## Clinical Priority Tiers

Patients are considered unboosted if eligible for their **first booster** and overdue

### Tier 1
- **Severe immunocompromise** (e.g., transplant, active chemo, rituximab)
- **Moderate immunocompromise** (e.g., anti-TNF, chronic prednisone)
- **Oxygen dependence** (any vaccination status)
- **Not fully vaccinated or unboosted and age $\geq 75$ years** (no high-risk condition)
- **Not fully vaccinated or unboosted and age $\geq 55$ years + high risk condition**

### Tier 2
- **Not fully vaccinated or unboosted and age $\geq 55$ years**
- **Not fully vaccinated or unboosted and age $< 55$ years + high risk condition**
- **Sickle cell disease** (any vaccination status)
- **BMI $\geq 40$** (any vaccination status)
- **Chronic kidney disease, eGFR < 30 or ESRD** (any vaccination status)

### Tier 3
- **Fully vaccinated and boosted and age $\geq 75$ years** (no high-risk condition)
- **Fully vaccinated and boosted and age $\geq 55$ years + high risk condition**
- **Fully vaccinated and boosted and pregnant**

### Tier 4
- **Fully vaccinated and boosted and age $\geq 55$ years** (no high-risk condition)
- **Fully vaccinated and boosted and age $< 55$ years + high risk condition**

### High Risk Conditions

**Severe immunocompromise**: Active anti-CD20 therapy, chronic corticosteroids (prednisone $>20$mg daily or equivalent), cyclosporin, multiple agents (e.g., prednisone and mycophenolate), abatacept, Bruton tyrosine kinase inhibitors (e.g., ibrutinib, acalabrutinib, zanabrutinib), solid organ transplant, stem cell transplant, active chemotherapy, advanced HIV infection, moderate or severe congenital immunodeficiency

**Moderate immunocompromise**: corticosteroids (prednisone $<20$mg daily, or equivalent), TNF alpha inhibitors (infliximab, adalimumab, certolizumab, golimumab, etanercept), methotrexate, leflunomide, azathioprine, fingolimod, JAK inhibitors (e.g., ruxolitinib, upadacitinib), tyrosine kinase inhibitors (axitinib, dasatinib, erlotinib, pazopanib, sunitinib, cyclophosphamide, mycophenolate, tacrolimus, sirolimus, other congenital and acquired immunocompromise states.

**Cardiovascular disease**: Heart failure, cardiomyopathy, coronary artery disease, congenital heart disease.

*Note: hypertension alone is not considered a high-risk condition*

**Chronic lung disease**: Moderate to severe asthma (does not include mild asthma with no recent exacerbations, exercise-induced asthma, or albuterol prescription alone), bronchiectasis, COPD (emphysema and chronic bronchitis), interstitial lung disease, pulmonary embolism, pulmonary hypertension, cystic fibrosis

**Chronic liver disease**: Cirrhosis, fatty liver disease, autoimmune hepatitis, alcohol liver disease

**Neurologic disease**: Stroke, dementia

**Obesity**: BMI $>30$; **Pregnancy**; **Chronic kidney disease**; **Diabetes**; other medical conditions as per CDC

**Multimorbidity**: Patients with multiple or advanced comorbidities limiting ADLs can be considered one tier higher as guided by clinician judgement

Guidance regularly updated, last revised April 18, 2022
Outpatient Treatment for Early COVID-19

Non-pregnant adults

Confirmed symptomatic COVID-19 (Antigen or PCR)

7 days or less of non-improving symptoms

Clinical Priority Tier 1, 2, 3, or 4

Symptoms for 5 days or less by time of treatment

GFR >30 mL/min

Class A or B medications only

Molnupiravir
800mg po q12h x 5 days
(if 5 days or less of symptoms)

IV Therapies
preferred therapy directed by availability and expected susceptibility of circulating variants

Remdesivir
200mg IV x 1 followed by 100mg IV q24h x 2

— or —

Bebtelovimab
175mg IV x 1

Nirmatrelvir-Ritonavir (Paxlovid)

GFR>60:
300mg/100mg po q12h x 5 days

GFR 30-60:
150mg/100mg po q12h x 5 days

Supportive therapy

Clinical priority
Factors associated with increased severity of COVID-19

Class A medications
No expected interaction with nirmatrelvir-ritonavir

Class B medications
Medications that potentially interact with nirmatrelvir-ritonavir but can be safely suspended, dose-reduced, or monitored

Class C medications
Medications that cannot be safely taken with nirmatrelvir-ritonavir

Guidance regularly updated, last revised April 18, 2022
Outpatient Treatment for Early COVID-19

Pregnant adults

Confirmed symptomatic COVID-19 (Antigen or PCR)
7 days or less of non-improving symptoms

Symptoms for 5 days or less by time of treatment

GFR >30 mL/min

Class A or B medications only

Remdesivir
200mg IV x 1 followed by 100mg IV q24h x 2

– or –
(f/remdesivir not available or inappropriate)
Bebtelovimab
175mg IV x 1

Nirmatrelvir-Ritonavir (Paxlovid)
GFR>60:
300mg/100mg po q12h x 5 days
GFR 30-60:
150mg/100mg po q12h x 5 days

Supportive therapy

IV Therapies preferred therapy directed by availability and expected susceptibility of circulating variants

No expected interaction with nirmatrelvir-ritonavir

Medications that potentially interact with nirmatrelvir-ritonavir but can be safely suspended, dose-reduced, or monitored

Medications that cannot be safely taken with nirmatrelvir-ritonavir

Class A medications
Class B medications
Class C medications

Guidance regularly updated, last revised April 18, 2022
Outpatient Treatment for Early COVID-19
Children ≥12 years (40 kg or greater) and young adults (age ≤ 21) in pediatrics

Confirmed symptomatic COVID-19 (Antigen or PCR)
7 days or less of non-improving symptoms

Clinical priority Tier
1, 2, 3, or 4

Clinical priority
Factors associated with increased severity of COVID-19

Supportive therapy

Symptoms for 5 days or less by time of treatment

GFR >30 mL/min

Remdesivir
200mg IV x 1 followed by 100mg IV q24h x2

– or –
(if remdesivir not available or appropriate)
Bebtelovimab
175mg IV x 1

Nirmatrelvir-Ritonavir (Paxlovid)

GFR >60:
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Class C medications
Medications that cannot be safely taken with nirmatrelvir-ritonavir

If you think your patient qualifies for outpatient oral or IV therapy, page Pediatric ID (virtual pager 14290).

Referring providers are responsible for patient/family counseling as well as prescriptions and ongoing monitoring.

Guidance regularly updated, last revised April 18, 2022
## Medication Categories for Nirmatrelvir-Ritonavir

Interactions can be complex. Advise caution and consultation.

### Category A — No expected interaction

**Most medications.** Advise reviewing interaction alerts in Epic, utilizing *Liverpool Covid-19 Drug Interaction Checker*, and *FDA EUA document* that includes detailed guidance.

### Category B — Potential interaction but *may* be manageable

- **Statins** — hold 8 days, pitavastatin and pravastatin do not need to be held
- **Alpha-1 blockers** — hold tamsulosin and others for 8 days
- **Inhaled beta agonists** — hold salmeterol for 8 days, formoterol/albuterol fine
- **Calcium channel blockers** — may increase CCB concentration, monitor or dose reduce
- **Opiates** — consider dose decrease by 50-75% for 8 days, except methadone
- **Oral corticosteroids** — monitor, consider 50-75% dose reduction
- **Sildenafil/tadalafil/vardenafil** — hold for 8 days

- **DOACs** — dabigatran and edoxaban likely safe, apixaban seek expert advice, avoid rivaroxaban
- **Warfarin** — monitor, INR may fall out of therapeutic range
- **Calcineurin inhibitors** — Avoid if possible, careful monitoring and dose adjustment
- **Antipsychotics** — Many in Category C, avoid if possible, dose reduction needed
- **Oral contraceptives** — Barrier method recommended until next cycle
- **Triptans** — hold eletriptan, sumatriptan fine

### Category C — Nirmatrelvir-ritonavir should not be used

Commonly used medications *(top 300)* in **bold**.

<table>
<thead>
<tr>
<th>Category</th>
<th>Medication</th>
<th>Interaction Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category B</td>
<td><strong>Statins</strong> — hold 8 days, pitavastatin and pravastatin do not need to be held</td>
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<td></td>
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<td>Chemotherapy and small molecule inhibitors — review with oncology</td>
</tr>
</tbody>
</table>

**Amiodarone**

**Eplerenone**

**Pimozide**

**Apalutamide**

**Ergot derivatives**

**Propafenone**

**Bosentan**

**Flecainide**

**Quinidine**

**Carbamazepine**

**Flibanserin**

**Ranolazine**

**Cisapride**

**Glecaprevir/pibrentasivr**

**Rifampin / Rifapentine**

**Clopidogrel** *(in high risk for thrombosis)*

**Ivabradine**

**Rivaroxaban**

**Clozapine**

**Lumateperone**

**Sildenafil** *(for pulmonary hypertension)*

**Colchicine** *(in hepatic/renal impairment)*

**Lurasidone**

**St. John’s wart**

**Disopyramide**

**Mexiletine**

**Taladafil** *(for pulmonary hypertension)*

**Dofetilide**

**Phenobarbital**

**Ticagrelor**

**Dronedarone**

**Phenytoin**

**Vorapaxar**

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**Guidance regularly updated, last revised Mar 3, 2022**
Referral for Parenteral Therapy COVID-19 Pathway

Confirmed symptomatic COVID-19 (Antigen or PCR)
7 days or less of non-improving symptoms

Clinical priority Tier 1, 2, 3, or 4

Yes

Contact ordering provider that not appropriate for parenteral therapy
Options to suggest: Nirmatrelvir-ritonavir Molnupiravir Supportive care

No

Contraindication to nirmatrelvir-ritonavir
- eGFR <30 or ESRD
- Receipt of Class C medication
- Non-modifiable Class B medication with provider justification
- Known allergy or hypersensitivity
- 6 or 7 days of COVID-19 symptoms

Yes

Bebtelovimab 175mg IV x 1

No

AST or AST < 10x upper limit of normal

Yes

GFR > 30 mL/min OR weight > 48kg

Yes

Patient understands and assets to possible charges

Remdesivir 200mg IV x1 followed by 100mg IV q24h x2

No

Elevated AST and ALT
Patients known to have active hepatitis with AST/ALT elevation may be at risk of worsening with remdesivir. Measurements in last 90 days used. Contact provider if uncertain.

Stage IV Kidney Disease
Following PINETREE trial criteria patients with GFR < 30 are eligible if weight > 48 kg. Contact provider if uncertain.

Contraindications to nirmatrelvir-ritonavir
- eGFR <30 or ESRD
- Receipt of Class C medication
- Non-modifiable Class B medication with provider justification
- Known allergy or hypersensitivity
- 6 or 7 days of COVID-19 symptoms

Yes

No

Charges
Depending on patient’s insurance plan and its co-payment/deductibles, patient may be responsible for charges for therapy.

Yes

No

Guidance regularly updated, last revised March 28, 2022

Used by central clinical team to manage referrals