CoLab Network

Summary Report

Nirmatrelvir-Ritonavir for the Treatment of COVID-19

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Executive Summary

The objective of the evidence review was to synthesize the current evidence on nirmatrelvir-ritonavir (NMV-r). NMV-r is likely safe and may be effective in reducing emergency department visits, hospitalization, and death. It appears to be comparably effective to other antivirals (i.e., molnupiravir and remdesivir), but NMV-r may have a higher incidence of mild to moderate adverse events. NMV-r also appears to be more effective in people who are partially vaccinated or not vaccinated compared to those who are fully vaccinated. The studies demonstrating these findings (2 randomized controlled trials [RCTs] and 27 observational studies) lack a diverse lens, which may limit their generalizability to the population in Canada.

Background

Several drug treatments for the management of COVID-19 are approved for use in Canada. Currently, the federal government, through the Public Health Agency of Canada, is responsible for overseeing the procurement and allocation of these drugs to ensure their availability for federal, provincial, and territorial health care systems. The following drugs, which are in high demand, are currently funded by the Public Health Agency of Canada: NMV-r (Paxlovid), remdesivir (Veklury), and tocilizumab (Actemra).

Policy Issue

Gathering post-market drug evidence on the safety, efficacy, and effectiveness of NMV-r is needed to help inform future decisions about its procurement, allocation, and equitable distribution within Canadian health care systems.

Objective

The objective of the evidence review was to synthesize the current evidence on NMV-r, updating an existing CADTH evidence review that was conducted when NMV-r was first introduced to the Canadian market (i.e., when data were limited), and the implementation advice was made in light of a supply shortage of NMV-r.

Policy Questions

1   What new evidence on the efficacy, effectiveness, and safety of NMV-r is available since the publication of the CADTH report?

2   Which patients are most likely to benefit from treatment with NMV-r?

Results

Selection of Studies

Researchers used a systematic review approach to identify clinical trials and observational studies published from November 2021 onward. Twenty-nine unique studies across 30 publications were included in the final analysis: 2 RCTs across 3 publications, and 27 observational studies.

Randomized Controlled Trials

Findings from the 2 RCTs suggest that, when compared to placebo or standard therapy, NMV-r reduces the risk of:

- progression to severe COVID-19
- hospitalization or death when treatment is started within 3 to 5 days of symptom onset in those who are not vaccinated.

These findings apply to outpatient adults with mild to moderate acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection who are considered high-risk.

Serious adverse events were rare in these 2 RCTs, and adverse events were mild to moderate and transient after treatment with NMV-r.

Both RCTs were assessed at a low to moderate risk of bias .

Observational Studies

Fifty-six percent of the included observational studies collected data during the Omicron wave.

NMV–r Versus No Treatment or Standard of Care

Findings from 14 observational studies suggest that NMV-r is significantly more effective compared to no treatment or standard of care in reducing the risk of:

- emergency department visits
- hospitalization
- death.

These findings apply to outpatient adults with mild to moderate acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection who are considered high-risk, regardless of age or vaccination status.

These 14 studies were assessed at a moderate to high risk of bias.

NMV–r Versus Molnupiravir or Remdesivir

Findings from 19 observational studies suggest that NMV-r is comparable to molnupiravir or remdesivir in reducing the risk of:

- COVID-19–related hospitalization
- hospitalization from any cause
- death.

These findings apply to outpatient adults with mild to moderate SARS-CoV-2 infection who are considered high-risk.

The incidence of mild to moderate adverse events like dysgeusia (a distorted sense of taste) or diarrhea may be higher in people who receive NMV-r than in those who receive molnupiravir or remdesivir. However, NMV-r was associated with a faster time to a negative test compared to molnupiravir and remdesivir.

These 19 studies were assessed at a moderate to high risk of bias.

Studies Assessing Specific Populations

The evidence review identified 5 treatment populations for NMV-r: older adults; recipients of a solid organ transplant; and those with inflammatory bowel disease, hematological malignancies, or systemic autoimmune rheumatic disease. For all 5 populations, effectiveness was found to be similar to the general population: NMV-r reduces hospitalization and death compared to no treatment and is similarly effective compared to other treatments.

Vaccination Status and Effectiveness

Grouping by vaccination status was not commonly reported in the included studies. However, when it was reported, NMV-r appeared to be more effective in those who are partially or unvaccinated compared to those who are fully vaccinated.

Limitations

There are 6 key limitations to the studies included in the evidence review. Notably, none of the studies grouped outcomes by racialized populations. Other limitations include the small number of comparators within the RCTs, the potential effect of prior infection on outcomes, and the moderate to critical risk of bias in more than 90% of the included studies.

Implications for Policy-Making

NMV-r is likely safe and may be effective in reducing emergency department visits, hospitalization, and death. It appears to be comparably effective to other antivirals (i.e., molnupiravir and remdesivir).

Results should be interpreted and used with caution due to:

- the limited generalizability of the RCT results
- the high-risk populations included in the observational studies
- the evolving and emerging evidence on the role of vaccination.

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