This algorithm is intended to help clinicians at the point of care initiate oral antiviral treatment for COVID-19. Based on efficacy data, nirmatrelvir/ritonavir (NMV/r) is the preferred agent, followed by molnupiravir.

**Signs of SEVERE MEDICAL ILLNESS?**

- STOP. Evaluate patient for a higher level of care.

**<5 days from SYMPTOM ONSET?**

- YES
- No

**DRUG INTERACTIONS:** Is the patient on any drugs that interact with NMV/r or cannot be substituted?

- YES
- NO

**Known/expected severe RENAL (GFR <30) or HEPATIC impairment?**

- YES
- NO

**HIGH RISK PATIENT?**

- YES
- NO

**Assess for NMV/r treatment**

- Consider NMV/r
- Not eligible for NMV/r. Assess for molnupiravir.

**Not eligible for oral antivirals. Consider IV therapeutics, see accompanying table.**

**Consider molnupiravir**

- If molnupiravir is not available, consider IV antivirals.

**E.g. worsening dyspnea, SpO2 <94% on room air,** new O2 requirement, confusion, respiratory distress, need for labs/imaging

**Symptomatic COVID-19 infection confirmed by PCR, NAAT, Antigen test or home test**

- YES
- NO

**AGE: Is the patient ≥18, or ≥12yrs AND ≥40kg?**

- YES
- NO

**≥18 years old?**

- YES
- NO

**Is the patient pregnant, trying to get pregnant, breastfeeding?**

- YES
- NO

**Is the patient ≥18, or ≥12yrs AND ≥40kg?**

- YES
- NO

**Confirm: This algorithm is intended to be educational in nature and is not a substitute for clinical decision making based on the medical condition presented. It is the responsibility of the user to ensure all information contained herein is current and accurate and applicable to the local context by using published references.**

**Assess: Common symptoms:**

- Fever
- Cough
- Rhinorrhea
- Chills
- Dyspnea

**Respond:**

- Common indications to test:
  - New severe symptoms
  - Symptoms with a COVID-19 exposure
  - Symptoms in an area with high COVID-19 prevalence

**Evaluate:**

- This algorithm is intended to get eligible symptomatic COVID-19 patients treated as soon as possible. If the patient has symptoms but tests negative, consider re-testing at a later point.

**Manageable drug interactions with NMV/r include:**

- Dopamine—hold if QT prolongation or prolongation do not need to be hold
- DOACs—dabigatran and edoxaban likely safe, apixaban seek expert advice, avoid rivaroxaban
- Alpha-1 blockers—hold tamsulosin and others for 8 days
- Warfarin—monitor, NMV may fall out of therapeutic range
- Inhaled beta agonists—hold for 8 days, formoterol/salmeterol fine
- Calcium channel blockers—avoid if possible, careful monitoring and dose adjustment
- Calcium channel blockers—monitor and consider dose decrease
- Antipsychotics—avoid if possible, dose reduction needed
- Opiates—consider dose decrease by 50-75% for 8 days, except methadone
- Oral contraceptives—Barrier method recommended until next cycle
- SSRI—monitor, locally available in short course
- Triglides—hold for 8 days, ezetimibe/simvastatin fine
- Benzodiazepines—monitor, consider dose reduction, don't use triazolam
- Chemotherapy and small molecule inhibitors—review with oncology
- Oral corticosteroids—monitor, consider 50-75% dose reduction
- Sildenafil/tadalafil/vardenafil—hold for 8 days
- Tramadol—consider use contraindicated
- Enoxaparin—consider use contraindicated
- Established renal therapy—do not change established dosing

For a comprehensive list visit: https://covid19-druginteractions.org/checker

Other interactions may be manageable. If an interacting drug cannot be managed, another antiviral (e.g. molnupiravir) might be indicated.

**Renal and liver function do not need to be routinely assessed before starting treatment.**

- Patients with mild renal impairment (GFR 30-60) should receive a reduced dose
- Severe hepatic impairment means decompensated liver failure, or Child-Pugh Class C liver disease. To calculate Child-Pugh, go to: www.hepatitis.uw.edu/page/clinical-calculators/ctp

**WHO defines “high-risk” as those with:**

- Immunodeficiency syndromes
- Solid organ transplants or autoimmune illnesses on immunosuppressants

Other factors increasing risk include:

- Age ≥ 65
- BMI ≥ 30 kg/m2
- Pregnancy
- Diabetes
- Sickle cell disease
- Chronic cardiopulmonary, kidney or liver disease
- Active cancer
- Those with disabilities
- Other clinician-determined high-risk factor (medical or demographic)

**Disclaimer:**
NMV/r

**Indications**
Age ≥18, or ≥12yrs and ≥40kg

**Modifications**
Renal impairment: Moderate, reduce dose as below. Severe impairment, avoid use. Hepatic: Not recommended in severe impairment

**Dose**
Nirmatrelvir 300mg + ritonavir 100mg every 12 hours x5 days. For moderate renal impairment use nirmatrelvir 150mg + ritonavir 100mg.

**Special requirements**
Drug interactions with CYP3A metabolized medications require special management

**Pregnancy/Lactation**
Limited data (see * at right). May reduce hormonal contraception efficacy, alternative method should be used. No renal adjustment. No hepatic adjustment.

**Route**
Oral

**Cost**
Brand name: $$
Generic: $

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Molnupiravir

**Indications**
Age ≥18

**Modifications**
No renal adjustment. No hepatic adjustment.

**Dose**
800mg orally every 12 hours for 5 days

**Special requirements**
Outpatient only

**Pregnancy/Lactation**
Not recommended, contraception should be used while taking and for 4 days (females) or 3 months (males) after

**Route**
Oral

**Cost**
Brand name: $$
Generic: $

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**Prioritization of therapeutics for COVID-19 when there are logistical constraints**

It may not always be possible to treat every patient who meets criteria. If this is the case, patients with the highest risk for progression to severe disease should be treated first (Tier 1), followed by those in successive tiers.

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccination status</th>
<th>Tier 1</th>
<th>Tier 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥65</td>
<td>Not vaccinated, or no booster</td>
<td></td>
<td>Tier 1</td>
</tr>
<tr>
<td>&lt;65</td>
<td>Fully vaccinated and boosted</td>
<td>Tier 3</td>
<td></td>
</tr>
</tbody>
</table>

All severely or moderately immunocompromised patients are considered Tier 1, regardless of immunization status or other conditions.

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**High risk conditions**
- Cancer
- Cardiovascular disease: e.g. heart failure, coronary artery disease (not isolated hypertension)
- Chronic kidney disease
- Diabetes
- Pregnancy
- Chronic lung disease (e.g. moderate/severe asthma, COPD, ILD, pulmonary hypertension)
- Immunocompromising conditions or receipt of immunosuppressive medications
- Obesity (e.g. body mass index ≥30)

**Immunocompromising conditions**
- Active treatment with high dose corticosteroids (e.g. 20mg prednisone x2 weeks), immunosuppressive cancer therapeutics, or alkylating agents/immunomodulatory biologic agents
- Transplant recipients:
  - Chimeric antigen receptor T cell (CAR T-cell), or hematopoietic cell transplant (HCT), within 2 years of transplant or receiving immunosuppressive therapy
  - Received a solid organ transplant and are receiving immunosuppressive therapy
- Undergoing active treatment for solid or hematologic malignancies
- Hematologic malignancy (e.g., chronic lymphocytic leukemia, non-Hodgkin lymphoma, multiple myeloma, acute leukemia) associated with poor response to COVID-19 vaccines
- Patients with moderate or severe primary immunodeficiencies
- Patients with HIV (especially untreated or advanced HIV infection with CD4 <200 cells/mm3, or AIDS-defining illness)

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