COVID-19

Test-to-Treat: Oral antiviral outpatient therapy algorithm

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.

**START HERE**

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

- **YES**
  - **Signs of SEVERE MEDICAL ILLNESS?**
    - **YES**
      - **STOP. Evaluate patient for a higher level of care.**
    - **NO**
      - **<5 days from SYMPTOM ONSET?**
        - **YES**
          - **HIGH RISK PATIENT?**
            - **YES**
              - **Assess for NMV/r treatment**
            - **NO**
              - **Reflect on accompanying table**
        - **NO**
          - ***pregnant patients, see note in table on accompanying page**

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

There are several potential drug-drug interactions with NMV/r. See sidebar for more information.

- **YES**
  - **Not eligible for oral antivirals. Consider IV therapeutics, see accompanying table.**
- **NO**

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

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

- **YES**
  - **Not eligible for NMV/r. Assess for molnupiravir.**
  - **If molnupiravir is not available, consider IV antivirals.**
- **NO**

**Is the patient ≥18 years old?**

- **YES**
  - **Known/expected severe RENAL (GFR <30) or HEPATIC impairment?**
    - **YES**
      - **Consider NMV/r**
      - **If NMV/r is not available, assess for molnupiravir eligibility.**
    - **NO**
      - **Consider molnupiravir**

**Confirm**

**Assess**

**Respond**

**Evaluate**

**Has your patient tested positive for COVID-19?**

If you are not sure if your patient has COVID-19, consider testing.

- **Common symptoms:**
  - Fever
  - Cough
  - Rhinorrhea
  - Chills
  - Dyspnea
- **Common indications to test:**
  - New severe symptoms
  - Symptoms with a COVID-19 exposure
  - Symptoms in an area with high COVID-19 prevalence

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.

**High-risk factors include:**

- **AGE:**
  - ≥18 yrs AND ≥40kg?
    - **YES**
      - **Is the patient on any SSRIs?**
        - **YES**
          - **Dose adjustments may be necessary for the following drugs**
            - Rifampin
            - Oral contraceptives
            - Antipsychotics
            - Opiates
            - Sildenafil/tadalafil/vardenafil
            - Statins
            - Oral corticosteroids
            - DOACs
            - Triptans
            - Established ritonavir therapy
            - Therapy with small molecule inhibitors
            - Benzodiazepines
            - Chemotherapy and small molecule inhibitors
          - **Consider IV therapeutics, see accompanying table.**
        - **NO**
          - **Not eligible for molnupiravir. Assess for NMV/r.**
      - **NO**
        - **Consider molnupiravir**
        - **If molnupiravir is not available, consider IV antivirals.**
- **BMI ≥ 30 kg/m2**
  - **Pregnancy**
  - **Diabetes**
  - **Sickle cell disease**
  - **Neurodevelopmental disorders**
  - **Cardiovascular disease, hypertension, or lung disease**
  - **Chronic kidney disease, stage 3b or worse**
  - **Neurodevelopmental disorders**
  - **Corticosteroids**
  - **Thrombus**
  - **Hepatic impairment**
  - **Malignancy**
  - **Clinical-determined medical condition, or demographic factor presumed to place the patient at high risk for disease progression**

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

- **Dose adjustments may be necessary for the following drugs**
  - Rifampin
  - Oral contraceptives
  - Antipsychotics
  - Opiates
  - Sildenafil/tadalafil/vardenafil
  - Statins
  - Oral corticosteroids
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**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:**
  - [https://covid19-druginteractions.org/checker](https://covid19-druginteractions.org/checker)
  - For a comprehensive list visit:
    - [https://covid19-druginteractions.org/checker](https://covid19-druginteractions.org/checker)
    - [https://www.hepatitisc.uw.edu/page/clinical-calculators/ctp](https://www.hepatitisc.uw.edu/page/clinical-calculators/ctp)
    - [https://www.hepatitisc.uw.edu/page/clinical-calculators/ctp](https://www.hepatitisc.uw.edu/page/clinical-calculators/ctp)

**Disclaimer:** 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.

Modified from the WHO COVID-19 CLINICAL CARE PATHWAY v2022.5

www.hepatitisc.uw.edu/page/clinical-calculators/ctp
**Indications**

- Age ≥18, and ≥12yrs and ≥40kg
- 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 for 5 days. For moderate renal impairment use nirmatrelvir 150mg + ritonavir 100mg.
- 800mg orally every 12 hours for 5 days

**Special requirements**

- Drug interactions with CYP3A metabolized medications require special management
- Limited data (see * at right). May reduce hormonal contraception efficacy, alternative method should be used.

**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: $

* Consensus does not exist on the recommendation of NMV/r for pregnant patients. The FDA states that for a mother and unborn baby, the benefit of taking NMV/r may be greater than the risk from the treatment, given existing animal studies and the extensive use of ritonavir in pregnant women with HIV. By contrast, WHO states that their strong recommendation for its use does not apply to pregnant patients.

**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.

**Vaccination status**

- Not fully vaccinated, or no booster
- Fully vaccinated and boosted

**Age**

- ≥ 75
- 60 ≤ Age < 75
- Age < 60

**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**

- Patients who are within 1 year of receiving B cell–depleting therapies (e.g., rituximab, ocrelizumab, ofatumumab, alemtuzumab)
- Patients receiving Bruton’s tyrosine kinase inhibitors
- Chimeric antigen receptor T cell recipients
- Transplant recipients:
  - Post-hematopoietic cell transplant recipients who have chronic graft-versus-host disease or who are taking immunosuppressive medications for another indication
  - Lung transplant recipients
  - Patients who are within 1 year of receiving a solid organ transplant (other than lung transplant)
  - Solid organ transplant recipients who had recent treatment with T cell– or B cell–depleting agents for acute rejection
- Cancer
- Patients with hematologic malignancies who are on active therapy
- Patients with severe combined immunodeficiencies
- Patients with HIV

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