Clinical Reference Group Recommendations: Therapies for COVID-19

UPDATED: June 2nd, 2020

The British Columbia COVID-19 Therapeutics Committee (CTC) meets weekly to discuss the most current research on the use of therapies in the management of COVID-19.

Position Statement on Unproven Therapies for COVID-19:

“There are no proven therapies for the prevention or treatment of COVID-19. All agents have the possibility of associated harm, and pharmaceutical supplies province-wide and nationally for many of the possible agents are severely limited. It is recognized that compassionate use of drugs will be pursued for ill patients with no known therapy. Ideally, use of these agents would be through a controlled clinical trial to better inform practice; in the absence of research studies, patients should be aware of the risks and benefits of novel therapies, and with efficacy and safety data collected to inform the larger community.”

*Position statements provide information/direction and express or clarify intent on a particular matter. They are intended as guidance for stakeholders in areas where events are evolving or changing rapidly, the implementation of processes and procedures may be premature, or it is timely to communicate the intent before or as policies and procedures are developed.

Currently, international bodies such as the World Health Organization (WHO), recommend that pharmacologic treatment for COVID-19 should not be used outside of clinical trials. There are practitioners throughout the world who are using various therapies that contradict this WHO recommendation. Within British Columbia, the use of specific COVID-19 drug therapies outside of clinical trials is NOT recommended. In the setting of a pandemic, it is not just one or a few individuals with a rare clinical disorder, but many with a common novel disease. Without ethically conducted clinical trials, the true efficacy and safety of investigational agents are largely unknown. Any inconsistencies in usage may also lead to confusion amongst clinicians and the public. Additionally, there are limited supplies of many of these agents. This results in limited supplies of therapies for patients with established indications for existing drugs. As new data emerges from research conducted around the world, recommendations regarding pharmacologic treatment of COVID-19 may change.

It is recognized that there may be extenuating clinical circumstances where clinicians decide to use unproven therapies when clinical trials are unavailable. In those circumstances where unproven therapies are used, the WHO has provided a standardized case report form for data collection to ensure that there is contribution to scientific research and the clinical community.
Recommendations for Specific Therapies

1. Lopinavir / Ritonavir (Kaletra®)
   **Recommendation:** Recommend against the use of lopinavir/ritonavir outside a randomized-controlled trial.

2. Remdesivir
   **Recommendation:** Recommend against the use of remdesivir outside a randomized-controlled trial.

3. Chloroquine and Hydroxychloroquine
   **Recommendation:** Recommend against the use of chloroquine and hydroxychloroquine for treatment or prophylaxis outside a randomized-controlled trial.

4. Oseltamivir
   **Recommendation:** Recommend against the use of oseltamivir unless suspected or confirmed influenza infection.

5. Ribavirin and Interferon
   **Recommendation:** Strongly recommend against the use of ribavirin and/or interferon for risk of harm.

6. Colchicine
   **Recommendation:** Recommend against the use of colchicine for treatment or prophylaxis outside a randomized-controlled trial.

7. Ascorbic Acid
   **Recommendation:** Recommend against the use of ascorbic acid for treatment or prophylaxis outside a randomized-controlled trial.

8. Tocilizumab and Sarilumab
   **Recommendation:** Recommend against the use of tocilizumab or sarilumab outside a randomized-controlled trial. If considered on an individual basis in patients with cytokine storm, it should only be done so with expert consultation (Infectious Diseases and Hematology/Rheumatology).

9. Convalescent Plasma
   **Recommendation:** Recommend against the use of convalescent plasma outside a randomized-controlled trial.

10. Intravenous Immunoglobulin G (IVIG)
    **Recommendation:** Recommend against the use of IVIG outside a randomized-controlled trial.

11. Corticosteroids
    **Recommendation:** Recommend against the routine use of corticosteroids outside a randomized-controlled trial. However, corticosteroids, via all routes of administration, may be used if another compelling indication is present (e.g. asthma exacerbation, refractory septic shock, obstetric use for fetal lung maturation). There is insufficient evidence at this time to
recommend for or against the use of corticosteroids for acute respiratory distress syndrome (ARDS).

12. Antibiotics
   \textbf{Recommendations:} If bacterial infection is suspected, antibiotics should be initiated based on local institutional antibiograms and sensitivities.

13. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)
   \textbf{Recommendation:} Recommend acetaminophen use preferentially for symptomatic management of COVID-19 but do not recommend against the use of NSAIDs such as ibuprofen.

14. Angiotensin Converting Enzyme (ACE) inhibitors and Angiotensin Receptor Blockers (ARBs)
   \textbf{Recommendation:} Recommend that patients on ACE inhibitors and ARBs continue these agents as indicated and not cease therapy solely on the basis of COVID-19.

15. Venous Thromboembolism (VTE) prophylaxis
   \textbf{Recommendation:} Suggest enoxaparin 30 mg SC bid as the preferred dose for VTE prophylaxis in critically ill patients with COVID-19. Consider enoxaparin 30 mg SC bid as the preferred dose for VTE prophylaxis in hospitalized ward-based patients with COVID-19. This dose was selected to reduce incident VTE and potentially save health care resources with patient transport and minimize risk of COVID-19 transmission to staff and others. Suggest even higher doses of enoxaparin for hospitalized patients with weight above 100 kg or BMI above 40 kg/m$^2$.

16. Other investigational therapies
   \textbf{Recommendation:} Recommend against any other investigational agent, including arbidol, ASC09, azvudine, baloxavir marboxil/favipiravir, camostat mesylate, darunavir/cobicistat, camrelizumab, ivermectin, niacin, thymosin, natural health products, and traditional Chinese medicines due to lack of data, lack of availability, or both.

*Denotes that a clinical trial of named therapy is currently planned or underway in British Columbia. Links below for registered trials in Canada and British Columbia.

Canada: https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-clinical-trials/list-authorized-trials.html

British Columbia: https://bcahsn.ca/covid-19-response/inventory/

*Recommendations are consistent with guidelines from the World Health Organization (WHO), the Surviving Sepsis Campaign (SSC) (a joint initiative of the Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM)), the Public Health Agency of Canada (PHAC), the Canadian Critical Care Society (CCCS), the Association of Medical Microbiology and Infectious Diseases Canada (AMMI), and The Australian and New Zealand Intensive Care Society (ANZICS)
The Clinical Reference Group (CRG) is made up of senior individuals from relevant healthcare areas (including critical care, epidemiology, infectious disease, microbiology, public health, and clinical specialties) acting as a collective resource for current COVID-19 knowledge. They provide clinical advice and guidance to support the overall work being done by the BC Centre for Disease Control, the Provincial Health Office, and the Ministry of Health. The CRG includes representation from the provincial health authorities and works with the other Ministry areas in order to provide cross-input on all COVID-19 content.