BC COVID THERAPEUTICS COMMITTEE (CTC)

Algorithm for Treatment of COVID-19 in Hospitalized Patients

APRIL 2025

This flow chart can be used in therapeutic decision making for **ADULT, NON-PREGNANT** patients who are hospitalized with a positive COVID-19 test across any disease severity. This tool includes pearls for consideration; however, as each clinical situation is unique, judgement is required. See notes on the second page for rationale. Seek expert consultation if patients do not fit these severity categories (e.g., recalcitrant or recurring COVID-19) or in deviations from these recommendations (e.g., non-formulary use of agents, prolonging treatment courses)

- Most patients in hospital settings who are SARS-CoV-2 test positive are NOT hospitalized DUE TO COVID-19 and do NOT require initiation of COVID-19 therapeutics
- Patients who require oxygen or organ support often have other reasons for needing these interventions besides COVID-19

Asymptomatic or minimally symptomatic	Mild – Moderate Not requiring consistent O_2 support	Severe COVID-19 Requiring low-flow supplemental O_2	Critical COVID-19 Requiring invasive and non-invasive high-flow ventilation (flow rate > 30 L/min and FiO_2 > 0.4, CPap, BiPap) or organ support
Patients can shed virus after recovering from infection or be incidentally test-positive. Testing or treatment is not required.	Patients can have respiratory symptoms such as nasal congestion, cough, sore throat, and may have pneumonia or tachypnea, but do not require ongoing supplemental oxygen. Such patients are usually hospitalized for other reasons.	Patients require supplemental O_2 for COVID pneumonia and not underlying conditions or other indications. Minimal or intermittent O_2 should be considered as moderate COVID-19, not severe disease.	Check that ventilator or organ support is required due to COVID-19 and not other indications.

Steroids

Steroids are NOT recommended in asymptomatic COVID

Steroids are NOT recommended in mild-moderate COVID

Dexamethasone 6mg PO/IV daily x 10 days or until discharge **is recommended**

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AND

Immunomodulators

Is Antiviral Treatment Recommended?

- Moderately and severely immunosuppressed
- Patients 60 years and older with:
  - End-stage renal disease (eGFR< 30ml/min)
  - Severe or end stage lung disease (COPD, asthma, interstitial lung disease)
  - Diabetes regularly treated with insulin
  - Severe developmental or intellectual disability
  - Rare blood and metabolic disorders

Nosocomial COVID and **moderate disease** (pneumonia, systemic illness) are most likely to progress; have a low threshold for treatment

NO | YES

Baricitinib & Tocilizumab are NOT recommended in asymptomatic, mild or moderate COVID

Inflammatory Markers Elevated?

Signs of COVID-19 related inflammation (CRP ≥ 50 mg/L, ferritin ≥ 1000 µg/L)?

NO | YES

Baricitinib
4 mg po daily (GFR ≥ 60 mL/min) or **2 mg po daily** (GFR 30-59 mL/min) or **2 mg po every 2nd day** (GFR 15-29 mL/min) up to 14 days, or until discharge **may be considered**

If contraindications to baricitinib (neutrophils <1.0 x 10^9/L lymphocytes <0.2 x 10^9/L , GFR <15 mL/min, ALT or AST 5x ULN), use **tocilizumab 400mg IV x 1 dose**

Tocilizumab
400mg IV x 1 dose is recommended

Reflection Point:
If deteriorating due to ongoing inflammation, and no contraindications (neutrophils <1.0 x 10^9/L lymphocytes <0.2 x 10^9/L, GFR <15 mL/min, ALT or AST 5x ULN)

AND

Baricitinib
4 mg po daily (GFR ≥ 60 mL/min) or **2 mg po daily** (GFR 30-59 mL/min) or **2 mg po every 2nd day** (GFR 15-29 mL/min) up to 14 days, or until discharge **may be considered**

Reflection Point:
Assess symptom trajectory – do not treat patients who are improving on their own

Contraindications to Paxlovid?

unmanageable drug-drug interactions, end-stage liver disease

NO | YES

Antivirals

Antivirals are NOT recommended in asymptomatic COVID or in patients without significant risk factors for severe disease

Nirmatrelvir/ritonavir (Paxlovid)
300/100mg PO BID (GFR ≥ 60 mL/min) OR **150/100mg PO BID** (GFR 30-59 mL/min) OR **300/100mg PO day 1** then **150/100mg PO ONCE daily days 2-5** (GFR <30mL/min) **x 5 days is recommended** within 5 days of symptom onset

Remdesivir
200mg IV x 1 then 100mg IV daily x 2 days (GFR ≥ 30 mL/min) or **200mg IV x 1 then 100mg IV 48 hours later x 1 dose** (GFR < 30mL/min) **is recommended** within 7 days of symptom onset

Remdesivir is NOT recommended in severe COVID

Reflection Point:
If deteriorates in 48 hrs despite first-line therapies, is excessively high-risk (e.g., elderly on rituximab), has recurring or recalcitrant severe infection, seek expert consultation for additional treatment options. See notes

Remdesivir is NOT recommended in critical COVID

Anticoagulation

High risk of bleeding?

age 75 or greater, GFR less than 30 mL/min, any coagulopathy, platelet count less than 50, use of dual antiplatelet therapy, recent history of serious GI bleed or recent intracranial condition (stroke, neurosurgery, aneurysm, cancer), epidural/spinal catheter

NO | YES

No specific anticoagulation regimen is recommended for VTE prophylaxis in asymptomatic, mild or moderate COVID-19. Follow standard of care for VTE prophylaxis in hospitalized patients

Therapeutic anticoagulation (LMWH preferred) **may be considered**
If used, anticoagulation for COVID-19 should start within 72 hours of admission and continue for 14 days or until hospital discharge

Prophylactic-intensity dosing of low molecular weight heparin (LMWH) for VTE prophylaxis **is recommended**

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Follow-up

No or Minimal Symptoms
- Do not repeat testing
- Assess daily for 2-3 days for symptom progression or development

Mild-Moderate COVID-19
- Patients started on antivirals should **finish antivirals**
- Patients started on dexamethasone for severe COVID should **finish 10 days of dexamethasone** or stop at discharge, whichever is sooner
- Patients started on baricitinib for severe COVID who improve (e.g., stop oxygen) **may stop baricitinib or continue if improvement is slow**
- Patients started on therapeutic anticoagulation for severe COVID **should continue therapeutic anticoagulation for 14 days** or until discharge, whichever is sooner

Severe COVID-19
- Patients started on remdesivir who progress to severe disease **can complete a 5-day course of remdesivir.** Do not prolong or extend treatment
- **Stop nirmatrelvir/ritonavir** if patient progresses from mild-moderate to severe disease
- Do not repeat testing or use cycle thresholds to guide treatment

Critical COVID-19
- Patients started on antivirals should **stop antivirals**
- Patients started on baricitinib can **continue baricitinib, continue baricitinib AND receive tocilizumab x 1 dose, OR stop baricitinib and receive tocilizumab x 1 dose.** The decision depends on reason for deterioration, degree of inflammation, initial response to baricitinib and patient factors such as contraindications and gastric access
- Patients started on therapeutic anticoagulation **should continue therapeutic anticoagulation** if they progress

Testing

- Polymerase Chain Reaction (PCR) testing for diagnosis of COVID-19 is indicated in all acute care settings, even if a rapid antigen test was self-administered prior to admission. See: Provincial Testing Guidelines
- As PCR is exquisitely sensitive and a positive test may indicate recovered infection or chronic shedding, symptom assessment and trajectory are paramount in guiding treatment decisions.

Corticosteroids

- Severe and Critical COVID-19:

  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.

  ** e.g., asthma exacerbation, refractory septic shock, history of chronic steroid use, obstetric use for fetal lung maturation.*

Immunomodulators

- Severe COVID-19:

  Baricitinib 4 mg PO daily (for GFR ≥60 mL/min), or 2 mg PO daily (for GFR 30-59 mL/min), or 2 mg PO every 2nd day (for GFR 15-29 mL/ min) up to 14 days**, or until hospital discharge (whichever occurs first) **is recommended** (COV-BARRIER, RECOVERY) for patients hospitalized from COVID-19 requiring supplemental oxygen who show signs of systemic inflammation/cytokine storm (e.g., elevated C-reactive protein ≥ 50 mg/L, ferritin ≥ 1000 µg/L). Baricitinib should only be initiated when oxygen support is required due to COVID-19 pneumonia (not from other causes such as heart failure, pulmonary embolism, etc.). Baricitinib should not be administered to patients with neutrophils <1.0 x 10^9/L, lymphocytes <0.2 x 10^9/L, ALT or AST >5 x ULN, GFR<15 mL/min/1.73 m^2. Patients who received immunosuppressants (high-dose corticosteroids, biologics, or JAK inhibitors) were generally excluded from RCTs of baricitinib; if baricitinib is being considered in these patients, benefits vs. risks of over-immunosuppression should be assessed on a case-by-case basis.

  **Limited data exist on baricitinib in pregnancy. Risks and benefits should be discussed on a case-by-case basis with pregnant patients with severe COVID-19*
  ***Early baricitinib discontinuation should be considered in patients who have clinically improved and no longer require supplemental oxygen*

  Tocilizumab is not recommended for patients receiving low-flow oxygen support. The RECOVERY trial found a survival benefit of 4% (28-day mortality: tocilizumab 29% vs. usual care 33%) in patients who had CRP >75 mg/L and on low-flow oxygen, non-invasive respiratory support, or invasive mechanical ventilation. However, considering the scarcity of IL-6 blockers in Canada, CTC and CTRAWG recommend prioritizing tocilizumab use only for critically ill patients at this time, which is the population shown to benefit most in both the REMAP and RECOVERY trials.

- Critical COVID-19:

  Tocilizumab AND/OR Baricitinib are recommended 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. While head-to-head comparative data are lacking, the magnitude of benefit of each agent appears equivalent. However, more robust data exist to support the use of tocilizumab. Baricitinib also carries the additional challenges related to gastric access and cytotoxic precautions. The ultimate choice of agent depends on patient characteristics and practical considerations. Patients receiving baricitinib prior to becoming critically ill may stop baricitinib and be switched to a one-time dose of tocilizumab or continue baricitinib. In patients who continue to deteriorate on immunomodulator monotherapy due to COVID-19-related inflammation/cytokine storm, the combination of tocilizumab and baricitinib can be considered as the addition of baricitinib to tocilizumab has been shown to provide an incremental survival benefit of 2.4% (OR 0.79, CI 0.63-0.97; RECOVERY).

  Tocilizumab 400 mg IV (single dose) is recommended (REMAP-CAP, RECOVERY). Dose-capping continues to be recommended over 8mg/kg due to a lack of robust drug supply and similar benefits between the two doses seen in observational studies. Tocilizumab should only be initiated when life support is required because of COVID-19 rather than other causes (such as bacterial infection, pulmonary embolism, etc.).

  Baricitinib 4 mg po daily (for GFR ≥ 60 mL/min) or 2 mg po daily (for GFR 30-59 mL/min) or 2 mg po every 2nd day (for GFR 15-29 mL/min) up to 14 days, or until discharge from hospital (whichever occurs first) **is recommended** (COV-BARRIER, RECOVERY). Baricitinib should only be initiated when life support is required because of COVID rather than other causes (such as bacterial infection, pulmonary embolism, etc.). Baricitinib should not be administered to patients with neutrophils < 1.0 x 10^9/L, , lymphocytes < 0.2 x 10^9/L, , ALT or AST > 5 x ULN, or eGFR < 15 mL/min (or CRRT)

  **Limited data exist on baricitinib in pregnancy. Risks and benefits of baricitinib should be discussed on a case-by-case basis with pregnant patients with critical COVID-19*

Antivirals

- Mild-Moderate COVID-19:

  Nirmatrelvir/ritonavir 300/100mg PO BID x 5 days (150/100mg PO BID x 5 days in eGFR 30-60ml/min; 300/100mg PO on day 1 followed by 150/100mg PO ONCE daily in eGFR <30ml/min) **is recommended** within 5 days of symptom onset for patients at high risk of progression to severe COVID-19 (see Clinical Practice Guide for recommendations) OR, if nirmatrelvir/ritonavir cannot be due to drug-drug interactions or contraindications **Remdesivir 200mg IV on day 1, followed by 100mg IV on days 2 and 3** (200mg IV on day 1, followed by 100mg IV 48-72 hours later in eGFR <30ml/min) **is recommended** within 7 days of symptom onset as an alternative to nirmatrelvir/ritonavir.

- Severe COVID-19:

  Remdesivir is not recommended in patients with severe COVID-19. While remdesivir has demonstrated a small survival benefit (14.6% vs. 16.3%, p=0.03) in the final analysis of SOLIDARITY, this difference was not observed when mortality was lower. Since current mortality is approximately 50% lower than in SOLIDARITY, the benefit of remdesivir is unlikely. Observational trials with positive results no longer show benefit in late Omicron periods when mortality is low and patients have hybrid immunity. Remdesivir is non-formulary in BC hospitals due to lack of benefit in the general population with severe COVID-19. Seek expert consultation before pursuing non-formulary remdesivir for patients who are deteriorating despite optimal therapy, those with excessive risk of mortality (e.g., elderly on rituximab) or those with recurring or recalcitrant severe infection. However, the lack of evidence of benefit of remdesivir in these scenarios needs to be seriously considered.

- Critical COVID-19:

  Remdesivir is not recommended in patients with critical COVID-19 as it has not demonstrated to improve survival or time to clinical recovery.

Anticoagulation

- Severe COVID-19:

  Therapeutic anticoagulation (LMWH preferred) can be considered in patients without high-risk features for serious bleeding*. It should start within 72 hours of admission and continue for 14 days or until hospital discharge. Patients who decompensate and require organ support while on therapeutic anticoagulation should continue therapeutic anticoagulation, if the risk of bleeding remains low.

  Pooled data from RCTs showed that therapeutic anticoagulation with LMWH/UFH significantly reduces major thrombotic events (OR 0.47; 95% CI 0.24-0.90) but may increase major bleeding (OR 1.45; 95% CI 0.77-2.70) compared with lower doses. Organ support-free days alive were significantly increased with therapeutic heparin (OR 1.29; 95% CI 1.07-1.57). Benefit is more likely in those with elevated D-dimer level or additional risk factors for thrombosis. No differences were observed in the need for invasive mechanical ventilation, intracranial hemorrhage or all-cause mortality.

  **High risk features for bleeding include age ≥75, eGFR less than 30 mL/min, any coagulopathy, platelet count less than 50, use of dual antiplatelet therapy, recent history of serious GI bleed or recent intracranial condition (stroke, neurosurgery, aneurysm, cancer), epidural or spinal catheter.*

- Critical COVID-19:

  Prophylactic-intensity dosing of low molecular weight heparin (LMWH) is recommended for VTE prophylaxis in patients who do not have suspected or confirmed VTE (or other indications for therapeutic anticoagulation). There is a high probability of harm when therapeutic anticoagulation is initiated in patients who have received organ support for greater than 48 hours (n=1074; NIH mpRCT). 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.