Ivermectin

What is it?

- **An antiparasitic agent primarily used for treatment of roundworms. It is proposed to have antiviral activity by disrupting the transport of viral proteins into the nucleus, thus reducing overall viral replication.**
- **In vitro, ivermectin has shown inhibition of SARS-CoV-2 replication in cell cultures at concentrations higher than achieved with standard human anti-parasitic dosing.[1]**

Health Canada Indications:	Intestinal strongyloidiasis and onchocerciasis (parasitic infections).

Health Canada issued a public advisory that ivermectin is not authorized for the treatment of COVID-19 and it may cause serious health issues. There is no evidence that ivermectin works to prevent or treat COVID-19 and Health Canada had not received any drug submissions or applications for clinical trials for ivermectin used for the prevention or treatment of COVID-19 (Oct. 19, 2021).[2]

Evidence: Ivermectin has been investigated for its role in COVID-19 treatment and prophylaxis, frequently in combination with other therapies. Many studies are still underway.[6]

- Some previously released studies with positive findings, have been withdrawn over ethical concerns, including plagiarism and potentially falsified data. These results have also had an impact on conclusions drawn by review articles.[3,4]
- A meta-analysis of 10 randomized controlled trials found that ivermectin, compared with the standard of care or placebo, did not reduce all-cause mortality, LOS, or viral clearance in patients with mostly mild COVID-19.[5]
- A Cochrane review of 14 randomized controlled trials found that ivermectin, compared to no treatment, placebo or standard of care, did not reduce mortality at 28 days, or clinical worsening at up to 28 days (inpatients) and up to 14 days (outpatients).[6] Details below:

Cochrane review [5]: 14 RCTs total; 9 RCTs of inpatients, 4 RCTs of outpatients, 1 RCT for prevention of COVID-19

Results (primary analysis, excluded studies assessed to be high risk of bias)

Outcomes	Inpatient treatment (Mod-Severe; WHO scale 4-5)	Outpatient Treatment (Mild; WHO scale 1-3)
All-cause mortality (up to 28 days)	185 participants (2 RCTs) RR 0.60 (CI 0.14 to 2.51) Certainty of evidence (GRADE): Very Low	422 participants (2 RCTs) RR 0.33 (CI 0.01-8.05) Certainty of evidence (GRADE): Very Low
Clinical worsening	**Need invasive mechanical ventilation at up to 28 days** 185 participants (2 RCTs) RR 0.55 (CI 0.11 to 2.59) Certainty of evidence (GRADE): Very Low	**Need invasive mechanical ventilation at up to 14 days** 398 participants (1 RCT) RR 2.97 (CI 0.12 to 72.47) Certainty of evidence (GRADE): Very Low
Adverse events (any grade) (up to 28 days)	152 participants (1 RCT) RR 1.21 (CI 0.50 to 2.97) Certainty of evidence (GRADE): Very Low	422 participants (2 RCTs) RR 0.95 (CI 0.86 to 1.05) Certainty of evidence (GRADE): Low
Viral clearance (at 7 days)	159 participants (2 RCTs) RR 1.82 (CI 0.51 to 6.48) Certainty of evidence (GRADE): Very Low	24 participants (1 RCT) RR 3.00 (CI 0.13 to 67.06) Certainty of evidence (GRADE): Low

National Institute of Health (NIH), World Health Organization (WHO), Infectious Diseases Society of America (IDSA): recommend against the use of ivermectin for COVID-19, except in a clinical trial.[7-9]

Canadian Agency for Drugs and Technologies in Health (CADTH), Canadian guidelines (British Columbia, Nova Scotia, Ontario), and the manufacturer (Merck): do not recommend ivermectin for the treatment or prevention of COVID-19.[10-14]

Practical Considerations

- **Ivermectin supply is very limited due to inappropriate use for COVID-19, and supply is needed for parasitic infections.[13]**
- **Ivermectin is metabolized via cytochrome P450 3A4 and is prone to drug interactions The concentration of ivermectin required to inhibit SARS-CoV-2 in vitro is unlikely to be achieved at standard dosing.[15]**

Prepared by: COVID-19 Clinical Pharmacy Working Group
Last Update: January 16, 2022

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