

# 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.



### 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. 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.
- **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).
  - 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.
  - 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.
- **Prophylactic dose low molecular weight or unfractionated heparin** is recommended in critically ill patients hospitalized with COVID-19.
  - These patients **should not receive therapeutic dose anticoagulation** unless they have a separate indication for this treatment.
- **Remdesivir** is not recommended for critically ill patients with COVID-19 receiving mechanical ventilation.
  - ▲ 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 9 days **may be considered** for suspected or confirmed COVID-19.
- 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 or stop based on microbiology results and clinical judgment.
- ▶ For recommendations for **SARS-CoV-2 neutralizing antibodies**, see [Box 1](#) on page 2.

#### Moderately Ill Patients

Patients newly requiring low-flow supplemental oxygen. 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.
  - ▲ 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 9 days is recommended for moderately ill patients with suspected or confirmed COVID-19.
- ▲ **Therapeutic dose anticoagulation may be considered** over prophylactic dose anticoagulation in moderately ill patients who are felt to be at low risk of bleeding.
- **All other patients should receive prophylactic dose anticoagulation.**
- **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).
  - 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.
  - 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.
- ▶ For recommendations for **SARS-CoV-2 neutralizing antibodies**, see [Box 1](#) on page 2.

#### Mildly Ill Patients

Patients who do not require new or additional supplemental oxygen from their baseline status, intravenous fluids, or other physiological support. These patients are usually managed in an ambulatory/outpatient setting.

- **Dexamethasone** is not recommended for mildly ill patients with suspected or confirmed COVID-19.
- **Remdesivir** is not recommended for mildly ill patients with suspected or confirmed COVID-19.
- **Tocilizumab** is not recommended outside of clinical trials for mildly ill patients with suspected or confirmed COVID-19.
- ◆ There is currently **insufficient evidence** to make a recommendation around **anticoagulation** for mildly ill patients.
- ▲ **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).
- ▶ 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

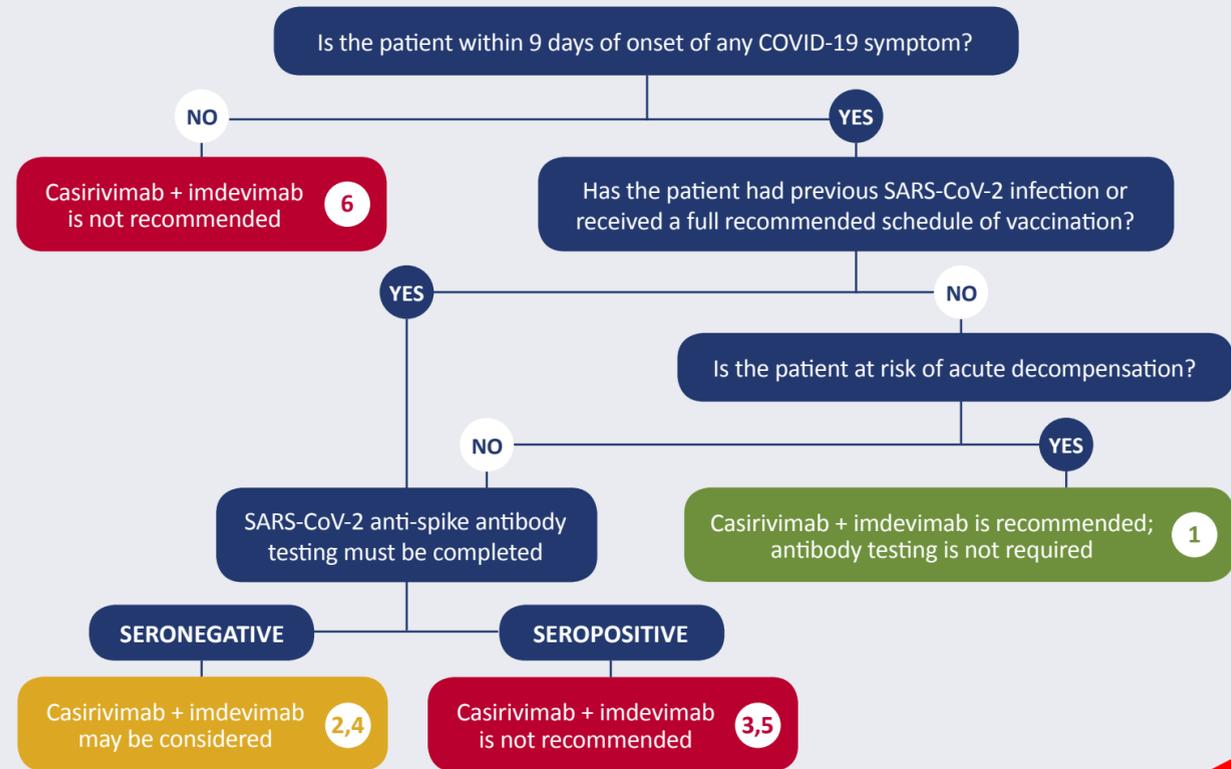
### RECOMMENDED AGAINST

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

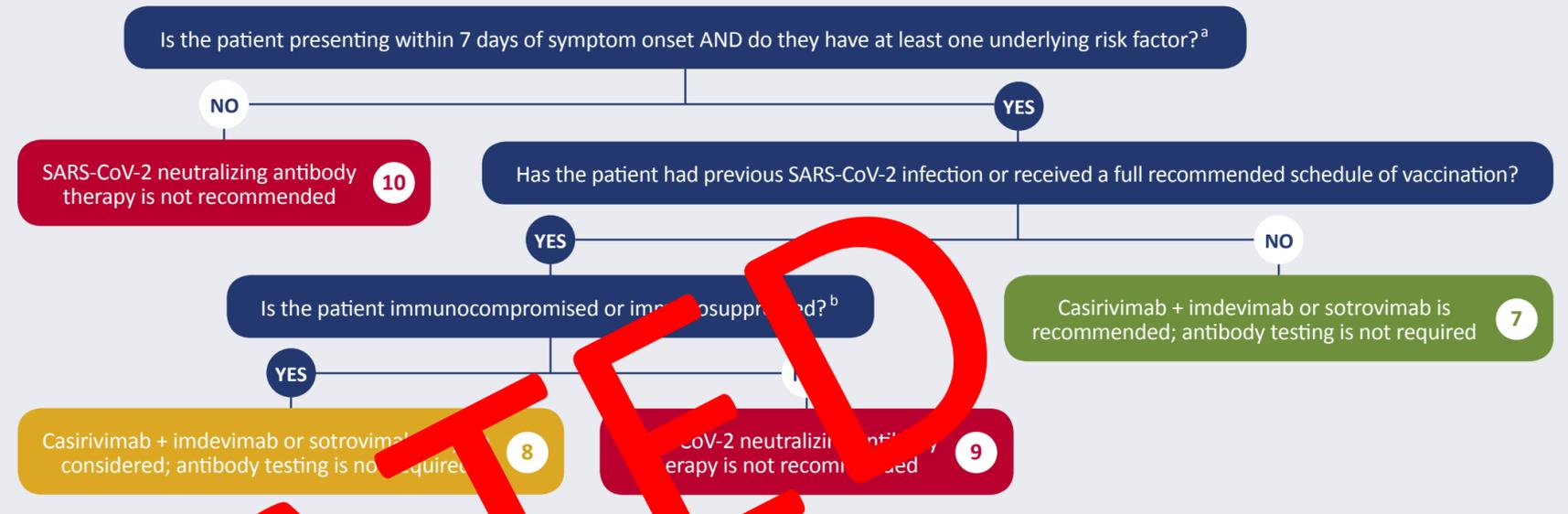
[Click here for dosing and pharmacologic considerations for medications approved or under investigation for COVID-19](#)

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



SCENARIO	RECOMMENDATION
<b>No history of vaccination or SARS-CoV-2 infection, within 9 days of onset of any COVID-19 symptom</b>	<ul style="list-style-type: none"> <li>1 Casirivimab + imdevimab 2400 mg IV <b>is recommended</b> 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.</li> <li>2 Casirivimab + imdevimab 2400 mg IV <b>may be considered</b> 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. SARS-CoV-2 anti-spike antibody testing demonstrates they are seronegative.</li> <li>3 Casirivimab + imdevimab is <b>not recommended</b> 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.</li> </ul>
<b>History of vaccination or SARS-CoV-2 infection, within 9 days of onset of any COVID-19 symptom</b>	<ul style="list-style-type: none"> <li>4 Casirivimab + imdevimab 2400 mg IV <b>may be considered</b> 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.</li> <li>5 Casirivimab + imdevimab is <b>not recommended</b> 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.</li> </ul>
<b>Beyond 9 days of onset of COVID-19 symptoms</b>	<ul style="list-style-type: none"> <li>6 Casirivimab + imdevimab is <b>not recommended</b> 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.</li> </ul>

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



SCENARIO	RECOMMENDATION <sup>a</sup>
<b>No history of vaccination or SARS-CoV-2 infection, with risk factors<sup>b</sup></b>	7 Casirivimab + imdevimab 1200 mg IV/SC OR sotrovimab 500 mg IV <b>is recommended</b> 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 <sup>b</sup> . Anti-spike antibody testing is not required.
<b>History of vaccination or SARS-CoV-2 infection, immunocompromised or immunosuppressed<sup>c</sup></b>	8 Casirivimab + imdevimab 1200 mg IV/SC OR sotrovimab 500 mg IV <b>may be considered</b> 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 <sup>c</sup> . Anti-spike antibody testing is not required.
<b>History of vaccination or SARS-CoV-2 infection, with risk factors<sup>b</sup> other than immunocompromise or immunosuppression</b>	9 Monoclonal antibody therapy is <b>not recommended</b> 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).
<b>No risk factors<sup>b</sup></b>	10 Monoclonal antibody therapy is <b>not recommended</b> 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<sup>c</sup>, or receipt of immunosuppressants<sup>c</sup>.

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
<ul style="list-style-type: none"> <li>1 Casirivimab + imdevimab 1200 mg IV/SC OR sotrovimab 500 mg IV <b>is recommended</b> 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.</li> </ul>

OUTDATED