Clinical Management of COVID-19 in Hospitalised Adults (including in pregnancy)

Introduction

Interim update 13 September 2022

- Updated Pharmac access criteria for antiviral treatment of COVID-19 not requiring oxygen

Updated 26 August 2022 – Next planned update 26 October 2022

- NEW recommendations to offer Evusheld (tixagevimab/cilgavimab) for treatment of patients who are eligible, but yet to receive pre-exposure prophylaxis (PrEP)
- NEW recommendation against offering Evusheld (tixagevimab/cilgavimab) to patients who are not eligible for pre-exposure prophylaxis
- NEW description of 'rebound' COVID-19 and advice against treatment of 'rebound'
- MODIFIED discussion for clinicians considering prescribing Paxlovid (nirmatrelvir + ritonavir) to patients with advanced kidney disease and dialysis
- MODIFIED recommendation that Evusheld (tixagevimab/cilgavimab) administration be planned during discharge process of eligible patients.

New content in this update is highlighted in red.

This guideline is intended to be an accessible summary of hospital management of **ADULTS** (including in pregnancy) with **confirmed or probable COVID-19**. It has been adapted from international 'living' guidelines for the New Zealand context by the Ministry of Health COVID-19 Therapeutics Advisory Group (a group of New Zealand clinicians, including representation from Infectious Diseases, Respiratory Medicine, Intensive Care, General Medicine, Obstetric Medicine, Primary Care, Emergency Medicine and Pharmacy).

New evidence informing the optimal management of patients with COVID-19 continues to accumulate rapidly. This document will be reviewed and updated periodically, or in response to significant changes in evidence and/or recommendations by international guideline groups. Download the Ministry of Health Āwhina app to be notified when guideline updates are made.

Further detailed guidance, including treatments that are either not recommended, or recommended only within a clinical trial, can be accessed in links to international guidance at the end of this document. Local specialist services with expertise in managing COVID-19 may consider emerging treatments outside of this guideline.

Additional details or differences on managing a pregnant woman are highlighted in orange rows just below the adult guidance.

Lastly, the management of COVID-19 in immunocompromised patients (including patients suspected to have persistent SARS-CoV-2 infection) presents unique challenges that are outside the scope of this guideline. Specialist advice from a patient's primary specialist ***and*** an Infectious Diseases physician is strongly recommended.

<table>
<tr><td rowspan="4">Assessment and Definition</td><td>Severity</td><td colspan="2">Mild</td><td colspan="2">Moderate</td><td colspan="2">Severe/Critical</td></tr>
<tr><td>Clinical definition</td><td>No symptoms</td><td>Any COVID symptoms without features of pneumonitis</td><td colspan="2">A clinically stable patient with any evidence of COVID-19 pneumonitis:
• New onset (or worsening) shortness of breath OR
• Infiltrates on plain chest radiograph OR
• Hypoxaemia that is EITHER:
…mild (92-94%), transient, or exercise-induced only (i.e. not requiring continuous oxygen therapy OR
…sustained but able to maintain ≥ 92% (≥90% for patients with chronic lung disease) with up to 4L/min oxygen via standard prongs</td><td>Any of the following:
• Requiring CPAP or high-flow nasal oxygen to maintain saturation ≥ 92% OR
• Acute respiratory distress e.g. RR >30 OR
• Rapidly deteriorating clinical trajectory</td><td>Any of the following:
• Requiring mechanical ventilation to maintain saturation ≥ 92% OR
• Requiring advanced circulatory support</td></tr>
<tr><td>Stage of infection</td><td colspan="2">Almost all cases in the first 5 days; throughout in most vaccinated patients without risk factors</td><td colspan="4">Progression to moderate/severe disease most commonly develops ~ 5-7 days post onset of illness in patients with significant risk factors; the trajectory of deterioration can sometimes be rapid</td></tr>
<tr><td>Site of care</td><td colspan="2">Community</td><td>Individual decision</td><td colspan="3">Hospital</td></tr>
<tr><td></td><td>Anti-viral therapy</td><td colspan="3">Paxlovid OR remdesivir OR molnupiravir
If <5 days illness AND meets high risk criteria</td><td colspan="2">Consider remdesivir if <7d illness</td><td>Nil</td></tr>
<tr><td rowspan="5">Therapeutics</td><td>Respiratory support</td><td colspan="3">Nil</td><td>Oxygen via NP</td><td>CPAP (or HFNO)</td><td>Mechanical ventilation</td></tr>
<tr><td>VTE prophylaxis</td><td>Nil</td><td colspan="2">Low dose enoxaparin
if hospitalised</td><td>Low dose enoxaparin (or consider therapeutic dose)</td><td colspan="2">Low dose enoxaparin</td></tr>
<tr><td>Corticosteroids</td><td>Nil</td><td colspan="2">Consider inhaled budesonide
if meets high risk criteria</td><td colspan="3">Dexamethasone</td></tr>
<tr><td>Immune modulation</td><td colspan="3">Nil</td><td colspan="2">Baricitinib or Tocilizumab</td><td>Tocilizumab</td></tr>
<tr><td></td><td>Antibody therapy</td><td colspan="6">Offer Evusheld if eligible for PrEP</td></tr>
</table>

Figure 1 - Severity assessment and therapeutic options in COVID-19 management.

Initial management

	MILD	MODERATE	SEVERE / CRITICAL
DEFINITION	No symptoms **OR** URTI symptoms only **OR** cough, new myalgia or asthenia without new shortness of breath or reduction in resting oxygen saturation	Stable adult patient presenting with shortness of breath and/or reduction in resting oxygen saturation while breathing air. Able to maintain oxygen saturation ≥92% (or ≥90% for patients with chronic lung disease) with up to 4 L/min oxygen via nasal prongs	Adult patients meeting any of the following criteria: • Respiratory rate ≥30/min • Oxygen saturation <92% on 4L/min oxygen via nasal prongs • Clinically deteriorating
	Pregnancy: use an oxygen saturation **target of ≥ 94%** rather than ≥92%		
BASELINE TESTING & WORK-UP	• Pulse oximetry • Other tests only as clinically indicated • Low value testing is discouraged	• FBC, Creat, electrolytes, LFTs, CRP • ECG only if specific indication • Chest x-ray • Venous blood gas (consider arterial) • Investigations for CAP (e.g. urinary antigens, sputum PCR panel) if radiography suggests bacterial infection • Consider d-dimer & ferritin	• FBC, Creat, electrolytes, LFTs, CRP • ECG • Chest x-ray • Venous blood gas (consider arterial) • Investigations for CAP (e.g. urinary antigens, sputum PCR panel) if radiography suggests bacterial infection • Blood cultures if febrile or shocked • Coag screen, d-dimer, ferritin, BNP, Troponin
	• Note – in vaccinated individuals with Omicron variant infection, COVID-19 may not be the primary diagnosis responsible for hospital presentation. It is important to consider concurrent non-COVID-19 medical conditions during evaluation.		
	• **Pregnancy:** also request urine protein:creatinine ratio, coagulation profile, group and screen (or cross match if delivery is thought to be imminent) • *NB* CXR and CT chest / CTPA can safely be performed in pregnancy if clinically indicated. • Laboratory results should be cautiously interpreted, using pregnancy-specific ranges where available. There are no validated pregnancy-specific values for D-dimer; consider monitoring trend for prognostic purposes in severe/deteriorating COVID-19.		
TREATMENT ESCALATION PLANNING	• Assess ability to safely isolate in community. • Notify and refer through local pathways • Consider & document risk factors for severe COVID-19	• Assess & document individual **risk factors for poor outcome** • Early discussion of patient goals of care, including existing advanced care plans, with patient and their family/whānau • Early, clear documentation of resuscitation decision and treatment escalation plan for all patients, specifically including appropriate modalities of respiratory support	
	• **NOTE – any new deterioration > 5 days post onset of illness requires careful assessment. Deterioration to severe COVID-19 can occur rapidly. Pneumonitis continues to develop in the second (or sometimes third) week of illness, particularly in older or unvaccinated patients**		
	• For pregnant and post-partum observations, utilise a maternity-specific chart (if available) • If hospitalised for COVID-19, all pregnant women should have multidisciplinary assessment by obstetricians, midwives, neonatologists +/- an obstetric physician at the earliest opportunity		

DISPOSITION DECISION	• Encourage discharge • Offer COVID-19 treatment on discharge if meet **eligibility criteria** • Liaise with local Public Health Unit or Regional Isolation and Quarantine (RIQ) according to regional processes	• Discuss with local COVID team • Admit to hospital if **Sa02 <93%** • Consider discharge if Sa02 ≥93% according to local protocols and availability of acute community COVID-19 care (e.g. primary care or hospital in the home service) • Offer COVID-19 treatment on discharge if meet **eligibility criteria**	• Admit to hospital • ICU and/or Respiratory review
MONITORING & MARKERS OF CLINICAL DETERIORATION	• Risk of deterioration is significantly reduced by vaccination and infection with Omicron variants. Individualised risk assessment should include consideration of vaccination status, day of illness, age, immunocompromise and comorbidities that increase risk of severe disease. • Ferritin and d-dimer are suggested as severity/prognosis markers, as part of an overall assessment • Monitor for progressive respiratory failure and sepsis, especially after day 5 of illness • Only repeat CXR during admission for confirmed COVID-19 for specific clinical indications • Perform a chest CT scan only if it would change management, in particular if concern for pulmonary embolism • Anticipate complications such as delirium, pulmonary embolism, other thromboembolism, arrhythmias, cardiac impairment, acute kidney injury, sepsis, shock and multi-organ dysfunction, and address using existing standards of care. Also be aware of potential medication complications • Repeat baseline investigations periodically in patients who are not clearly improving, in order to detect & manage the above complications		
	Additional considerations in pregnancy: • Screen for pre-eclampsia in all pregnancies > 20/40 gestation and review at each assessment: i.e., systolic BP ≥ 140mmHg and/or diastolic ≥ 90, worsening peripheral oedema, headache, visual changes or upper abdominal pain. Risk of pre-eclampsia is increased in COVID-19. • Consider repeating laboratory investigations if there is a deterioration in maternal condition • Appropriateness and frequency of foetal heart rate monitoring and ultrasound to be considered on an individual basis, accounting for gestational age and clinical severity. Consider parameters for delivery (in discussion with neonatologists, anaesthetists ± intensive care team) • Consider steroids for the fetal lung maturation, and magnesium sulphate for neuroprotection or severe pre-eclampsia as per local obstetric guidelines • Consider emergency delivery if required for maternal resuscitation (including need for prone positioning) or for immediate foetal concern		
NOTIFICATION	• Discuss all admitted cases with local COVID team at the earliest opportunity, according to local protocols		
CLINICAL TRIALS	• As the optimal management of COVID-19 is not yet known, the **standard of care is to be offered enrolment in a clinical trial,** if available • **All** patients should be screened for eligibility for a locally available COVID-19 clinical trial (e.g. 'REMAP-CAP' and 'ASCOT-ADAPT')		

COVID-19 Therapeutics: patients **not requiring oxygen**

The main benefit of these therapeutics is to reduce progression to more severe COVID-19, with a possible small reduction in mortality. The benefit in vaccinated individuals and / or infection with Omicron variant is likely to be restricted to patients at high risk of developing severe COVID-19. The recently expanded Pharmac access criteria for antiviral treatments outlines groups who are at higher absolute risk of COVID-19-associated hospitalisation in New Zealand. Within these groups, it is important to recognise that older age (particularly over the age of 75), incomplete vaccination and severe immunocompromise remain the most important risk factors for severe COVID-19. As such, **we recommend offering treatments** (including antivirals and budesonide) **to patients not requiring oxygen to people who are:**

1) Aged **65 years** or older
2) OR **Māori or Pacific** aged **50 years** or older
3) OR other ethnicity aged **50 years** or older and have **not completed a primary course of vaccination**
4) OR have any of the following **specific clinical risk scenarios**:
    a. **immunocompromised**[1] and not expected to reliably mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection, regardless of vaccination status
    b. Previous critical COVID-19 requiring treatment in Intensive Care
    c. Down syndrome
    d. Sickle cell disease
5) OR are have **at least *three* risk factors for severe COVID-19 disease**[2]

For these treatments, patients should **not** already have COVID-19 associated pneumonitis requiring oxygen. If a patient requires oxygen for COVID-19, **different therapeutics recommendations** apply.

The definition of **immunocompromise** in PHARMAC access criteria aligns with the eligible population for a **three-dose primary vaccine** series. However, a subgroup of **severely immunocompromised** individuals are at higher risk of severe outcomes, including:

- Solid organ transplant recipient, particularly if within 12 months of transplantation, if requiring more than routine maintenance immunosuppression, treated with mycophenolate mofetil, or treated for rejection within past 12 months
- Within 24 months of haematopoietic stem cell transplant or CAR-T cell therapy.
- Graft-versus-host disease treated with multi-modal immunosuppressive therapy
- Treated B-cell haematologic malignancy (e.g. chronic lymphocytic leukaemia, lymphoma, multiple myeloma) within the past 6 months
- Receipt of anti-CD20 monoclonal antibody therapy (e.g. rituximab) within the past 12 months
- Primary or acquired hypogammaglobulinaemia (IgG <3), even if now on replacement immunoglobulin
- Primary immunodeficiency associated with severe B-cell or combined cellular defects
- Advanced HIV with CD4 <200
- Other conditions (on case by case basis) felt to have profound immunocompromise on the basis of combined immunosuppression, functionally equivalent to the above groups

Risk factors are detailed on the Ministry of Health (MOH) website and include: obesity, chronic lung disease, chronic kidney disease, heart disease, diabetes, hypertension, chronic liver disease, active malignancy, chronic neurologic disease and severe mental health illness.

MODALITY	PATIENT SUB-GROUPS	RECOMMENDATION
ANTIVIRALS	Adults who meet **access criteria** AND are within 5 days of symptom onset AND do not have severe hepatic dysfunction (Childs-Pugh class C) AND do not have a potentially serious drug-drug interaction with ritonavir	Give Paxlovid (nirmatrelvir and ritonavir):[1] • (nirmatrelvir 300mg + ritonavir 100mg) PO q12h for 5 days • eGFR 30-59ml/min: nirmatrelvir 150mg + ritonavir 100mg po q12h for 5 days • eGFR <30: *consider*[2] nirmatrelvir 300mg + ritonavir 100mg po daily on day 1, then nirmatrelvir 150mg + ritonavir 100mg po daily for 4 days • Peritoneal or haemodialysis: *consider*[2], with dose for eGFR <30 ml/min, but dose after dialysis. Suggested[2] dosing for weight <40kg **here**. • Use barrier contraception for 7 days after last dose • Do not prescribe Paxlovid for **'rebound' COVID-19** [1] *NB Paxlovid prescriber advice available here. Management of common drug interactions highlighted here.* [2] *The NZ Medsafe datasheet currently advises against use of Paxlovid in patients with eGFR <30 due to insufficient data available. Subsequently, dosing for CKD4 and dialysis has been **suggested by an Ontario working group** due to increased risk of severe COVID-19 in this group.*
	Adults who meet **access** criteria AND are unable to receive Paxlovid AND are within 7 days of symptom onset *Guidance for further prioritisation of remdesivir to patients at highest risk is available **here**.*	Consider remdesivir: • 200mg IV on day 1, then 100mg IV q24h for further 2 days (maximum 3 days total) • Limited data of safety in patients with eGFR <30ml/min or peritoneal dialysis.* Use if benefits felt to clearly outweigh potential risks. Likely to be safe in haemodialysis. • Do not prescribe remdesivir for **'rebound' COVID-19** **Consider a two dose regimen (i.e. omission of day 3 dose) for patients with eGFR<30: modelling suggests this may provide equivalent drug concentrations to patients with normal renal function.*
	Adults who meet **access** criteria AND are unable to receive Paxlovid AND are unable to receive remdesivir AND are within 5 days of symptom onset	Consider molnupiravir [#]: • 800mg PO q12h for 5 days • Use barrier contraception while taking molnupiravir and for 4 days after last dose • Do not prescribe molnupiravir for **'rebound COVID-19'** *[#]NB molnupiravir is less effective at reducing risk of severe COVID-19 than other antivirals, and is not recommended for regular use in high-risk patients presenting to hospital.*
	Adults with COVID-19 after day 7 of illness	• Do not start antivirals • Complete course if started earlier in illness
	Discuss all severely immunocompromised patients with Infectious Diseases or Microbiology	
	Pregnancy (meeting the same clinical criteria as above)	• Do not use Paxlovid or molnupiravir in pregnancy • Avoid breastfeeding during and for 7 days after Paxlovid or 4 days after molnupiravir • Use remdesivir if >12/40 gestation as per Adult Guideline indications with the same dosing as above • Remdesivir is compatible with breastfeeding

STEROIDS	Adults who meet high risk criteria AND are ineligible for antivirals AND are within 14 days of symptom onset	Consider inhaled budesonide 800micrograms BD for up to 14 days if respiratory symptoms • Updated budesonide guidance available here Do not use systemic steroids to treat COVID-19 without an oxygen requirement
	Adults without oxygen requirement, but another evidence-based indication for systemic steroids (e.g. asthma/COPD exacerbations)	Steroids as per usual practise
ANTIBODY THERAPY	**Severely immunocompromised** adults **within 7 days** of illness: AND are **eligible for Evusheld pre-exposure prophylaxis (PrEP)** AND have not received Evusheld in the past 6 months	Offer tixagevimab/cilgavimab (Evusheld) 600mg IM STAT • Limited data suggest benefit in early treatment, but current approval only for PrEP (requires rapid NPPA) • Caution if significant coronary artery disease
	Adults who are **not severely immunocompromised**	**Do not give tixagevimab/cilgavimab (Evusheld)**
	Adults with **any severity of illness**	**Do not use casivirimab/imdevimab (Ronapreve)** or **sotrovimab** due to lack of predicted efficacy against currently circulating SARS-CoV-2 variants. *Guidance about use of Ronapreve in specific cases if advised by an expert clinician is available here.

Supportive management: **all patients in hospital**

MODALITY	PATIENT SUB-GROUPS	RECOMMENDATION
RESPIRATORY SUPPORT	All patients	• Switch nebulisers to metered dose inhalers via spacer if possible • Monitor closely for worsening hypoxia if elevated work of breathing or respiratory rate
	SpO_2 <92% at rest	• Administer dry oxygen (1-4 L/min) via standard nasal prongs • Use Hudson mask (5-10 L/min), Venturi device or high flow nasal oxygen (HFNO) if required • Aim for SpO_2 92–96% (88–92% for those at risk of hypercapnic respiratory failure) • Encourage use of self-proning
	Unable to maintain SpO2 ≥92% on conventional oxygen or high flow nasal oxygen [HFNO] (requiring Fi02 >40%)	• Consider CPAP. Settings should be individualised, but a starting pressure of 8-10cm H_20 is common • Continue HFNO if CPAP unavailable, during meal breaks from CPAP or patient intolerance of CPAP • Encourage use of self-proning
	Hypercapnic patients with underlying COPD or OHS	• Consider BiLevel Non-Invasive Ventilation (NIV) in addition to above
	Pregnancy	• SpO2 target is ≥ 94%; ideally aim for 96-98%. • After 20/40 avoid positioning flat on back: use a wedge for lateral supine positioning. Left lateral during resuscitation or if hypotensive. • Self-proning may be possible (depending on gestation and habitus).

<table>
<tr><td>FLUID MANAGEMENT</td><td colspan="2">• Assess for hypovolaemia and correct as required.
• Avoid excessive resuscitation or ‘maintenance’ fluids
• Anticipate and monitor ongoing fluid losses</td></tr>
<tr><td rowspan="5">VTE PROPHYLAXIS</td><td>Hospitalised adults with:
• mild COVID-19
• OR severe and critical COVID-19

AND no contra-indication to anticoagulation e.g. risk for major bleeding</td><td>Enoxaparin 40mg SC once daily (standard prophylaxis)
• Adjust dose for impaired renal function

(NB Therapeutic-dose anticoagulation is not beneficial and probably hazardous when initiated prophylactically in severe and critical COVID-19)</td></tr>
<tr><td>Hospitalised adults with moderate COVID-19 AND no contra-indication to anticoagulation e.g. risk for major bleeding

(NB moderate = stable adult patient presenting with shortness of breath and/or reduction in resting oxygen saturation while breathing air. Able to maintain oxygen saturation ≥92% (or ≥90% for patients with chronic lung disease) with up to 4 L/min oxygen via nasal prongs)</td><td>Therapeutic dose anticoagulation should be considered over standard prophylaxis for up to 14 days, or until clinical recovery (discharge or resolved hypoxia)
Enoxaparin 1mg/kg SC twice daily (max 150mg BD)
• Adjust dose for impaired renal function

All other patients should receive standard prophylaxis as detailed above</td></tr>
<tr><td>Hospitalised pregnant adults with mild OR severe/critical COVID-19 UNLESS:
• Delivery expected within 24 hours (if only on enoxaparin 40mg SC once daily then 12 hourly)
• Platelets < 50
• Actively bleeding / coagulopathy
• Severe hypertension (>160/110)</td><td>Enoxaparin 40mg SC once daily (standard prophylaxis)
• dose adjustment may be necessary if current weight ≥90kg</td></tr>
<tr><td>Hospitalised pregnant or postpartum adults with moderate COVID-19 AND no contra-indication to anticoagulation (as above)</td><td>Consider therapeutic anticoagulation as for non-pregnant adults (above)</td></tr>
<tr><td colspan="2">Anticoagulation in pregnancy should be considered for a longer duration if post-partum or has additional risk factors for VTE (discuss with Obstetrics)</td></tr>
<tr><td>INTENSIVE CARE</td><td colspan="2">Regular, open and early discussions between ward-based clinicians and local ICU team is strongly encouraged. In addition to local referral guidelines, ICU review should be prompted by the following:
• Significant oxygen requirement (e.g. requiring FiO2 of >40% to maintain SpO_2 >92%, or needing CPAP)
• Increased work of breathing with impending respiratory failure
• Haemodynamically unstable and / or hypotension not responsive to fluid bolus
• Rapidly worsening tachypnoea or hypoxaemia

Detailed clinical guidance for ICU care of COVID-19 is beyond the scope of this guideline</td></tr>
<tr><td rowspan="2">ANTIBIOTIC THERAPY</td><td colspan="2">Antibiotics should not be used to treat COVID-19 pneumonitis: bacterial co-infection is uncommon.</td></tr>
<tr><td>Severe/critical COVID-19 especially with any deterioration occurring >7 days post onset and/or >3 days after hospital admission</td><td>• Evaluate for secondary infection, including hospital-acquired infection
• Discuss with local Infectious Diseases / Microbiology team if concern for secondary infection</td></tr>
</table>

COMMUNICATION & HOLISTIC CARE	Encourage for all patients: • Clearly communicate typical symptoms and anticipated clinical course with patient, family/whānau or carers • Reinforce importance of complying with all Public Health messages, including self-isolation and testing • When possible, explain risks, benefits and likely outcomes of treatments with patients, family/whānau or carers • Use an interpreting service to assist communication if required • Facilitate regular clinical updates, and video calls between patient family/whānau or carers • Routinely refer to local cultural and/or spiritual support services • Consider early involvement of Palliative Care and/ or Liaison Psychiatry services to assist with symptom management, particularly anxiety, dyspnoea and delirium/agitation • Ensure appropriate housing, financial and social support is in place prior to discharge (including a working phone). If concerns, refer to social work • If welfare or cultural support issues identified, liaise with Public Health or Regional Isolation Quarantine (RIQ) according to regional processes as part of discharge planning	
	• Ensure Maternity services including lead maternity carer are alerted so wrap-around antenatal and post-natal care can be provided for the mother and baby	
THERAPIES FOR EXISTING INDICATIONS	• Nocturnal CPAP for Obstructive Sleep Apnoea (inpatients)	Consider changing usual vented CPAP mask to a non-vented mask + expiratory port + filter (decision depends on equipment availability and staff expertise)
	• ACE-inhibitors / ARBs • Oral contraceptive pill (with or without oestrogen)	• Usual care (i.e. may be continued in COVID-19 unless otherwise contra-indicated)
	• Corticosteroids for asthma/COPD (inhaled or oral, with or without bronchodilators)	• Usual care • Do not use a nebuliser unless definite clinical need
	• Oral menopausal hormone therapy / HRT	• Consider stopping until after recovery
	• All pregnancy-related supplements and medications should be continued	
SURGERY	• Elective minor surgery should generally be deferred until at least four weeks, and major surgery until 8-12 weeks, following recovery from COVID-19 if patient outcome is not compromised • Acute surgical procedures that are indicated during active COVID-19 infection should be discussed with local ID and infection control services • Comprehensive preoperative and ongoing assessment must be carried out to ensure optimal clinical decision-making	
	• Caesarean section (including emergency) should not be deferred if clinically indicated, e.g. if needed for maternal resuscitation or immediate fetal concern; mode of delivery should otherwise remain based on obstetric indication	

COVID-19 Therapeutics: patients **requiring oxygen**

MODALITY	PATIENT SUB-GROUPS	RECOMMENDATION
STEROIDS	Adults with sustained oxygen requirement	Dexamethasone 6mg* daily PO/IV for 10 days OR until hospital discharge Do not routinely continue after discharge if completed at least 5 days in hospital *consider dexamethasone 12mg PO/IV on day 1 if would qualify for immunomodulation, but medication is unavailable within next 24 hours
	Pregnancy with sustained oxygen requirement to maintain SpO2 ≥94%	If steroids needed for fetal lung maturation (usually < 34^{+6} weeks): • dexamethasone 6mg IM every 12 hours for four doses • THEN either prednisone 40mg PO daily, OR hydrocortisone 80mg IV twice daily If steroids not required for fetal lung maturation, use non-fluorinated steroids: • prednisone 40mg PO daily OR hydrocortisone 80mg IV twice daily OR methylprednisolone 40mg IV once daily Total duration is 10 days total OR until discharge, whichever is sooner.
	Risk of **gestational diabetes:** monitor blood glucose levels closely and start treatment if elevated.	
ANTIVIRAL THERAPY	***All patients enrolled in ASCOT-ADAPT trial (anti-viral domain)***	***As per trial protocol & randomisation (in addition to remdesivir, if indicated below)***
	Adults with new sustained oxygen requirement within first 7 days of illness and not requiring mechanical ventilation	Consider remdesivir (especially if **high risk** patient) • 200mg IV on day 1, then 100mg IV q24h for 2-4 days (maximum 5 days total) • If short-lived oxygen requirement without evidence of pneumonitis, suggest 3-day course rather than 5 days
	Adults with COVID-19 after day 7 of illness	• Do not start remdesivir • Complete course (3 days) if started earlier in illness
	Adults with severe immunocompromise with any stage/severity of COVID-19	Discuss with local infectious diseases team
	Pregnancy (meeting the same clinical criteria as above)	• Use remdesivir if >12/40 gestation as per Adult Guideline indications with the same dosing as above • Remdesivir is compatible with breastfeeding
ANTIBODY THERAPY	**Severely immunocompromised** adults **within 12 days** of illness: • AND are eligible for Evusheld PrEP • AND have not received Evusheld in the past 6 months	Offer tixagevimab/cilgavimab (Evusheld) 600mg IV STAT • Limited data suggest benefit in early treatment, but current approval only for PrEP (requires rapid NPPA) • Caution if significant coronary artery disease • May be given in addition to antiviral therapy
	Adults who are **not severely immunocompromised**	**Do not give Evusheld**

<table>
<tr><td></td><td>Adults with any severity of illness</td><td>Do not use casivirimab/imdevimab (Ronapreve) or sotrovimab due to lack of predicted efficacy currently circulating SARS-CoV-2 variants

*Guidance about use of Ronapreve in specific cases if advised by an expert clinician is available here.</td></tr>
<tr><td rowspan="6">IMMUNE MODULATION THERAPY</td><td colspan="2">In patients receiving systemic steroids in combination with immune modulation, we recommend screening for, and consider empiric treatment of latent infection, e.g. Hepatitis B or strongyloidiasis (in patients who have lived in an endemic region)</td></tr>
<tr><td colspan="2">There are no trials of immune modulation therapies currently recruiting in New Zealand</td></tr>
<tr><td>Adults with moderate COVID-19
• AND receiving systemic steroids
• AND elevated CRP or other evidence of severe systemic inflammation OR clinically deteriorating
• AND there is not another active, severe concurrent infection</td><td>Give baricitinib:
• 4mg PO/NG daily for 14 days or until hospital discharge
• Reduce to 2mg PO daily if eGFR 30-60mL/min
• Reduce to 1mg PO daily if eGFR 15-29mL/min*
• Do not use if eGFR <15mL/min
• Avoid in pregnancy or breastfeeding
• Baricitinib is a section 29 product

OR tocilizumab:
• 8mg/kg IV (actual body weight) rounded to nearest 80mg or 200mg vial (max dose 800mg), as a single dose
• Notes: risk of secondary infection may be increased; CRP response is inhibited, and consequent reduction in CRP does not necessarily correlate with response to treatment

*baricitinib 2mg PO every 48 hours is an alternative</td></tr>
<tr><td>Adults with severe / critical COVID-19 requiring non-invasive or mechanical ventilation or organ support:
• AND receiving systemic steroids
• AND there is not another active, severe secondary infection</td><td>Give tocilizumab as above
• Start as soon as possible if requiring NIV, mechanical ventilation or other organ support

OR baricitinib, if tocilizumab is unavailable (as above).
• If tocilizumab is available and baricitinib commenced earlier in illness, suggest change to tocilizumab

Do not treat with both baricitinib and tocilizumab together</td></tr>
<tr><td>COVID-19 not meeting the criteria above</td><td>Do not use immune modulation therapy</td></tr>
<tr><td>Pregnancy (meeting the same clinical criteria as above)</td><td>Give tocilizumab (same dosing as above):
• Notes: Tocilizumab crosses the placenta after 28/40, but no evidence of harm to date. Suggest deferring live vaccination (i.e. Rotarix, BCG) up to 6 months in neonates with antenatal exposure. All other vaccinations are safe.
• Compatible with breastfeeding.
• May cause raised ALT and thrombocytopenia, mimicking pre-eclampsia / HELLP.
• Do not use baricitinib (as above)</td></tr>
</table>

Discharge Planning and Follow-up

Patients with Suspected, Probable or Confirmed COVID-19 who are being considered for discharge need to have specific decisions made about the following aspects of post-discharge care:

FURTHER INVESTIGATIONS	• Follow-up investigations are not universally required after COVID-19 • A repeat chest x-ray in 6-12 weeks to confirm resolution of pulmonary opacities should be arranged for individuals with significant radiographic abnormalities and / or risk factors for lung cancer	
DISCHARGE DESTINATION	• Anyone with COVID symptoms or suspected infection being discharged before PCR results are available should be tested using a RAT. If the RAT (or a PCR) is negative, the person should be advised to stay home until symptoms resolve and seek a further test if symptoms worsen. • Anyone who tests positive (on RAT or PCR) should be able to be discharged home but should be linked in through the Care in the Community Model if needed for follow-up, and household members should be advised to self-isolate as per standard advice for positive cases. Note that positive RAT results need to be recorded in My COVID Record. • The local Medical Officer of Health does not need to be notified of discharge of a positive case.	
CLEARANCE FROM ISOLATION	• The decision to end isolation should be consistent with Public Health policies and local hospital infection prevention and control policies, which may be different. • **Local hospital isolation policy should be followed until point of discharge** • Release from isolation after discharge should align with the current Public Health Policy for community isolation: this is now taken as **7 days from date of onset of symptoms or date of positive test** (whichever is earlier, starting from day zero). • **'Rebound' COVID-19** is characterised by recurrence of symptoms and/or a new positive viral test after having tested negative, irrespective of prior antiviral therapy. It occurs within a week of symptom improvement or completion of antiviral treatment. Data informing the approach to 'rebound' COVID-19 is limited, although 'rebound' does not appear to be associated with increased risk of severe COVID-19. It is important that 'rebound' be differentiated from both re-infection (rare within the first 4 weeks of COVID-19 recovery) and persistent SARS-CoV-2 infection (very rare and affects only **severely immunocompromised** hosts). We suggest clinicians discuss possible 'rebound' COVID-19, and **all COVID-19 in severely immunocompromised patients** with an infectious disease specialist or clinical microbiologist. • Exceptions to this duration may include severe immunocompromise and severe/critical COVID-19. It is advisable to seek the advice of an infectious disease specialist or microbiologist for severely immunocompromised individuals. Additional testing may be useful, such as serial NAAT/PCR testing suggestive of low viral load (i.e. negative or with high cycle threshold), high or increasing antibody levels or repeatedly negative RAT tests.	
	All patients	**Encourage vaccination if not completed eligible vaccination course (including booster dose[s]).** • If not completed primary vaccination series before infection, vaccination is recommended from 4 weeks after clinical recovery, even if treated with anti-SARS-CoV-2 antibody therapy (convalescent plasma or monoclonal antibody such as Ronapreve) • If completed primary vaccination series before infection, booster vaccination is recommended from 12 weeks after clinical recovery Educate about anticipated gradual recovery from COVID-19, and potential for persistent symptoms. • Encourage those with persistent symptoms after 6 weeks to arrange assessment by their GP.

	Severely immunocompromised	Suggest discuss all patients with infectious diseases or clinical microbiology to clarify duration of isolation (if inpatient) and consider screening for persistent SARS-CoV-2 infection. If eligible for Evusheld and not treated in the past 6 months, suggest discuss timing of administration during discharge process. Further guidance available here.
	Patients with significant respiratory failure (and/or persistent dyspnoea), or other persistent organ dysfunction	Specialist clinic follow-up, investigations and support following discharge (as advised by local specialty services)
	Pregnancy (or recently post-partum)	• VTE prophylaxis - refer to specific guidelines above • Recommend follow up growth scan within 2 weeks • If possible, delay follow-up CXR until post-partum

Links to other guidelines

- Australian COVID-19 living guidelines: https://covid19evidence.net.au/
- NICE (UK) living guideline: https://www.nice.org.uk/guidance/ng191
- National Institute of Health (USA): https://www.covid19treatmentguidelines.nih.gov/
- WHO COVID-19 living guideline: https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2022.1
- Ontario COVID-19 Science Advisory Group guideline (Canada): https://covid19-sciencetable.ca/sciencebrief/clinical-practice-guideline-summary-recommended-drugs-and-biologics-in-adult-patients-with-covid-19-version-11-0/