Health PEI

ANTIMICROBIAL STEWARDSHIP SUBCOMMITTEE

COVID-19 in Adults

Definitions

- Viral infection with SARS-CoV-2

Diagnostic Considerations

- Clinical presentation varies from asymptomatic to critical illness.
- Common symptoms include: new tiredness, new or worsening cough, fever (chills, sweats), new shortness of breath (SOB) or difficulty breathing, change in smell or taste, sore throat, runny/stuffy nose/sneezing, headache, nausea, diarrhea, or vomiting
- Rapid antigen testing or PCR testing may be used to diagnose COVID-19, depending on setting.

COVID-19 Severity Definitions

1. **Asymptomatic infection:** No symptoms of COVID-19

2. **Mild-to-moderate COVID-19: Outpatient (or admitted for non-respiratory needs)**
   - patients NOT requiring supplemental oxygen
   - Clinical signs of pneumonia may or may not be present
   - No signs of severe pneumonia
3. **Severe COVID-19: Hospitalized, non ICU-based care**
   - patients requiring supplemental oxygen therapy
   - Fever or suspected respiratory infection plus one of the following:
     - Respiratory rate > 30 breaths/min
     - Severe respiratory distress
     - SpO2 ≤ 92% on room air
4. **Critical COVID-19: Hospitalized, ICU-based care**
   - Patients requiring respiratory support (i.e., high-flow oxygen, noninvasive ventilation, or mechanical ventilation) and/or vasopressor or inotropic support
   - May be characterized by ARDS, sepsis or septic shock

Management considerations

- Initiate droplet/contact precautions and escalate to airborne precautions if performing aerosol generating medical procedures.
- The mainstay of treatment for all patients is supportive care (symptom management, rest, etc.) including supplemental oxygen, ventilation, and prone positioning as appropriate.
- Initiation of COVID-19 treatments should take into consideration the patient's disease severity, duration of symptoms, immunization history, risk factors for progressing to more severe disease, and patient-specific factors such as pregnancy, drug-drug-interactions, etc.

Medication Management by Disease Severity

Asymptomatic COVID-19

NO treatment recommended (regardless of risk factors)

- Follow-up is reasonable in high-risk patients who would qualify for treatment if otherwise symptomatic.

Mild-to-moderate COVID-19

Immunocompetent	Supportive care
Patients with moderate to severe immunosuppression*	Supportive care +/- Antiviral therapy ***Nirmatrelvir 300 mg + ritonavir 100 mg [Paxlovid®] po BID x 5 days** • Initiate as early as possible and within 5 days of symptom onset • MANY drug-drug interactions which may require temporary adjustment of chronic medications. • Dose adjustment required in renal impairment **OR** if unable to use Nirmatrelvir/ritonavir: ****Remdesivir 200 mg IV on day 1 then 100 mg IV q24h on days 2 and 3** • Initiate as early as possible and within 7 days of symptom onset

Additional information

- Antiviral therapy should be considered for patients who are **appreciably symptomatic** or have a **concerning clinical trajectory**. Immunosuppression alone does not warrant automatic initiation of antiviral therapy.
- Antivirals are NOT required for patients that have improved significantly without treatment.
- Systemic corticosteroids are NOT recommended in mild-to-moderate COVID-19
- Inhaled corticosteroids are NOT recommended
- See below for information on VTE prophylaxis in COVID-19

*See **Appendix 1** for more information on Paxlovid eligibility, renal dosing, definitions of immunosuppression etc

See **Appendix 2 for more information on remdesivir eligibility and exclusion criteria

This document is designed to aid Prince Edward Island practitioners in the appropriate use of antimicrobials. These guidelines provide general recommendations and are not a substitute for clinical judgement or consultation with Infectious Disease experts.

Severe or Critical COVID-19	
Corticosteroid	**Dexamethasone 6 mg IV/PO q24h x 10 days** (or until discharge if earlier) in hospitalized patients with COVID-19 who require **mechanical ventilation** or those who require **supplementary oxygen**.
+/- non-corticosteroid immunomodulator therapy	***Tocilizumab** 8 mg/kg IV x 1 dose ONLY, maximum of 800 mg/dose **OR** ****Baricitinib** 4 mg PO q24h x 14 days (or until hospital discharge, if sooner) • Dose adjustment required in renal impairment

Additional Information

- Immunomodulators should only be considered as an adjuvant treatment to corticosteroids.
- Immunomodulators may render the patient more susceptible to infections.
  - Do **NOT** use baricitinib or tocilizumab if co-existing severe infection (i.e. any active, severe infection other than COVID-19).
  - Exercise caution when considering their use in patients with a history of recurrent/chronic infections or with underlying conditions which may predispose patients to infection.
- In patients with rapid improvement (e.g. supplemental oxygen weaned), may consider stopping baricitinib before 14 days of therapy.
- Routine combined use of baricitinib and tocilizumab for treatment of COVID-19 is NOT recommended.
  - However, in situations where a patient has clinically deteriorated despite treatment with tocilizumab, clinical judgment may deem added use of baricitinib appropriate after first receiving tocilizumab.
- See below for information on VTE prophylaxis in COVID-19

*See **Appendix 3** for more information on tocilizumab eligibility/exclusion criteria and dose banding

See **Appendix 4 for more information on baricitinib eligibility/exclusion criteria and renal dose adjustments

Prevention

- Review patient vaccine record in provincial all immunizations registry (AIR) to ensure they are up to date with all eligible vaccinations

These guidelines are an adaptation of Horizon Health's COVID-19 guideline (2025)

VTE Prophylaxis in COVID-19

Mild to moderate COVID-19 • *patients NOT requiring supplemental oxygen* • *Clinical signs of pneumonia may or may not be present* • *No signs of severe pneumonia*	**No specific anticoagulation regimen is recommended for VTE prophylaxis in asymptomatic, mild or moderate COVID-19.** Follow standard of care for VTE prophylaxis in hospitalized patients

Severe COVID-19
• *patients requiring supplemental oxygen therapy*
• *Fever or suspected respiratory infection plus one of the following:*
  ○ *Respiratory rate > 30 breaths/min*
  ○ *Severe respiratory distress*
  ○ *SpO2 ≤ 92% on room air*
	Therapeutic anticoagulation (LMWH preferred) may be considered in patients without high-risk features for serious bleeding*.
	
	It should start within 72 hours of admission and continue for 14 days or until hospital discharge.
	
	Patients who decompensate and require organ support while on therapeutic anticoagulation should continue on therapeutic anticoagulation, if the risk of bleeding remains low.
	
	Pooled data from RCTs showed that therapeutic anticoagulation with LMWH/UFH significantly reduces major thrombotic events (OR 0.47; 95% CI 0.24- 0.90) but may increase major bleeding (OR 1.45; 95% CI 0.77-2.70) compared with lower doses. Organ support-free days alive were significantly increased with therapeutic heparin (OR 1.29; 95% CI 1.07-1.57). **Benefit is more likely in those with elevated D-dimer level or additional risk factors for thrombosis.** No differences were observed in the need for invasive mechanical ventilation, intracranial hemorrhage or all-cause mortality.
	
	***High risk features for bleeding include:** age 75 or greater, eGFR less than 30 mL/min, any coagulopathy, platelet count less than 50, use of dual antiplatelet therapy, recent history of serious GI bleed or recent intracranial condition (stroke, neurosurgery, aneurysm, cancer), epidural or spinal catheter.

Critical COVID-19 • *Patients requiring respiratory support (i.e., high-flow oxygen, noninvasive ventilation, or mechanical ventilation) and/or vasopressor or inotropic support* • *May be characterized by ARDS, sepsis or septic shock*	**Prophylactic-intensity dosing of low molecular weight heparin (LMWH) is recommended for VTE prophylaxis in patients who do not have suspected or confirmed VTE (or other indications for therapeutic anticoagulation).** There is a high probability of harm when therapeutic anticoagulation is initiated in patients who have received organ support for greater than 48 hours (n=1074; NIH mpRCT). Patients receiving therapeutic anticoagulation for COVID-19 prior to organ support should REMAIN on therapeutic anticoagulation and continue for up to 14 days or until hospital discharge.

Reference: BC CDC

Appendix 1: Nirmatrelvir/ritonavir

Eligibility Criteria:

- COVID-19 infection confirmed, AND
- Patient 18 years of age or older, AND
- Presenting with mild to moderate symptoms of COVID-19 that started within the last 5 days, AND
- ONE of the criteria below:
  - **Severe immunosuppression, OR
  - *Moderate immunosuppression

****Severe Immunosuppression**	**Examples include:** • Solid organ transplant recipients ○ Note: patients on tacrolimus, sirolimus, and cyclosporine are EXCLUDED from Paxlovid treatment due to significant drug-drug interactions • Treatment for malignant hematological condition • Bone marrow, stem cell transplant or transplant-related immunosuppressant use • Receipt of Anti-CD20 agents or B-cell depleting agents (such as rituximab) in the previous 2 years • Severe primary immunodeficiencies [combined immunodeficiencies affecting T cells, immune dysregulation (particularly familial hemophagocytic lymphohistiocytosis), or type 1 interferon defects (caused by a genetic primary immunodeficiency disorder or secondary to anti-interferon autoantibodies)
***Moderate Immunosuppression**	**Examples include:** • Treatment for cancer including solid tumors • Significantly immunosuppressing drugs (e.g. biologic in the last 3 months, oral immune suppressing medication in the past month, oral steroid [20 mg/day of prednisone equivalent taken on an ongoing basis] in the past month, or immune-suppressing infusion or injection in past three months) • Advanced HIV Infection (treated or untreated) • Moderate primary immunodeficiencies • Renal conditions (i.e. hemodialysis, peritoneal dialysis, glomerulonephritis and dispensing of a steroid, eGFR <15 mL/min) ○ Note: patients on tacrolimus, sirolimus, and cyclosporine are EXCLUDED from Paxlovid treatment due to significant drug-drug interactions
NOTE: Prior to prescribing Paxlovid for a patient who has received a solid organ transplant (provided it is either a renal transplant patient or is ACTIVELY being followed by Nephrology) and taking an immunosuppressant, Nephrology MUST be consulted)	

For consideration, PEI Pharmacare criteria for coverage also includes patients aged 65 years or older with at least one of the following chronic high-risk conditions:

- *Diabetes treated with insulin*
- *Severe or end-stage lung conditions (e.g. cystic fibrosis, severe chronic obstructive pulmonary disease, asthma)*
- *Rare blood and genetic disorders such as sickle cell disease, thalassemia, urea cycle defects*
- *Severe intellectual or developmental disability*
- *Glomerular Filtration Rate less than 30 mL/min*

Dose adjustments:

Hepatic impairment

- Mild (Childs Pugh A): 100% of dose
- Moderate (Childs Pugh B): 100% of dose
- Severe (Childs Pugh C): **Contraindicated**

Renal Impairment

eGFR greater than 60 mL/min (Usual dosing)	Nirmatrelvir 300 mg + ritonavir 100 mg taken together PO BID for 5 days
eGFR 30 to 60 mL/min	Nirmatrelvir 150 mg + ritonavir 100 mg taken together PO BID for 5 days
eGFR less than 30 mL/min	Nirmatrelvir 300 mg + ritonavir 100 mg taken together PO **once** on day 1, **then** nirmatrelvir 150 mg + ritonavir 100 mg taken together PO once daily on days 2-5
Hemodialysis And patient weight **40 kg or greater**	Nirmatrelvir 300 mg + ritonavir 100 mg taken together PO **once** on day 1, **then** nirmatrelvir 150 mg + ritonavir 100 mg taken together PO once daily on days 2-5 *Give after dialysis*
Hemodialysis And patient weight **less than 40 kg**	Nirmatrelvir 150 mg + ritonavir 100 mg taken together q48h for 3 doses *Give after dialysis*

Managing Drug Interactions:

- Ritonavir inhibits CYP3A4; therefore, many patients will be at risk of drug interactions.
    - Real-world studies observed that as many as 70% of patients may have clinically significant drug-drug interactions requiring mitigation.
    - Cases of harm from drug interactions have been published; however, the true incidence of harm from drug interactions is unknown.
- It is recommended to use multiple resources to manage drug interactions, as some information may be conflicting or incomplete.
- Strategies should be considered for the 5-day duration of treatment and for at least 2 to 5 days after treatment completion, and for potentially longer if nirmatrelvir/ritonavir is administered with an interacting concomitant medication that has a long half-life.
    - Please note, the onset of inhibition is **rapid** and clinically significant drug-drug interactions can occur despite the short treatment course.

Drug interaction tools and resources:

- Liverpool COVID-19 Drug Interaction Checker
- BC COVID Therapeutics Committee (CTC) - Practice Tool: Drug-Drug Interactions & Contraindications

Appendix 2: Remdesivir

Eligibility criteria:

- **Moderately-to-severely immunosuppressed patients** (see above) presenting with **mild-to-moderate COVID-19**, within 7 days of symptom onset, **and who are eligible for, but unable to use, nirmatrelvir/ritonavir.**

Exclusion criteria:

- Weight less than 40 kg
- ALT elevation greater than or equal to 5 times the upper limit of normal at baseline

Renal Impairment:

No dose adjustment is required in renal dysfunction

- Initially, remdesivir was not recommended in patients with an eGFR <30 mL/min; however, more recent evidence has shown that remdesivir can be used without any dose adjustment in patients with advanced renal failure (including dialysis).

Hepatic Impairment:

- Remdesivir should not be initiated in patients with Alanine Aminotransferase (ALT) greater than or equal to 5 times the upper limit of normal (ULN).
- Remdesivir should be STOPPED in patients who develop ALT greater than or equal to 5 times the ULN during treatment or if the ALT elevation is accompanied by signs and symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase or international normalized ration (INR).

Monitoring Recommendations

- T, HR, RR, BP, SpO2 at baseline, q30min during infusion and PRN
- CBC, electrolytes, serum creatinine, INR, ALT, AST, bilirubin, alkaline phosphate prior to starting treatment and then **as clinically appropriate during treatment**.
- Clinical assessments to watch for signs of infusion-related reactions (fever, chills, hypotension, rash, pruritis and hypersensitivity/anaphylaxis) at baseline, during infusion and PRN

Appendix 3: Tocilizumab

Eligibility Criteria

1. Patient is 18 years of age or older; **AND**
2. COVID-19 pneumonia; **AND**
3. Receiving dexamethasone or an equivalent corticosteroid unless contraindicated; **AND**
4. One of the two following oxygenation support criteria:
   - Oxygen saturation of less than 92% on room air on repeated measurement OR an ongoing requirement for supplementary oxygen; AND with a C-reactive protein level greater than or equal to 75 mg/L;
     OR
   - Within 24 - 48 hours of starting respiratory support via high flow nasal oxygen; continuous positive airway pressure (CPAP) or non-invasive ventilation; invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO).

Exclusion Criteria

- Known hypersensitivity tocilizumab.
- Co-existing severe infection[1] that might be worsened by tocilizumab.
- Previous receipt of a non-corticosteroid immunomodulator agent for treatment of the current episode of COVID-19.
- A baseline ALT or AST more than 5 times the upper limit of normal (caution is recommended if level more than 1.5 times upper limit of normal).
- A baseline platelet count less than 50 x 10^9 /L.
- A baseline absolute neutrophil count of less than 2 x 10^9/L

[1] Any active, severe infection other than COVID-19; caution is advised when considering the use of tocilizumab in patients with a history of recurring or chronic infections or with underlying conditions which may predispose patients to infections.

Tocilizumab Dosing: 8 mg/kg IV x 1 dose ONLY, maximum of 800 mg/dose

The following dose bandings are suggested to avoid wastage:

Weight (kg)	Dose (mg)
≤40 kg	8mg/kg, rounded to nearest 20mg
> 40 kg and ≤ 65 kg	400mg
> 65 kg and ≤ 90 kg	600mg
> 90 kg	800mg

Additional Information:

- Half-life of 11-17 days
- CRP is no longer a reliable inflammatory biomarker after a dose of tocilizumab (as it can cause prolonged depression of CRP levels*)

** does not apply for baricitinib*

Appendix 4: Baricitinib

Eligibility Criteria:

1. Patient is 18 years of age or older; **AND**
2. COVID-19 pneumonia; **AND**
3. Informed patient or caregiver consent (written or verbal); **AND**
4. Oxygen saturation less than 92% on room air on repeated measurement, receiving supplementary oxygen, oxygen through a high-flow device, non-invasive ventilation, invasive ventilation or ECMO; AND
5. At least one elevated inflammatory marker (C-reactive protein, D-dimer, lactate dehydrogenase, or ferritin).

Exclusion Criteria:

- Known hypersensitivity baricitinib.
- Previous receipt of tocilizumab for treatment of the current episode of COVID-19, unless the patient is clinically deteriorating.
- Co-existing severe infection[1] that might be worsened by baricitinib.
- A baseline ALT or AST more than 5 times the upper limit of normal.
- An estimated glomerular filtration rate less than 15 mL/min per 1.73 m^2.
- A baseline absolute neutrophil count of less than 1 x 10^9/L
- A baseline absolute lymphocyte count less than 0.2 x 10^9/L

[1] Any active, severe infection other than COVID-19; caution is advised when considering the use of baricitinib in patients with a history of recurring or chronic infections or with underlying conditions which may predispose patients to infections.

Baricitinib Dosing:

Usual dose (eGFR greater than or equal to 60 ml/min/1.73 m^2): Baricitinib 4 mg PO q24h x 14 days (or until hospital discharge, if sooner)

- **If eGFR 30 to 59 mL/min/1.73 m^2:** Baricitinib 2 mg PO q24h
- **If eGFR 15 to 29 mL/min/1.73 m^2:** Baricitinib 2 mg PO q48h
- **If eGFR <15 mL/min/1.73 m^2:** Do NOT use

Use of baricitinib in patients with eGFR 15 – 29 mL/min:

- Patients with an eGFR less than 30 mL/min per 1.73 m^2 were excluded from the COV-BARRIER trial – use only if the potential benefit outweighs the risk
- Please use informed consent when considering use in this patient group

Intermittent hemodialysis and peritoneal dialysis: Not recommended

Additional Information

- Half-life of 12-16 hours (shorter duration of immunosuppression than tocilizumab).
- In patients with **rapid improvement** (e.g. supplemental oxygen weaned), may consider stopping baricitinib before 14 days of therapy.

References

1. Horizon Health Network – Anti-infective stewardship committee. Firstline: COVID-19; Accessed Dec 2025
2. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19.
3. British Columbia COVID-19 Therapeutics Committee (CTC) and COVID-19 Therapeutics Review and Advisory Working Group (CTRAWG).
4. Nova Scotia Health Authority – Antimicrobial Stewardship Handbook. COVID-19 ld.php. Accessed Dec 2025

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