Ontario COVID-19 Drugs and Biologics Clinical Practice Guidelines Working Group

Therapeutic Management of Adult Patients with COVID-19

Recommendations apply to patients >18 years of age. Recommendations are based on the best available data and may change as additional data becomes available. Science Briefs can be found on the Ontario COVID-19 Science Advisory Table website.

SCIENCE TABLE
COVID-19 ADVISORY FOR ONTARIO

SEVERITY OF ILLNESS	RECOMMENDATIONS

Critically Ill Patients

Patients requiring ventilatory and/or circulatory support, including high-flow nasal oxygen, non-invasive ventilation, invasive mechanical ventilation, or ECMO

- ● **Dexamethasone** 6 mg PO/IV daily for 10 days (or until discharge if sooner) **is recommended**.
- ● **Tocilizumab is recommended** for patients who are on recommended doses of dexamethasone therapy (or a dose-equivalent corticosteroid) AND are within 14 days of hospital admission (or within 14 days of a new COVID-19 diagnosis if the infection was nosocomially acquired).
  - **In drug shortage situations, a single dose of tocilizumab 400 mg IV or sarilumab 400 mg IV** should be used for all eligible patients. A second dose of tocilizumab or sarilumab should not be given to any patient.
- ▲ **Baricitinib** 4 mg PO/NG daily for 14 days (or until discharge if sooner) **may be considered** in patients who are on recommended doses of dexamethasone therapy (or a dose-equivalent corticosteroid) or who have a contraindication to corticosteroid treatment. The panel does not recommend combined use of baricitinib and IL-6 inhibitors due to absence of safety and efficacy evidence.
- ● **Prophylactic dose low molecular weight or unfractionated heparin is recommended**.
- ■ These patients **should not receive therapeutic dose anticoagulation** unless they have a separate indication for this treatment.
- ■ **Remdesivir** is **not recommended** for patients receiving mechanical ventilation.
- ▲ **Remdesivir** 200 mg IV on day 1, then 100 mg IV daily for 4 days **may be considered** in patients requiring high-flow oxygen (i.e., oxygen by mask, oxygen by high-flow nasal cannula, or non-invasive mechanical ventilation).
- ■ **SARS-CoV-2 neutralizing antibodies** are **not recommended** for critically ill patients. For symptomatic inpatients with nosocomial infection, see mildly ill recommendations below for sotrovimab.
- ■ Bacterial co-infection is uncommon in COVID-19 pneumonia at presentation. **Do not add empiric antibiotics for bacterial pneumonia** unless bacterial infection is strongly suspected. Continue empiric antibiotics for no more than 5 days, and de-escalate on the basis of microbiology results and clinical judgment.

Moderately Ill Patients

Patients newly requiring low-flow supplemental oxygen

- ● **Dexamethasone** 6 mg PO/IV daily for 10 days (or until discharge if sooner) **is recommended**.
- ▲ If patients are discharged with home-based oxygen therapy, **dexamethasone** 6 mg PO daily until oxygen is no longer required (for a maximum of 10 days) **may be considered**.
- ● **Remdesivir** 200 mg IV on day 1, then 100 mg IV daily for 4 days **is recommended**.
- ▲ **Therapeutic dose anticoagulation may be considered** over prophylactic dose anticoagulation in patients who are felt to be at low risk of bleeding.
- ● **All other patients should receive prophylactic dose anticoagulation.**
- ■ **SARS-CoV-2 neutralizing antibodies** are **not recommended** for moderately ill patients. For symptomatic inpatients with nosocomial infection, see mildly ill recommendations below for sotrovimab.
- ● **Tocilizumab is recommended** for patients who have evidence of systemic inflammation, defined as a serum CRP of 75 mg/L or higher, AND have evidence of disease progression (i.e., increasing oxygen or ventilatory requirements) despite 24-48 hours of recommended doses of dexamethasone therapy (or a dose-equivalent corticosteroid), AND are within 14 days of hospital admission (or within 14 days of a new COVID-19 diagnosis if the infection was nosocomially acquired).
  - **In drug shortage situations, a single dose of tocilizumab 400 mg IV or sarilumab 400 mg IV** should be used for all eligible patients. A second dose of tocilizumab or sarilumab should not be given to any patient.
- ▲ **Baricitinib** 4 mg PO daily for 14 days (or until discharge if sooner) **may be considered** in patients who are on recommended doses of dexamethasone (or a dose-equivalent corticosteroid) or who have a contraindication to corticosteroid treatment. The panel does not recommend combined use of baricitinib and IL-6 inhibitors due to absence of safety and efficacy evidence.

Mildly Ill Patients

Patients who do not require new or additional supplemental oxygen from their baseline status

- ● **Sotrovimab** 500 mg IV x 1 dose **is recommended** for mildly ill patients who present within 7 days of symptom onset and meet any one of the following criteria:
  - Symptomatic residents of long-term care facilities, retirement homes, and other congregate care living settings
  - Symptomatic inpatients with nosocomial infection
  - High-risk patients: (a) ≥70 years of age AND have at least one additional risk factor; or (b) ≥50 years of age AND First Nations, Inuit, or Métis, AND have at least one additional risk factor (e.g., obesity (BMI ≥30), dialysis or stage 5 kidney disease (eGFR <15 mL/min/1.73 m^2), diabetes, cerebral palsy, intellectual disability of any severity, sickle cell disease, receiving active cancer treatment, solid organ or stem cell transplant recipients)
- ▲ **Sotrovimab may be considered** in patients who do not meet the above criteria if they present within 7 days of symptom onset and if, in the opinion of a physician, they have other important risk factors for disease progression (e.g., immunosuppression, receipt of immunosuppressants).

  Previous SARS-CoV-2 infection and vaccination status do not need to be considered. Serologic testing does not need to be done.

  It is recommended that monoclonal antibody therapy be administered to non-hospitalized individuals across Ontario using a hybrid network that includes, but is not limited to, mobile integrated healthcare services, community paramedicine, and outpatient infusion clinics.
- ▲ **Budesonide** 800 mcg inhaled twice daily for 14 days **may be considered** for symptomatic high-risk outpatients (as described under sotrovimab recommendation for mildly ill patients).
- ▲ **Fluvoxamine** 50 mg PO daily titrated up to 100 mg PO TID for 15 days **may be considered** for mildly ill patients presenting within 7 days of symptom onset. This recommendation is based on very low certainty evidence of reduction in hospitalization, and the need for outpatient treatment options with a reasonable safety profile during an anticipated spike in COVID-19 cases due to the Omicron variant. Pharmacist consultation and outpatient provider follow-up is important to avoid any significant adverse drug interactions with fluvoxamine.
- ◆ There is currently **insufficient evidence** to make a recommendation around **anticoagulation** for mildly ill patients.
- ■ The following therapies are **not recommended** in mildly ill patients: dexamethasone, remdesivir, tocilizumab, and baricitinib.

CURRENTLY NOT RECOMMENDED

There is insufficient evidence to support the use of the following therapies in the treatment of COVID-19 outside of clinical trials or where other indications would justify its use:

- ◆ Colchicine
- ◆ Interferon (with or without lopinavir-ritonavir and ribavirin)
- ◆ Vitamin D

RECOMMENDED AGAINST

The following therapies are not recommended for treatment of COVID-19 due to lack of benefit, potential harm, and system implications of overuse:

- ■ Antibiotics (azithromycin)
- ■ Casirivimab-imdevimab due to lack of neutralizing activity against the Omicron variant
- ■ Hydroxychloroquine or chloroquine
- ■ Ivermectin
- ■ Lopinavir/ritonavir

Click here for dosing and pharmacologic considerations for medications approved or under investigation for COVID-19

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