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See [COVID-19 Information for AHS Staff & Health Professionals](#) for current version.

Current Guidance for the Management of Adult Hospitalized Patients with COVID-19

Prepared By: The COVID-19 Therapeutics Working Group, Alberta Health Services

Note: This document represents updated guidance (previous update May 13, 2022) and will be updated as relevant new information becomes available. As such, the most current web-based version of this document should preferentially be used.

The COVID-19 Therapeutics Working Group (WG) has updated the evolving evidence base for this document as best as possible but recognizes that future updates will be required based on ongoing therapeutic trials and emerging evidence. Supportive care remains an important component of therapy for individuals infected with SARS-CoV-2. Updated COVID-19 management guidelines from the [Public Health Agency of Canada \(PHAC\)](#), [Association of Medical Microbiology and Infectious Diseases \(AMMI\)](#), [Canada/Canadian Critical Care Society](#) (August 21, 2020)¹, [the Infectious Diseases Society of America \(IDSA\)](#) (November 21, 2022)² and the [Alberta Health Services COVID-19 Scientific Advisory Group](#)³ have been reviewed in preparing this update. Full details are available in the hyperlinks above and the referenced documents below.

Consultation with other specialties (e.g. Infectious Diseases, Respiratory Medicine, Critical Care, General Internal Medicine) who are most likely to be familiar with the rapidly evolving literature can be considered to help assess the risks and benefits for an individual patient. As recommended by AHS Ethics, any off-label use of medication requires the prescriber's careful consideration of risk/benefit, consultation between experts and attending physician as needed, and documenting consent from the patient or alternate decision-maker after discussion of the current state of evidence of benefit and harms. Adverse events with respect to off-label use of medications for inpatient treatment should be documented and reported by clinicians through the [AHS Reporting and Learning System for Patient Safety](#).

The guidance provided in this document does not replace best clinical judgment and/or expert consultation but rather is meant to inform clinicians of the most current management guidelines to facilitate best use of therapeutic options for patients with COVID-19.

Guiding Principles

- 1) The use of antiviral or other immunomodulatory treatments, other than those recommended below, for patients with COVID-19 should occur within the context of controlled clinical trials wherever possible, given the currently available limited therapeutic options for which evidence-based data are available.
- 2) If the use of antiviral or immunomodulatory agents for COVID-19 outside of clinical trials is being considered, the potential risks (adverse reactions, drug interactions (see [COVID drug interactions](#) or [Lexicomp](#)) versus unverified benefits must be considered and discussed with the patient or caregiver, and consent documented on the chart.
- 3) Bacterial co-infection in patients with early COVID-19 is uncommon. Do NOT routinely add antibacterials unless bacterial infection is strongly suspected. If indicated, antibacterials should be reassessed within the first 3 days after initiation to determine if continuation is necessary, or to de-escalate and/or optimize therapy in accordance with the principles of stewardship to avoid short-term adverse-effects and negative long-term consequences of increased microbial resistance.

Current Practice Guidance

1. General Considerations

- Patients with mild suspected or confirmed COVID-19 should not require hospitalization, unless there is a clinical concern for rapid deterioration, significant underlying co-morbidities, extenuating sociodemographic circumstances, or an inability to return promptly to hospital. Patients with mild COVID-19 and their caregivers should be provided with information on symptom management and informed of the signs and symptoms of complications that should prompt medical re-evaluation.
- Patients with moderate suspected or confirmed COVID-19 (i.e. with clinical signs of pneumonia, SpO₂ ≥ 90% on room air, but no signs of severe pneumonia) who are not determined to be at high risk of deterioration may not require hospitalization, but they should self-monitor and be counseled along with their caregivers about the signs and symptoms of complications that should prompt medical re-evaluation.
- Patients with severe suspected or confirmed COVID-19 and respiratory distress, hypoxemia, or shock should receive supplemental oxygen therapy immediately with target saturations of > 94% SpO₂ during resuscitation. Patients with severe illness should be closely monitored for signs of clinical deterioration, specifically rapidly progressive respiratory failure, or shock.

- In hospitalized adult patients who meet criteria for severe disease (defined by the IDSA as SpO₂ <94% on room air), and requiring supplemental oxygen, mechanical ventilation or extracorporeal membrane oxygenation, clinicians should prescribe dexamethasone 6 mg IV/PO daily for 10 days (or equivalent glucocorticoid dose)⁴, or until off oxygen or discharged, whichever is earlier. Glucocorticoids are not recommended in patients who do not have hypoxemia requiring supplemental oxygen.

2. Antibacterials

- For those patients with suspected or confirmed mild to moderate COVID-19, antibiotics should **not** be routinely prescribed unless there is clinical suspicion of a bacterial infection.
- For patients with severe COVID-19 but not critically ill, do NOT routinely add antibacterials unless bacterial infection is strongly suspected.
- For critically ill patients with suspected or confirmed severe COVID-19, empiric antibacterial agents to treat all likely pathogens causing severe acute respiratory bacterial infection and sepsis as soon as possible are reasonable, and optimally should be initiated within 1 hour of initial patient assessment for patients with sepsis.
- If indicated, empiric antibiotic treatment should be based on the working clinical diagnosis (e.g., community-acquired pneumonia, health care-associated pneumonia or sepsis), local epidemiology, and susceptibility data. See references such as [Bugs & Drugs](#) for empiric antibacterials.
- Use of antibacterial therapy should be judicious with reassessment after 3 days for de-escalation and/or optimization of therapy, in accordance with the principles of stewardship, after review of the clinical status, laboratory and imaging findings, and microbiology results.

3. Antivirals/Immunomodulators

- Remdesivir has two approved formulary indications in AHS. Hospitalized patients with COVID-19 pneumonia, defined as having oxygen requirements above pre-hospitalization baseline (SpO₂ less than 94% on room air, or requiring O₂ supplementation to maintain SpO₂ greater than 94%) and/or new infiltrates on chest X-ray not caused by other health conditions, who are not invasively mechanically ventilated, are eligible for a 5-day course of remdesivir (200 mg IV on day 1, followed by 100 mg IV daily on days 2-5)^{5,6}. High risk inpatients admitted for non-COVID reasons with incidental or hospital-acquired COVID-19 are eligible for a 3-day course of remdesivir (200 mg IV on day 1, followed by 100 mg IV daily on days 2 and 3)⁷. See the AHS formulary for full eligibility criteria. In select clinical circumstances where multi-agent therapy including remdesivir, or extended duration remdesivir is being considered for highly immunocompromised people, Infectious Diseases consultation is required (in person or phone).
- Tocilizumab is approved for use in patients with severe COVID-19 pneumonia⁸. To be eligible, patients must have been admitted to hospital for COVID-19 pneumonia 7 or fewer days ago, or have developed

symptoms from hospital-acquired COVID-19 pneumonia 7 or fewer days ago. They must also be experiencing significant progressive respiratory failure due to COVID-19 pneumonia that requires they receive ventilation (invasive or non-invasive) or supplemental oxygen to achieve a minimum SpO₂ of 90%. Supplemental oxygen is defined as heated high flow oxygen with FiO₂ ≥ 0.5, nasal prong delivered oxygen at a rate of 6 L/minute, or mask delivered oxygen with FiO₂ ≥ 0.5. Furthermore, tocilizumab must be initiated within 24 hours of initiation of mechanical ventilation or, if not mechanically ventilated, as soon as possible. Tocilizumab is restricted for this indication to one dose per patient per hospitalization, dosed as follows:

≤ 40 kg:	8 mg/kg
> 40 kg:	400 mg

Tocilizumab should not be used in patients who have received baricitinib for the treatment of COVID-19 during their current hospitalization. They each work on the same inflammatory pathway, so added benefit is unlikely. Due to their immunosuppressant effects, combination therapy may have adverse effects.⁹

- Sarilumab is approved as an alternative to tocilizumab when tocilizumab is not available, using the same eligibility criteria as tocilizumab. It is available in Canada in a subcutaneous formulation, but is administered intravenously as a single 400mg dose for the treatment of COVID-19. It has the same mechanism of action as tocilizumab but has not been studied as widely. It was directly compared to tocilizumab in the REMAP-CAP trial¹⁰, and was found to lead to a similar reduction in mortality, albeit with less precision due to the much smaller number of patients given sarilumab. A network meta-analysis¹¹ done in support of the World Health Organization (WHO) living guidelines for COVID-19 therapeutics¹² concluded that sarilumab likely has similar effectiveness to tocilizumab, although their recommendation to use sarilumab has less certainty due to the smaller number of subjects and studies included in the meta-analysis. Approval of sarilumab was based on the similar mechanisms of action, direct trial evidence, and indirect network meta-analysis evidence. Sarilumab should not be used in patients who have received tocilizumab or baricitinib for the treatment of COVID-19 during their current hospitalization. They each work on the same inflammatory pathway, so added benefit is unlikely. Due to their immunosuppressant effects, combination therapy may have adverse effects.⁹
- Baricitinib is approved for use in patients with severe COVID-19 pneumonia. To be eligible patients must be experiencing significant progressive respiratory failure due to COVID-19 pneumonia that requires they receive ventilation (invasive or non-invasive) or supplemental oxygen to achieve a minimum SpO₂ of 90%. Supplemental oxygen is defined as heated high flow oxygen with FiO₂ ≥ 0.5, nasal prong delivered oxygen at a rate of 6 L/minute, or mask delivered oxygen with FiO₂ ≥ 0.5. Baricitinib is an oral tablet given by mouth or enteral tube 4 mg once daily for 14 days or until discharge, whichever is sooner. The main trial¹³ upon which approval of use was based excluded patients with eGFR < 30 mL/min/1.73m². It was dosed at 2 mg daily for those with eGFR 30 to < 60 mL/min/1.73m². However, the US Food and Drug Administration Emergency Use Authorization (FDA

EUA)¹⁴ also lists dosing of 1 mg for patients with eGFR 15 to < 30 mL/min/1.73m². Baricitinib 1 mg tablets are not available in Canada, so for patients with eGFR in this range, the recommended dose is 2 mg every other day. Baricitinib should not be used in patients who have received tocilizumab or sarilumab for the treatment of COVID-19 during their current hospitalization. They each work on the same inflammatory pathway, so added benefit is unlikely and due to their immunosuppressant effects, combination therapy may have adverse effects.⁹

- Bamlanivimab, bamlanivimab-etesevimab, casirivimab-imdevimab, sotrovimab, and tixagevimab-cilgavimab are no longer recommended as treatments for COVID-19. Tixagevimab-cilgavimab is no longer recommended for pre-exposure prophylaxis of COVID-19. Neutralization data¹ suggest that none of these agents effectively neutralize the dominant circulating variants of the SARS-CoV-2 virus in Alberta, as of January 2023.
- Nirmatrelvir-ritonavir (Paxlovid[®]) is an oral COVID-specific antiviral approved for use in high-risk outpatients, as well as inpatients admitted for non-COVID reasons with incidental or hospital-acquired COVID-19, if therapy can be initiated within 5 days of symptom onset. See the AHS formulary for full eligibility criteria. Published data suggests it significantly reduces risk of hospitalization or death in outpatients at high risk for progression to severe disease¹⁸. Paxlovid[®] has numerous significant drug interactions that may make patients ineligible for treatment. Outpatients who think they may be eligible for treatment with Paxlovid[®] are advised to call the dedicated Alberta HealthLink phone line at 1-844-343-0971. Centralized assessing and prescribing physicians will determine eligibility and arrange for treatment in the community, if appropriate.

- Consideration of all other investigational antivirals or immunomodulators (e.g. lopinavir/ritonavir, famotidine, and colchicine) should be only under ethics approved, controlled trials.
- There is currently insufficient evidence to recommend routine use of fluvoxamine in outpatients^{2,20}. It is not recommended for inpatient use.
- The use of hydroxychloroquine, or any hydroxychloroquine combinations (e.g. hydroxychloroquine plus azithromycin), is not recommended as a treatment in patients with COVID-19.
- Ivermectin should not be used for the prevention or treatment of COVID-19.²¹ Its use is not supported by evidence²².
- Convalescent plasma is not recommended as a treatment in patients with COVID-19. Evidence suggests it has no benefit²³.

4. General Investigations

Please note the listed investigations below are for clinical consideration and not required tests. Please use the laboratory tests and Investigations incorporated into care pathways and order sets if there are differences between those and the list below.

4.1 General Laboratory tests:

Laboratory tests may not be required in otherwise ambulatory patients who are clinically stable, and not felt to be at elevated risk of decompensation. In the presence of higher clinical severity and/or comorbidities, the following laboratory tests may be considered:

- CBC & differential - *low lymphocyte count and/or neutrophil/lymphocyte ratio of >3.13 may be suggestive of COVID-19/more severe disease*
- AST, ALT, bilirubin, Cr, CRP, Urea
- D-dimer, INR
- Blood cultures
- COVID-19 PCR and RPP swabs OR sputum or ET aspirate or bronchoscopic samples for COVID-19 PCR

Also consider for select patients:

- HIVAb
- MRSA nasal swab (to determine need for empiric MRSA pneumonia coverage pending cultures)

4.2 CXR - AP (portable) or PA/LAT depending on site policies for ED based COVID-19 patients

4.3 Laboratory tests that can be considered in specific patients based on clinical status and comorbidities (NB: the current literature does not support a specific role for these parameters in guiding clinical management but they may be useful in evolving prognostic models):

- ABG
- fibrinogen
- ferritin
- troponin
- If immunocompromised and clinically indicated, ET aspirate, bronchoscopy (if required), or induced sputum for PJP and/or mycobacterial and /or fungal assessment

5.0 Other considerations

- Clinical progression to more severe disease usually begins between 5-7 days after symptom onset. Risk factors for disease progression include older age and presence of underlying medical conditions (e.g. hypertension, obesity, diabetes, chronic lung diseases, and immunocompromised state). However, younger, previously healthy individuals can develop severe illness
- If oxygen demand is increasing, consider early referral for appropriate respiratory supports depending on access and infrastructure.
- There is no evidence that ACE Inhibitors and Angiotensin Receptor Blockers need to be stopped. There is a theoretical concern about ACE inhibition and viral receptors but there are no clinical data supporting risk. Major cardiovascular societies ([Hypertension Canada Statement on COVID-19 ACEi/ARB](#)) recommend that suspected and confirmed COVID-19 patients on ACE inhibition should be maintained on their therapy if it is otherwise indicated to avoid decompensation of cardiac disease.
- There is no specific contraindication to NSAIDs: [AHS SAG Use of NSAIDs Review](#). As other symptomatic therapy can be substituted (acetaminophen, appropriately dosed) it may be reasonable to prefer acetaminophen to NSAIDs for COVID-19 symptoms, but patients with inflammatory conditions on stable doses of NSAIDs should remain on them.

Submitted by the COVID-19 Therapeutics Working Group and reviewers (Critical Care, Infectious Diseases, Pharmacy, Emergency Medicine, Pulmonary Medicine, Immunology). Reviews of this document were also done by members of the Divisions of Infectious Diseases in the Departments of Medicine at the University of Calgary and the University of Alberta.

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