COVID-19

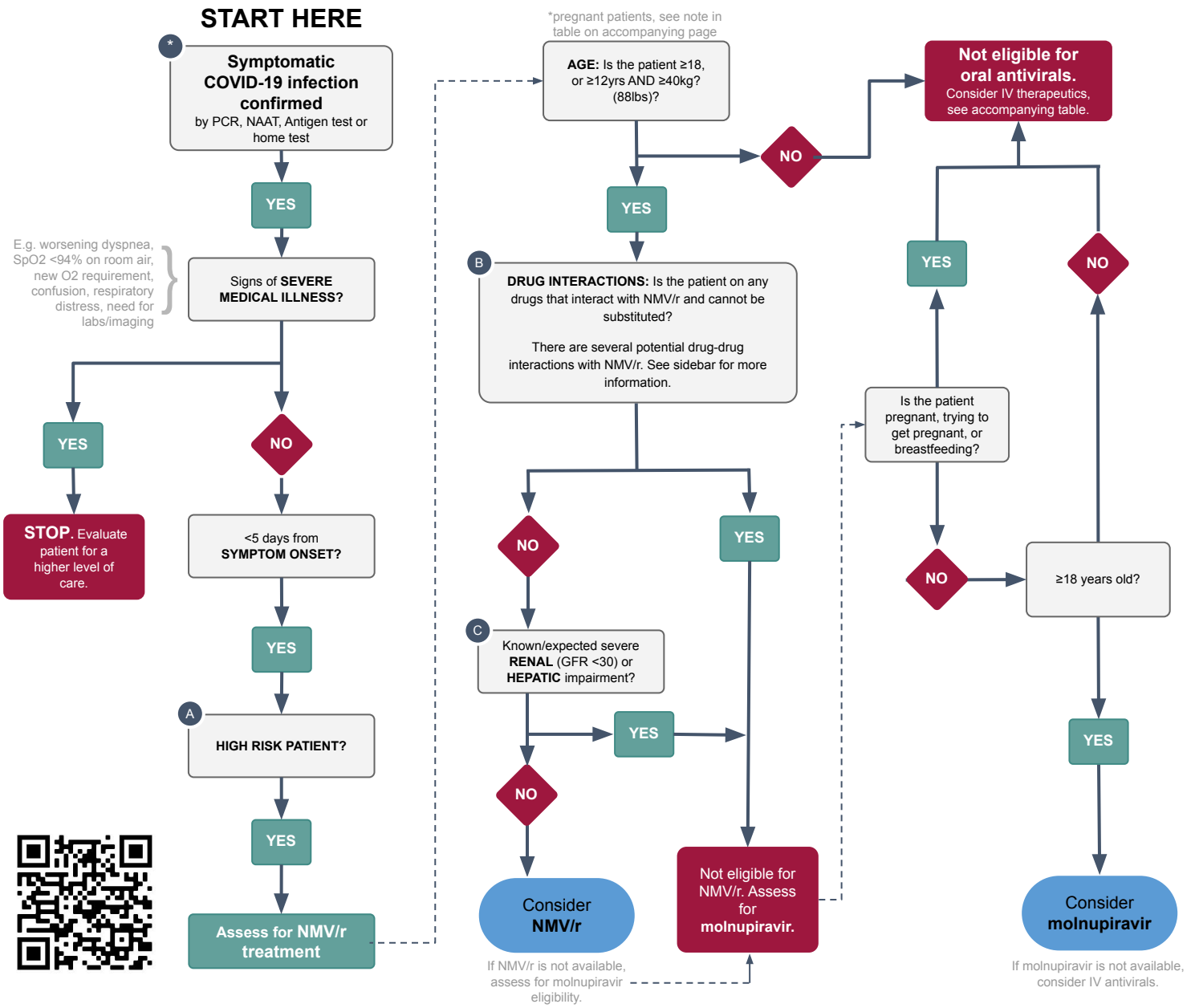
Test-to-Treat: Oral antiviral outpatient therapy algorithm

v2024.2.1

Modified from the **WHO COVID-19 CLINICAL CARE PATHWAY**

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.**

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.

A 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
- Tuberculosis
- Chronic cardiopulmonary, kidney or liver disease
- Active cancer
- Those with disabilities,
- Other clinician-determined high-risk factor (medical or demographic)

B Manageable drug interactions with NMV/r include:
Dose adjustments may be necessary for the following drugs
- **Statins** – hold 8 days, pitavastatin and pravastatin do not need to be held
- **DOACs**—dabigatran and edoxaban likely safe, apixaban seek expert advice, avoid rivaroxaban
- **Alpha-1 blockers** – hold tamsulosin and others for 8 days
- **Warfarin** —monitor, INR may fall out of therapeutic range
- **Inhaled beta agonists** — hold salmeterol for 8 days, formoterol/albuterol fine
- **Calcineurin inhibitors** — 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
- **SSRIs** — monitor, toxicity unlikely in short course
- **Triptans** — hold eletriptan and zolmitriptan, sumatriptan 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
- **Rifampin** — concomitant use contraindicated
- **Established ritonavir therapy** — do not change established ritonavir dose

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.

C **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.hepatitisc.uw.edu/page/clinical-calculators/ctp

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C A **R** E
Confirm Assess **Respond** Evaluate

Additional medication specific information

	NMV/r	Molnupiravir
Indications	Age ≥18, or ≥12yrs and ≥40kg	Age ≥18
Modifications	Renal impairment: Moderate, reduce dose as below. Severe impairment, avoid use. Hepatic: Not recommended in severe impairment	No renal adjustment. No hepatic adjustment.
Dose	Nirmatrelvir 300mg + ritonavir 100mg every 12 hours x5 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	Outpatient only
Pregnancy/ Lactation	Limited data (see * at right). May reduce hormonal contraception efficacy, alternative method should be used.	**Not recommended**, contraception should be used while taking and for 4 days (females) or 3 months (males) after
Route	Oral	Oral
Cost	Brand name: $$ Generic: $	Brand name: $$ Generic: $

FDA and WHO guidelines agree on the possible benefit of NMV/r in pregnant patients. The FDA suggests that the benefits outweigh the risks, while WHO recommends NMV/r be offered after fully informed shared decision-making.

Note: The test-to-treat strategy relies on oral agents, as they can be easily initiated at the point of care. If these agents are not available, consider the use of IV therapeutics (e.g. remdesivir, sotrovimab).

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	Age ≥ 75	Tier 1	Tier 3
	≥ 65 Age <75	High risk condition = Tier 1	High risk condition = Tier 3
		No high risk condition = Tier 2	No high risk condition = Tier 4
	Age <65	High risk condition = Tier 2	High risk condition = Tier 4

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

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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