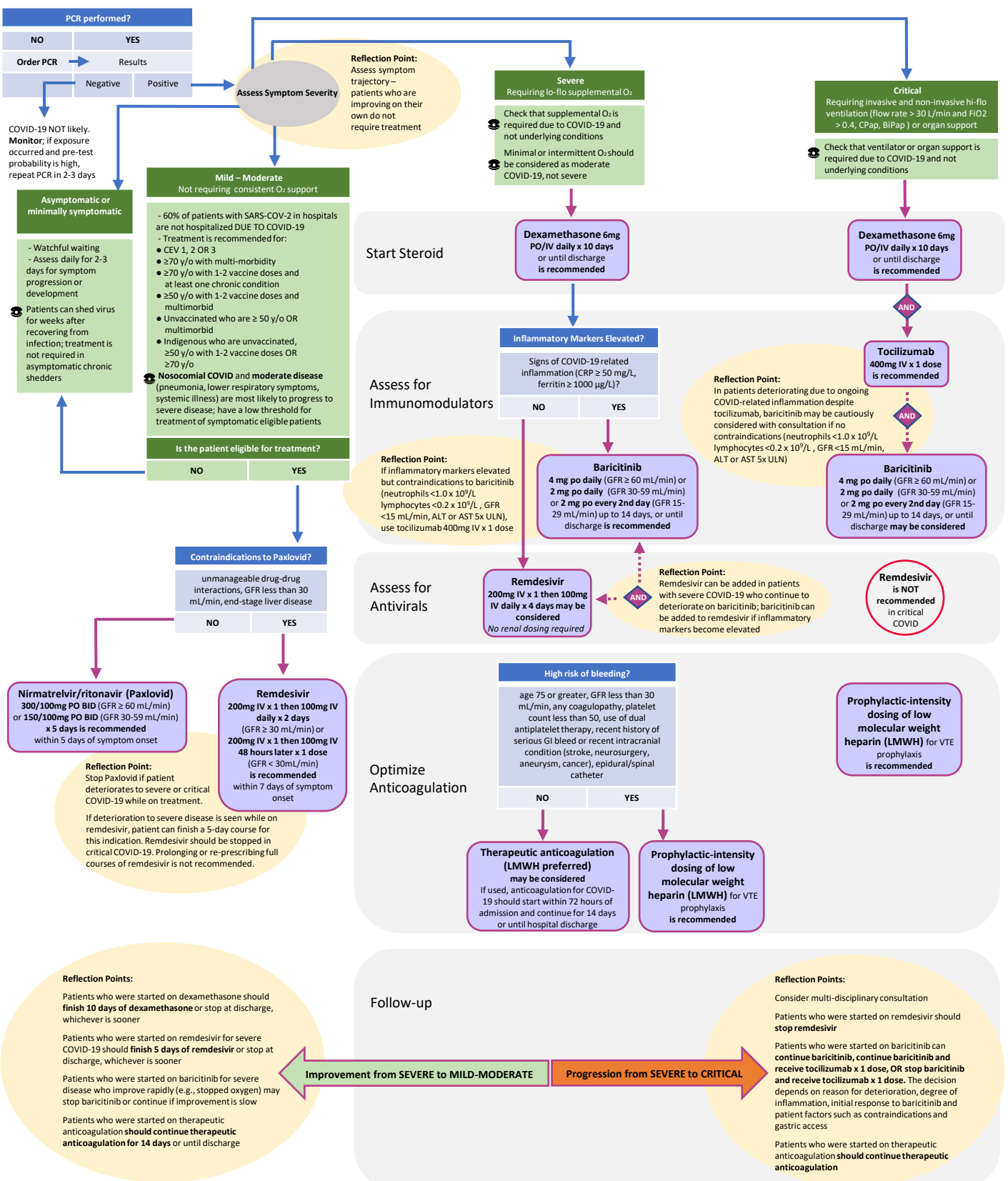


**BC COVID THERAPEUTICS COMMITTEE (CTC)** Algorithm for Treatment of COVID-19 in Hospitalized Patients **DEC 2022**

This flow chart can be used in therapeutic decision making for **ADULT, NON-PREGNANT** patients who are hospitalized and have a positive COVID-19 test or have symptoms consistent with COVID-19 across any disease severity. This tool includes pearls for consideration; however, as each clinical situation is unique, strong judgement is required. Expert consultation can be considered for assistance.



## Testing

- 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  $\geq 60$  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  $\geq 50$  mg/L, ferritin  $\geq 1000$   $\mu$ g/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  $<1.0 \times 10^9/L$ , lymphocytes  $<0.2 \times 10^9/L$ , ALT or AST  $>5 \times$  ULN, GFR  $<15$  mL/min/1.73 m<sup>2</sup>. 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  $FiO_2 > 0.4$  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  $\geq 60$  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  $< 1.0 \times 10^9/L$ , lymphocytes  $< 0.2 \times 10^9/L$ , ALT or AST  $> 5 \times$  ULN, or eGFR  $< 15$  mL/min (or receiving renal replacement therapy).

\*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) **is recommended** within 5 days of symptom onset for patients at high risk of progression to severe COVID-19 (see [Clinical Practice Guide](#) for eligibility criteria) 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  $<30$ ml/min) **is recommended** within 7 days of symptom onset as an alternative to nirmatrelvir/ritonavir.

- Severe COVID-19:

**Remdesivir 200mg IV on day 1 followed by 100mg IV on days 2-5 can be considered** in patients who are not receiving baricitinib for COVID-19-related inflammation/cytokine storm. Remdesivir has demonstrated a small survival (14.6% vs. 16.3%,  $p=0.03$ ) in the final analysis of SOLIDARITY and need for requiring mechanical ventilation (8% vs. 15%) as a secondary endpoint of CATCO. As data supporting the use of baricitinib is stronger, baricitinib should be initiated first in those meeting criteria. Remdesivir may be added in patients who are deteriorating (but not requiring organ support), or not improving despite baricitinib as the combination has been shown to reduced recovery time and improved clinical status for patients with severe COVID-19 (ACTT-2). If remdesivir is used for this indication, a 5-day course is recommended as a 10-day course was shown to be equivalent but increased the length of hospital stay.

- 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 on 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  $\geq 75$ , 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.