Clinical Reference Group Recommendations: Therapies for COVID-19

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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 Therapies for COVID-19:

“Evidence for the role of various therapies for the prevention or treatment of COVID-19 is quickly emerging and represents a rapidly evolving area of research. Since all agents have the possibility of associated harm, and pharmaceutical supply chains are fragile, it is essential that therapies are used in an evidence-based fashion. With a focus on knowledge translation, it is recommended that all clinical studies are critically appraised for quality and generalizability, and a decision to use any treatment is made in the context of provincially harmonized best practices and patients’ informed consent. It is recognized that compassionate use of drugs may be pursued based on extrapolated or preliminary data or where data is lacking. Ideally, use of such agents would be through participation in a controlled clinical trial to better inform practice. In the absence of research studies or definitive results, patients should be aware of the risks and benefits of novel therapies, and 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.

While positive results for a small number of treatments are being published, the efficacy, safety and role in therapy for most pharmacological treatments for COVID-19 remain unknown. Currently, international bodies such as the World Health Organization (WHO), recommend that unproven pharmacological therapies for COVID-19 not be used outside of clinical trials. **Within British Columbia, the use of unproven COVID-19 drug therapies outside of clinical trials is NOT recommended.** Participation in clinical trials allows for ethical evaluation of the efficacy and safety of potential agents, minimizes inconsistencies in usage that is harmful to the clinical community and the public, and protects the drug supply chain. It is recognized that there may be extenuating individual circumstances where clinicians decide to use such therapies when
clinical trials are unavailable. In settings 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.

In circumstances where practice-changing results become available, such data should be carefully interpreted with particular attention to effect size, applicability, safety and practical issues of incorporating the evidence into practice that are specific to patients in British Columbia. The recommendations listed below have been written with careful consideration of these points.

For recommendations pertaining to Multisystem Inflammatory Syndrome in Children (MIS-C) and COVID-19 please visit BCCDC website at: http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID19_MIS-C_ClinicianGuidance.pdf
Recommendations for Specific Therapies

1. Corticosteroids
Dexamethasone 6 mg IV/PO q24h for up to 10 days is strongly recommended (RECOVERY trial), unless higher doses are clinically indicated.** Hydrocortisone 50 mg IV q6h is recommended as an alternative (REMAP-CAP trial). If dexamethasone and hydrocortisone are not available, methylprednisolone 32 mg IV q24h or prednisone 40 mg PO daily are recommended.

2. Lopinavir / Ritonavir (Kaletra®)
Lopinavir/ritonavir is not recommended for treatment or prophylaxis of COVID-19 outside of approved randomized-controlled trials.

3. Remdesivir
Remdesivir* has received conditional approval by Health Canada for the treatment of COVID-19. Remdesivir shortened time to clinical recovery but failed to show any survival benefit in the ACTT-1 trial. At this time in British Columbia, the CTC encourages a focused use of remdesivir in clinical trials due to international clinical equipoise.

4. Chloroquine or Hydroxychloroquine
Chloroquine or hydroxychloroquine (with or without azithromycin) is not recommended for treatment or prophylaxis of COVID-19.

5. Oseltamivir
Oseltamivir is not recommended for treatment or prophylaxis of COVID-19.

6. Ribavirin and Interferon
Ribavirin and/or interferon is not recommended for treatment or prophylaxis of COVID-19 outside of approved randomized-controlled trials.

7. Colchicine
Colchicine is not recommended for treatment or prophylaxis of COVID-19 outside of approved randomized-controlled trials.

8. Ascorbic Acid
Ascorbic acid is not recommended for treatment or prophylaxis of COVID-19 outside of approved randomized-controlled trials.

9. Tocilizumab and Sarilumab
Tocilizumab, sarilumab, or anakinra is not recommended outside of approved clinical trials; where clinical trials are not available, it remains unknown whether tocilizumab provides any benefit for treatment of patients with cytokine storm. If treatment is considered, expert consultation is recommended (Infectious Diseases, Hematology, and/or Rheumatology).

10. Convalescent Plasma
Convalescent plasma is not recommended for treatment or prophylaxis of COVID-19 outside of approved randomized-controlled trials.
11. **Intravenous Immunoglobulin G (IVIG)**
Intravenous immunoglobulin G (IVIG) is not recommended for treatment or prophylaxis of COVID-19 outside of approved randomized-controlled trials.

12. **Antibiotics**
Antibiotics should be initiated based on local institutional antibiograms and sensitivities if bacterial infection is suspected.

13. **Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)**
Acetaminophen is recommended 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)**
Patients on ACE inhibitors and ARBs are recommended to continue these agents as indicated and not cease therapy solely on the basis of COVID-19.

15. **Venous Thromboembolism (VTE) prophylaxis**
Enoxaparin 30 mg SC bid is suggested as the preferred dose for VTE prophylaxis in critically ill patients with COVID-19. Enoxaparin 30 mg SC bid should be considered 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/m².

16. **Other investigational therapies**
Other investigational agents including arbidol, ASC09, azvudine, baloxavir marboxil/favipiravir, camostat mesylate, darunavir/cobicistat, camrelizumab, famotidine, ivermectin, niacin, thymosin, natural health products, and traditional Chinese medicines are not recommended for treatment or prophylaxis of COVID-19 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.


*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)
About the Clinical Reference Group
*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.