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

*Updated in the setting of Omicron subvariant BA.2*

<table>
<thead>
<tr>
<th>Illness Severity</th>
<th>Current Potential Therapy Options</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Asymptomatic</strong></td>
<td>Supportive care</td>
<td></td>
</tr>
<tr>
<td><strong>Symptomatic not requiring supplemental oxygen (&gt; 94% on room air)</strong></td>
<td>Supportive care</td>
<td>In both inpatients and outpatients, corticosteroids are not recommended for asymptomatic individuals diagnosed with COVID-19.</td>
</tr>
<tr>
<td><strong>Outpatient:</strong></td>
<td><strong>Paxlovid™</strong> (nirmatrelvir/ritonavir) is preferred for the treatment of COVID-19 in patients at high risk for progression.</td>
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<tr>
<td>For oral antivirals, like Paxlovid™, please see details below:</td>
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<tr>
<td></td>
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<td>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 either monoclonal antibody treatment or remdesivir.</td>
</tr>
<tr>
<td></td>
<td>• Patient cannot be hospitalized for COVID-19</td>
<td><strong>Nirmatrelvir/Ritonavir (Paxlovid™)</strong></td>
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<tr>
<td></td>
<td>• Patient must be able to initiate treatment within 5 days of symptom onset</td>
<td>Paxlovid™ is an oral antiviral which is a combination of nirmatrelvir/ritonavir which received an EUA on December 22, 2021 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. Paxlovid™ is currently only available through designated pharmacies at this time with prioritization outlined by New York State and New York City public health departments. 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.</td>
</tr>
<tr>
<td></td>
<td>• Patient must have a medical condition that increases their risk for severe illness or death from COVID-19</td>
<td><strong>Molnupiravir</strong> (Lagevrio™)</td>
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<tr>
<td></td>
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<td>Molnupiravir is an oral antiviral which received an EUA on December 23, 2021 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. Molnupiravir is currently only available through designated pharmacies at this time with limited allocation and prioritization outlined by New York State and New York City public health departments. Patients must start treatment within 5 days of symptom onset and must have a positive test result for SARS-CoV-2 infection.</td>
</tr>
<tr>
<td>SARS-CoV-2 specific <a href="#">monoclonal antibody therapy</a> 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 <a href="#">referral form</a>.</td>
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</tr>
<tr>
<td>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.</td>
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<tr>
<td><strong>Inpatient:</strong></td>
<td>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.</td>
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</tbody>
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MSHS COVID-19 Treatment Guidance March 24, 2022

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MSHS COVID-19 Treatment Guidance March 24, 2022
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.

**Bebtelovimab**
Bebtelovimab is a SARS-CoV-2 specific monoclonal antibody which received an emergency use authorization (EUA) on February 11, 2022 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 subvariant. Due to logistical and supply constraints prioritization for treatment has been outlined by the New York State and New York City public health departments.

<table>
<thead>
<tr>
<th>Hospitalized requiring low-flow nasal cannula (SpO2 ≤ 94% on RA)</th>
<th>Supportive care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider:</td>
<td></td>
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<tr>
<td>• SARS-CoV-2 specific antibody therapy*</td>
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<tr>
<td>• Dexamethasone</td>
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<tr>
<td>• Remdesivir</td>
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<tr>
<td>In addition to remdesivir, anticoagulation, and dexamethasone consider referring for enrollment in available Clinical Trials.</td>
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<tr>
<td>*Inpatient monoclonal antibody therapy requires ID consultation and site-specific approval</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hospitalized requiring non-rebreather, high flow nasal cannula, or non-invasive ventilation (i.e., BiPAP)</th>
<th>Supportive care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommended:</td>
<td></td>
</tr>
<tr>
<td>• Dexamethasone</td>
<td></td>
</tr>
<tr>
<td>• Remdesivir</td>
<td></td>
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<tr>
<td>• Baricitinib or tocilizumab</td>
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</tbody>
</table>

**Remdesivir — non-formulary, requires ID consultation and 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 ≥ 12 years old and ≥ 40 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.

**Dexamethasone 6 mg IV/PO once daily for up to 10 days**
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.

<table>
<thead>
<tr>
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<tr>
<td>• Baricitinib or tocilizumab</td>
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</tbody>
</table>

**See above**
Baricitinib requires non-formulary ID and Critical Care approval
On November 19, 2020, the FDA issued an EUA for the use of baricitinib for COVID-19. This EUA was updated on July
In addition to remdesivir, anticoagulation, and dexamethasone consider referring for enrollment in available Clinical Trials.

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 and within 24 hours of rapid progression to high-flow nasal cannula and non-invasive ventilation.

**Tocilizumab requires non-formulary ID and Critical Care approval**

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 and within 24 hours of rapid progression to high-flow nasal cannula, non-invasive ventilation, or mechanical ventilation.

Currently, there is a limited supply of tocilizumab and baricitinib may be considered in the appropriate patient population.

<table>
<thead>
<tr>
<th>Hospitalized requiring mechanical ventilation or ECMO</th>
<th>Supportive care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider</td>
<td></td>
</tr>
<tr>
<td>• Dexamethasone</td>
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<tr>
<td>• Tocilizumab</td>
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<tr>
<td>In addition to anticoagulation and dexamethasone,</td>
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<tr>
<td>consider referring for enrollment in available Clinical Trials.</td>
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</tbody>
</table>

Remdesivir is not recommended. See above.

**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. 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. 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. Most patients in both arms received concomitant corticosteroids and primarily dexamethasone. Currently, use of baricitinib for the treatment of COVID-19 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) with a recent CRP of ≥75. 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, those unable to take enteral medications, 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 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

**Bebtelovimab**


- 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](https://www.fda.gov/medwatch).

**Dexamethasone**

- 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 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 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.\(^5\)\(^7\)

**Caution:**

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

**Nirmatrelvir/ritonavir (Paxlovid™)**

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 88% 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.

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.
- Patients on other medications relying on CYP3A for clearance (e.g., alfuzosin, amiodarone, flecainide, colchicine, clozapine, ergot derivatives, lovastatin, simvastatin, sildenafil (Revatio®) when used for pulmonary arterial hypertension) where elevated drug levels are associated with serious or life-threatening reactions. Please review Section 4 of the Fact Sheet for Healthcare Providers.
- Patients on other medications which are CYP3A inducers (e.g., anticonvulsants like carbamazepine, phenobarbital, phenytoin; rifampin, St. Jon’s Wort) which can decrease Paxlovid™ concentrations and potentially decrease potency of Paxlovid™ or lead to resistance. Please review Section 4 of the Fact Sheet for Healthcare Providers.
Caution must be used with multiple other medications including but not limited to calcium channel blockers, oral contraceptives, immunosuppressants commonly used in organ transplantation and hematopoietic stem cell transplantation, antifungals, chemotherapeutics, corticosteroids, and anticoagulation. Please review Section 7 of the Fact Sheet for Healthcare Providers and your patient’s medications prior to prescribing.

Paxlovid™ can be considered in the treatment of symptomatic adults and pediatric patients (≥ 12 years of age weighing at least 40 kg or 88 pounds) who have tested positive for SARS-CoV-2 infection. The patient/caregiver must be informed of the following prior to prescribing:

- Paxlovid™ is not FDA-approved and its use is authorized for emergency use by the FDA.
- There are no approved treatments for mild-moderate COVID-19, however other agents are authorized for similar indications under emergency use.
- Please give patient a hard copy of the Fact Sheet for Patients and Caregivers

Due to limited supply, the New York State and New York City Health Departments have offered detailed information regarding prioritization and prescribing. A limited number of designated outpatient pharmacies are capable of filling prescriptions. Please visit this website prior to prescribing outside of New York City and please see this website for instructions and availability in New York City.

In New York City, Paxlovid™ can only be prescribed through Alto Pharmacy. Fulfilled prescriptions will be delivered to 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.

- Patients must be symptomatic and able to start treatment within 5 days of symptom onset. Symptom onset must be documented in the pharmacist note section of the prescription order.
- Patient must be considered at increased risk for severe COVID-19 and fulfillment of prescription will be based on supply and prioritization by New York State and New York City Health Departments.
- 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. Please review Section 7 of the Fact Sheet for Healthcare Providers and your patient’s medications prior to prescribing. This link can be used to assess for drug interactions.
Hepatotoxicity has occurred in patients receiving ritonavir

Adverse events should be reported to FDA Medwatch.

**Molnupiravir** (Legevrio®)

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.

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.

Molnupiravir can be considered in the treatment of symptomatic adults (≥ 18 years of age weighing at least 40 kg or 88 pounds) who have tested positive for SARS-CoV-2 infection. The patient/caregiver must be informed of the following prior to prescribing:

- Molnupiravir is not FDA-approved and its use is authorized for emergency use by the FDA.
- There are no approved treatments for mild-moderate COVID-19, however other agents are authorized for similar indications under emergency use.
- Please give patient a hard copy of the Fact Sheet for Patients and Caregivers

Due to limited supply, the New York State and New York City Health Departments have offered detailed information regarding prioritization and prescribing. A limited number of designated outpatient pharmacies are capable of filling prescriptions. Please visit this website prior to prescribing outside of New York City and please see this website for instructions and availability in New York City.

In New York City, molnupiravir can **only** be prescribed through Alto Pharmacy. Fulfilled prescriptions will be delivered to 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.

- Patients must be symptomatic and able to start treatment within 5 days of symptom onset. Symptom onset must be documented in the pharmacist note section of the prescription order.
- Patient must be considered at increased risk for severe COVID-19 and fulfillment of prescription will be based on supply and prioritization by New York State and New York City Health Departments.
- 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.
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 pregnancy surveillance at 1-877-888-4231 or https://pregnancyreporting.msd.com/

Remdesivir (Veklury®)⁹,¹⁰
Remdesivir was FDA-approved for the treatment of COVID-19 on October 22, 2020 in hospitalized patients ≥ 12 years of age and weighing ≥ 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. A randomized placebo-controlled trial¹¹ was conducted evaluating off-label administration of remdesivir for three days in the setting of symptomatic COVID-19 in unvaccinated outpatients at high-risk for progression. The single study noted an 87% decrease in the risk of hospitalization compared with placebo. Currently, SARS-CoV-2 specific monoclonal antibody therapy and oral antivirals are preferred in this scenario. However, remdesivir may be considered if neither monoclonal antibody or oral antivirals are not indicated or available.

- 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.
- 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.
- Use of remdesivir in pediatric patients (< 12 years of age) and patients weighing < 40 kg would be considered off-label use. Use of the lyophilized powder for hospitalized pediatric patients weighing ≥ 3.5 kg is available under an EUA. 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:
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 days¹² 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 not requiring supplemental oxygen who are ≥ 40 kg, 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.
**Sotrovimab (Xevudy)**\(^{13,14}\)
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 variant, however decreased activity against the BA.2 subvariant.

- Patients ≥ 12 years of age (and ≥ 40 kg) referred for sotrovimab 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 sotrovimab will be limited to those determined to be highest risk for progression to severe COVID-19 and hospitalization based on 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 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.

**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)**\(^{15-22}\)
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. 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 with questions:

<table>
<thead>
<tr>
<th>Medication</th>
<th>Notes</th>
</tr>
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<tbody>
<tr>
<td>ACE inhibitors and ARBs(^{23})</td>
<td>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.</td>
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<tr>
<td>Azithromycin(^{24})</td>
<td>Azithromycin with or without hydroxychloroquine is NOT recommended for the treatment of COVID-19.</td>
</tr>
<tr>
<td>Bamlanivimab(^{25})</td>
<td>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.</td>
</tr>
<tr>
<td>Bamlanivimab/Etesevimab(^{26,27})</td>
<td></td>
</tr>
<tr>
<td>Casirivimab/Imdevimab (REGEN-COV)(^{28-30})</td>
<td>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.</td>
</tr>
<tr>
<td>Colchicine(^{31})</td>
<td>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.</td>
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<tr>
<td>Famotidine(^{32})</td>
<td>Use of H2 blockers or proton pump inhibitors specifically for the treatment of COVID-19 is not recommended.</td>
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<tr>
<td>Fluvoxamine(^{33-35})</td>
<td>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.</td>
</tr>
<tr>
<td>Hydroxychloroquine(^{24,36-39})</td>
<td>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.</td>
</tr>
<tr>
<td>Interferons(^{41})</td>
<td>Data specific to SARS CoV-2 are lacking. Interferon is currently not recommended for the treatment of COVID-19. Clinical trials are ongoing.</td>
</tr>
<tr>
<td>Ivermectin(^{42-45})</td>
<td>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.</td>
</tr>
<tr>
<td>Treatment</td>
<td>Description</td>
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<tr>
<td>Ivermectin</td>
<td>If disseminated strongyloidiasis is being considered, ivermectin remains the treatment of choice and requires ID approval.(^{46,47})</td>
</tr>
<tr>
<td>IVIG</td>
<td>Use of IVIG for COVID-19 is not recommended outside of use for MIS-C and MIS-A.</td>
</tr>
<tr>
<td>Nitazoxanide(^{48})</td>
<td>Displays inhibitory activity against the SARS-CoV-2 \textit{in vitro}. Nitazoxanide is currently not recommended for the treatment of COVID-19 for ambulatory or hospitalized patients with COVID-19.</td>
</tr>
<tr>
<td>Ribavirin</td>
<td>There are insufficient data to recommend the use of ribavirin for the treatment of COVID-19.</td>
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<tr>
<td>Tofacitinib(^{49})</td>
<td>Tofacitinib(^{49}) 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.</td>
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</tbody>
</table>
References:


