SA Health

COVID-19: Treatment recommendations for hospitalised adult patients

Statewide Clinical Guideline - Adoption of CALHN Guideline

Endorsed by CALHN Drugs and Therapeutics Committee: 29/04/2024

Version 5.1

Approval date: 29/04/2024

Government of South Australia | Health
Central Adelaide Local Health Network

GUIDELINE

Reference	CALHN-GDE05778			
Title	COVID-19: Treatment recommendations for hospitalised adult patients			
Scope	All CALHN clinical staff in acute care hospitals			
Document owner	Infectious Diseases – Speciality Medicine 2			
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Oversight committee	CALHN Drug and Therapeutics Committee			
Committee endorsement	29 April 2024			
Sponsor	Dr Renjy Nelson – Head of Unit, Infectious Diseases/IPCU, CALHN			
Sponsor approval	22 April 2024			
Priority Care Committee (PCC)	PCC: National Standard 4 Medication Safety			
Risk rating	☐ Extreme	☐ High	☒ Medium	☐ Low
Title and reference of parent SA Health Policy	N/A			
Summary (three sentences maximum)	This guideline provides recommendations on the antiviral and immunomodulatory medications available for patients hospitalised with COVID-19 in CALHN.			
Keywords (five to eight)	COVID-19, Baricitinib, Molnupiravir, Nirmatrelvir, Ritonavir, Remdesivir, Tocilizumab, Sarilumab, Dexamethasone, Sotrovimab.			

Clinical Governance	Partnering with Consumers	Preventing and Controlling Healthcare Associated Infections	Medication Safety	Comprehensive Care	Communicating for Safety	Blood Management	Recognising and Responding to Acute Deterioration
☒	☐	☒	☒	☐	☐	☐	☒

Version	Change summary	Next scheduled review
5.1	Non-scheduled minor review. Removal of tables for classification of immunosuppressed patients and link to PBS criteria inserted. Removal of declaration form requirement and sotrovimab and removal of critical shortage statement for tocilizumab. Clarification eligibility criteria for nirmatrelvir/ritonavir and molnupiravir for patients aged 50-69. Change in recommendations for remdesivir and nirmatrelvir/ritonavir in renal impairment. Additional section for immunocompromised patients with reactivation of COVID-19 infection.	April 2027
5.0	Non-scheduled minor review. Patients aged > 50 years with 1 risk factor eligible for PBS treatment with nirmatrelvir/ritonavir. Removed “not up to date vaccination status” as requirement for treatment eligibility for patients < 50 years.	July 2026
4.9	Non-scheduled update. Indications for anti-viral treatment updated to include individuals previously hospitalised with COVID-19 infection, independent of age and other risk factors.	May 2026
4.8	Non-scheduled review. Updated eligibility for access to oral antiviral medications to be in line with PBS changes made at the start of April 2023.	April 2026
4.7	Non-scheduled review. Updated risk factors for severe illness to be in line with changes made to the PBS in Jan 2023.	February 2026

GUIDELINE

COVID-19: Treatment recommendations for hospitalised adult patients

Introduction

- Since the emergence of COVID-19 there have been significant developments in the antiviral and immunomodulatory medications recommended for patients hospitalised with COVID-19.
- This guideline only addresses the use of disease-modifying treatments for COVID-19 in hospitalised adult patients.
- This guideline **DOES NOT:**
  - provide guidance of the overall care for patients with COVID-19
  - provide advice regarding supportive therapies recommended for COVID-19
  - provide information regarding the prevention or chemoprophylaxis for the prevention of COVID-19.
- For information related to the management and care of patients with COVID-19 please refer to:
  - COVID–19 (SARS–COV–2) – Management Guide (CALHN–PRC05409)
  - CALHN COVID–19 internet page
- Medication recommendations for COVID-19 can change rapidly due to medication shortages, ongoing research and as novel agents are discovered. For the most up to date Australian guidelines and recommendations refer to:
  - National COVID-19 Clinical Evidence Taskforce (The Australian Living Guidelines)
  - Clinical Excellence Commission: Medication Safety Updates

Topics covered in this guideline

For detailed information on the following topics click on the links below:

1. Definition of COVID-19 disease severity for adults
2. Risk factors for progressing to severe or critical illness
3. Classification of immunocompromised patients including medications associated with a reduced immune response to COVID-19 vaccination
4. COVID-19 treatment recommendations for hospitalised adults according to disease severity (excluding pregnancy/breastfeeding) – mild illness
5. COVID-19 treatment recommendations for hospitalised adults according to disease severity (excluding pregnancy/breastfeeding) – moderate to critical illness
6. Assessing a patient for nirmatrelvir plus ritonavir (Paxlovid®)
7. COVID-19 treatment recommendations for hospitalised pregnant and breastfeeding adults
8. Approach to treatment of immunocompromised patients with persistent or relapsed COVID-19 infection
9. Access and restrictions to therapy
10. Treatments for COVID-19 - Drug Monographs

Remdesivir
Molnupiravir
Nirmatrelvir plus ritonavir
Dexamethasone
Baricitinib
Tocilizumab

1. Definition of COVID-19 disease severity for adults[1]

Mild illness (outpatient or inpatients admitted with another condition)	Adults not presenting any clinical features suggestive of moderate or severe disease or a complicated course of illness.
	• Characteristics:
	  ○ no symptoms; or
	  ○ mild upper respiratory tract symptoms; or
	  ○ cough, new myalgia or asthenia without new shortness of breath or a reduction in oxygen saturation
	  ○ oxygen saturations > 95% on room air

Moderate illness (ward based care)	Stable patient presenting with respiratory and/or systemic signs or symptoms. Able to maintain oxygen saturation above 92% at rest (or above 90% for patients with chronic lung disease) with up to 4L/min oxygen via nasal prongs.
	• Characteristics:
	  ○ fatigue, fever > 38ºC or persistent cough
	  ○ clinical or radiological signs of lung involvement
	  ○ no clinical or laboratory indicators of clinical severity or respiratory impairment

Severe illness (specialised ward or ICU)	Adult patients meeting any of the following criteria: • respiratory rate ≥ 30 breaths/min • oxygen saturation ≤ 92% at a rest state on ≥ 4L/min oxygen via nasal prongs • arterial partial pressure of oxygen (PaO_2) / inspired oxygen fraction (FiO_2) ≤ 300

Critical illness (ICU)	Adult patients meeting any of the following criteria:
	• Respiratory failure as defined by:
	  ○ severe respiratory failure (PaO_2/FiO_2 < 200), respiratory distress or acute respiratory distress syndrome
	  ○ deterioration despite advanced forms of respiratory support (non-invasive ventilation, high flow nasal oxygen) OR requiring mechanical ventilation
	OR
	• Other signs of significant deterioration:
	  ○ hypotension or shock
	  ○ impairment of consciousness
	  ○ other organ failure

2. Risk factors for progressing to severe or critical illness[1,28,29]

- Immunosuppression
- Renal impairment (eGFR < 60mL/min or equivalent renal impairment for pregnant women)
- Age ≥ 50 years, or age ≥ 30 years if Aboriginal and/or Torres Strait Islander*
- Diabetes (requiring medication) or gestational diabetes (requiring medication) in pregnant women
- Obesity (BMI > 30 kg/m^2 or > 40 kg/m^2 for pregnant patients)
- Chronic liver disease (cirrhosis)
- Respiratory compromise including:
    - history of chronic bronchitis, bronchiectasis, chronic obstructive pulmonary disease (COPD) or moderate-to-severe asthma requiring an inhaled steroid to control symptoms or caused by neurological or musculoskeletal disease
- Neurological conditions including stroke, dementia and demyelinating conditions
- Coronary artery disease
- Heart failure or cardiomyopathies
- Residing in residential aged care
- Disability with multiple comorbidities and/or frailty
- Past COVID-19 infection episode resulting in hospitalisation
- Reduced, or lack of, access to higher level healthcare and lives in an area of geographic remoteness classified by the Modified Monash Model as Category 5 or above
- Pregnancy (see page 9)

Please note the following conditions previously listed as risk factors are now included in conditions considered immunosuppressive as per the PBS

- People with disability with multiple comorbidities and/or frailty
- Down Syndrome
- Cerebral palsy
- Congenital heart disease
- Thalassemia
- Sickle cell disease
- Other haemoglobinopathies not already listed

* Age ≥ 50 years or ≥ 30 years if Aboriginal and/or Torres Strait Islander as a risk factor for developing severe COVID-19 illness has been taken into account in the flow charts on pages 7-10 and hence is not included in the box containing risk factors for developing severe disease on those pages.

3. Classification of Immunocompromised Patients

Immunocompromised patients are not expected to mount an adequate immune response to COVID-19 vaccination, or the COVID-19 infection due to their underlying conditions regardless of their vaccine status. Early access to treatment with COVID-19 antiviral medications is important for immunocompromised patients to reduce the likelihood of progression to more severe COVID-19 illness.

For more information regarding eligibility for treatment of early COVID-19 with antiviral medications for patients with immunocompromising medical conditions or taking immunosuppressive medications, see the PBS criteria here.

4. COVID-19 treatment recommendations for hospitalised adult patients (excluding pregnancy/breastfeeding- see page 9)

See page 10 for information on prescribing restrictions and access to therapies in CALHN

Mild illness not requiring oxygen

For all hospitalised patients consider VTE prophylaxis and empiric influenza treatment* until results of respiratory viral panel available

- **Immunosuppressed** patients (all ages) irrespective of vaccination status
- **Previous COVID-19 infection requiring hospitalisation** (all ages) irrespective of vaccination status or risk factors
- **Aged ≥ 70 years** irrespective of vaccination status or risk factors
- **Aged 50 to 69 years** irrespective of vaccination status **PLUS** ≥ 2 risk factor (Box 1)
- **Aboriginal or Torres Strait Islander AND Aged ≥ 30 years** irrespective of vaccination status **PLUS** ≥ 1 risk factor (Box 1)
- **Aged < 50 years or < 30 years if Aboriginal or Torres Strait Islander** irrespective of vaccination status **PLUS** ≥ 3 risk factors (Box 1)

First Line:
If symptom onset **≤ 5 days AND NO** contraindications or drug interactions
Nirmatrelvir plus ritonavir

Second Line:
Symptom onset **≤ 7 days AND** contraindications to nirmatrelvir plus ritonavir
Remdesivir

Third Line:
Symptom onset **≤ 5 days AND** nirmatrelvir plus ritonavir and remdesivir contraindicated or unavailable
Molnupiravir (see Box 3)

- **Aged < 50 years** (or < 30 years if Aboriginal or Torres Strait Islander) **PLUS** ≥ 2 risk factors (Box 1)

First Line:
If symptom onset **≤ 5 days AND NO** contraindications/ drug interactions
Nirmatrelvir plus ritonavir

See Box 3 for patients contraindicated from taking nirmatrelvir plus ritonavir

NOTE: Supportive care alone recommended for patients who are at **low risk of progressing to severe illness** (i.e. not up to date vaccination status) with no risk factors for progressing to severe illness (box 1) and patients who have mild disease symptoms and are > 7 days since symptom onset

Box 3: Consider risk versus benefits of molnupiravir as limited evidence in patients <70 years. For patients who are contraindicated from taking nirmatrelvir/ritonavir and/or remdesivir only prescribe molnupiravir if benefits outweigh risks AND appropriate reproductive counselling can be provided.

Box 1: Risk factors for progressing to severe illness

- Renal impairment (eGFR < 60mL/min)
- Diabetes (requiring medication)
- Obesity (BMI > 30 kg/m^2)
- Chronic liver disease (cirrhosis)
- Coronary artery disease
- Heart failure and cardiomyopathies
- Respiratory compromise including: history of chronic bronchitis, cystic fibrosis, bronchiectasis, chronic obstructive pulmonary disease, moderate-to-severe asthma requiring an inhaled steroid to control symptoms or caused by neurological or musculoskeletal disease
- Neurological conditions e.g. stroke, dementia, demyelinating conditions (inc multiple sclerosis)
- Residential aged care
- Disability with multiple comorbidities and/or frailty
- Past COVID-19 infection episode resulting in hospitalisation
- Reduced, or lack of, access to higher level healthcare and lives in an area of geographic remoteness classified by the Modified Monash Model as Category 5 or above

Please note the following "High risk conditions" are now included in the list of immunocompromised conditions as per PBS criteria:

- People with disability with multiple comorbidities and/or frailty
- Down Syndrome
- Cerebral palsy
- Congenital heart disease
- Thalassemia
- Sickle cell disease
- Other haemoglobinopathies not already listed

Box 2: Dosing Recommendations

Nirmatrelvir plus ritonavir: **eGFR > 60 mL/min:** 300mg nirmatrelvir (2x150mg capsules) + 100mg ritonavir (1x100mg capsule) orally twice daily for 5 days. **eGFR < 60mL/min**: 150mg nirmatrelvir (1x150mg capsule) + 100mg ritonavir (1x100mg capsule) orally twice daily for 5 days. Use with caution in patients with eGFR < 30 mL/min (see drug monograph on page 12)
Molnupiravir: 800mg (4 x 200mg capsules) orally 12-hourly for 5 days
Remdesivir: 200mg IV infusion loading dose day 1 then 100mg IV daily on day 2 and 3. Total 3 day course.
***Oseltamivir:** **CrCl >30mL/min:** 75mg orally twice daily, **CrCl 10-30mL/min**: 75mg orally once daily, **CrCl <10mL/min**: 75mg orally alternate daily for 5 days **IF** Influenza confirmed. Cease immediately if viral panel negative for influenza

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5. COVID-19 treatment recommendations for hospitalised adult patients (excluding pregnancy/breastfeeding- see page 9)

See page 10 for information on prescribing restrictions and access to therapies in CALHN

Moderate illness on supplemental oxygen	Severe illness on high flow oxygen	Critical illness on non-invasive or mechanical ventilation
For all hospitalised patients: VTE prophylaxis^ Consider empiric influenza treatment* until results of respiratory viral panel available		
dexamethasone PLUS remdesivir If no improvement or increasing oxygen requirement and elevated markers of systemic inflammation@ **ADD** **baricitinib** (if baricitinib contraindicated contact ID)	**dexamethasone PLUS remdesivir** If elevated markers of systemic inflammation@ **ADD** **baricitinib** **OR** If clinical signs of deterioration# and not already on baricitinib **tocilizumab**	**Non-invasive ventilation / high flow oxygen/mechanical ventilation** **dexamethasone** **PLUS** If elevated markers of systemic inflammation@ **baricitinib** **OR** **tocilizumab** (can continue **remdesivir** if already commenced)

@ Consider clinical situation taking into account systemic inflammatory markers i.e CRP, LDH and ferritin

rapidly increasing oxygen requirement despite high flow oxygen (≥ 4L/min), respiratory distress or signs of acute respiratory distress syndrome, sepsis or other organ failure

Box 1: Dosing Recommendations

Baricitinib: Daily oral dose for up to 14 days. Modify dose according to renal function**: eGFR > 60mL/min** 4mg daily, **eGFR 30-60mL/min** 2mg daily, **eGFR 15-30mL/min** 2mg every second day. **eGFR < 15mL/min:** not recommended

Dexamethasone: 6mg oral or IV for up to 10 days (can be ceased at discharge if this is before 10 days). Seek specialist advice if on long term or high dose corticosteroids prior to admission

Remdesivir: Do not start remdesivir if > 10 days since symptom onset OR in patients on mechanical ventilation but it may be continued if commenced prior to ventilation. Dose: 200mg IV load on day 1 then 100mg IV daily for another 4 days (total 5-day course but can be ceased after 3 days if patient well enough to discharge).

Tocilizumab (ID approval required outside of ICU): IV single dose based on weight. If ≤ 40kg: **8mg/kg**, > 40kg and ≤ 65kg: **400mg**, > 66kg and ≤ 90kg: **600mg**, > 90kg: **800mg**

^VTE Prophylaxis: Recommended for all hospitalised patients with COVID-19 unless contraindicated (i.e. major bleeding). **CrCl > 30mL/min**: enoxaparin 40mg subcutaneous injection daily. **CrCl < 30mL/min**: enoxaparin 20mg subcutaneous injection daily

Note: Patients in ICU requiring initiation of these medications after hours (between 10pm and 8am) do NOT require ID approval however they should be discussed the next day during the ICU/ID COVID ward round

***Oseltamivir: CrCl >30mL/min:** 75mg orally twice daily, **CrCl 10-30mL/min**: 75mg orally once daily, **CrCl <10mL/min**: 75mg orally alternate daily for 5 days **IF** Influenza confirmed. Cease immediately if viral panel negative for influenza

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6. Assessing a patient for nirmatrelvir plus ritonavir (Paxlovid®) – contraindications and drug interaction considerations

Modified from University of Liverpool – COVID-19 Drug Interactions

Contraindications to nirmatrelvir plus ritonavir

- Age < 12 years and <40kg
- Pregnant or breastfeeding
- Solid organ transplant recipients
- Severe liver disease (i.e. Child Pugh Class C)
- Unable to swallow tablets
- Cognitively impaired or unable to manage medications
- Prescribed any of the medications **below:**

Amiodarone	Midazolam (oral)
Aliskiren	Neratinib
Apixaban*	Pethidine
Avanafil	Phenobarbital
Bosentan	Primidone
Carbamazepine	Pimozide
Ciclosporin	Phenytoin
Cisapride	Quetiapine
Clonazepam	Quinidine
Clopidogrel^	Rifampicin
Clozapine	Rivaroxaban*
Colchicine	Salmeterol*
Diazepam*	Sildenafil (for pulmonary hypertension)
Disopyramide	Simvastatin*
Domperidone*	Sirolimus
Dronedarone	Sodium fusidate
Eplerenone	St John's Wort
Everolimus	Tacrolimus
Ergometrine	Tadalafil (for pulmonary hypertension)
Flecainide	Ticagrelor
Ivabradine	Vardenafil (for pulmonary hypertension)
Lercanidipine*	Venetoclax
Lurasidone	

* Paxlovid® will increase exposure to these medications – assess if medicine can be safely stopped for 8 days.
^ Paxlovid will decrease efficacy of clopidogrel. Consider risk of thrombotic events before commencing Paxlovid®.
For more information on when medications can be recommenced check University of Liverpool COVID-19 resource page
Note: list of medications is not exhaustive and may change.

→ Yes (any contraindication): **No nirmatrelvir plus ritonavir (Paxlovid)**

→ No:

Check http://www.covid19-druginteractions.org and/or product information to check for potential drug interactions including:

- Over the counter medications including all herbal and vitamin supplements
- Recreational drugs
- Other medications including medications given infrequently or in a hospital setting including:
  - Chemotherapy or other biologic/targeted immune therapy in the last month
  - Opiate substitution
  - HCV/HBV/HIV treatment
  - Hormonal contraceptives (except implant/depot)
  - Steroid injections
  - Depot antipsychotics
  - Multiple sclerosis treatment

ANY RED or AMBER interactions?

No → **Give nirmatrelvir plus ritonavir (Paxlovid)**

Yes →

Review interaction information available on University of Liverpool COVID-19 resource page and consider the following things:

- Can the medicine be safely withheld for 8 days? E.g. simvastatin
- Can a dose adjustment be easily made? Take into account patient understanding, use of compliance aids such as webster packs and whether different strengths of medication(s) will be required.
- Will the patient understand if advised of adverse reactions to monitor for and what to do if they occur?
- How long since intervention has occurred? I.e. clopidogrel

Clinical decision based on all the individual patient information, discussion with specialist if required and patient to determine if nirmatrelvir plus ritonavir is appropriate.

Yes → **Give nirmatrelvir plus ritonavir (Paxlovid)**

No → **No nirmatrelvir plus ritonavir (Paxlovid)**

Medications unlikely to interact or to have a significant interaction with nirmatrelvir plus ritonavir

ACE inhibitors
Acid reducing agents (antacids, PPIs, histamine receptor antagonists)
Aspirin
Azathioprine
Beta blockers
Corticosteroids (oral, inhaled, topical)
Fluvastatin
Furosemide
Gabapentin
HRT/Contraceptive implant or depot
Immunoglobulin
Inhalers (except salmeterol)
Insulin
Levothyroxine
Metformin
Methotrexate
Monoclonal antibodies (mAbs)
Mycophenolate
Non-steroidal anti-inflammatories (NSAIDs)
Pravastatin
Pregabalin

Give nirmatrelvir plus ritonavir (Paxlovid)

Nirmatrelvir plus ritonavir (Paxlovid®) dosing

eGFR > 60 mL/min:
300mg nirmatrelvir (2x150mg capsules) + 100mg ritonavir (1x100mg capsule) twice daily for 5 days.

eGFR < 60mL/min:
150mg nirmatrelvir (1x150mg capsule) + 100mg ritonavir (1x100mg capsule) twice daily for 5 days – use with caution in patients with eGFR < 30ml/min (see drug monograph)

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7. COVID-19 treatment recommendations for hospitalised pregnant and breastfeeding adult patients

(refer to Box 3 for dosing recommendations)

See page 10 for information on prescribing restrictions and access to therapies in CALHN

NOTE 1: There is limited evidence for disease modifying therapies in pregnant and breastfeeding patients and the decision to treat should be based on risk factors for progressing to severe illness (as listed in Box 2) taking into account the harm benefit ratio for both mother and fetus. Seek advice from ID.

Mild illness not requiring oxygen	**Moderate illness** on supplemental oxygen	**Severe illness** high flow oxygen	**Critical illness** non-invasive ventilation or mechanical ventilation

VTE Prophylaxis (recommended for all hospitalised patients with COVID-19 unless contraindication e.g. major bleeding)
Consider empiric influenza treatment* until results of respiratory viral panel available

For all patients with moderate to critical illness consider corticosteroid e.g. dexamethasone (obtain guidance from obstetric medicine for preferred corticosteroid in pregnancy; prednisolone or hydrocortisone may be preferred first – for appropriate dose conversion see here. Seek specialist advice for patients taking long term or high dose corticosteroids prior to admission)

immunosuppressed (regardless of vaccination status) **OR** unvaccinated or vaccination status not up to date (Box 1) with one or more risk factor(s) for progressing to severe illness (Box 2) **All patients must be ≤ 7 days since symptom onset** 1st trimester: **Contact ID** 2nd or 3rd trimester or breastfeeding: **remdesivir*** (discuss with ID if patient is ineligible/declines remdesivir therapy)	**remdesivir** **PLUS** If no improvement (e.g. evidence of systemic inflammation) or increasing oxygen requirement **tocilizumab**	**remdesivir** **PLUS** If elevated markers of systemic inflammation **tocilizumab**	If elevated markers of systemic inflammation **tocilizumab** Continue **remdesivir** if commenced prior to ventilation

Box 1: Definition of "not up to date" vaccine status: Unvaccinated **OR** single dose vaccination **OR** less than 2 weeks since primary course of COVID-19 vaccination **OR** less than 7 days since first booster vaccination **OR** ≥ 3 months since primary COVID-19 vaccination course with no booster vaccination. Refer to the Australian Immunisation Handbook for recommendations regarding COVID-19 vaccination in pregnancy

Box 2: Risk factors for progressing to severe illness (see page 4 for more detail): Immunosuppressed, diabetes/gestational diabetes, obesity (BMI >40kg/m^2), renal impairment , coronary artery disease, cardiomyopathies or heart failure, respiratory compromise, chronic liver disease (cirrhosis), disability with multiple comorbidities and/or frailty , reduced, or lack of, access to higher level healthcare and lives in an area of geographic remoteness classified by the Modified Monash Model as Category 5 or above neurological diseases including: dementia, stroke, demyelinating conditions (i.e. multiple sclerosis), past COVID-19 infection episode resulting in hospitalisation

Box 3: Dosing Recommendations

Dexamethasone: 6mg orally or IV for up to 10 days (can be ceased at discharge if this is before 10 days).

Remdesivir* (mild illness): 200mg IV on day 1 then 100mg on day 2 and 3. 3 day course only).

Remdesivir* (moderate to critical illness): 200mg IV load on day 1 then 100mg IV daily for another 4 days (total 5 day course but can be ceased after 3 days if patient well enough to be discharged). There is a paucity of evidence of efficacy for remdesivir in COVID-19 infection. Consider using remdesivir for selected pregnant or breastfeeding patients hospitalised with moderate to severe COVID-19 illness who do not require ventilation, with ID guidance. Pregnant patients were excluded from all clinical trials of remdesivir in COVID-19.

Tocilizumab: IV single dose based on weight at the time of clinical need. If ≤ 40kg: 8mg/kg, > 40kg and ≤ 65kg: 400mg, > 66kg and ≤ 90kg: 600mg, > 90kg 800mg

VTE Prophylaxis: Enoxaparin 40mg subcut injection daily if CrCl > 30mL/min or enoxaparin 20mg subcut injection daily if CrCl < 30mL/min. VTE prophylaxis should also be considered for pregnant women with mild disease with any of the following risk factors for VTE: prior VTE, age > 35 years, BMI > 40 or BMI > 30 with another risk factor for VTE, blood dyscrasias or smoker

***Oseltamivir:** **CrCl >30mL/min:** 75mg orally twice daily, **CrCl 10-30mL/min**: 75mg orally once daily, **CrCl <10mL/min**: 75mg orally alternate daily for 5 days **IF** Influenza confirmed. Cease immediately if viral panel negative for influenza

NOTE 2: Given the limited data in pregnant and breastfeeding patients, **baricitinib** should only be used in clinical trials. Molnupiravir and nirmatrelvir plus ritonavir are not recommended in pregnant or breastfeeding women.

NOTE: If corticosteroids are required for fetal lung maturity in women at risk of preterm birth obtain guidance from obstetric medicine regarding the appropriate steroid and dose to be prescribed.

8. Approach to the treatment of immunocompromised patients with persistent or relapsed COVID-19 infection[38, 39,40,41]

Active, persistent COVID-19 infection can uncommonly occur in immunocompromised patients. Immunocompromised patients with persistent COVID-19 infection will often test positive on COVID-19 PCR testing for weeks to months with a low cycle threshold (CT) value which may indicate replicating, transmissible virus. Patients most at risk of persistent infection include those with severe B-cell depletion due to cancer therapy (ie patients treated with anti-CD 20 monoclonal antibodies within the previous 6-12 months and/or haematopoietic stem cell transplant recipients).

There is limited data about the optimal management of patients with persistent COVID-19 infection. Small observational studies and case reports suggest some efficacy with combination antiviral treatment and/or extended courses of antiviral medications however therapeutic management remains challenging and there are no guidelines currently available.

All patients with persistent COVID-19 infection should be seen as a formal consult by Infectious Diseases. The use of combination antiviral therapy, antiviral treatments more than 10 days after initial symptom onset or antiviral treatment courses beyond 5 days for nirmatrelvir/ritonavir and 10 days for remdesivir is “off-label” and will require an IPU as well as patient consent.

9. Access and restrictions

Disease-modifying therapy	ID Approval required*	Available on PBS for COVID-19	Registered in Australia for COVID-19	Verbal Consent required@	After hours access Available¥
Baricitinib	No*	No	No – off label use	Yes	Yes
Dexamethasone	No	No	No – off label use	Yes	Yes
Molnupiravir	No*	Yes	Provisionally	Yes	No
Nirmatrelvir plus ritonavir	No*	Yes	Provisionally	Yes	No
Remdesivir#	No*	No	Provisionally	Yes	Yes
Tocilizumab*	Yes	No	Provisionally	Yes	4G178 (fridge)

@ Informed consent should be obtained for the use of medicines to treat COVID-19, especially those that are unregistered or used in an off-label manner. The consent should be documented in the patient’s Health Record, including when verbal informed consent is obtained. More information regarding where consent is recommended or required can be found here.

¥ After hours availability may change according to usage, patient numbers and stock availability. Molnupiravir and nirmatrelvir plus ritonavir are not available after hours (unless the patient is day 5 of symptoms, it can be dispensed the next day). If stock not available in machines mentioned above after searching “global find” in ADC then please contact on-call pharmacist on pager 22161

* ID approval not required for baricitinib, remdesivir, molnupiravir, nirmatrelvir plus ritonavir if prescribed in line with recommendations within these guidelines. Tocilizumab requires ID approval except when given overnight in ICU.

During business hours (7 days per week 8:45am-5pm)

- Place a medication requisition order through Sunrise and mark as urgent
- Contact in-patient pharmacy (ext. 44988) to arrange stock delivery/collection

10. Treatments for COVID-19 – Drug Monographs

Nirmatrelvir plus Ritonavir (Paxlovid®) [1,7,15,16, 35 , 35, 37,47,49, 50,51]

Patient consent required (verbal or written).

Stock not available after hours in CALHN

For more detailed information on the use of nirmatrelvir plus ritonavir in patients with COVID-19 visit the product information available on the TGA website

Drug Class	• Nirmatrelvir is a protease inhibitor that blocks the activity of the SARS-CoV-2-3CL protease thus inhibiting viral replication. Low dose ritonavir is given concurrently with nirmatrelvir as a 'booster' to maintain nirmatrelvir plasma levels during treatment through inhibition of the CYP3A4 mediated metabolism of nirmatrelvir.
Indications	• First line treatment of mild COVID-19 for non-pregnant adults who do NOT require supplemental oxygen and are ≤ 5 days since symptom onset AND: ○ Are immunosuppressed (regardless of vaccination status or age) **OR** ○ Have previously experienced COVID-19 infection requiring hospitalisation (regardless of vaccination status or age) **OR** ○ Aged < 50 years (or < 30 years if Aboriginal or Torres Strait Islander) **with** TWO or more risk factors for severe or critical illness (regardless of vaccination status) **OR** ○ Aged 50 to 69 years with TWO or more risk factors for severe or critical illness (regardless of vaccination status) **OR** ○ Aboriginal or Torres Strait Islander AND aged ≥ 30 years with ONE or more risk factors for severe or critical illness (regardless of vaccination status) **OR** ○ Aged ≥ 70 years regardless of vaccination status or risk factors for progressing to severe or critical illness • **Check for contraindications and drug interactions before prescribing.** • Treatment should not be commenced in hospitalised patients with severe or critical COVID-19 illness, however the course can be completed if commenced prior to initiation of supplemental oxygen or hospitalisation.
Contra-indications	• Hypersensitivity to nirmatrelvir or ritonavir or any of the excipients listed in the product information. • Children less than 12 years old and weighing <40kg • **Pregnancy** – the use of nirmatrelvir plus ritonavir in pregnant patients is not recommended as there is no human data to evaluate the drug-associated risk of adverse developmental outcomes. Women of childbearing age should be advised to use effective contraception for the duration of treatment and for 7 days after the last dose of nirmatrelvir plus ritonavir. These recommendations are based on animal studies, the use of nirmatrelvir has not been assessed in human trials. • **Breastfeeding** – limited data. Based on the potential for adverse reactions on the infant, breastfeeding is not recommended during AND for 7 days after treatment. • **Contraception** – Ritonavir may reduce the efficacy of combined hormonal contraceptives therefore alternative contraceptive methods or additional barrier protection is advised during treatment and for one full menstrual cycle after completing the nirmatrelvir plus ritonavir course. • **Severe hepatic impairment** – avoid due to insufficient data.

	• **Drug interactions**
	  ○ Co-administration of medications that are highly dependent on CYP3A4 for clearance and could be associated with serious/life-threatening reactions with elevated serum concentrations. See below for examples.
	  ○ Co-administration of medications which are potent CYP3A4 inducers which can result in significantly reduced plasma concentrations of nirmatrelvir plus ritonavir and could be associated with loss of virologic response and possible resistance. See below for examples.

Precautions	• **Severe renal impairment** (eGFR < 30 mL/min) – use with caution. Dose recommendations are from the Renal Drug Database and are based on a study from Wales with small numbers of patients with end stage renal disease (ESRD). In this study patients with ESRD taking this dose experienced no serious adverse effects. • Exercise caution in patients with a history of anaphylaxis to other medicines. • **Hepatotoxicity** - Caution should be exercised in patients with pre-existing liver disease, or hepatitis. Hepatic transaminase elevations, clinical hepatitis and jaundice have been reported in patients using ritonavir. • **Risk of HIV-1 Resistance Development** - Due to the co-administration of low dose ritonavir, there may be a risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection.
Storage and presentation	• This is a combination therapy. The two components are provided as individual, co-packaged medications. **Each package contains 30 tablets in total**; 20 x 150mg nirmatrelvir tablets, and 10 x 100mg ritonavir tablets. This is the supply required to complete the standard adult 5-day course. • Store at room temperature, less than 25^{o}C
Dose	• **eGFR ≥ 60mL/min/1.73m^2**: Nirmatrelvir 300mg (two 150mg tablets) with ritonavir 100mg (one 100mg tablet) taken together orally every 12 hours for 5 days. • **eGFR < 60 mL/min/1.73m^2**: Nirmatrelvir 150mg (one 150mg tablet) with ritonavir 100mg (one 100mg tablet) taken together orally every 12 hours for 5 days. See precautions section above for patients with eGFR < 30mL/min/1.73m^2 No dose adjustment is required for patients with mild or moderate hepatic impairment. Avoid use in patients with severe hepatic impairment.

Administration	• Where possible swallow the tablets whole, with or without food.
	• There is little information regarding the safety or efficacy of nirmatrelvir plus ritonavir when tablets are crushed or dispersed, however the following instructions have been provided for those with swallowing difficulties or enteral feeding tubes:
	  ○ For patients with swallowing difficulties:
	  1. Disperse the nirmatrevir tablet(s) in water OR if the patient is unable to swallow thin fluids, crush the nirmatrelvir tablet(s) and mix with a spoonful of yoghurt or apple puree.
	  2. Crush the ritonavir tablet and mix with water, or a spoonful of yoghurt or apple puree.
	  ○ For patients with enteral feeding tubes:
	  1. Flush the tube with 30mL of water.
	  2. Disperse the nirmatrelvir tablet(s) in 10-20mL of water in an enteral syringe. The tablet(s) will form a milky, light pink dispersion within a few minutes.
	  3. Check carefully that the tablet(s) is completely dispersed and then give via enteral tube.
	  4. Flush tube with 5mL of water.
	  5. Crush the ritonavir tablet and mix with water, then draw into an enteral syringe.

<table>
<tr><td></td><td>
6. Give the mixture via enteral tube ensuring all the mixture has been administered.
7. Flush the tube with 30mL of water.

• If a dose of nirmatrelvir and ritonavir is missed within eight hours of the time it is usually taken, this dose should be taken as soon as remembered. If a dose is missed by more than eight hours, this dose should be skipped, and the next dose taken at the regular time. The dose should not be doubled up to make up for the missed doses of nirmatrelvir and ritonavir.

• The blister strips for Paxlovid® contain two tablets of nirmatrelvir and one tablet of ritonavir corresponding to the daily administration at the standard dose (morning and night doses are separated within the same blister strip). Therefore, patients with moderate renal impairment should be alerted to the fact that only one tablet of nirmatrelvir should be taken every 12 hours (with the tablet of ritonavir).
</td></tr>
<tr><td>Monitoring</td><td>
• Baseline creatinine, electrolytes and urea, LFTs and complete blood exam.
• Monitor the patient for adverse effects.
• If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue and initiate appropriate medications and/or supportive care.
</td></tr>
<tr><td>Adverse Effects</td><td>
• It may be difficult to distinguish between adverse effects of nirmatrelvir or ritonavir and the signs and symptoms of COVID-19.
• As a new medication, adverse reactions to nirmatrelvir continue to be investigated. Refer to the Paxlovid® product information for a complete list of possible adverse effects.
• To date the most common adverse reactions reported include:
  ○ altered sense of taste
  ○ headache
  ○ diarrhoea
  ○ vomiting
  ○ hypertension
  ○ myalgia
• Suspected or confirmed adverse reactions should be reported via Safety Learning System and also via the Therapeutic Goods Administrations adverse effects online form: TGA adverse event reporting
</td></tr>
<tr><td>Patient Information / consent forms</td><td>
• Nirmatrelvir plus ritonavir patient information leaflets can be found here
</td></tr>
<tr><td>Drug Interactions</td><td>
• Ritonavir has many drug-drug and drug-herbal interactions which are complex and can be difficult to predict. Ritonavir is known to inhibit and induce CYP3A4 as well as many other CYP enzymes. It is also a strong inducer of UGT enzymes that mediate glucuronidation.
• Always check the University of Liverpool COVID-19 resource page or Up-To-Date interaction checker prior to prescribing nirmatrelvir plus ritonavir.
• Some of the more significant interactions are listed below however this is not an exhaustive list and information may change over time. Where it states ‘consider risk vs benefit’ refer to the Australian Medicines Handbook, the Liverpool resource page, Up-To-Date interaction checker or the Paxlovid® product information for more information on the mechanism of the interaction.
<table>
<tr><th>Medicine</th><th>Recommendation</th><th></th><th>Medicine</th><th>Recommendation</th></tr>
<tr><td>Abemaciclib</td><td>Consider risk vs benefit</td><td></td><td>Acalabrutinib</td><td>Consider risk vs benefit</td></tr>
<tr><td>Apalutamide</td><td>Consider risk vs benefit</td><td></td><td>Amiodarone</td><td>Do not use</td></tr>
<tr><td>Avanafil</td><td>Do not use</td><td></td><td>Apixaban</td><td>Do not use*</td></tr>
<tr><td>Bosentan</td><td>Do not use</td><td></td><td>Bedaquiline</td><td>Consider risk vs benefit</td></tr>
<tr><td>Carbamazepine</td><td>Do not use</td><td></td><td>Budesonide</td><td>Consider risk vs benefit</td></tr>
<tr><td>Ciclosporin</td><td>Do not use</td><td></td><td>Ceritinib</td><td>Consider risk vs benefit</td></tr>
</table>
</td></tr>
</table>

Clonazepam	Do not use		Cisapride	Do not use
Clozapine	Do not use		Clopidogrel	Do not use^
Contraceptives	Consider risk vs benefit		Colchicine	Do not use
Delamanid	Consider risk vs benefit		Dabigatran	Consider risk vs benefit
Diazepam	Do not use*		Dexamphetamine	Consider risk vs benefit
Disopyramide	Do not use		Digoxin	Consider risk vs benefit
Domperidone	Do not use*		Dronedarone	Do not use
Encorafenib	Consider risk vs benefit		Eletriptan	Consider risk vs benefit
Eplerenone	Do not use		Enzalutamide	Consider risk vs benefit
Everolimus	Do not use		Ergometrine	Do not use
Flecainide	Do not use		Fentanyl	Consider risk vs benefit
Ibrutinib	Consider risk vs benefit		Fluticasone	Consider risk vs benefit
Ivabradine	Do not use		Illegal drugs	Check Liverpool page
Lamotrigine	Consider risk vs benefit		Ketoconazole	Consider risk vs benefit
Letermovir	Consider risk vs benefit		Lercanidipine	Do not use
Lurasidone	Do not use		Levothyroxine	Consider risk vs benefit
Methylphenidate	Consider risk vs benefit		Methadone	Consider risk vs benefit
Neratinib	Do not use		Midazolam	Do not use
Phenobarbital	Do not use		Pethidine	Do not use
Piroxicam	Do not use		Phenytoin	Do not use
Pimozide	Do not use		Primidone	Do not use
Quinidine	Do not use		Quetiapine	Do not use
Rifampicin	Do not use		Rifabutin	Consider risk vs benefit
Rivaroxaban	Do not use*		Riociguat	Consider risk vs benefit
Salmeterol	Do not use*		Rosuvastatin	Consider risk vs benefit
Simvastatin	Do not use*		Sildenafil	Do not use
Sodium fusidate	Do not use		Sirolimus	Do not use
Tacrolimus	Do not use		St John's Wort	Do not use
Theophylline	Consider risk vs benefit		Tadalafil	Do not use
Vardenafil	Do not use		Ticagrelor	Do not use
Venetoclax	Do not use		Valproate	Consider risk vs benefit
Vincristine	Consider risk vs benefit		Vinblastine	Consider risk vs benefit
Warfarin	Consider risk vs benefit		Voriconazole	Consider risk vs benefit

*unless medicine can be safely stopped for 8 days. For more information re when medications can be recommenced check University of Liverpool COVID-19 resource page

^ Paxlovid will decrease efficacy of clopidogrel. Consider risk of thrombotic events before commencing Paxlovid.

Molnupiravir (Lagevrio®) [1,7,14,17,20]

Patient consent (verbal or written) required

Stock not available after hours in CALHN

For more detailed information on the use of molnupiravir in patients with COVID-19 visit the product information available on the TGA website

Drug Class	• Antiviral pro-drug, which once metabolised to an active ribonucleoside triphosphate (NHC-TP), is incorporated into SARS-CoV-2 viral RNA resulting in an accumulation of transcribed mutations with each viral replication cycle, thus inhibiting further replication.
Indications	The National Clinical Evidence Taskforce recommends against routine use of molnupiravir except in specific circumstances and where all other treatment options are contraindicated OR inappropriate, based on the results of the PANORAMIC Trial. The median age of patients in the PANORAMIC trial was 56 years (younger than target treatment groups in Australia) and a reduction in time to recovery was shown for all patients and trend to reduced hospitalisation/death in patients aged ≥ 80 years. The AMS Committee note recent Victorian data which showed a reduction in hospitalisation and death in patients aged ≥ 70 years who received molnupiravir. Molnupiravir should continue to be considered when nirmatrelvir/ritonavir and/or remdesivir are contraindicated, inappropriate or inaccessible. Consider risk versus benefits of molnupiravir as limited evidence in patients < 70 years. For patients aged < 70 years who are contraindicated from taking nirmatrelvir/ritonavir and/or

	remdesivir, only prescribe molnupiravir if benefits outweigh risks AND appropriate reproductive counselling can be provided • Second or third line treatment of mild COVID-19 for non-pregnant adults where nirmatrelvir plus ritonavir AND remdesivir are not available or contraindicated and benefits of treatment outweigh risks and appropriate reproductive counselling is provided. Patients must have symptom onset of no more than 5 days, not require supplemental oxygen and be: ○ Immunosuppressed irrespective of vaccine status **OR** ○ Aged ≥ 70 years irrespective of vaccination status or risk factors for progressing to severe or critical illness **OR** ○ Aged 50 to 69 years PLUS ≥ 2 risk factors for progressing to severe or critical illness (irrespective of vaccination status) ○ **OR** ○ A past COVID-19 infection requiring hospitalisation **OR** ○ Aboriginal or Torres Strait Islander and aged ≥ 30 years PLUS ≥ 1 risk factor for progressing to severe or critical illness (irrespective of vaccination status) **OR** ○ Aged < 50 years or < 30 years if Aboriginal or Torres Strait Islander **PLUS** ≥ 3 risk factors) for progressing to severe or critical illness (irrespective of vaccination status) • Treatment should not be commenced in hospitalised patients with severe or critical COVID-19 illness, however the course can be completed if commenced prior to initiation of supplemental oxygen or hospitalisation.
Contra-indications	• Hypersensitivity to molnupiravir or any of the excipients in the product. • Children less than 18 years old • **Pregnancy** – the use of molnupiravir in pregnant patients is **not recommended** due to potential risk of reduced foetal growth and development. • **Breastfeeding** – it is unknown whether molnupiravir is present in human breastmilk, affects breastmilk production, or has an effect on the breastfed infant. Based on the potential for adverse reactions on the infant, breastfeeding is **not recommended** during AND for 4 days after treatment. • **Contraception -** Prescribers should consider a pregnancy test prior to commencement of therapy. Advise women of childbearing potential to use effective contraception for the duration of treatment and for 4 days after the last dose of molnupiravir. Advise men who are sexually active with a partner of childbearing potential to use an adequate form of contraception during and 3 months after treatment with molnupiravir.
Precautions	• Exercise caution in patients with a history of anaphylaxis to other medicines. • **Renal Impairment -** Patients with eGFR < 30mL/min and patients on dialysis were excluded from the Phase 3 MOVe-OUT trial. Molnupiravir is a prodrug hydrolysed to NHC. The fraction of dose excreted as NHC was ≤ 3% therefore renal impairment is not expected to have a significant effect on NHC exposure. • **Hepatic impairment -** the pharmacokinetics of molnupiravir and NHC has not been evaluated in patients with hepatic impairment. Hepatic elimination is not expected to be a major route of NHC elimination.
Drug Interactions	• No formal interaction studies have been conducted with molnupiravir

	• The metabolite of molnupiravir is not a substrate of major drug metabolising enzymes or transporters. Neither molnupiravir nor its substrate are inhibitors or inducers of major drug metabolising enzymes or transporters. • While the potential for drug interactions with molnupiravir are considered unlikely, as this is a new drug, continue to check the University of Liverpool COVID-19 resource page
Presentation and storage	• Available as 200mg capsules supplied as a bottle of 40 capsules. • Store at room temperature, less than 30^{o}C
Dose	• 800mg (4 x 200mg capsules) orally 12-hourly for 5 days • No dose adjustment is required for renal or hepatic impairment or the elderly (see precautions above). • If the patient misses a dose of molnupiravir within 10 hours of the time it is usually taken, the patient should take it as soon as possible and resume the normal dosing schedule. If a patient misses a dose by more than 10 hours, the patient should not take the missed dose and instead take the next dose at the regularly scheduled time. The patient should not double the dose to make up for a missed dose.

Administration	• Capsules can be taken with or without food.
	• Administration of molnupiravir via an oral solution has not been evaluated in clinical trials however the following advice has been provided for patients with swallowing difficulties and or for administration via an enteric tube.
	• Preparation of the solution:
	  ○ Open FOUR (4) capsules and transfer contents into an oral syringe. Discard empty capsule shells
	  ○ Add approximately 40 mL of water to the oral syringe.
	  ○ Mix/stir the capsule contents and water for 3 minutes.
	  1. Insoluble capsule contents may not dissolve completely.
	  2. Reconstituted solutions prepared according to directions may have visible undissolved particulates and are acceptable for oral administration.
	  ○ Administration should occur as soon as possible after the preparation and no later than 2 hours after the preparation.
	• For administration via enteral tube:
	  ○ Prior to administration redisperse the suspension by mixing or stirring the oral syringe for 1 minute prior to administration
	  ○ Flush enteral tube with 5 mL of water prior to administration.
	  ○ Administer entire volume from the administration syringe.
	  ○ Flush tube with 5 mL of water TWICE (10 mL total) after administration of the suspension.

Handling	• Occupational exposure to non-intact tablets may be harmful. Staff who are actively trying to conceive or who are pregnant or breastfeeding should not prepare or handle a dispersed dose. • For all other staff, use standard Personal Protective Equipment (PPE) if preparation or administration of a dispersed tablet is required.
Monitoring	• Baseline creatinine, electrolytes and urea, LFTs and complete blood exam. • Monitor the patient for adverse effects. • If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue and initiate appropriate medications and/or supportive care.
Adverse Effects	• It may be difficult to distinguish between adverse effects of molnupiravir and the signs and symptoms of COVID-19. • As a new medication, adverse reactions to molnupiravir continue to be investigated. Refer to the product information for a complete list of possible adverse effects. To date reactions include: ○ Common (>1%): diarrhoea, nausea, dizziness, headache

	○ Uncommon (0.1-1%): rash, urticaria • Suspected or confirmed adverse reactions should be reported via Safety Learning System and also via the Therapeutic Goods Administrations adverse effects online form: TGA adverse event reporting
Patient Information and consent forms	• Molnupiravir patient information leaflets can be found here (IH-CIS05843)

Remdesivir[1,2,5,7,8,10,11,12,25, 45, 46,48] **Patient consent (verbal or written) required** **For more detailed information on the use of remdesivir in patients with COVID-19 visit the product information available on the TGA website**	
Drug Class	• Antiviral, a nucleotide analogue prodrug that binds to the viral RNA-dependent RNA polymerase and inhibits viral replication through premature termination of RNA transcription.
Indications	• **Treatment of mild COVID-19 Illness:** • Second line treatment (when nirmatrelvir plus ritonavir is contraindicated or not suitable) of mild COVID-19 for non-pregnant adult patients who do not require supplemental oxygen and are **within 7 days of symptom onset** **AND** ○ Are immunosuppressed (regardless of vaccination status) **OR** ○ Have previously experienced COVID-19 infection requiring hospitalisation (regardless of vaccination status or age) **OR** ○ Aged 50 to 69 years with **TWO** or more risk factors for progressing to severe illness **OR** ○ Aged ≥ 30 years if Aboriginal and/or Torres Strait Islander irrespective of vaccination status with **ONE** or more risk factors for progressing to severe illness **OR** ○ Aged ≥ 70 years irrespective of vaccination or risk factors for progressing to severe illness **OR** ○ Aged < 50 years or < 30 if Aboriginal and/or Torres Strait Islander **with THREE** or more risk factors for progressing to severe illness (regardless of vaccination status) • Treatment of breastfeeding or pregnant patients in their second or third trimester **within 7 days of symptom onset** and do not require supplemental oxygen AND: ○ Are immunosuppressed irrespective of vaccine status **OR** ○ Who have reduced immunity to COVID-19 e.g. not vaccinated or do not have an up-to-date vaccine status **AND** who have one or more risk factors for progressing to severe or critical illness. • **Treatment of moderate to critical illness:** ○ Remdesivir may be considered for patients with a confirmed diagnosis of COVID-19 or known contact of a confirmed case with syndrome consistent with COVID-19 awaiting confirmation by diagnostic testing; **AND**

	○ Aged ≥ 18 years, or aged 12 to 17 years and weighing > 40 kg; **AND** ○ With oxygen saturation ≤ 92% on room air and requiring supplemental oxygen; **AND** ○ ≤ 10 days since symptom onset ○ For use in moderate disease vaccination status of the patient does NOT matter • Remdesivir is **NOT** indicated for patients requiring invasive mechanical ventilation or ECMO, although it may be continued if it was started prior to ventilation commencing. • Unless corticosteroids are contraindicated (see dexamethasone monograph above), remdesivir should be given in conjunction with dexamethasone for patients requiring supplemental oxygen (i.e. patients being treated for moderate to critical COVID-19) • Remdesivir is available via the National Medical Stockpile and availability is expected to fluctuate with demand and constraints in the supply chain. In the context of shortages remdesivir should be reserved for those patients who will likely benefit the most including: ○ ≤ 7 days since symptom onset ○ Not requiring high flow nasal oxygen ○ Life expectancy greater than ONE year
Contra-indications	• Known hypersensitivity to any ingredient of remdesivir product or remdesivir metabolites. • Mechanical ventilation for >48 hours at the time of commencement. • Hepatic impairment: ALT ≥ 5 times the upper normal limit (ULN) at baseline. • Patients with evidence of multiorgan failure, including coagulopathy (significant thrombocytopenia), hepatic failure, renal failure or significant cardiomyopathy are not eligible to access remdesivir from the National Medicines Stockpile (NMS).
Precautions	• Severe Renal impairment[1]: eGFR < 30mL/min/1.73m^2 ○ Formulated with the excipient sulfobutyl betadex sodium (SBECD) which accumulates in renal impairment. For most patients with an eGFR < 30mL/min/1.73m^2 the benefit of treatment will outweigh the risks of treatment as the reported toxic doses of SBECD are 50-100 times higher than exposure during a 5-10 day course of remdesivir. ○ The Renal Drug Database and FDA have recently updated dosing recommendations for patients with eGFR < 30mL/min/1.73m^2 and both state remdesivir can be used in patients with eGFR < 30mL/min/1.73m^2 without need for dose adjustment. • Factors where the benefit of remdesivir is uncertain & requires careful consideration before use: ○ Presence of an intercurrent illness likely to lead to patient death within one year; ○ Advanced age with limitations on activities of daily living; ○ Need for more than a 5 day treatment course (not available via NMS).
Drug Interactions	• Drug-drug interaction trials of remdesivir and other concomitant medications have not been conducted in humans. Remdesivir is a substrate for several drug metabolising enzymes however clinical relevance of these interactions has not been established. • Use with hydroxychloroquine or chloroquine is not recommended as it may reduce antiviral activity of remdesivir.

[1] NOTE: Dose adjustments are based on eGFR (CKD-EPI). For patients with extremes of body size, multiply the eGFR by the patient's body surface area (in m^2) and divide by 1.73 m^2

	• For detailed information regarding drug interactions with remdesivir please check the University of Liverpool COVID-19 resource page.

Preparation	• There are 2 preparations available in Australia via the NMS:
	  ○ Powder for injection
	  ▪ 100 mg sterile, preservative-free, white to off-white to yellow lyophilised powder vial.
	  ▪ Requires storage below 30°C.
	  ▪ Contains sulfobutyl betadex sodium (SBECD 3 g), hydrochloric acid & sodium hydroxide.
	  ○ Concentrated solution vial
	  ▪ 100 mg/20 mL concentrate solution (clear colourless to yellow) vial; sterile preservative-free.
	  ▪ Requires refrigerated storage at 2–8°C.
	  ▪ Stable for up to 12 hours at room temperature (20–25°C) prior to dilution.
	  ▪ Contains sulfobutyl betadex sodium (SBECD 6 g), hydrochloric acid & sodium hydroxide.
	  ▪ Concentrated solution not recommended in children < 12 years of age or adolescents weighing <40kg

Dose	• **Mild illness:** 200mg via IV infusion on day 1, then 100mg IV daily for a further 2 days (total 3 days treatment). • **Moderate to critical illness:** 200mg via IV infusion on day 1, then 100mg IV daily for a further 4 days (total 5 days treatment). Can be ceased after 3 days of therapy if patients are well enough to be discharged i.e. no longer requiring supplemental oxygen.
Administration	• There are different formulations of remdesivir available via the NMSand administration instructions may vary. • For administration details please refer either to the Australian Injectables Drugs Handbook and the NSW Therapeutic Advisory Group page on remdesivir.

Monitoring	• As experience with remdesivir at these doses and for this duration is limited patients should have appropriate clinical and laboratory monitoring including:
	  ○ Baseline and daily creatinine, electrolytes, urea, LFTs and complete blood exam
	  ▪ Discontinue remdesivir if:
	  ➢ eGFR < 30mL/min/m^2 (contact ID to discuss risk vs benefit)
	  ➢ ALT ≥ 5 times ULN during treatment with remdesivir (remdesivir may be restarted when ALT is < 5 times ULN), OR
	  ➢ ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR.
	  ○ Perform baseline and DAILY coagulation profile testing, including prothrombin time.
	  ○ Heart rate
	  ○ Observe for infusion-related reactions. If present, immediately discontinue administration of remdesivir and initiate supportive therapy if required.

Adverse Effects	• As experience with remdesivir at these doses and for this duration is limited patients it is important to document and report all suspected adverse effects. To date, the following adverse effects have been observed: ○ Very common (>10%): graded elevations in ALT, AST and bilirubin.

	○ Common (>1%): prolonged prothrombin time, gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea), headache, rash. ○ Rare (<0.1%): hypersensitivity reactions (anaphylactic reactions are rare but are a medical emergency; stop the infusion and begin treatment immediately). • Infusion-related reactions may include hypotension, nausea, vomiting, diaphoresis, shivering. • Post-marketing adverse effects reported include bradycardia (including severe bradycardia and sinus bradycardia), cardiac failure and hypotension. • Suspected or confirmed adverse reactions should be reported via Safety Learning System and also via the Therapeutic Goods Administrations adverse effects online form: TGA adverse event reporting.
Patient information and consent forms	• CALNH Remdesivir Consumer Information leaflets can be found here • Remdesivir patient information leaflets are also available via the NSW Clinical Excellence Commission

Dexamethasone[1,2,5,7,9,11]

For more detailed information on the use of dexamethasone in patients with COVID-19 visit the COVID-19 National Clinical Evidence Taskforce Guidelines

Drug Class	• Corticosteroid
Indications	• Dexamethasone is recommended for all adult patients with confirmed COVID-19 infection AND are receiving oxygen (including mechanically ventilated patients). • Do not routinely use in patients with COVID-19 who do not require oxygen.
Contra-indications	• Hypersensitivity to dexamethasone or any excipients of the tablet or injection or to other corticosteroids. • Concomitant administration of live virus vaccines (risk of severe systemic infection).
Precautions	• Seek specialist advice for patients taking long term or high dose corticosteroids prior to admission ○ Patients with primary or secondary adrenal insufficiency, rheumatologic and other chronic conditions treated with corticosteroids may not be able to mount a normal stress response in the event of COVID-19 infection. Administration of physiologic stress doses of corticosteroids may need to be considered to avoid potentially fatal adrenal failure. • Pregnancy: corticosteroid treatment is recommended for the treatment of moderate/severe or critical COVID-19 infections. Choice of steroid should be guided by Obstetric Medicine, Infectious Diseases and ICU (if required) at the time of treatment. Patients may be offered dexamethasone or prednisolone depending on their gestation, pregnancy details, comorbidities and other illness factors. • Given the short duration of treatment for COVID-19 many of the recognised precautions for the use of corticosteroids may not apply. • The treating doctor should assess if treatment with dexamethasone puts the patient at substantial risk of harm due to concurrent (non COVID-19) infection. This assessment must not delay treatment with dexamethasone. • For a full list of precautions and considerations for special populations such as pregnancy and breastfeeding please visit the dexamethasone drug guideline available via the NSW Therapeutic Advisory Group.

Drug Interactions	• Dexamethasone is a moderate inducer of CYP3A4 and P-glycoprotein (P-gp) and a substrate for CYP3A4. Use with CYP3A4 inhibitors may increase dexamethasone concentrations, while use with CYP3A4 inducers may decrease dexamethasone concentrations and efficacy. • The effects of anticoagulant agents are usually decreased (but may be increased in some patients) with concurrent corticosteroid treatment. Close monitoring of the INR or prothrombin time is recommended. • Concomitant use of drugs that irritate the gastrointestinal lining with dexamethasone may increase the risk of peptic ulceration and bleeding. • For more detailed information regarding drug interactions with dexamethasone check the University of Liverpool COVID-19 resource page.
Preparation	• Intravenous formulations: 4mg/mL or 8mg/2mL • Oral formulation: 4mg and 0.5mg tablets

Dose and administration	• 6mg via intravenous injection or 6mg orally with food ONCE daily for up to 10 days*
	  ○ If giving via intravenous injection give as a slow injection over 3-5 minutes
	  ○ May be diluted with 10 mL of sodium chloride 0.9% to facilitate slow injection
	* If well enough to discharge prior to the 10 day course being completed dexamethasone can be ceased on discharge.

Adverse Effects	• Given the short duration for COVID-19 of treatment many known corticosteroid adverse effects are unlikely to occur.
	• Some common adverse effects that may occur with short term use of dexamethasone include:
	  ○ Transient itching, burning or tingling in perineal area (after high dose rapid IV bolus)
	  ○ Infection
	  ○ Electrolyte and fluid disturbances including: hypernatraemia, hypervolaemia, hypokalaemia
	  ○ Hypertension,
	  ○ Hyperglycaemia,
	  ○ GI disturbances including increased appetite and dyspepsia
	  ○ Delayed wound healing and bruising
	  ○ Facial flushing
	  ○ Myopathy, muscle weakness
	  ○ Psychiatric effects (euphoria, hypomania, depression, disturbances of mood, cognition, sleep and behaviour. Delirium or psychosis are less common).

Monitoring	• Clinicians should monitor for potential adverse effects listed above including monitoring blood sugar levels (especially if known diabetic) and creatinine and electrolytes. • Baseline testing for hepatitis B, HIV, HCV should be undertaken for all patients and consider strongyloides and tuberculosis testing according to epidemiological risk factors. Dexamethasone treatment should **NOT** be delayed pending results of baseline tests.
Patient information	• Dexamethasone product information and consumer medicines information leaflets are available via MIMS .

Baricitinib[1,2,3,7,8,11,13,14,15, 43, 44]

ID approval and patient consent (verbal or written) required

For more detailed information on the use of baricitinib in patients with COVID-19 visit the Clinical Excellence Commission baricitinib guideline	
Drug Class	• Janus Kinase (JAK) 1 and 2 inhibitor, disease-modifying anti-rheumatic drug (DMARD), immunomodulator
Indications	• Off-label use of baricitinib may be considered for patients with a current diagnosis of COVID-19 who require supplemental oxygen, high-flow oxygen and/or non-invasive ventilation including those who may be intolerant of steroid therapy particularly where there is evidence of systemic inflammation such as: ○ Elevated ESR, C-reactive protein (CRP, D-dimers, lactate dehydrogenase • Baricitinib is equal first line therapy for patients on mechanical ventilation and can be continued if a patient progresses from needing high-flow oxygen/non-invasive ventilation to mechanical ventilation. • Baricitinib should **NOT** be given to patients who have already received sarilumab or tocilizumab. • Unless corticosteroids are contraindicated (see dexamethasone monograph above), baricitinib should be given in conjunction with dexamethasone.
Contraindications	• Hypersensitivity: contraindicated in patients with known hypersensitivity to baricitinib or any of the excipients in the product. • Pregnancy and breastfeeding. • Renal impairment [2]: Not recommended for patients on dialysis or patients with acute kidney injury or eGFR < 15mL/min/1.73m^2. • Patients with serious active infections (other than COVID-19). • Live vaccines should not be given concomitantly.
Precautions	• Thrombosis: Baricitinib may increase the risk of venous thromboembolism (VTE). Use with caution in individuals with an increased risk of thrombosis. • Use with caution if haemoglobin < 80 g/L, lymphocyte count < 0.2 x 10^9/L or neutrophil count < 0.5 x 10^9/L. • Renal impairment: Dose reduction required in patients with eGFR 30-60 mL/min/1.73m^2 • Hepatic: Baricitinib has not been studied in patients with severe hepatic impairment. It should only be used in patients with severe hepatic impairment if the potential benefit outweighs the potential risk of harm. • Gastrointestinal (GI): GI perforations have been reported. Use with caution in patients at risk of GI perforation. Evaluate new onset abdominal symptoms. • Infection: use is associated with an increased risk of serious infection including bacterial, viral, fungal and opportunistic infection, additive risk when used in combination with other immunosuppressive therapy. Patients should be monitored for signs and symptoms of infection. Patients should be evaluated for latent tuberculosis infection.
Drug Interactions	• Strong OAT3 inhibitors such as gemfibrozil and probenecid may increase concentrations of baricitinib – see below for dose adjustments. • Additive immunosuppressive risk when used with other immunomodulatory agents e.g. methotrexate, corticosteroids (excluding dexamethasone given for COVID-19), tocilizumab, adalimumab, rituximab and anakinra. Use of monoclonal antibodies targeting cytokines (e.g. TNF-alpha, interleukin-1, interleukin-6) or T-cells within the

[2] NOTE: Dose adjustments are based on eGFR (CKD-EPI). For patients with extremes of body size, multiply the eGFR by the patient's body surface area (in m^2) and divide by 1.73 m^2

	last 4 weeks and monoclonal antibodies targeting B-cells within the last 3 months are contraindicated. • Clozapine: increased risk of agranulocytosis. • Live vaccines should be avoided just prior to and during treatment with baricitinib. Specialist input should be obtained regarding timing of future vaccinations. • For a full list of drug interactions check the University of Liverpool COVID-19 resource page.
Presentation and storage	• Available as: ○ 2 mg film-coated tablets ○ 4 mg film-coated tablets • Store below 30^{O}C in original package
Dose	• NOTE: Dose adjustments are based on eGFR (CKD-EPI). For patients with extremes of body size, multiply the eGFR by the patient's body surface area (in m^2) and divide by 1.73 m^2. • Oral daily dose for up to 14 days or until discharge – whichever comes first ○ 4mg orally daily if eGFR > 60mL/min/1.73m^2 ○ 2mg orally daily if eGFR 30-60mL/min/1.73m^2 ○ 2mg orally every second day if eGFR 15-29mL/min/1.73m^2 ○ Do NOT use if eGFR < 15mL/min/1.73m^2 • Patients taking strong OAT3 inhibitors, such as probenecid or gemfibrozil, prescribe half the dose which would be given for patient's renal function.
Administration	• Can be given with or without regard to food. • Do not crush or break the tablet. • For patients who are unable to swallow whole tablets, place tablet(s) to achieve desired dose in a closed oral syringe with room temperature water and disperse by gentle swirling until an even suspension is formed. Tablet may take 5 minutes to completely disperse. • Dispersed tablets are stable in water for up to 4 hours; however, the solution should be administered immediately whenever possible. The container should be rinsed with additional room temperature water and these contents also administered. **Dispersion instructions for 2mg and 4mg baricitinib tablets** **Administration via** / **Dispersion volume of water** / **Container rinse volume** Oral dispersion / 5-10 mL / At least 5 mL Gastrostomy tube / 15 mL / At least 15 mL Nasogastric tube* / 30 mL / At least 15 mL * To avoid clogging of small diameter tubes (smaller than 12 Fr), the syringe can be held horizontally and shaken several times • See special instructions in NSW Therapeutic Advisory Group baricitinib drug guideline for further information.
Handling	• Intact baricitinib tablets can be handled with standard precautions for handling of oral medications. • Occupational exposure to non-intact tablets may be harmful. Staff who are actively trying to conceive or who are pregnant or breastfeeding should not prepare or handle a dispersed dose.

	• For all other staff, use standard Personal Protective Equipment (PPE) if preparation or administration of a dispersed tablet is required.

Monitoring	• As baricitinib is a new medication, patients should have appropriate clinical and laboratory monitoring including:
	  ○ Baseline and daily creatinine, electrolytes and urea as well as LFTs and complete blood exam.
	• Interrupt treatment if:
	  ○ Neutrophil count < 0.5 x 10^9 cells/L
	  ○ Lymphocyte count < 0.2 x 10^9 cells/L
	  ○ Haemoglobin < 80g/L
	  ○ Increases in ALT or AST are observed and drug-induced liver injury is suspected
	• Baseline testing for hepatitis B, HIV, HCV should be undertaken for all patients and consider strongyloides and tuberculosis testing according to epidemiological risk factors. Baricitinib treatment should **NOT** be delayed pending results of baseline tests.

Adverse Effects	• As the use of baritinib for COVID-19 is off-label, it is important to document and report all (from possible to confirmed) adverse effects experienced by the patient during treatment to inform its safety profile and future use. • Common (>1%): infections (including serious and opportunistic), hypercholesterolaemia, thrombocytosis (not associated with thrombotic events), nausea (especially in first 2 weeks), abdominal pain, headache, increased creatine kinase • Infrequent (0.1–1%): thrombosis, neutropenia, lymphopenia, anaemia, acne, vomiting, hypertriglyceridaemia, increased liver enzymes. • Suspected or confirmed adverse reactions should be reported via Safety Learning System and also via the Therapeutic Goods Administrations adverse effects online form: TGA adverse event reporting.
Patient information and consent forms	• Baricitinib patient information leaflets are available via the NSW Therapeutic Advisory Group. • Example patient consent forms can be found here

Tocilizumab[1,2,3,5,7,8,9,11,16,17,19,20] **ID approval and patient consent (verbal or written) required** **For more detailed information on the use of tocilizumab in patients with COVID-19 visit the product information available on the TGA website**	
Drug Class	• Anti-rheumatic, cytokine modulator, monoclonal antibody (humanised)
Indications	• Off-label use of tocilizumab may be considered for patients with a current diagnosis of COVID-19, who require supplemental oxygen, particularly where there is evidence of systemic inflammation such as: ○ Elevated ESR, C-reactive protein (CRP, D-dimers, lactate dehydrogenase, ferritin) • Unless corticosteroids are contraindicated (see dexamethasone monograph above), tocilizumab should be given in conjunction with dexamethasone for patients.
Contraindications	• Hypersensitivity to any component of the product, Chinese hamster ovary cell products or other recombinant human or humanised antibodies. • Sepsis or active, severe infections from non-COVID-19 pathogens.

	• Live and live-attenuated vaccines should not be given concurrently.
Precautions	• A history of anaphylaxis to other medicines. • A history of recurring or chronic infection, or with underlying conditions (e.g. diabetes) which may predispose patients to infections. • A history of HIV, positive core antibody for hepatitis B, prior HCV infection or symptomatic EBV infection. • A history of tuberculosis/tuberculosis exposure. • Concurrent immunosuppressive/anti-rejection therapy increases the risk of infection and should be avoided. • In patients with haematological abnormalities including the possibility of macrophage activation syndrome (MAS) or haemophagocytic lymphohistiocytosis, advice from a haematologist should be sought especially in those with ○ Absolute neutrophil count < 2 x 10^9/L ○ Platelets < 100 x 10^9/L • Active hepatic disease or hepatic impairment including abnormal liver enzymes (transaminases 3–5 times the upper limit of normal). • Patients with current or previous history of diverticulitis or intestinal ulceration.
Drug Interactions	• Concurrent immunosuppressive/anti-rejection therapy increases the risk of infection and should be avoided. • Tocilizumab has no inhibitory or inducing effects on cytochromes. However, patients with COVID-19 may experience an elevation of IL-6, which has been shown to suppress activity of drug metabolising enzymes, namely CYP3A4, but also others. Tocilizumab will normalise cytochrome activity (via inhibition of IL-6). • The indirect effect of tocilizumab on CYP450 enzyme activity in this setting is unknown but the effects may persist for several weeks after administration. • Specialist input should be obtained regarding timing of future vaccinations. Live and live-attenuated vaccines should be avoided for 6 months. • For a full list of drug interactions check the University of Liverpool COVID-19 resource page.
Presentation and storage	Available as: • 80 mg/4 mL concentrate solution for IV infusion vial • 200 mg/10 mL concentrate solution for IV Infusion vial • 400 mg/20 mL concentrate solution for IV Infusion vial Store vials at 2–8°C. (Refrigerate. Do not freeze.)
Dose	• The suggested dose is dependent on actual body weight (for pregnant women use the weight at the time of clinical need): ○ Patients > 90 kg: 800 mg IV single dose ○ Patients > 65 and ≤ 90 kg: 600 mg IV single dose ○ Patients > 40 and ≤ 65 kg: 400 mg IV single dose ○ Patients ≤ 40 kg: 8 mg/kg IV single dose These dosing ranges are based on the doses used in the REMAP-CAP trial[17].
Administration	• Administer as a single intravenous infusion over 60 minutes 1. Ascertain the volume of tocilizumab solution that will be required and withdraw the same volume from a 100mL sodium chloride 0.9% infusion bag. 2. Withdraw the tocilizumab dose from the vial(s) & add to the sodium chloride 0.9% infusion bag.

	3. Invert gently when mixing to avoid foaming. Do NOT shake. Inspect the bag, which must be clear to opalescent, colourless to pale yellow and free from visible particles. 4. Do not use the same IV line to administer other medications at the same time 5. Prime the line with tocilizumab infusion and then infuse intravenously over 60 minutes via either a central or peripheral line. 6. After completion of the tocilizumab infusion, at least 20mL of 0.9% sodium chloride should be used to flush the giving set.
Monitoring	• Monitor for adverse effects by performing including complete blood exam and electrolytes, creatinine, urea, LFTs and CRP (tocilizumab inhibits the production of CRP therefore a reduction in CRP should not be used as a marker of clinical improvement). • New onset gastrointestinal symptoms • Observe for hypersensitivity reaction during, and for 30 minutes after IV infusion. Resuscitation facilities must be readily available. • Baseline testing for hepatitis B, HIV, HCV should be undertaken for all patients and consider strongyloides and tuberculosis testing according to epidemiological risk factors. Tocilizumab treatment should **NOT** be delayed pending results of baseline tests.
Adverse Effects	• As tocilizumab is provisionally registered by the TGA for use in patients with COVID-19, it is important to document and report all (from possible to confirmed) adverse effects experienced by the patient during treatment to inform its safety profile and future use. • Common (>1%): Infections (including opportunistic), neutropenia, hypofibrinogenaemia, increased liver enzymes, gastritis, mouth ulcers, hypertension, infusion-related reactions (below), antibodies to tocilizumab, rash, itch, headache, dizziness. • Infrequent (0.1–1%): GI perforation (possibly dose-related), thrombocytopenia, hypersensitivity reactions (e.g. urticaria, angioedema), dyspnoea, cough, conjunctivitis • Rare (<0.1%): Serious hepatotoxicity (including acute liver failure, hepatitis and jaundice, in some rare cases treatment has required liver transplant), pancreatitis, pulmonary fibrosis. • Infusion-related reactions: Occur within 24 hours of IV infusion; they include hypertension, headache, rash, hypersensitivity (anaphylaxis 0.2%). • Suspected or confirmed adverse reactions should be reported via Safety Learning System and also via the Therapeutic Goods Administrations adverse effects online form: TGA adverse event reporting.
Patient information and consent forms	• Tocilizumab patient information leaflets are available via the NSW Clinical Excellence Commission.

DEFINITIONS/ACRONYMS/ABBREVIATIONS

ALP Alkaline Phosphatase
ALT Alanine Aminotransferase
AST Aspartate Aminotransferase

CRP	C-Reactive Protein
EBV	Epstein Barr Virus
ECMO	Extracorporeal membrane oxygenation
eGFR	estimated Glomerular Filtration Rate
ESR	Erythrocyte Sedimentation Rate
GI	Gastrointestinal
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
IV	Intravenous
LFTs	Liver Function Tests
NMS	National Medical Stockpile
PFS	Prefilled syringe
SBECD	Sulfobutyl betadex sodium
ULN	Upper Limit of Normal
VTE	Venous Thromboembolism

LINKS TO RESOURCES

- National COVID-19 Clinical Evidence Taskforce (The Australian Living Guidelines)
- COVID-19 Resources: NSW Therapeutic Advisory Group
- IPCU: COVID–19 (SARS–COV–2) – Management Guide (CALHN–PRC05409)
- Anaphylaxis: Management Guidelines (CALHN-CPA04038)
- CALHN COVID–19 internet page
- World Health Organisation. Therapeutics and COVID-19: Living Guideline
- Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. 2020.
- Australian Technical Advisory Group on Immunisation (ATAGI)
- Clinical Excellence Commission: Medication Safety Updates
- COVID-19: Medication Management of mild illness in the outpatient setting (CALHN-GDE05808)

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