British Columbia COVID-19 Therapeutics Committee (CTC) and COVID-19 Therapeutics Review and Advisory Working Group (CTRAWG) Clinical Practice Guidance for

Antimicrobial and Immunomodulatory Therapy in Adult Patients with COVID-19

SUMMARY
last updated April 18th, 2021

Recommendations in this document apply to patients > 18 years of age. For details including special populations, refer to the complete summary document.

There is limited clinical evidence to guide antiviral therapy for patients with COVID-19.

Specialist consultation (e.g., Critical Care, Infectious Disease, Hematology, or Rheumatology) is recommended if any investigational treatment is offered to a patient with COVID-19 outside of approved clinical trials. Informed consent should be obtained from the patient or the substitute decision maker.

SEVERITY OF ILLNESS	ANTIVIRAL THERAPY Unless otherwise specified, recommendations include antivirals alone or in combination	ANTIBACTERIAL THERAPY	IMMUNOMODULATORY THERAPY	OTHER THERAPEUTICS
Critically Ill COVID-19 Patients *Hospitalized, ICU-based* Patients requiring respiratory support (high-flow oxygen, noninvasive ventilation, mechanical ventilation) and/or vasopressor/ inotropic support	**Chloroquine** or **Hydroxychloroquine** is **not** recommended for the treatment of COVID-19 **Lopinavir/ritonavir** is **not** recommended for the treatment of COVID-19 **Remdesivir#** is **not** recommended outside of approved clinical trials **Interferon IV/SC** is **not** recommended for the treatment of COVID-19. **Ribavirin/ Interferon (Inhaled)** is **not** recommended outside of approved clinical trials **Ivermectin** is **not** recommended outside of approved clinical trials	**Ceftriaxone 1-2 g IV q24h x 5 days** is recommended if there is concern for bacterial co-infection (alternative for severe beta-lactam allergy: moxifloxacin 400 mg IV q24h x 5 days) **Azithromycin 500 mg IV q24h x 3 days** is recommended if atypical bacterial infection is suspected (not required if on moxifloxacin) De-escalate on the basis of microbiology results and clinical judgment	**Dexamethasone 6 mg IV/SC/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. **Tocilizumab 400 mg IV (single dose)** OR **Sarilumab 400 mg IV (single dose)** is **recommended** (REMAP-CAP, RECOVERY) for patients requiring life support due to confirmed COVID-19. This includes high-flow oxygen support (e.g., Optiflow) if flow rate > 30 L/min and FiO2 > 0.4 OR invasive or non-invasive ventilation OR vasopressor or inotropic support. Tocilizumab/Sarilumab must be administered within 24 hours of the initiation of life support measures. Patients admitted to hospital for more than 14 days with symptoms of COVID-19 should not receive tocilizumab/ Sarilumab for this indication. Tocilizumab/Sarilumab should only be initiated when life support is required because of COVID-19 rather than other causes (such as bacterial infection, pulmonary embolism, etc). **Passive Immunotherapies (Convalescent Plasma/IVIG/Monoclonal antibodies/Antibody cocktail therapies/Regn-COV2/Bamlanivimab), Colchicine and biologics (Anakinra, Baricitinib)** are **not** recommended outside of approved clinical trials	**Enoxaparin 30 mg SC q12h is suggested for VTE prophylaxis.** Patients receiving therapeutic anticoagulation for COVID-19 PRIOR to organ support should REMAIN on therapeutic anticoagulation and continue for up to 14 days or until hospital discharge. Therapeutic anticoagulation for COVID-19 should NOT be initiated in patients who have received organ support for greater than 48 hours due to a high probability of harm (n=1074; NIH mpRCT). **ACE inhibitors** and **ARBs** should not be discontinued solely on the basis of COVID-19 **NSAIDs** should not be discontinued solely on the basis of COVID-19
Severely Ill COVID-19 Patients *Hospitalized, ward-based, long-term care* Patients requiring supplemental oxygen therapy	**Chloroquine** or **Hydroxychloroquine** is **not** recommended for the treatment of COVID-19 **Lopinavir/ritonavir** is **not** recommended for the treatment of COVID-19 **Remdesivir#** has not demonstrated benefit in survival, progression to ventilation or length of hospital stay and remains uncertain with respect to shortening time to recovery by 5 days. The World Health Organization (WHO) has issued a conditional recommendation against the use of remdesivir in hospitalized COVID-19 patients. Further evaluation in approved clinical trials is strongly encouraged. If remdesivir is used outside of clinical trials, full disclosure of risks and benefits with consideration of patient values and preferences are necessary, as it is not considered standard of care. Furthermore, it should be restricted to hospitalized patients requiring supplemental oxygen but not requiring non-invasive or invasive mechanical ventilation." **Interferon IV/SC** is **not** recommended for the treatment of COVID-19. **Ribavirin/ Interferon (Inhaled)** is **not** recommended outside of approved clinical trials **Ivermectin** is **not** recommended outside of approved clinical trials	Antibacterial therapy is **not** routinely recommended outside of approved clinical trials unless other indications justify its use (e.g., suspected bacterial co-infection in COVID-19 positive patients)	**Dexamethasone 6 mg IV/SC/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. **Tocilizumab** is **not** recommended for patients receiving low-flow oxygen support. The RECOVERY trial found a survival benefit of 4% (tocilizumab 29% vs. usual care 33% 28-day mortality) in patients who had CRP >75 mg/L AND low-flow oxygen, non-invasive respiratory support, or invasive mechanical ventilation. However, considering the scarcity of IL-6 blockers in Canada, drug therapy should be prioritized to the persons with both the highest need and the greatest likelihood of benefiting from the therapy. Combined with outstanding issues in the preliminary findings of the RECOVERY trial (e.g. 17% of patients randomized to tocilizumab not receiving the drug), the CTC recommends prioritizing tocilizumab use only for critically ill patients at this time, which is the population shown to benefit in both the REMAP and RECOVERY trials. **Passive Immunotherapies (Convalescent Plasma/IVIG/Monoclonal antibodies/Antibody cocktail therapies/Regn-COV2/Bamlanivimab), Colchicine and biologics (Anakinra, Baricitinib)** are **not** recommended outside of approved clinical trials	**Therapeutic anticoagulation (LMWH preferred) should be initiated in patients without high risk features for serious bleeding** and **NOT** requiring organ support. **Therapeutic anticoagulation for COVID-19 should start within 72 hours of admission and be continued for 14 days or until hospital discharge, even if there is deterioration requiring organ support during this period.**Therapeutic anticoagulation was superior to usual care (intermediate or prophylactic intensity) in reducing mechanical ventilation and all-cause mortality (n=2221). High risk features for bleeding include age>75y; creatinine clearance<30 mL/min; any coagulopathy; platelet count<50 x 109/L; use of DAPT; recent history of serious GI bleed or recent intracranial condition (stroke; neurosurgery; aneurysm; cancer). This recommendation is based on preprint data awaiting peer review (NIH mpRCT). **ACE inhibitors** and **ARBs** should not be discontinued solely on the basis of COVID-19 **NSAIDs** should not be discontinued solely on the basis of COVID-19
Mildly Ill COVID-19 Patients *Ambulatory, outpatient, long-term care* Patients who do not require supplemental oxygen, intravenous fluids, or other physiological support	**Chloroquine** or **Hydroxychloroquine** is **not** recommended for the treatment of COVID-19 **Lopinavir/ritonavir** is **not** recommended for the treatment of COVID-19 **Remdesivir#** is **not** recommended outside of approved clinical trials **Interferon IV/SC** is **not** recommended for the treatment of COVID-19. **Ribavirin/ Interferon (Inhaled)** is **not** recommended outside of approved clinical trials **Ivermectin** is **not** recommended outside of approved clinical trials	Antibacterial therapy is **not** routinely recommended outside of approved clinical trials unless other indications justify its use (e.g., suspected bacterial co-infection in COVID-19 positive patients)	In adults with mildly ill COVID-19 aged 65 and over OR aged 50 and over with underlying health conditions and within 14 days of symptom onset, **inhaled budesonide 800 µg twice daily for 14 days** may be considered on a case by case basis in discussion with the patient by clearly highlighting the uncertainty in the benefit of treatment, and the risks and potential adverse effects. Informed consent should be obtained and treatment initiated as soon as possible. Underlying health conditions include weakened immune system due to illness or medication; heart disease and/or hypertension; chronic lung disease; diabetes; hepatic impairment; stroke or other neurological condition; obesity or BMI above 35. **Biologics/Small molecules (Tocilizumab, Sarilumab, Anakinra, Baricitinib)** are **not** recommended outside of approved clinical trials **Passive Immunotherapies (Convalescent Plasma/IVIG/Monoclonal antibodies/Antibody cocktail therapies/Regn-COV2/Bamlanivimab)** are **not** recommended outside of approved clinical trials In patients aged 40 years or older with PCR-confirmed COVID-19 who have at least one risk factor† and no contraindications††, **colchicine 0.6 mg PO BID x 3 days, then 0.6 mg daily x 27 days may be considered** on a case-by-case basis in discussion with the patient by clearly highlighting the uncertainty in the benefit of treatment, and the risks and potential adverse effects. Informed consent should be obtained and treatment initiated as soon as possible.	**ACE inhibitors** and **ARBs** should not be discontinued solely on the basis of COVID-19 **NSAIDs** should not be discontinued solely on the basis of COVID-19
Prophylaxis Patients with known COVID-19 exposure	**Chloroquine** or **hydroxychloroquine** is **not** recommended for prophylaxis in patients with known COVID-19 exposure. **Lopinavir/ritonavir** is **not** recommended outside of approved clinical trials **Ivermectin** is **not** recommended outside of approved clinical trials		†Age >70 years, obesity (BMI >30 kg/m2), diabetes, hypertension (systolic >150 mmHg), respiratory or coronary disease, heart failure, fever 38.4°C, and dyspnea. ††Contraindications – GFR <30 mL/min (recent GFR recommended), inflammatory bowel disease, chronic diarrhea or malabsorption, neuromuscular disease, severe liver disease, chemotherapy, current colchicine treatment, hypersensitivity to colchicine, or existing prescriptions any of the following potential drug interactions (e.g. carvedilol, verapamil, amiodarone, azoles, cyclosporine, macrolides, protease inhibitors).	
Discharge Patients with known COVID-19 that have recovered and are discharged from hospital	No COVID-19 specific medications are recommended on discharge (includes corticosteroids and DVT chemoprophylaxis; unless indicated for other reasons)			

** e.g., asthma exacerbation, refractory septic shock, history of chronic steroid use, obstetric use for fetal lung maturation*
 # The Remdesivir Review and Advisory Working Group evaluates the evidence and utility of remdesivir, provides recommendations on its use, and determines its allocation within the province.

This document is dynamic and addresses key therapeutic areas of concern for clinicians. The complete and most up-to-date version of the guidelines is available at http://www.bccdc.ca/health-professionals/clinical-resources/covid-19-care/clinical-care/treatments

Vancouver Coastal Health — Promoting wellness. Ensuring care.
fraserhealth — Better health. Best in health care
Provincial Health Services Authority — Province-wide solutions. Better health.
Providence Health Care — How you want to be treated
island health
Interior Health — Every person matters
northern health — the northern way of caring
British Columbia Ministry of Health
BC Patient Safety & Quality Council — Working Together. Accelerating Improvement.
First Nations Health Authority — Health through wellness