARS-CoV-2 specific monoclonal antibody therapy is available for patients at high risk of progression to severe COVID-19 who cannot be prescribed Paxlovid™ – provider referrals can be submitted through this referral form. 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. **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 monoclonal antibody treatment or remdesivir if not requiring supplemental oxygen. Infectious diseases consultation is required.	In both inpatients and outpatients, corticosteroids are not recommended for those who do not require supplemental oxygen for COVID-19. Patients should not be admitted solely to receive monoclonal antibody treatment and/or remdesivir. **Nirmatrelvir/Ritonavir (Paxlovid™)** Paxlovid™, nirmatrelvir/ritonavir, is an oral antiviral available for the treatment of non-hospitalized patients with *symptomatic* COVID-19 who do not require supplemental oxygen and who are at high risk for progression to severe COVID-19. Prescriptions for Paxlovid™ can be filled through designated pharmacies. Patients must start treatment within 5 days of symptom onset and must have a positive test result for SARS-CoV-2 infection. *Caution must be used with concomitant medications. Please see below for detailed information.* **Bebtelovimab** Bebtelovimab is a SARS-CoV-2 specific monoclonal antibody available for treatment of non-hospitalized patients with *symptomatic* COVID-19 not requiring supplemental oxygen and who are high risk for progression to severe COVID-19. Bebtelovimab retains activity against omicron and the BA.2 omicron subvariants. **Molnupiravir** (Lagevrio®) Molnupiravir is an oral antiviral available for the treatment of non-hospitalized patients with *symptomatic* COVID-19 who do not require supplemental oxygen and who are high risk for progression to severe COVID-19. Prescriptions for molnupiravir can be filled through designated pharmacies. Patients must start treatment within 5 days of symptom onset and must have a positive test result for SARS-CoV-2 infection.

		Caution must be used in persons of childbearing potential and those who are sexually active with persons of childbearing potential. Please see below for detailed information.
Hospitalized requiring low-flow nasal cannula (SpO2 ≤ 94% on RA)	Supportive care **Recommend::** • **SARS-CoV-2 specific antibody therapy*** • **Dexamethasone** • **Remdesivir** In addition to remdesivir, anticoagulation, and dexamethasone consider referring for enrollment in available Clinical Trials. ***Inpatient monoclonal antibody therapy requires ID consultation and site-specific approval**	**Remdesivir — non-formulary, requires ID approval.** Remdesivir is not recommended in patients with an ALT > 5 times with upper limit of normal. Remdesivir is FDA approved for the treatment of patients > 28 days old and ≥ 3 kg who are hospitalized with COVID-19. On January 21, 2022, the approval was expanded to include a 3-day course for outpatients at high risk for progression to severe COVID-19 or hospitalization. Patients who require minimal oxygen support may receive remdesivir alone without dexamethasone. **Dexamethasone 6 mg IV/PO once daily for up to 10 days** Dexamethasone should not be continued after discharge unless patient has a history of being on chronic steroid therapy.
Hospitalized with rapidly escalating oxygen needs and/or requiring non-rebreather, high flow nasal cannula, or non-invasive ventilation (i.e., BiPAP)	Supportive care **Recommend:** • **Dexamethasone** • **Remdesivir** • **Baricitinib or tocilizumab** In addition to remdesivir, anticoagulation, and dexamethasone consider referring for enrollment in available Clinical Trials.	See above **Baricitinib requires ID consult and non-formulary ID and Critical Care approval** **Tocilizumab requires ID consult and non-formulary ID and Critical Care approval** Oral baricitinib, a JAK inhibitor, for 14 days (or until discharge whichever is shorter) or a single-dose of tocilizumab, an IL-6-receptor antagonist, should be given in combination with dexamethasone in most patients requiring high-flow nasal cannula or non-invasive ventilation. Combination therapy of baricitinib and tocilizumab is not recommended due to insufficient evidence and potential for increased risk of adverse events.
Hospitalized requiring mechanical ventilation or ECMO	Supportive care **Recommend:** • **Dexamethasone** • **Baricitinib or tocilizumab**	Remdesivir is not recommended. See above.

	In addition to anticoagulation and dexamethasone, consider referring for enrollment in available Clinical Trials.	

Medications used for TREATMENT of COVID-19:

Anticoagulation The Mount Sinai Health System COVID-19 Anticoagulation Protocol

Baricitinib (Olumiant®)

On May 10, 2022, the FDA approved baricitinib, a JAK inhibitor, for the treatment of hospitalized adult patients with COVID-19 requiring supplemental oxygen based on the findings of the RECOVERY[2] trial and associated meta-analysis. RECOVERY demonstrated mortality benefit in patients requiring supplemental oxygen when used in combination with corticosteroids. The results of this large pragmatic placebo-controlled trial added to existing data which informed the prior EUA for baricitinib including the ACTT-2[3] and COV-BARRIER[4] trials. Currently, use of baricitinib for the treatment of COVID-19 requires ID consultation and site designated ID and Critical Care approval.

Baricitinib, in combination with dexamethasone, is recommended in most patients with rapidly escalating oxygen requirements (e.g., requiring non-rebreather, HFNC, non-invasive ventilation, or mechanical ventilation).

- 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, those unable to take enteral medications, those with evidence of thrombosis, 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 appropriate teams.
- The use of baricitinib in a pregnant person must be discussed with maternal fetal medicine.

For patients <18 years old, 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 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 by mouth 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
- Possible side effects include venous thrombosis and concomitant infections.

Adverse events should be reported to FDA Medwatch.

Bebtelovimab

The FDA issued an EUA for bebtelovimab on February 11, 2022 for the treatment of symptomatic mild to moderate COVID-19. Bebtelovimab is a recombinant neutralizing human IgG1k monoclonal antibody targeting the spike protein of SARS-CoV2. Bebtelovimab retains *in vitro* activity against the omicron variant and the BA.2 subvariant.

- Patients ≥ 12 years of age (and ≥ 40 kg) referred for bebtelovimab must have a documented direct SARS-CoV2 viral test (lab-based antigen or PCR), symptoms of COVID-19 for ≤ 5 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.

In the setting of logistical and supply constraints, administration of bebtelovimab will be limited to those determined to be highest risk for progression to severe COVID-19 and hospitalization based on availability and eligibility for oral antivirals, age, vaccination status, ability to mount a response to vaccination, and underlying medical comorbidities. Please review if your patient would benefit from an oral antiviral and has no contraindication to use of an oral antiviral prior to referral. Please refer to recommendations from the New York State and New York City Health Departments and the NIH COVID-19 Treatment Guidelines for prioritization when there are logistical or supply constraints.

- The following must be documented in the medical record prior to prescribing bebtelovimab: the patient/caregiver has received the appropriate fact sheet and that the patient has been informed of potential alternatives, and that bebtelovimab is not FDA-approved but is authorized for use under an EUA.
- A monoclonal antibody consent form will need to be completed.

Dosing:
175 mg/2 mL administered as a single IV push over 30 seconds

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

Adverse events should be reported to FDA Medwatch.

Dexamethasone[5,6]

- 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.
- 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 be continued.

Dosing:
Dexamethasone 6 mg PO or IV q 24 hours for up to 10 days or until discharge whichever is earlier.
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 or until discharge whichever is earlier.

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.[6-8]

Caution:

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

Nirmatrelvir/ritonavir (Paxlovid™)[9]

On December 22, 2021, the FDA issued an EUA for the use of Paxlovid™. EPIC-HR, a phase 2/3 randomized placebo-controlled trial in non-hospitalized high-risk adult patients with symptomatic COVID-19 demonstrated an 89% reduction in hospitalization and death in those taking Paxlovid™ versus placebo within 5 days of symptom onset. Nirmatrelvir (PF-07321332) inhibits the SARS-CoV-2 protease and inhibits protein synthesis and viral replication. Nirmatrelvir is co-packaged with ritonavir which helps “boost” levels of nirmatrelvir. Ritonavir has been used in this capacity to treat HIV disease. Drug interactions are common with ritonavir and must be reviewed prior to prescribing. Paxlovid™ may lead to persons with HIV-1 developing HIV protease inhibitor resistance if given without complete antiretroviral therapy.

Paxlovid™ should be considered in *symptomatic* patients (≥ 12 years of age weighing at least 40 kg or 88 pounds) who have ≤ 5 days of symptoms **and** have tested positive for SARS-CoV-2 infection **and** are high-risk for progression to severe COVID-19, including hospitalization and death.

When prescribing please note the following.

- Paxlovid™ is not FDA-approved and its use is authorized for emergency use by the FDA.
- Please give patient a hard copy of the Fact Sheet for Patients and Caregivers.
- Patients should be informed that Paxlovid™ may cause altered taste and gastrointestinal symptoms such as nausea, vomiting and diarrhea

Treatment with Paxlovid™ is contraindicated in the following patients:

- History of hypersensitivity reactions to ritonavir.
- Patients with kidney disease (eGFR < 30 mL/min) or Childs-Pugh Class C liver disease.

Attention must be paid to potential drug-drug interactions including but not limited to calcium channel blockers, oral contraceptives, immunosuppressants commonly used in organ transplantation and hematopoietic stem cell transplantation, antifungals, chemotherapeutics, and anticoagulation. Please use the below tools to review management of potential drug-drug interactions.

Potential drug-drug interactions can be evaluated using the following tools:

- University of Liverpool COVID-19 Drug Interactions
- Infectious Diseases Society of America (IDSA) Management of Drug Interactions with Nirmatrelvir/Ritonavir (Paxlovid™): Resource for Clinicians
- Fact Sheet for Healthcare Providers
- NIH COVID-19 Treatment Guidelines: drug-drug interactions between ritonavir-boosted nirmatrelvir (Paxlovid) and concomitant medications.

Designated pharmacies can fill prescriptions for Paxlovid™.

In New York City, Paxlovid™ can also be prescribed through Alto Pharmacy. Alto will deliver fulfilled prescriptions will to the patient's preferred New York City address. Prescriptions confirmed by 5 pm on weekdays or 1 pm on weekends will be delivered the same day. Phone prescriptions can be called to 800-874-5881. Please note the below when prescribing through Alto Pharmacy.

- Symptom onset must be documented in the pharmacist note section of the prescription order.
- Verify patient's phone number and address for delivery.
- In the pharmacist note section, document race/ethnicity from the following options: Asian/Native Hawaiian or other Pacific Islander; Black; Hispanic/Latino; native American/Alaskan Native; and White.
- If you feel that your patient meets criteria and does not have a contraindication to the use of molnupiravir as an alternative, you can write a similar prescription with the same details and include "To be used in case Paxlovid™ prescription cannot be filled because of supply limitation."

Dosing:
300 mg of nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet), with all three tablets taken together twice a day for a total of 5 days.
The medications can be taken with or without food
These medications must be swallowed whole and CANNOT be chewed, broken or crushed

For patients with eGFR ≥ 30 to < 60 mL/min, the dose must be adjusted: 150 mg of nirmatrelvir (one 150 mg tablet) with 100 mg ritonavir

If the patient misses a dose of Paxlovid™ within 8 hours of the time it is usually taken, the patient should take it as soon as possible and resume the normal dosing schedule. If the patient misses a dose by more than 8 hours, the patient should not take the missed dose and instead take the next dose at the regularly scheduled time.

Caution:

- Use of Paxlovid™ and certain other drugs may result in significant drug interactions.
- Hepatotoxicity has occurred in patients receiving ritonavir

Adverse events should be reported to FDA Medwatch.

Molnupiravir (Legevrio®)[10]

On December 23, 2021, the FDA issued an EUA for molnupiravir for the treatment of mild to moderate COVID-19. The MOVe-OUT trial, a randomized double-blinded placebo-controlled trial demonstrated a 30% reduction in hospitalization or death in high-risk adult participants taking molnupiravir versus placebo. Molnupiravir is a pro-drug of a nucleoside analog that can be incorporated in to the RNA and cause mutations that lead to an antiviral effect. Molnupiravir should considered for patients ≥18 years old for whom an alternative treatment is not accessible or clinically appropriate. Paxlovid™ is considered the preferred oral antiviral, if available.

Molnupiravir can be considered in the treatment of symptomatic adults (≥ 18 years of age weighing at least 40 kg or 88 pounds) who have ≤ 5 days of symptoms **and** have tested positive for SARS-CoV-2 infection **and** are high-risk for progression to severe COVID-19, including hospitalization and death. When prescribing please note the following.

- Molnupiravir is not FDA-approved and its use is authorized for emergency use by the FDA.
- Please give patient a hard copy of the Fact Sheet for Patients and Caregivers

Treatment with molnupiravir is contraindicated in the following patients:

- Patients < 18 years old due to effects on bone and cartilage growth
- Pregnant persons due to embryo-fetal toxicity in animal studies. Providers must assess if the person is pregnant or of childbearing potential.
- **In persons of childbearing potential, it is recommended that individuals use effective contraception correctly and consistently for *the duration of treatment and for 4 days after the last dose* of molnupiravir**.
- Breastfeeding is not recommended *during treatment and for 4 days after the last dose* of molnupiravir. A lactating individual may consider interrupting breastfeeding and pumping and discarding breast milk during this time
  Males of reproductive potential who are sexually active with persons of childbearing potential should use reliable method of contraception correctly and consistently *during treatment and for at least 3 months after the last dose*.

Designated pharmacies can fill prescriptions for molnupiravir.

In New York City, molnupiravir can also be prescribed through Alto Pharmacy. Alto will deliver fulfilled prescriptions will to the patient's preferred New York City address. Prescriptions confirmed by 5 pm on weekdays or 1 pm on weekends will be delivered the same day. Phone prescriptions can be called to 800-874-5881. Please note the below when prescribing through Alto Pharmacy.

- Symptom onset must be documented in the pharmacist note section of the prescription order.
- Verify patient's phone number and address for delivery.
- In the pharmacist note section, document race/ethnicity from the following options: Asian/Native Hawaiian or other Pacific Islander; Black; Hispanic/Latino; native American/Alaskan Native; and White.

- If you feel that your patient meets criteria and does not have a contraindication to the use of molnupiravir as an alternative, you can write a similar prescription with the same details and include "To be used in case Paxlovid™ prescription cannot be filled because of supply limitation."

Dosing:
800 mg (four 200 mg capsules) twice a day with or without food for a total of 5 days
These medications must be swallowed whole and CANNOT be chewed, opened, broken or crushed

If a dose is missed and it has been over 10 hours since the scheduled dose, resume the prescribed dosing schedule and discard the missed dose. If within 10 hours, take dose as soon as possible and resume dosing schedule.

Adverse events should be reported to FDA Medwatch.
Pregnancy surveillance is occurring through Merck Sharp & Dohme's at 1-877-888-4231 or https://pregnancyreporting.msd.com/

Remdesivir (Veklury®)[11,12]
Remdesivir is FDA-approved for the treatment of COVID-19 in hospitalized patients> 28 days of age and weighing ≥ 3 kg. 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. A randomized placebo-controlled trial[13] was conducted evaluating ambulatory administration of remdesivir for three days in the setting of symptomatic COVID-19 in unvaccinated non-hospitalized patients at high-risk for progression. The single study noted an 87% decrease in the risk of hospitalization compared with placebo. Currently, SARS-CoV-2 oral antivirals are preferred in this scenario.

- 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).
- Remdesivir is non-formulary and requires ID approval.
- Patients should not be admitted solely to receive remdesivir and should not be hospitalized solely to complete a course of remdesivir. Remdesivir is likely more effective earlier in symptom onset, ideally within 7 days of symptom onset.

Dosing:
For patients requiring supplemental oxygen:
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 days[14] 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.

For patients < 40 kg: 5 mg/kg IV on day 1, then 24 hours later start 2.5 mg/kg IV for 4 days for a total duration of 5 days or until hospital discharge, whichever is sooner.

For patients not requiring supplemental oxygen, the recommended duration of remdesivir treatment is 3 days.

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.

Tocilizumab (Actemra®)[15-22]

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. Meta-analysis of 27 trials noted a 28-day mortality benefit with the use of IL-6 antagonists with concomitant corticosteroids.[22] A single dose of tocilizumab in combination with dexamethasone can be considered in patients with rapidly escalating oxygen requirements (e.g., requiring HFNC, BiPAP, or mechanical ventilation). Currently, use of tocilizumab for the treatment of COVID-19 requires ID consultation and site designated ID and Critical Care approval.

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 appropriate teams.
- 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

Adverse events should be reported to FDA Medwatch.

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

ACE inhibitors and ARBs[23]	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.
Azithromycin[24]	Azithromycin with or without hydroxychloroquine is NOT recommended for the treatment of COVID-19.
Bamlanivimab[25] **Bamlanivimab/Etesevimab**[26,27]	The FDA issued an emergency use authorization (EUA) for 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. On September 16, 2021 the EUA was expanded to include the use of bamlanivimab/etesevimab for post-exposure prophylaxis. Due to increasing recovery of variants of interest and variants of concern (i.e., Omicron) neither bamlanivimab nor bamlanivimab/etesevimab are recommended.
Casirivimab/Imdevimab (REGEN-COV)[28-30]	The FDA issued an EUA on November 21, 2020, for casirivimab/imdevimab, a dual monoclonal SARS-CoV2 antibody cocktail targeting the spike protein of SARS-CoV-2. An update to the EUA was released on July 30, 2021, to include the use of casirivimab/imdevimab for post-exposure prophylaxis. Due to increasing recovery of variants of interest and variants of concern (i.e., Omicron BA.1) casirivimab/imdevimab is not recommended. Casirivimab/imdevimab does have activity against the BA.2 omicron subvariant.
Colchicine[31]	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.
Famotidine[32]	Use of H2 blockers or proton pump inhibitors specifically for the treatment of COVID-19 is not recommended.
Fluvoxamine[33-35]	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[24,36-39]	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.[40] Patients prescribed hydroxychloroquine for preexisting rheumatologic conditions should be continued on their current dose.
Interferons[41]	Data specific to SARS CoV-2 are lacking. Interferon is currently not recommended for the treatment of COVID-19. Clinical trials are ongoing.
Ivermectin[42-46]	*In vitro* 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.[47,48]
IVIG	Use of IVIG for COVID-19 is not recommended outside of use for MIS-C and MIS-A.
Nitazoxanide[49]	Displays inhibitory activity against the SARS-CoV-2 *in vitro*. Nitazoxanide is currently not recommended for the treatment of COVID-19 for ambulatory or hospitalized patients with COVID-19.
Ribavirin	There are insufficient data to recommend the use of ribavirin for the treatment of COVID-19.
Sotrovimab (Xevudy)[50,51]	The FDA issued an EUA for sotrovimab on May 26, 2021 for the treatment of symptomatic mild to 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 for COVID-19. Sotrovimab retains *in vitro* activity against the omicron BA.1 variant, however decreased activity against the BA.2 subvariant.
Tofacitinib[52]	Tofacitinib[52] 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. 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.

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