For patients at high risk of severe COVID-19 not requiring hospitalization or supplemental oxygen, NIH guidelines identify ritonavir-boosted nirmatrelvir and remdesivir as preferred therapies. Bebtelovimab and molnupiravir are recommended as alternative therapies, to be used only when preferred therapies are not available, feasible, or clinically appropriate.

Antivirals

Ritonavir-boosted nirmatrelvir is the preferred outpatient treatment option.

- Treatment should begin within 5 days of symptom onset.
- It is vital for clinicians to consider all medications before prescribing given its significant drug interactions. This web-based checker helps identify and manage interactions. For special populations, clinicians should consult patients’ specialist.
- Contraindications include a history of Stevens-Johnson syndrome or toxic epidermal necrolysis; clinicians should consider renal and hepatic function.
- There is a risk of rebound infection with this antiviral, so monitoring patients during and after treatment is critical.

Remdesivir should be considered for patients who cannot tolerate oral antiviral treatment or when ritonavir-boosted nirmatrelvir is unavailable.

Molnupiravir should only be considered when preferred therapies cannot be used. It is contraindicated for patients under 18 and is not recommended during pregnancy or lactation.

Monoclonal Antibodies

Monoclonal antibodies (mAbs) should be considered if:

- A patient has poor renal function or drug interaction with ritonavir-boosted nirmatrelvir
- More than 5 days since symptom onset (up to 7 days)
- Renal or hepatic disease is present

mAbs are safe for pregnant or lactating patients as well as those who are immunocompromised. Because mAbs are administered intravenously or intramuscularly, they may be harder for patients in rural and underserved areas to access.

For patients at high risk of serious COVID-19 that cannot be vaccinated, tixagevimab plus cilgavimab is recommended as a pre-exposure prophylaxis (PrEP) treatment.

Special Populations

Special populations at greatest risk of severe disease from an acute COVID-19 infection include those with medical comorbidities, underlying conditions, and compromised immune systems, as well as recent immigrant, refugee, pregnant and pediatric patients. These patients require unique considerations for treatment and should be monitored closely throughout.

Access to Treatment Options

COVID-19 has exacerbated existing health disparities and barriers to access to treatment options for racial minorities, rural populations, and recent immigrants. It is critical clinicians take into account these factors and other social determinants of health when considering treatment and seek ways to reach vulnerable patients.

Considerations for Outpatient Treatment of COVID-19

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