McLeod Health Outpatient COVID-19 Treatment Algorithm

For patients eligible to receive outpatient therapy for mild to moderate COVID-19, **treatment should be started as soon as possible after developing COVID-19 symptoms and/or test positive for SARS-CoV-2**. These therapies have proven beneficial only in mild to moderate disease; therefore, patients do not qualify for these treatments if they have a new requirement for supplemental oxygen or an increased need from their baseline supplemental oxygen rate due to COVID-19 since this classifies them as severe disease.

- The greatest benefit is **within 5 days of symptom onset,** but some therapies may be used up to 7 days.
- All therapies listed are authorized for use in individuals **aged 12 years and older** except molnupiravir is only approved for people aged 18 years and older.
- These therapies have not been studied in combination. Patients should only receive **one** regimen.
- All listed medications (except remdesivir) are under Emergency Use Authorization (EUA) through the FDA. Patients should be counseled on the risks and benefits of therapy and provided with a Fact Sheet for Patients and Caregivers for the specific medication before prescribing EUA therapies. Remdesivir is FDA approved and therefore does not require the Fact Sheet.

Tier	Risk Group	Preferred Outpatient Therapy Options (in order of preference, taking into account availability) SELECT ONLY ONE
1A	**Unvaccinated pregnant person OR** **Severely immune compromised** individual (see Table 1) not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccination status	1. Nirmatrelvir/ritonavir (PAXlovid) PO BID x 5 d 2. Bebtelovimab IV once – **priority for hyperemesis or major drug interactions to PAX (see Table 3)** 3. Remdesivir IV daily x 3 d – priority if major drug interactions to PAX (see Table 3)
1B	**Vaccinated pregnant** person **without** a booster **OR** **Unvaccinated** individuals at the highest risk of severe disease, defined as at least one of the following: • Aged ≥ 75 years • Aged ≥ 65 years with any clinical risk factor (see Table 2)	
2	**Vaccinated pregnant** person **with** a booster **OR** **Unvaccinated** individuals at risk of severe disease not included in Tier 1 AND meeting at least one of the following: • Aged ≥ 65 years • Aged < 65 years with any clinical risk factor (see Table 2)	1. Nirmatrelvir/ritonavir (PAXlovid) PO BID x 5 d 2. Bebtelovimab IV once – **priority for hyperemesis or major drug interactions to PAX (see Table 3)** 3. Remdesivir IV daily x 3 d – priority if major drug interactions to PAX (see Table 3) 4. Molnupiravir oral twice daily x 5 d*
3	**Vaccinated** individuals **regardless of booster** status but at risk of severe disease, defined as at least one of the following: • Aged ≥ 75 years • Aged ≥ 65 years with any clinical risk factor (see Table 2)	
4	**Vaccinated** individuals **regardless of booster** status but at risk of severe disease, defined as at least one of the following: • Aged ≥ 65 years • Aged < 65 years with any clinical risk factor (see Table 2)	

*DO NOT use molnupiravir in pregnancy. Patients of reproductive age should be counseled on the risks of fetal toxicity.

MEDICATION AVAILABILITY MAY BE LOCATED AT:

https://healthdata.gov/Health/COVID-19-Public-Therapeutic-Locator/rxn6-qnx8

5/20/22

Supplemental Information:

Nirmatrelvir/ritonavir (Paxlovid) - FREE

- **Dose:** Two 150 mg tablets of nirmatrelvir (300 mg total per dose) + one 100 mg tablet of ritonavir PO twice daily (dispensed from pharmacy in blister packs)
  - AVOID if creatinine clearance (CrCl) is less than 30 mL/min or end stage renal disease
  - CrCl between 30-59 mL/min: 1 tablet nirmatrelvir 150 mg + 1 tablet ritonavir 100 mg PO twice daily x 5 days
  - AVOID in patients with severe hepatic impairment
- **FDA EUA Indication:** 12+ years old weighing > 40 kg
  - Paxlovid Fact Sheet for Patients, Parents, and Caregivers
- **Drug interaction screening is extremely important due to known major and potentially life-threatening drug interactions with ritonavir (see NIH Statement on Paxlovid Drug Interactions for more information).**
- **Access Pathway:** Prescriptions must be sent to SC DHEC-designated pharmacy (see therapeutic locator)

Bebtelovimab

- **Dose:** 175 mg IV push once
- **FDA EUA Indication:** 12+ years old weighing > 40 kg
  - Fact Sheet will be provided at infusion center
- **Access Pathway:** Patient referral to COVID infusion center by visiting McLeodHealth.org

Remdesivir (Veklury)

- **Dose:** 200 mg IV once x 1 day then 100 mg IV daily x 2 days (3 days total)
  - Avoid if CrCl < 30 mL/min, known hepatic disease or ALT > 10 x ULN
- **FDA Approved Indication:** 12+ years old weighing > 40 kg
- **Access Pathway:** Patient referral to COVID infusion center by visiting McLeodHealth.org (Only offered when monoclonal antibody not available)

Molnupiravir (Lagevrio) - FREE

- **Dose:** Four 200 mg tablets (800 mg total per dose) by mouth twice daily x 5 days
- **FDA EUA Indication:** 18+ years old
  - Molnupiravir Fact Sheet for Patients and Caregivers
- DO NOT USE in pregnancy. Consider confirming negative pregnancy test.
- Patients of reproductive potential should be counseled to use a reliable method of contraception correctly and consistently for the 5-day duration of molnupiravir plus an additional 4 days after completing therapy for females and an additional 3 months for males with partners who may become pregnant.
- **Access Pathway:** Prescriptions must be sent to SC DHEC-designated pharmacy (see therapeutic locator)

Table 1. Severe Immune Compromising Conditions

- Within 1 year of receiving B cell-depleting therapies (e.g., rituximab, ocrelizumab, ofatumumab, alemtuzumab)
- Receiving Bruton tyrosine kinase inhibitors
- Chimeric antigen receptor T cell (CAR-T) recipients
- Post-hematopoietic cell transplant recipients who have chronic graft versus host disease (GVHD) or who are taking immunosuppressive medications for another indication
- Hematologic malignancies on active therapy
- Lung transplant recipients, regardless of date of transplant
- Within 1 year of receiving a solid-organ transplant (other than lung)
- Severe combined immunodeficiencies
- Untreated HIV with a CD4 cell count < 50 cells/mm^3

Table 2. Clinical Risk Factors for Progression to Severe COVID-19

- Adult with BMI > 35 or pediatric patient > 85^{th} percentile for weight
- Immune compromising condition other than Tier 1 severe immune compromising condition (listed in Table 1)
- Cancers other than Tier 1 hematologic malignancies (listed in Table 1)
- Diabetes mellitus, type 1 or 2
- Chronic kidney disease
- Chronic lung disease
- Neurodevelopmental disorder
- Cerebrovascular disease
- Chronic liver disease
- Heart condition
- Hypertension
- Medical-related technology dependence (e.g., tracheostomy, gastrostomy)
- Sickle cell disease
- Smoking, current or former

Paxlovid™ Prescribing Algorithm

Does patient have positive SARS-CoV-2 **AND** active, new symptoms?

No → Screen for SARS-CoV-2 vaccination

Yes

Meet EUA criteria for Paxlovid™?
≥ 12 years and ≥ 40 kg and risk of progression to severe disease (refer to reference 1)

No → No outpatient treatment currently recommended

Yes

How many days **since symptom onset**?

≥ 6 days → Consider **bebtelovimab** outpatient infusion if symptoms ≤ 7 days
See COVID-19 Outpatient Infusion Referral Form[2]

≤ 5 days

Does patient have **contraindicated medications**?[3]

Ex: anticonvulsants (except levetiracetam), antiarrhythmics, anticoagulants/antiplatelets, pulmonary hypertension therapy, and immunosuppressants (including chemotherapy)

Yes → **Avoid Paxlovid™, consider bebtelovimab** outpatient infusion if symptoms ≤ 7 days
See COVID-19 Outpatient Infusion Referral Form[2]

No

Presence of **severe hepatic disease (Child-Pugh C)** or **unable to take oral medications**?

Yes → Consider **bebtelovimab** outpatient infusion if symptoms ≤ 7 days
See COVID-19 Outpatient Infusion Referral Form[2]

No

End-stage renal disease or CrCl < 30 mL/min?

Yes → Consider **bebtelovimab** outpatient infusion if symptoms ≤ 7 days
See COVID-19 Outpatient Infusion Referral Form[2]

No

Renal dosing (eGFR):
≥ 60 mL/min: 300 mg nirmatrelvir and 100 mg ritonavir orally twice daily for 5 days (3 tablets/dose)
30 to 59 mL/min: 150 mg nirmatrelvir and 100 mg ritonavir orally twice daily for 5 days (2 tablets/dose)

References:

1. https://www.mcleodhealth.org/wp-content/uploads/2022/04/McLeod-Health-Outpatient-COVID-Guidelines-4-6-22.pdf
2. https://www.mcleodhealth.org/wp-content/uploads/2022/04/COVID-Outpatient-Infusion-Form-4-6-22.pdf
3. https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ritonavir-boosted-nirmatrelvir--paxlovid-/paxlovid-drug-drug-interactions/

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