Symptomatic mild to moderate COVID-19 and onset within 5-7 days

Baseline Patient Risk Assessment → Treatment Considerations

Risk Low → High

Without risk factors for progression to severe disease	Increased but not high risk for progression to severe disease	High risk or with several factors associated with increased risk for progression to severe disease
Suggest **against** routine use of NIRMATRELVIR/RITONAVIR (conditional recommendation, moderate certainty evidence)	Suggest NIRMATRELVIR/RITONAVIR (conditional recommendation, moderate certainty evidence)	Recommend NIRMATRELVIR/RITONAVIR (strong recommendation, moderate certainty evidence
Suggest **against** routine use of REMDESIVIR (conditional recommendation, moderate certainty evidence)	Suggest REMDESIVIR (conditional recommendation, low certainty evidence)	Recommend REMDESIVIR (strong recommendation, moderate certainty evidence)
Recommend **against** MOLNUPIRAVIR (strong recommendation, moderate certainty evidence)	Suggest **against** MOLNUPIRAVIR (conditional recommendation, low certainty evidence)	Suggest MOLNUPIRAVIR (conditional recommendation, low certainty evidence)

Treatment Considerations:

- Lack of severe drug interaction or lack of contraindications to nirmatrelvir/ritonavir? — YES → Recommend NIRMATRELVIR/RITONAVIR; NO → Intravenous medications feasible?
- Intravenous medications feasible? — YES → Recommend REMDESIVIR; NO → No other treatment options available and no contraindications to molnupiravir
- No other treatment options available and no contraindications to molnupiravir — YES → Suggest MOLNUPIRAVIR

Example of increased but not high-risk factors for progression

Example health condition

- Age 65-74 years
- ASCVD
- Asthma
- Cardiomyopathy
- Cerebral Vascular Disease
- Chronic liver diseases
- Chronic lung diseases
- Cirrhosis
- Dementia
- Diabetes Mellitus
- Disabilities including Down Syndrome
- End stage renal disease
- Heart failure
- HIV with CD4 > 200
- Inflammatory bowel disease
- Mental health conditions
- Obesity
- Parkinson's Disease
- Physical inactivity
- Pregnancy (current or recent)
- Smoking history
- Solid tumor (> 12 months prior)
- Tuberculosis

Example therapeutics[1]

- Anti-IL-6
- Anti-IL-12 and 23
- Corticosteroids 10-20 mg for ≥4 weeks

Note: [1] Example therapeutics that are less likely to predispose to substantial immunosuppression

Example of high-risk factors for progression

Example health condition

- Age ≥ 75 years
- Fewer than 1% peripheral B-cells assessed in past 6 months
- Congenital agamma-globulinemia
- Hematopoietic stem cell transplant (HSCT) <2 years or active graft versus host disease
- Hematological malignancy on therapy
- HIV infection with CD4 <200
- Other severe primary immunodeficiency
- Solid organ transplant
- Solid tumor on treatment

Example therapeutics[2]

- B-cell depleting agents in past 12 months (e.g., rituximab, ofatumumab, ocrelizumab, others)
- CAR-T therapy in past 12 months
- Abatacept
- Tyrosine kinase inhibitor (e.g., ibrutinib, acalabrutinib, others)
- High-dose corticosteroids (≥20 mg prednisone or equivalent for ≥4 weeks)
- Anthracycline derivates

Note: [2] Example therapeutics that predispose to substantial immunosuppression

Oral nirmatrelvir/ritonavir *(Paxlovid)*

- eGFR ≥ 60 mL/min: 300 mg (2 x 150 mg tablets), plus ritonavir 100 mg (1 tablet) every 12 hours x 5 days
- eGFR ≥ 30 to < 60 mL/min: 150 mg (1 tablet) plus ritonavir 100 mg (1 tablet) every 12 hours for 5 days
- eGFR < 30 mL/min or HD: 300 mg (2 x 150 mg tablets), plus ritonavir 100 mg (1 tablet) daily x 1 day, then 150 mg (1 tablet) plus ritonavir 100 mg (1 tablet) daily for 4 days
- Within 5 days of symptom onset

Intravenous remdesivir *(Veklury)*

- Day 1: 200 mg i.v. once
- Day 2 and 3: 100 mg i.v. daily
- No renal or hepatic adjustments
- Within 7 days of symptom onset

Oral molnupiravir *(Lagevrio)*

- 800 mg (4 x 200 mg capsules) every 12 hours for 5 days
- No renal or hepatic adjustments
- Avoid pregnancy
- Within 5 days of symptom onset