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

<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>Corticosteroids are not recommended.</td>
</tr>
<tr>
<td></td>
<td><em>Outpatient:</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td>For oral antivirals, like Paxlovid™, please see details below:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Patient cannot be hospitalized for COVID-19</td>
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<tr>
<td></td>
<td>• Patient must be able to initiate treatment within 5 days of symptom onset with presumed or confirmed COVID-19.</td>
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<tr>
<td></td>
<td>• Patients considered to have a risk factor for severe COVID-19 including age over 50, being unvaccinated or not being up-to-date with COVID-19 vaccination, or specific medical conditions or behaviors.</td>
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<tr>
<td></td>
<td>For questions regarding Paxlovid™ please click <a href="#">here</a>.</td>
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<tr>
<td></td>
<td>Please visit the <a href="#">COVID-19 therapeutics locator</a> to find locations able to dispense antivirals.</td>
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<tr>
<td></td>
<td><strong>Inpatient:</strong></td>
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<td></td>
<td>Inpatients not hospitalized for COVID-19 but who develop symptomatic COVID-19 while hospitalized or are admitted for indications not related to COVID-19 can be considered for antivirals including Paxlovid™ or remdesivir in discussion with Infectious Diseases.</td>
<td></td>
</tr>
<tr>
<td><strong>Hospitalized requiring low-flow nasal cannula (SpO2 ≤ 94% on RA)</strong></td>
<td>Supportive care</td>
<td>Remdesivir (Veklury®) — non-formulary, requires ID approval.</td>
</tr>
<tr>
<td></td>
<td><strong>Recommend:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Dexamethasone</td>
<td>Remdesivir is not recommended in patients with an ALT &gt; 5 times with upper limit of normal. Patients who require minimal oxygen support may receive remdesivir alone without dexamethasone.</td>
</tr>
<tr>
<td></td>
<td>• Remdesivir</td>
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</tr>
</tbody>
</table>
In addition to remdesivir, anticoagulation, and dexamethasone consider referring for enrollment in available Clinical Trials.

<table>
<thead>
<tr>
<th>Hospitalized with rapidly escalating oxygen needs and/or requiring non-rebreather, high flow nasal cannula, or non-invasive ventilation (i.e., BiPAP)</th>
<th>Supportive care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommend:</strong></td>
<td>Dexamethasone 6 mg IV/PO once daily for up to 10 days</td>
</tr>
<tr>
<td>• Dexamethasone</td>
<td>Dexamethasone should not be continued after discharge unless patient has a history of being on chronic steroid therapy.</td>
</tr>
<tr>
<td>• Remdesivir</td>
<td></td>
</tr>
<tr>
<td>• Baricitinib or tocilizumab</td>
<td>See above</td>
</tr>
</tbody>
</table>

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.

<table>
<thead>
<tr>
<th>Hospitalized requiring mechanical ventilation or ECMO</th>
<th>Supportive care</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommend:</strong></td>
<td>Remdesivir is not recommended. See above.</td>
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<tr>
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<td></td>
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</table>
Medications used for TREATMENT of COVID-19 (listed alphabetically):

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 RECOVERY² 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-2³ and COV-BARRIER⁴ 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.

Dexamethasone⁵,⁶
- 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™)9,10
In May 2023, the FDA approved Paxlovid™ for the treatment of mild-moderate COVID-19 in patients at high risk for progression to severe disease. 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 as first line for the treatment of symptomatic patients (≥ 12 years of age weighing at least 40 kg or 88 pounds) who have ≤ 5 days of symptoms, have confirmed or high suspicion for COVID-19.

Paxlovid™ is not authorized for pre- or post-exposure prophylaxis or asymptomatic COVID-19.

Due to the current federal distribution of Paxlovid™ by Health and Human Services (HHS), it remains under an EUA and, as such, off-label use (e.g. pre-emptive prescribing for travel, prolonged courses, and treatment of severe or critical disease) is prohibited.

A comprehensive review of Frequently Asked Questions regarding EUA Paxlovid is available from the FDA.

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.

Most drug-drug interactions can be overcome with holding of medications or dose adjustment. Please use the below tools to assess and manage 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

Please visit the COVID-19 therapeutics locator to find locations able to dispense antivirals.
In New York City, Paxlovid™ can also be prescribed through Alto Pharmacy for home delivery. 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:

- Verify patient’s phone number and address for delivery and advise the patient that they will receive a call or text message to schedule delivery.
- In the pharmacist note section, document date of symptom onset
- For patients with moderate renal dysfunction (eGFR ≥30 to < 60 mL/min), specify dosing for the renal dose pack: 150 mg nirmatrelvir (one 150 mg tablet) with 100 mg ritonavir (one 100 mg tablet) taken together twice daily for 5 days.

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.

“Rebound” after receiving Paxlovid™ and without antiviral therapy11 has been reported between 2-8 days after initial recovery and is characterized by a recurrence in symptoms or a new positive viral test after a negative test. Re-treatment with Paxlovid™ or other anti-SARS-CoV-2 therapy is not recommended at this time. Concern about potential rebound should not influence offering Paxlovid™ to patients who may derive benefit.

Molnupiravir (Legevrio®)12,13
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 be 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 not contraindicated.

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 confirmed or high suspicion for COVID-19 and are at risk for progression to severe disease.

Molnupiravir is not authorized for pre- or post-exposure prophylaxis or asymptomatic COVID-19.

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. If a patient is pregnant and is unable to be prescribed alternative treatment, please consult Infectious Diseases and Maternal Fetal Medicine to make an appropriate treatment plan.
- **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.

Please visit the COVID-19 therapeutics locator to find locations able to dispense antivirals.

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.

- Verify patient’s phone number and address for delivery and advise the patient that they will receive a call or text message to schedule delivery.
- In the pharmacist note section, document date of symptom onset

**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/](https://pregnancyreporting.msd.com/)

**Remdesivir (Veklury®)**
 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. PINETREE, a randomized controlled trial, was conducted evaluating outpatient administration of remdesivir for three days in the setting of symptomatic COVID-19 in unvaccinated patients at high-risk for progression. The single study noted an 87% decrease in the risk of hospitalization compared with placebo.

- 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 early, 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 or until hospital discharge, whichever is sooner. Patients should not remain hospitalized solely to complete course of remdesivir if discharge is appropriate.

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®)\(^{18-25}\)
The FDA approved the use of tocilizumab for the treatment of hospitalized adult patients with COVID-19 who are receiving systemic corticosteroids and require supplemental oxygen on December 21, 2022. Use of tocilizumab for similar indications remains under emergency authorization by the FDA for pediatric patients (2-17 years old). A meta-analysis of 27 trials noted a 28-day mortality benefit with the use of IL-6 antagonists with concomitant corticosteroids.\(^{25}\) 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. For patients age 2 years to 17 years old, 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:

<table>
<thead>
<tr>
<th>Medication</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Anakinra</strong> (Kinaret®)</td>
<td>Anakinra is an IL-1 receptor antagonist that is authorized by the FDA as on November 8, 2022 for the treatment of COVID-19 in certain hospitalized patients at risk for developing severe respiratory failure based on the results of the SAVE-MORE trial. Enrollment into this clinical trial was based on plasma soluble urokinase plasminogen activator receptor (suPAR) level ≥ 6 ng/mL. This assay is not commercially available in the United States. At this time, use of anakinra in the treatment of COVID-19 requires ID consultation.</td>
</tr>
<tr>
<td><strong>Azithromycin</strong></td>
<td>Azithromycin with or without hydroxychloroquine is <strong>NOT</strong> recommended for the treatment of COVID-19.</td>
</tr>
<tr>
<td><strong>Colchicine</strong></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>
</tr>
<tr>
<td><strong>Fluvoxamine</strong></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 <strong>NOT</strong> recommended for the treatment of COVID-19 for ambulatory or hospitalized patients outside of a clinical trial.</td>
</tr>
<tr>
<td><strong>Hydroxychloroquine</strong></td>
<td>Hydroxychloroquine is <strong>NOT</strong> recommended for prophylaxis or treatment of COVID-19. Co-administration of remdesivir and hydroxychloroquine or may result in reduced antiviral activity of remdesivir. Patients prescribed hydroxychloroquine for preexisting rheumatologic conditions should be continued on their current dose.</td>
</tr>
<tr>
<td><strong>Ivermectin</strong></td>
<td><em>In vitro</em> 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. Recent trials (i.e., ACTIV-6) demonstrate did not support the use of ivermectin in patients with mild-moderate COVID-19. 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 <strong>not</strong> recommended. If disseminated strongyloidiasis is being considered, ivermectin remains the treatment of choice and requires ID approval.</td>
</tr>
<tr>
<td><strong>IVIG</strong></td>
<td>Use of IVIG for COVID-19 is <strong>not</strong> recommended outside of use for MIS-C and MIS-A.</td>
</tr>
<tr>
<td><strong>Tofacitinib</strong></td>
<td>Tofacitinib 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 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 <strong>not</strong> recommended due to the potential risk of infectious complications.</td>
</tr>
</tbody>
</table>
References:


