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.

RECOMMENDATIONS

SEVERITY OF ILLNESS

Critically Ill Patients

- 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 >60 and ≤65 kg; and 8 mg/kg if weight ≤60 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, as they have a separate indication for this treatment.

- Remdesivir is not recommended for critically ill patients with COVID-19 unless mechanical ventilation.
  - In critically ill patients requiring high flow oxygen (i.e., oxygen face mask, or oxygen by high-flow nasal cannula, or non-invasive mechanical ventilation), remdesivir 200 mg IV on day 1, then 100 mg IV daily thereafter may be considered for suspected COVID-19.

- Bacterial co-infection is uncommon in COVID-19 pneumonia at presentation. Do not administer empiric antibiotics for bacterial pneumonia unless bacterial infection is strongly suspected. Continuing antibiotic therapy for more than 5 days, and de-escalate empiric antibiotics and consider clinical judgment.

- For recommendations on SARS-CoV-2 neutralizing antibodies, see Box 2 on page 2.

Moderately Ill Patients

- 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 orally daily until oxygen is no longer required (for a maximum of 28 days) may be considered.

- Remdesivir 200 mg IV on day 1, then 100 mg IV daily thereafter is recommended for moderately ill patients with suspected or confirmed COVID-19.

- Therapeutic doses of tocilizumab may be considered over prophylactic dose anticoagulation in moderately ill patients who are in low risk of developing.

- All other patients should receive prophylactic dose anticoagulation.

- Tocilizumab is not recommended outside of clinical trials for mildly ill patients with suspected or confirmed COVID-19.

- If patients are discharged with home-based oxygen therapy, dexamethasone 6 mg orally daily 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 on SARS-CoV-2 neutralizing antibodies, see Box 2 on page 2.

Mildly Ill Patients

- 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 (265 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 on 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 systemic implications of overdose:

- 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

<table>
<thead>
<tr>
<th>History of vaccination or SARS-CoV-2 infection, within 9 days of onset of any COVID-19 symptom</th>
<th>RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casirivimab + imdevimab is not recommended</td>
<td>1</td>
</tr>
<tr>
<td>SARS-CoV-2 anti-spike antibody testing must be completed</td>
<td>2</td>
</tr>
<tr>
<td>Casirivimab + imdevimab is recommended; antibody testing is not required</td>
<td>3</td>
</tr>
</tbody>
</table>

#### RECOMMENDATION

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.
2. Casirivimab + imdevimab 2400 mg IV 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 seronegative.
3. Casirivimab + imdevimab 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, and are clinically at risk of acute decompensation if anti-spike antibody testing demonstrates they are seronegative.

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

#### SCENARIO

<table>
<thead>
<tr>
<th>History of vaccination or SARS-CoV-2 infection, immunosuppression or infection with risk factorsb</th>
<th>RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk factors</td>
<td>7</td>
</tr>
<tr>
<td>History of SARS-CoV-2 infection, immunosuppression or infection with risk factorsb</td>
<td>8</td>
</tr>
</tbody>
</table>

#### RECOMMENDATION

1. 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 1 underlying risk factor. Anti-spike antibody testing is not required.
2. 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).

### 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.