

Northern Health Interim Therapeutic Guidance for Adult Patients with Suspected or Confirmed COVID-19 Updated Mar 25/20

This guideline will be updated regularly as evolving evidence becomes available; to ensure that you are using the latest version, please access this guide online.

The suggestions below are based on limited, weak quality evidence and expert opinion.

It is important to note that current medication supplies are fragile and judicious use of the treatments listed below are strongly advised.

For more information on treatment, recommendations and patient risk factors for severe disease please refer to the Appendix.

Due to the current delay in test results (4+ days) and limited evidence – these treatment recommendations are for cases of SUSPECTED and or CONFIRMED COVID-19

Symptom Severity Suspected or Confirmed COVID-19	Treatment Recommendations	Comments
<p>Mild:</p> <p>Hospitalization not required</p> <p>No Supplemental O₂ required or no increase in baseline O₂ needs</p> <p>O₂ Sat greater than 90%#</p> <p>No acute dyspnea or changes to baseline dyspnea</p> <p>#patients with chronic underlying lung disease may have variable baseline O₂ ranges</p>	<p>Supportive treatment only (rest, hydration, and antipyretics)</p>	<p>Acetaminophen is currently the preferred analgesic/antipyretic. Avoid use of NSAIDs at this time. See appendix for further details.</p>
<p>Moderate/Severe:</p> <p>Hypoxemia requiring supplemental O₂ OR New infiltrates on chest x-ray</p> <p>AND/OR Requiring Hospitalization</p>	<p>Ceftriaxone 2g IV q24h x 7 days (re-assess in 48 - 72 hrs) PLUS Azithromycin 500 mg PO daily x 3 days</p> <p>**Hydroxychloroquine cannot be recommended outside of clinical trials at this time.</p>	<p style="text-align: center;">See above</p> <p>Steroids: Do not administer systemic corticosteroids unless other indication (consider discontinuing inhaled glucocorticoids in non-asthmatic patients). See appendix</p>

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<p>Critical:</p> <p>Decreased LOC</p> <p>Multi-organ failure</p> <p>Requires ICU admission With or without Mechanical ventilation</p>	<p>Ceftriaxone 2g IV q24h x 7 days (re-assess in 48 - 72 hrs)</p> <p>PLUS</p> <p>Azithromycin 500 mg PO daily x 3 days</p> <p>**Hydroxychloroquine cannot be recommended outside of clinical trials at this time.</p>	<p>See above</p> <p>Steroids: Do not administer systemic corticosteroids unless other indication (consider discontinuing inhaled glucocorticoids in non-asthmatic patients). See appendix</p>
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**** Investigational treatments:**

Hydroxychloroquine/chloroquine have the most promising evidence evolving for potential use in treatment of COVID-19. However, several provincial bodies (College of Physicians/Surgeons, Pharmacists and Nurses, BCCDC, Provincial Antimicrobial Clinical Experts group) have decided that there is still a lack of clinically convincing outcomes and due to the fragility of the supply chain, they are prohibiting the use of chloroquine and hydroxychloroquine for treatment or prophylaxis outside of a clinical trial. In order to align with the rest of the province at this time, the NH COVID-19 Therapeutics and Treatment reference group is unable to recommend use of these drugs at this time. The Group will be investigating whether participation in clinical trials will be possible although there are no current BC trials of this agent.

In a recent open-label randomized study, use of lopinavir/ritonavir (Kaletra®) in hospitalized adult patients with severe COVID-19 was compared to standard of care; no difference in time to clinical improvement was seen.⁸ Remdesivir is another investigational drug that might have a place in treatment of COVID-19 based on in-vitro/animal data with MERS (i.e. Sheahan 2020).⁹ Clinical trials are ongoing in China and U.S. (Canada is not included). Unfortunately, it is not commercially available and only a limited supply is accessible for compassionate use through the manufacturer; obtaining this drug in a pandemic situation will not be possible in a timely manner. Furthermore, exclusion criteria from the manufacturer are extensive and highly restrictive.^{4,9} Due to these reasons stated here, we are not recommending use of remdesivir or Kaletra® at this time.

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APPENDIX

Suspected versus confirmed: Patients enrolled in the open label study, which investigated use of hydroxychloroquine (\pm azithromycin), were initiated on therapy at 4 ± 3 days from symptom onset⁵. Since our Health Authority is seeing a COVID-19 swab result turnaround of 4 to 8 days, we have to consider initiating therapy in suspected cases that are presenting with moderate to severe symptoms.

Risk Factors for severe disease:

Patients presenting with mild disease plus any of the risk factors below are at an increased risk of progressing to severe disease. Although there are no changes to treatment recommendations for mild disease, patients should be advised to closely monitor their symptoms.

55 years or older	Renal or hepatic insufficiency
Diabetes	Cardiovascular disease (e.g. hypertension, heart failure)
Immunosuppression (drug induced or disease related)	Underlying lung disease (e.g. COPD, asthma)

Non-steroidal Anti-inflammatory Drugs (NSAIDs)^{1-3:}

There are some reports that NSAID use has been associated with clinical deterioration in some patients with severe COVID-19. The WHO has corrected their previous recommendation against use of NSAIDs and Health Canada has released a statement that there is not sufficient evidence at this time to link NSAID use to worsening of COVID-19 symptoms. However due to the limited nature of evidence available to support safe use of NSAIDs in patients with COVID-19, acetaminophen is currently the preferred analgesic/antipyretic in these patients. At this time, we recommend acetaminophen as the first line analgesic/antipyretic unless otherwise contraindicated) and for clinicians to prescribe NSAIDs in patients with suspected COVID-19 with caution. Patients that are currently taking NSAIDs on a chronic basis (i.e. ASA 81 mg) should not stop. Any suspected adverse events related to these drugs should be reported through the usual channels, as part of regular pharmacovigilance activities.¹

ACE-Inhibitors (ACEI) / Angiotensin Receptor Blockers (ARBs):

There is interest in the potential role of ACEI / ARBs in the pathophysiology of this disease since the SARS-CoV-2 virus binds to the ACE2 receptor for cellular entry. There are theories these may either help or worsen COVID-19 disease. Currently there are no data to support either starting or stopping ACEI/ARBs on any patients with COVID-19.⁴ We do not currently routinely recommend stopping these agents for patients with COVID-19, unless otherwise indicated (e.g. acute kidney injury, hypotension etc.). After patients have recovered from their viral syndrome, these medications can resume if stopped or if indicated, new ACEI/ARBs can be started if they

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have a primary indication.¹⁻² Any suspected adverse events related to these drugs should be reported through the usual channels, as part of regular pharmacovigilance activities.¹

Oseltamivir:

We recommend against the use of oseltamivir outside its current indication for suspected and confirmed influenza. Neuraminidase inhibitors have not been shown to have activity against COVID-19.³⁻⁴ Initial empiric therapy with oseltamivir may be reasonable during the influenza season in critically ill patients, if there is concern that the patient might have influenza pneumonia. Such patients can have confirmatory nasopharyngeal swabs for influenza. At this time the role for oseltamivir specifically for COVID-19 is limited.⁴

Nebules versus Metered Dose Inhalers (MDI):

For suspected or confirmed COVID-19 patients, nebulized therapy is considered an aerosol generating medical procedures (AGMPs) therefore nebulization poses a risk of aerosolization of the SARS-CoV-2 virus.^{2,7} If a bronchodilator is required (e.g. salbutamol), we recommend using a meter dose inhaler (MDI) in place of nebulization to reduce the risk of transmission to healthcare professionals. However if a nebulized medication is unavoidable ensure appropriate PPE and airborne precautions are followed.

Steroids:

The role of corticosteroids in the management of COVID-19 is controversial. It is currently unclear if any benefit is derived from their use and they may also cause harm.¹⁻⁴ The use of corticosteroids is not recommended at this time in the management of COVID-19, unless another indication for their use is present (e.g. acute exacerbation of COPD or asthma, refractory septic shock, etc.).⁴ Consider discontinuation of inhaled steroids as they may reduce local immunity and promote viral replication, unless necessary for acute indications.²

Questions related to these guidelines can be directed to Alicia Rahier, Antimicrobial Stewardship Pharmacist, at alicia.rahier@northernhealth.ca or 250-612-2030. If you are looking for advice about how to test or treat a patient with a suspected case of COVID-19, call the intensivists at the Rural Outreach Support group (ROSe) 24/7 for additional information, support, or guidance. Toll-Free: 1-888-918-0626.

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References

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7. Provincial Infection Control Network of BC (PICNet). 2019 Novel Coronavirus: Aerosol Generating Medical Procedures in Healthcare Settings. 2019NCOV_AGMP_V2_February 7 2020
8. Cao et al. A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19. NEJM. March 18, 2020. DOI: 10.1056/NEJMoa2001282
9. VGH-PHC COVID-19 Therapeutics Committee (CTC) Summary on Current Therapeutics for COVID-19 March 17, 2020

Membership of the NH Therapeutics and Treatment Reference Group for COVID-19:

- Physician Representation: Abu Hamour (Infectious Disease), Patrick Rowe (Emergency), MJ Slabbert (Critical Care), Brian Hillhouse (Family Medicine), Sharla Olsen (Internal Medicine & Respiriology)
- Pharmacy Representation: Alicia Rahier (Antimicrobial Stewardship Pharmacist), Ryan Doerksen & Jessica Brecknock (Medication Use Management Pharmacists) and Dana Cole (Regional Director, Pharmacy).