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**<br>Patients requiring ventilatory and/or circulatory support, including high-flow nasal oxygen, non-invasive ventilation, invasive mechanical ventilation, or ECMO.<br>These patients are usually managed in an intensive care setting. | ● **Dexamethasone** 6 mg PO/IV daily for 10 days (or until discharge if sooner) **is recommended** for critically ill patients with suspected or confirmed COVID-19.<br>● **Tocilizumab (dosed according to body weight) is recommended** for critically ill patients with suspected or confirmed COVID-19, 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).<br>• The dose of tocilizumab IV may be determined by a weight-based dose strategy (8 mg/kg, maximum dose 800 mg) OR by a weight-based dose banding strategy (800 mg if weight >90 kg; 600 mg if weight >65 and ≤90 kg; 400 mg if weight >40 and ≤65 kg; and 8 mg/kg if weight ≤40 kg). A second dose of tocilizumab may be considered after 24 hours if the patient is not improving.<br>• **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 should not be given to any patient.<br>● **Prophylactic dose low molecular weight or unfractionated heparin is recommended** in critically ill patients hospitalized with COVID-19.<br>■ These patients **should not receive therapeutic dose anticoagulation** unless they have a separate indication for this treatment.<br>■ **Remdesivir** is **not recommended** for critically ill patients with COVID-19 receiving mechanical ventilation.<br>▲ In critically ill patients requiring high-flow oxygen (i.e., oxygen by mask, oxygen by high-flow nasal cannula, or non-invasive mechanical ventilation), **remdesivir** 200 mg IV on day 1, then 100 mg IV daily for 4 days **may be considered** for suspected or confirmed COVID-19.<br>■ 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.<br>▶ For recommendations for **SARS-CoV-2 neutralizing antibodies**, see Box 1 on page 2. |
| **Moderately Ill Patients**<br>Patients newly requiring low-flow supplemental oxygen.<br>These patients are usually managed in hospital wards. | ● **Dexamethasone** 6 mg PO/IV daily for 10 days (or until discharge if sooner) **is recommended** for moderately ill patients with suspected or confirmed COVID-19.<br>▲ 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**.<br>● **Remdesivir** 200 mg IV on day 1, then 100 mg IV daily for 4 days **is recommended** for moderately ill patients with suspected or confirmed COVID-19.<br>▲ **Therapeutic dose anticoagulation may be considered** over prophylactic dose anticoagulation in moderately ill patients who are felt to be at low risk of bleeding.<br>● **All other patients should receive prophylactic dose anticoagulation.**<br>● **Tocilizumab (dosed according to body weight) is recommended** for moderately ill patients with suspected or confirmed COVID-19, 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).<br>• Weight-based dosing strategies are the same as for critically ill patients, and a second dose of tocilizumab may be considered after 24 hours if the patient is not improving.<br>• **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 should not be given to any patient.<br>▶ For recommendations for **SARS-CoV-2 neutralizing antibodies**, see Box 1 on page 2. |
| **Mildly Ill Patients**<br>Patients who do not require new or additional supplemental oxygen from their baseline status, intravenous fluids, or other physiological support.<br>These patients are usually managed in an ambulatory/ outpatient setting. | ■ **Dexamethasone** is **not recommended** for mildly ill patients with suspected or confirmed COVID-19.<br>■ **Remdesivir** is **not recommended** for mildly ill patients with suspected or confirmed COVID-19.<br>■ **Tocilizumab** is **not recommended outside of clinical trials** for mildly ill patients with suspected or confirmed COVID-19.<br>◆ There is currently **insufficient evidence** to make a recommendation around **anticoagulation** for mildly ill patients.<br>▲ **Inhaled budesonide** 800 mcg twice daily for 14 days **may be considered** in selected patients with increased risk of adverse COVID-19 outcomes (≥65 years of age, or ≥50 years of age with one or more of: immunosuppression; heart disease; hypertension; asthma; lung disease; diabetes; liver disease; stroke; neurologic disease; or obesity).<br>▶ For recommendations for **SARS-CoV-2 neutralizing antibodies**, see Box 2 on page 2. |

## 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

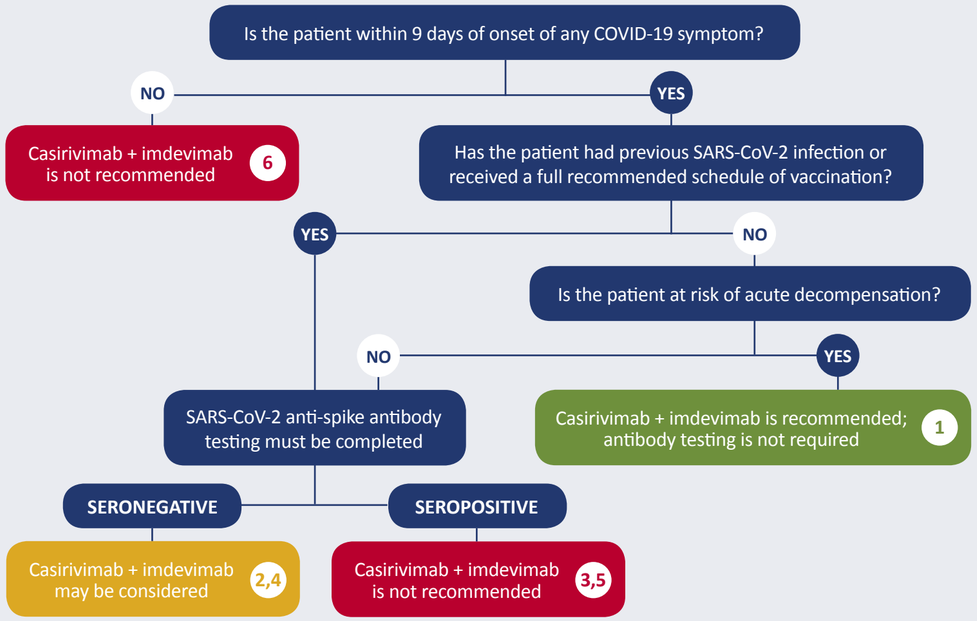
## RECOMMENDED AGAINST

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

- ■ Antibiotics (azithromycin)
- ■ Hydroxychloroquine or chloroquine
- ■ Ivermectin
- ■ Lopinavir/ritonavir

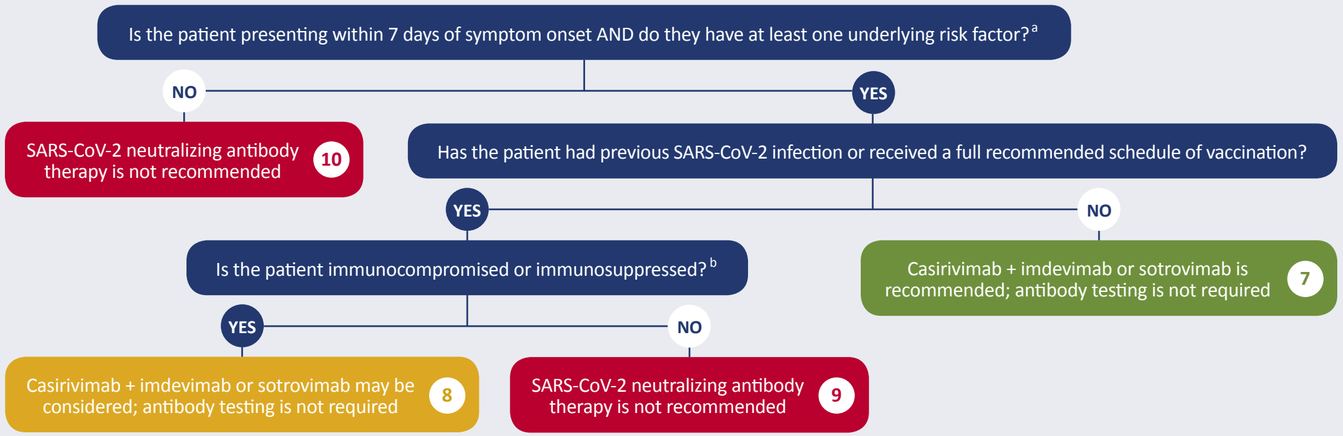
**Click here for dosing and pharmacologic considerations for medications approved or under investigation for COVID-19**

## Box 1. SARS-CoV-2 neutralizing antibodies for treatment of moderate or critical COVID-19




| SCENARIO | RECOMMENDATION |
|---|---|
| **No history of vaccination or SARS-CoV-2 infection, within 9 days of onset of any COVID-19 symptom** | ● 1 Casirivimab + imdevimab 2400 mg IV **is recommended** for moderately or critically ill patients with no history of SARS-CoV-2 infection or having received a full recommended schedule of vaccination, who are within 9 days of symptom onset, and have demonstrated rapid clinical deterioration. SARS-CoV-2 anti-spike antibody testing is not required.<br>▲ 2 Casirivimab + imdevimab 2400 mg IV **may be considered** for moderately or critically ill patients with no history of SARS-CoV-2 infection or having received a full recommended schedule of vaccination, who are within 9 days of symptom onset, and are not clinically at risk of acute decompensation, if anti-spike antibody testing demonstrates they are seronegative.<br>■ 3 Casirivimab + imdevimab is **not recommended** for moderately or critically ill patients with no history of SARS-CoV-2 infection or having received a full recommended schedule of vaccination, who are within 9 days of symptom onset, and are not clinically at risk of acute decompensation, if anti-spike antibody testing demonstrates they are seropositive. |
| **History of vaccination or SARS-CoV-2 infection, within 9 days of onset of any COVID-19 symptom** | ▲ 4 Casirivimab + imdevimab 2400 mg IV **may be considered** for moderately or critically ill patients with a history of SARS-CoV-2 infection or having received a full recommended schedule of vaccination, who are within 9 days of symptom onset, if anti-spike antibody testing demonstrates they are seronegative.<br>■ 5 Casirivimab + imdevimab is **not recommended** for moderately or critically ill patients with a history of SARS-CoV-2 infection or having received a full recommended schedule of vaccination, who are within 9 days of symptom onset, if anti-spike antibody testing demonstrates they are seropositive. |
| **Beyond 9 days of onset of COVID-19 symptoms** | ■ 6 Casirivimab + imdevimab is **not recommended** for moderately or critically ill patients who are beyond 9 days of symptom onset, whether or not they are presumed to have immunity through previous SARS-CoV-2 infection or having received a full recommended schedule of vaccination. |

## Box 2. SARS-CoV-2 neutralizing antibodies for treatment of mild COVID-19




| SCENARIO | RECOMMENDATION [a] |
|---|---|
| **No history of vaccination or SARS-CoV-2 infection, with risk factors [b]** | ● 7 Casirivimab + imdevimab 1200 mg IV/SC OR sotrovimab 500 mg IV **is recommended** for mildly ill patients who meet the following criteria: (1) no history of SARS-CoV-2 infection or having received a full recommended schedule of vaccination, AND (2) confirmed, symptomatic COVID-19, AND (3) within 7 days of onset of any COVID-19 symptom, AND (4) at least one underlying risk factor [b]. Anti-spike antibody testing is not required. |
| **History of vaccination or SARS-CoV-2 infection, immunocompromised or immunosuppressed [c]** | ▲ 8 Casirivimab + imdevimab 1200 mg IV/SC OR sotrovimab 500 mg IV **may be considered** for mildly ill patients who meet the following criteria: (1) history of SARS-CoV-2 infection or having received a full recommended schedule of vaccination, AND (2) confirmed, symptomatic COVID-19, AND (3) within 7 days of onset of any COVID-19 symptom, AND (4) immunocompromised or immunosuppressed [c]. Anti-spike antibody testing is not required. |
| **History of vaccination or SARS-CoV-2 infection, with risk factors [b] other than immunocompromise or immunosuppression** | ■ 9 Monoclonal antibody therapy is **not recommended** for mildly ill patients who are not immunocompromised or immunosuppressed and are presumed to have immunity (through receiving a full recommended schedule of vaccination or previous infection). |
| **No risk factors [b]** | ■ 10 Monoclonal antibody therapy is **not recommended** for patients at low risk of adverse outcomes, whether or not they are presumed to have immunity. |

a. 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 (MIH) services, community paramedicine (CP), and outpatient infusion clinics.
b. Risk factors: age >50 years, indigenous (First Nations, Inuit, or Métis), obesity, cardiovascular disease (including hypertension), chronic lung disease (including asthma), chronic metabolic disease (including diabetes), chronic kidney disease, chronic liver disease, immunosuppression [c], or receipt of immunosuppressants [c]
c. Examples include: active treatment for solid tumor and hematologic malignancies, receipt of solid-organ transplant and taking immunosuppressive therapy, receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy), moderate or severe primary immunodeficiency (e.g. DiGeorge syndrome, Wiskott-Aldrich syndrome), resident of long-term care, advanced or untreated HIV infection, active treatment with high-dose corticosteroids (i.e. ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis factor (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory. These individuals should have a reasonable expectation for 1-year survival prior to getting infected with SARS-CoV-2.

## Box 3. SARS-CoV-2 neutralizing antibodies for post-exposure prophylaxis

| RECOMMENDATION |
|---|
| ● Casirivimab + imdevimab 1200 mg IV/SC OR sotrovimab 500 mg IV **is recommended** for unvaccinated individuals or individuals not expected to mount an adequate immune response to SARS-CoV-2 vaccination (including immunosuppressed or immunocompromised as described in Box 2). Due to limited supply and implementation challenges, we recommend that post-exposure prophylaxis should currently be offered only to hospital inpatients, and those residing in congregate settings (e.g. long-term care, retirement homes, shelters, correctional facilities) who have had a high-risk exposure to SARS-CoV-2 (as determined by an expert in Infection Prevention and Control or Public Health) and who are at high-risk to progress to moderate or severe COVID-19. Determination of using a SARS-CoV-2 neutralizing antibody for post-exposure prophylaxis should take into account the nature and context of their exposure. |