Therapeutic Management of Hospitalized Adults with COVID-19◊

Alberta Health Services

COVID-19 Positive (symptomatic or asymptomatic): Assess Severity and Monitor for Change

COVID + and Asymptomatic

COVID + and Non-severe
(if progresses with hypoxia see "severe")

NOT moderately or severely immunocompromised*

Moderately or Severely Immunocompromised*

Supportive Management
NOT ELIGIBLE for Paxlovid® or remdesivir (no evidence of benefit)

If within 5 days of symptom onset:
Paxlovid® (nirmatrelvir-ritonavir)[a]
300mg-100mg PO bid x 5 days

Absolute contraindication to Paxlovid®

If within 7 days of symptom onset:
Remdesivir 200mg IV day 1, 100mg IV daily days 2- 3

COVID + and Severe disease
(SpO2 < 94% on room air or requiring supplemental O_2)

Deterioration

COVID + and requiring:
>6 LPM O_2
or FiO_2 > 0.5
or mechanical ventilation (MV)

Dexamethasone 6mg
PO or IV daily x 10[b] days
or until off O_2
or discharged

AND

Remdesivir 200mg IV day 1,
100mg IV daily days 2-5

Dexamethasone 6mg
PO or IV daily x 10[b] days
or until off O_2
or discharged

AND

If ≤ 7 days since hospital admission for COVID or, for nosocomial COVID, ≤ 7 days of symptoms:

Tocilizumab[c] 400mg single dose IV
(if MV, most effective within 24h of MV start)

OR

Baricitinib[c] 4mg PO daily x 14 days or until discharge

OR

If tocilizumab unavailable:

Sarilumab[c] 400mg single dose IV
(if MV, most effective within 24h of MV start)

ANTICOAGULATION: In moderately sick hospitalized COVID-19 patients (requiring oxygen up to 15 L/min via nasal cannula) with no contraindications to anticoagulation and low bleeding risk, therapeutic dose tinzaparin (175 units/kg) is recommended for 14 days or until discharge, to increase the probability of survival and reduce the need for ICU-level organ support. In critically ill hospitalized COVID-19 patients with no contraindications to anticoagulation, prophylactic dose tinzaparin (75 units/kg) is recommended.

*** Severe Immunocompromise:**

1. Recipient of solid organ transplant
2. Treatment for malignant hematologic condition
3. Bone marrow transplant-, stem cell transplant-, or transplant-related immunosuppressant use
4. Receipt of anti-CD20 drugs or B-cell depleting drugs in the past 2 years
5. Severe primary immunodeficiencies

*** Moderate immunocompromise:**

1. Treatment for cancer, including solid tumours
2. Treatment with significantly immunosuppressing drugs:
   a) Biologic or other immunosuppressing medication in the past 3 months
   b) Oral steroid (20 mg/day of prednisone equivalent on an ongoing basis) in the past month
3. Advanced HIV infection (untreated, or treated with CD4 count ≤ 200/mm^3
4. Moderate primary immunodeficiencies
5. Renal conditions: Dialysis (hemodialysis or peritoneal dialysis), eGFR < 15 mL/min, glomerulonephritis being treated with steroids)

◊ Orange/red arms reflect the need for oxygen or mechanical ventilation (MV) **related to COVID**.

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Treatment Footnotes

a. Paxlovid®

Contraindications:

- Transplant patient (except if under the guidance of the transplant team)
- Drug interactions that cannot be managed with medication changes (check Lexi-Comp via https://krs.libguides.com or the Liverpool COVID-19 Drug Interactions Checker at https://www.covid19-druginteractions.org/checker)

AHS supports crushing and splitting of Paxlovid® to be administered orally or for enteral tube administration – see Paxlovid crushing and splitting guidance.

Dosage:

	eGFR > 60mL/min	eGFR ≤ 60mL/min and ≥ 30mL/min	eGFR < 30mL/min	Dialysis
Paxlovid 150mg/100mg (Nirmatrelvir/Ritonavir)	300 mg nirmatrelvir + 100 mg ritonavir both twice a day for 5 days	150 mg nirmatrelvir + 100 mg ritonavir both twice a day for 5 days	300 mg nirmatrelvir + 100 mg ritonavir both on day 1, then 150 mg nirmatrelvir + 100 mg ritonavir once a day for 4 more days	300 mg nirmatrelvir + 100 mg ritonavir both on day 1 then 150 mg nirmatrelvir + 100 mg ritonavir once a day for 4 more days, to be dosed after dialysis[1]

b. **Dexamethasone duration**: Standard 10-day course. Some data suggests similar benefit with a 7-day course, so 7 days may be reasonable depending on risk to benefit ratio (prescriber discretion), see refere**nce:** *Open Forum Infectious Diseases*, Volume 10, Issue 3, March 2023, ofad105, https://doi.org/10.1093/ofid/ofad105

c. Receipt **of tocilizumab, baricitinib, sarilumab** in patients with highly suspected or proven non-COVID infections and severe underlying immunocompromise may increase the risk of secondary infection. Specialist consultation is suggested in these cases.

If patient meets tocilizumab / baricitinib / sarilumab criteria at presentation, favour one of these agents over remdesivir. If an immunocompetent patient has met criteria for, and been given tocilizumab / baricitinib / sarilumab, the presumption is that they are in a phase of their illness where remdesivir has not been proven beneficial, would not be expected to yield benefit, and should not be used.

Only one of baricitinib / sarilumab / tocilizumab should be used in the same patient; they all work on the same inflammatory pathway, they are unlikely to have added benefit and are potent immunosuppressants, so combination use could have adverse effects.

Adjust **baricitinib** dose based on eGFR:

- 30 to < 60 mL/min/1.73 m2: 2 mg PO/NG once daily
- 15 to < 30 mL/min/1.73 m2: 2 mg PO/NG every other day
- <15 mL/min/1.73 m2: Use is not recommended.