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

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.

RECOMMENDATIONS

- 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 body-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.

MODERATELY ILL PATIENTS

Patients newly requiring low-flow supplemental oxygen. These patients are usually managed in hospital wards.

RECOMMENDATIONS

- 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/IV 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 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.

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.

RECOMMENDATIONS

- Tocilizumab 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.↑
- Dexamethasone is not recommended 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.

RECOMMENDED AGAINST

The following therapies are not recommended for the treatment of COVID-19 outside of clinical trials or where other indications would justify its use:

- Chloroquine
- Hydroxychloroquine or chloroquine
- Ivermectin
- Lopinavir/ritonavir

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:

- Antibiotics (azithromycin)
- SARS-CoV-2 neutralizing antibodies
- Remdesivir
- Tocilizumab
- Therapeutic dose anticoagulation unless they have a separate indication for this treatment.

OUTDATED

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), inhaled budesonide 800 mcg twice daily for 14 days may be considered, as it may reduce patient-reported symptoms and time to recovery.

For recommendations for SARS-CoV-2 neutralizing antibodies, see Figure 1 on page 2.

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

Version 4.0 | Updated September 29, 2021 | https://doi.org/10.47326/ocsat.cpg.2021.4.0 | Design by Tiffany Kan PharmD | Page 1 of 2
Recommendations for SARS-CoV-2 Neutralizing Antibodies in Patients with COVID-19

The monoclonal antibody cocktail casirivimab + imdevimab is preferred over sotrovimab due to practical considerations; the former currently has greater availability, and has IV and SC formulations.

Figure 1. Casirivimab + imdevimab for moderate or critical COVID-19 (community-acquired or nosocomial)

Is the patient within 9 days of onset of any COVID-19 symptom?

<table>
<thead>
<tr>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casirivimab + imdevimab is not recommended</td>
<td>Casirivimab + imdevimab may be considered</td>
</tr>
</tbody>
</table>

Has the patient had previous SARS-CoV-2 infection, or are they fully vaccinated?

<table>
<thead>
<tr>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casirivimab + imdevimab is not recommended</td>
<td>Casirivimab + imdevimab is recommended; antibody testing is not required</td>
</tr>
</tbody>
</table>

Is the patient at risk of acute decompensation?

<table>
<thead>
<tr>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casirivimab + imdevimab is not recommended</td>
<td>Casirivimab + imdevimab 8000 mg IV demonstrated rapid clinical deterioration. Antibody testing is not required.</td>
</tr>
</tbody>
</table>

COVID-19 antibody testing must be completed

<table>
<thead>
<tr>
<th>SERONEGATIVE</th>
<th>SEROPOSITIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casirivimab + imdevimab may be considered</td>
<td>Casirivimab + imdevimab is recommended; antibody testing is not required</td>
</tr>
</tbody>
</table>

Figure 2. Casirivimab + imdevimab for mild COVID-19 (not for post-exposure prophylaxis)

Is the patient presenting within 7 days of symptom onset AND do they have at least one underlying risk factor?#

<table>
<thead>
<tr>
<th>NO</th>
<th>YES</th>
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<tbody>
<tr>
<td>Casirivimab + imdevimab is not recommended</td>
<td>Casirivimab + imdevimab 1200 mg IV or SC is recommended for mildly ill patients who meet the following criteria:</td>
</tr>
</tbody>
</table>

- No history of full vaccination or SARS-CoV-2 infection and
- Confirmed, symptomatic COVID-19 AND
- Within 7 days of onset of any COVID-19 symptom AND
- At least one underlying risk factor3 Antibody testing is not required.

History of full vaccination or SARS-CoV-2 infection, immunocompromised or immunosuppressed4

<table>
<thead>
<tr>
<th>NO</th>
<th>YES</th>
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</thead>
<tbody>
<tr>
<td>Casirivimab + imdevimab may be considered; antibody testing is not required</td>
<td>Casirivimab + imdevimab is recommended; antibody testing is not required</td>
</tr>
</tbody>
</table>

History of full vaccination or SARS-CoV-2 infection, with risk factors5 other than immunocompromise or immunosuppression

<table>
<thead>
<tr>
<th>NO</th>
<th>YES</th>
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</thead>
<tbody>
<tr>
<td>Casirivimab + imdevimab is not recommended</td>
<td>Casirivimab + imdevimab is recommended for mildly ill patients who meet the following criteria:</td>
</tr>
</tbody>
</table>

- History of full vaccination or SARS-CoV-2 infection AND
- Confirmed, symptomatic COVID-19 AND
- Within 7 days of onset of any COVID-19 symptom AND
- Immunocompromised or immunosuppressed Antibody testing is not required.

No risk factors

<table>
<thead>
<tr>
<th>NO</th>
<th>YES</th>
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<tbody>
<tr>
<td>Casirivimab + imdevimab is not recommended</td>
<td>Monoclonal antibody therapy is not recommended for mildly ill patients who are not immunocompromised or immunosuppressed and are presumed to have immunity (through full vaccination or previous infection).</td>
</tr>
</tbody>
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# Risk factors: age >50 years, obesity, cardiovascular disease (including hypertension), chronic lung disease (including asthma), chronic pulmonary disease (including diabetes), chronic kidney disease, chronic liver disease, immunosuppression, or receipt of immunosuppressant.

3. Examples include: 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., Di George syndrome, Wiskott-Aldrich syndrome), 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), utilizing agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapy agents classified as severely immunosuppressive, tumor-necrosis factor (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory.

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Updated September 29, 2021