

# COVID-19: Medication management of Mild Illness in the Outpatient Setting

Statewide Clinical Guideline - Adoption of  
CALHN Guideline

Endorsed by CALHN Antimicrobial Stewardship (AMS) Committee:  
08/04/2025









Endorsed by South Australian Medicines Advisory Committee  
(SAMAC): 07/08/2025

Version 5.2

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# GUIDELINE

<b>Reference</b>	CALHN-GDE05808
<b>Title</b>	COVID-19: Medication Management of Mild Illness in the Outpatient Setting
<b>Scope</b>	CALHN staff managing COVID-19 mild illness in the outpatient setting
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<b>Oversight committee</b>	South Australian Medicines Advisory Committee
<b>Committee endorsement</b>	07 August 2025
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<b>Sponsor approval</b>	08 April 2025
<b>Priority Care Committee (PCC)</b>	PCC: National Standard 4 Medication Safety
<b>Risk rating</b>	<input type="checkbox"/> Extreme <input type="checkbox"/> High <input type="checkbox"/> Medium <input checked="" type="checkbox"/> Low
<b>Title and reference of parent SA Health Policy</b>	N/A
<b>Summary</b> (three sentences maximum)	This guideline provides a pathway for the medication management of mild COVID-19 illness in the outpatient setting.
<b>Keywords</b> (five to eight)	COVID-19, molnupiravir, nirmatrelvir, ritonavir, remdesivir, mild, outpatient.

 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
<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Version	Change summary	Next scheduled review
5.2	Non-scheduled major review. Change to eligibility criteria and access to remdesivir. Removal of recommendations for treatment of COVID-19 illness in pregnancy and breastfeeding. Updated information regarding drug interactions with nirmatrelvir/ritonavir.	April 2028
5.1	Non-scheduled minor review. Clarification of PBS eligibility for nirmatrelvir/ritonavir and molnupiravir for patients aged 50-69. Change in recommendations for remdesivir and nirmatrelvir/ritonavir in renal impairment. Remove classification of immunocompromised patients and insert link to PBS instead. Remove sotrovimab drug monograph.	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 review. 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. Timeframe for checking blood results updated for haemodialysis patients on remdesivir.	February 2026

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## GUIDELINE

### COVID-19: Medication Management of Mild Illness in the Outpatient Setting

- This guideline addresses the use of disease-modifying treatments for COVID-19 in adult patients with mild illness who **DO NOT** require supplemental oxygen or hospitalisation for COVID-19. It is intended to guide treatment of patients in the outpatient setting, including SA Health Urgent Care Hubs.
- 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 advice regarding disease-modifying therapies recommended for patients hospitalised with COVID-19
  - provide information regarding the prevention of COVID-19
  - provide advice regarding the treatment and management of COVID-19 in pregnancy and breastfeeding.
- For information related to the management and care of patients with COVID-19 refer to:
  - [COVID-19: Disease-modifying treatment recommendations for hospitalised adult patients \(CALHN-GDE05778\)](#)
  - [COVID-19 \(SARS-COV-2\) – Management Guide \(CALHN-PRC05409\)](#)

#### Definition of COVID-19 mild illness

Adults not presenting any clinical features suggestive of moderate or severe illness or a complicated course of illness. Characteristics of mild illness include:

- No symptoms (PBS eligible for patients  $\geq 70$  years); or
- Mild upper respiratory tract symptoms (inc nasal congestion runny nose, headache or sore throat); or
- Cough, fever or chills, new myalgia or lethargy/weakness without new shortness of breath or a reduction in oxygen saturation
- Gastrointestinal disturbances including loss of taste or smell.

See [Appendix 1](#) for complete description of COVID-19 disease severity definition.

#### Changes to the National Medical Stockpile (NMS)

From 1 January 2024, the Commonwealth ceased supplying oral NMS COVID-19 medications to public hospitals free of charge. Nirmatrelvir/ritonavir (Paxlovid®) and molnupiravir (Lagevrio®) are available via the PBS for eligible outpatients, please refer to the PBS website for full eligibility criteria. Once the current supply of remdesivir is exhausted, it will be funded by individual Local Health Networks (LHNs).

#### Approximate cost of COVID-19 antivirals per course

Remdesivir: \$2300 (3 day course), \$3400 (6 day course)

Nirmatrelvir/ritonavir: \$1000 (if non-PBS)

Molnupiravir: \$1000 (if non-PBS)

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## Risk factors for progressing to severe or critical illness

- Immunosuppression (see below)
- 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<sup>2</sup> or > 40 kg/m<sup>2</sup> 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
- Cardiovascular disease including 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

Immunocompromised patients are not expected to mount an adequate immune response to either the COVID-19 vaccination or previous COVID-19 infection(s) due to their underlying illness, 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.

### The following patients are considered moderately to severely immunocompromised per the PBS and CALHN guideline:

- 1) Any primary or acquired immunodeficiency including:
  - a) Haematologic neoplasms: leukaemias, lymphomas, myelodysplastic syndromes, multiple myeloma and other plasma cell disorders
  - b) Post-transplant: solid organ (on immunosuppressive therapy), haematopoietic stem cell transplant (within 24 months)
  - c) Immunocompromised due to primary or acquired (HIV/AIDS) immunodeficiency; **OR**
- 2) Any significantly immunocompromising condition(s) where, in the last 3 months the patient has received:
  - a) Chemotherapy or whole body radiotherapy
  - b) High-dose corticosteroids (at least 20 mg of prednisone per day, or equivalent) for at least 14 days in a month, or pulse corticosteroid therapy,
  - c) Biological agents and other treatments that deplete or inhibit B cell or T cell function (abatacept, anti-CD20 antibodies, BTK inhibitors, JAK inhibitors, sphingosine 1-phosphate receptor modulators, anti-CD52 antibodies, anti-complement antibodies, anti-thymocyte globulin),
  - d) Selected conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) including mycophenolate, methotrexate, leflunomide, azathioprine, 6-mercaptopurine (at least 1.5mg/kg/day), alkylating agents (e.g. cyclophosphamide, chlorambucil), and systemic calcineurin inhibitors (e.g. cyclosporin, tacrolimus); **OR**
- 3) Any significantly immunocompromising condition(s) where, in the last 12 months the patient has received an anti-CD20 monoclonal antibody treatment, but criterion 2c above is not met; **OR**
- 4) Others with very high-risk conditions including Down Syndrome, cerebral palsy, congenital heart disease, thalassemia, sickle cell disease and other haemoglobinopathies; **OR**
- 5) People with disability with multiple comorbidities and/or frailty (irrespective of age or vaccination).



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## COVID-19 treatment recommendations for confirmed mild illness in non pregnant adults

For advice regarding the treatment and management of mild COVID-19 illness in pregnancy contact closest local health network with specialist perinatal services

### Eligible for oral antiviral medications via the PBS<sup>#</sup>

Patients with [disability with multiple/significant comorbidities and/or frailty are eligible per PBS](#) irrespective of age

- Immunocompromised patients (page 3) OR
- Aged ≥ 70 years irrespective of risk factors OR
- Aged ≥ 50 to 69 years with ≥ 2 risk factors (page 3) OR
- Aboriginal or Torres Strait Islander Aged ≥ 30 years AND ≥ 1 risk factor (page 3) OR
- Previous COVID-19 infection resulting in hospitalisation



**First line:** Symptom onset ≤ 5 days: **Nirmatrelvir plus ritonavir** via PBS

**Second line:**<sup>+</sup> Symptom onset ≤ 5 days: **Molnupiravir**<sup>β</sup> via PBS

<sup>+</sup> **Remdesivir** may be considered as second line therapy for mild COVID-19 illness in specific high-risk patients/circumstances, as described in **Box 1** below.

#### \*Box 1: Remdesivir Eligibility for Mild COVID-19 Illness

Remdesivir may be prescribed as **second line** therapy for patients where nirmatrelvir plus ritonavir is not appropriate due to **contraindications** or **significant drug-drug interactions** which **cannot** be managed **AND** symptom onset ≤ 7 days **AND** patient is/has:

- highly immunosuppressed, e.g.
  - solid organ transplant
  - haematological malignancy, or
  - received treatment with T or B cell depleting agents within previous 12 months, or
- cystic fibrosis
- nil by mouth (and without NGT/PEG), OR
- severely compromised gastrointestinal absorption (e.g. severe GVHD)

Infectious Diseases (ID) approval is required for all patients prescribed or referred for remdesivir for mild COVID-19 illness not meeting criteria above, or where local policy requires prescribing to be through ID approval.

**Remdesivir:** 200mg IV infusion loading dose day 1 then 100mg IV daily on day 2 and 3.  
**Total 3-day course for mild illness.**

**Not eligible for oral antiviral medications via PBS<sup>^</sup>**  
**Aged < 50 years or < 30 years if Aboriginal or Torres Strait Islander**  
**AND ≥ 2 risk factors (see page 3)**



**First line - Symptom onset ≤ 5 days: Nirmatrelvir plus ritonavir<sup>^</sup>**

#### Dosing recommendations:

##### Nirmatrelvir plus ritonavir:

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

**eGFR < 60mL/min:** 150mg nirmatrelvir (1x150mg tablet) + 100mg ritonavir (1x100mg tablet) orally twice daily for 5 days - use with caution in patients with eGFR < 30 mL/min (see drug monograph on page 10)

**Molnupiravir<sup>β</sup>:** 800mg (4 x 200mg capsules) orally 12-hourly for 5 days.

**β Molnupiravir:** Consider risk versus benefits of using molnupiravir as limited evidence in patients < 70 years. 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 for 3 months after treatment with molnupiravir.

Supportive care alone is recommended for patients who have symptom onset > 7 days and those considered at low risk of progressing to severe COVID-19 illness (i.e. immunocompetent patients aged < 50 years OR patients aged ≥ 50-70 years with no risk factors for progressing to severe illness).

**#** For patients without Medicare follow the same medication recommendations but prescribe as non-PBS<sup>^</sup>

**^ Non-PBS Oral Antiviral Medications:** When prescribed in a public hospital on discharge, dispensing from the public hospital pharmacy is preferred due to the high cost to the patient if obtained in the community.

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## Assessing a patient's suitability for nirmatrelvir plus ritonavir (Paxlovid®) – contraindications and drug-drug interactions

Paxlovid® (nirmatrelvir plus ritonavir) has a high potential to cause significant drug-drug and drug-herbal interactions. 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. Maximal inhibition of CYP3A4 is reached approximately 48 hours after initiating ritonavir and lasts several days after it is discontinued.

### 1. Obtain a complete list of patient's current medications including:

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

### 2. Check <http://www.covid19-druginteractions.org/checker> and/or another drug interaction checker, and/or the Paxlovid® product information for potential drug-drug interactions

### 3. Check for absolute contraindications to Paxlovid® use:

- Age < 12 years and weight < 40kg
- Severe liver disease (i.e., Child-Pugh Class C)
- Compromised gastrointestinal absorption (e.g. severe GVHD) or nil by mouth (note: both oral agents can be administered to those with swallowing difficulties, including via enteral tubes – refer to individual drug monographs for details).

### Interactions with Medicines and Nirmatrelvir + Ritonavir (Paxlovid®)

- Note: if a drug is not listed below, it cannot be assumed safe to prescribe: Check the Liverpool [website](#) or product information.
- Management of interactions with Paxlovid® is complex and full details should be obtained from the website where possible. *Reference: [Liverpool Drug Interactions Group](#) – last modified 31/5/23*

#### Legend

Colour/Symbol	Recommendation for Paxlovid Use
●	<p><b>Contraindicated – Do not co-administer</b></p> <p><b>Do not use Paxlovid® → risk of serious toxicity. Use alternative COVID-19 therapy</b></p> <p>Stopping the other drug will <b>not</b> mitigate the interaction (e.g., prolonged half-life, narrow therapeutic index, prolonged enzyme-inducing effects which may decrease effectiveness of nirmatrelvir/ritonavir).</p>
	<p><b>Do not co-administer unless the other drug can be held</b></p> <p><b>Significant ↑ in drug concentrations expected. Paxlovid® may be appropriate IF the other drug can be safely held</b> (see Liverpool <a href="#">website</a> for more information). Interacting drug can be resumed at least 3 days after completing Paxlovid®. If the medication cannot safely be held, use an alternative COVID-19 medication</p>
□	<p><b>Caution – potential interaction</b></p> <p><b>Dose modification required to allow use of Paxlovid®</b></p> <p>Significant ↑/↓ in drug concentrations expected, which may lead to toxicity or impaired efficacy. Only co-administer if the interacting drug can be safely held or dose-adjusted and closely monitored (see Liverpool <a href="#">website</a> for more information)</p>
	<p><b>Potential Interaction</b></p> <p>Manageable by counselling patient</p> <p><b>Proceed with Paxlovid®</b></p> <p>Interaction manageable by counselling the patient about potential interaction and advising to temporarily stop the drug if feeling unwell. Drug can be resumed 3 days after completing Paxlovid®</p>
	<p><b>Weak interaction</b></p> <p>No action needed</p> <p><b>Proceed with Paxlovid®</b></p> <p>Drug metabolised partially by CYP3A4 or with low risk of adverse event from interaction</p>
	<p><b>No interaction expected</b></p> <p><b>Proceed with Paxlovid®</b></p>

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Analgesics	
Aspirin	
Buprenorphine	
Celecoxib	
Codeine	
Diclofenac	
Fentanyl – see <a href="#">Liverpool</a>	
Hydromorphone	
Ibuprofen	
Mefenamic acid	
Methadone	
Morphine	
Naproxen	
Oxycodone – see <a href="#">Liverpool</a>	
Paracetamol	
Pethidine – see <a href="#">Liverpool</a>	
Tapentadol	
Tramadol	
Antiarrhythmics	
Amiodarone	
Digoxin – see <a href="#">Liverpool</a>	
Disopyramide – see <a href="#">Liverpool</a>	
Flecainide – see <a href="#">Liverpool</a>	
Lidocaine – see <a href="#">Liverpool</a>	
Quinidine	
Anticoagulants / Antiplatelets	
Note 1 Apixaban – see <a href="#">Liverpool</a>	
Aspirin	
Note 2 Clopidogrel	
Note 1 Dabigatran – see <a href="#">Liverpool</a>	
Dalteparin	
Dipyridamole	
Enoxaparin	
Heparin	
Prasugrel	
Note 1 Rivaroxaban- see <a href="#">Liverpool</a>	
Note 3 Ticagrelor	
Warfarin – monitor INR	

Anticonvulsants	
Brivaracetam	
● Carbamazepine	
Clonazepam	
□ Ethosuximide	
Gabapentin	
Lacosamide	
Lamotrigine	
Levetiracetam	
Oxcarbazepine	
● Phenobarbital	
● Phenytoin	
Pregabalin	
● Primidone	
Rufinamide	
□ Tiagabine	
Topiramate	
Valproate	
Vigabatrin	
Zonisamide	
Antidepressants	
Agomelatine	
Amitriptyline	
Bupropion	
Citalopram	
Clomipramine	
Desvenlafaxine	
Doxepin	
Duloxetine	
Escitalopram	
Fluoxetine	
Imipramine	
Lithium	
Mianserin	
Mirtazapine	
Nortriptyline	
Paroxetine	
□ Reboxetine – see <a href="#">Liverpool</a>	
Sertraline	
● St John’s Wort	
Venlafaxine	
Vortioxetine	

Antihistamines	
Cetirizine	
Fexofenadine	
Loratadine	
Antipsychotics	
Amisulpride	
□ Aripiprazole – see <a href="#">Liverpool</a>	
Asenapine	
□ Brexpiprazole – see <a href="#">Liverpool</a>	
Cariprazine – see <a href="#">Liverpool</a>	
Chlorpromazine	
Clozapine – see <a href="#">Liverpool</a>	
Droperidol	
Flupentixol	
□ Haloperidol	
Lurasidone – see <a href="#">Liverpool</a>	
Olanzapine	
Paliperidone	
Periciazine	
Quetiapine – see <a href="#">Liverpool</a>	
□ Risperidone – see <a href="#">Liverpool</a>	
Ziprasidone	
Zuclopenthixol	
Drugs for Anxiety and Sleep Disorders	
□ Alprazolam – see <a href="#">Liverpool</a>	
Bromazepam	
□ Buspirone – see <a href="#">Liverpool</a>	
□ Clobazam – see <a href="#">Liverpool</a>	
Clonazepam – see <a href="#">Liverpool</a>	
Diazepam – see <a href="#">Liverpool</a>	
□ Flunitrazepam – see <a href="#">Liverpool</a>	
Lorazepam	
Midazolam – see <a href="#">Liverpool</a>	
Nitrazepam – see <a href="#">Liverpool</a>	
Oxazepam	
Temazepam	
□ Zolpidem – see <a href="#">Liverpool</a>	
□ Zopiclone – see <a href="#">Liverpool</a>	
Bronchodilators	
Salbutamol	
Ipratropium	
Note 4 Salmeterol – see <a href="#">Liverpool</a>	
Cancer Drugs	
Seek specialist advice	

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Cardiovascular Drugs	
	Ambrisentan
	Amiloride
	<b>ACE-Inhibitors</b>
	<b>Beta Blockers</b> are not expected to interact except <b>Labetalol</b>
	Bosentan – see <a href="#">Liverpool</a>
☐	<b>Calcium Channel Blockers</b> Dose adjustment preferred if high risk of bradycardia or hypotension. Monitor.
	Candesartan
☐	Digoxin – see <a href="#">Liverpool</a>
	Eplerenone – see <a href="#">Liverpool</a>
	Eprosartan
	Furosemide
	Hydralazine
	Hydrochlorothiazide
	Iloprost
	Indapamide
	Irbesartan
	Ivabradine – see <a href="#">Liverpool</a>
	Losartan
	Macitentan
	Olmesartan
	Prazosin
☐	Riociguat – see <a href="#">Liverpool</a>
	Sacubitril
	Sildenafil – see <a href="#">Liverpool</a>
	Spironolactone
	Tadalafil – see <a href="#">Liverpool</a>
	Telmisartan
	Valsartan
Cystic Fibrosis – seek specialist advice	
☐	Elexacaftor with Tezacaftor and Ivacaftor
☐	Ivacaftor
●	Lumacaftor with Ivacaftor
☐	Tezacaftor with Ivacaftor
Diabetes Medication	
	Acarbose
	Alogliptin
	Dapagliflozin
	Dulaglutide
	Empagliflozin

	Exenatide
	Glibenclamide
	Gliclazide
	Glimepiride
	Glipizide
	Insulin
	Linagliptin
	Metformin
	Pioglitazone
☐	Saxagliptin – see <a href="#">Liverpool</a>
	Sitagliptin
	Vildagliptin
Gastrointestinal	
	Antacids
	Cisapride – see <a href="#">Liverpool</a>
☐	Aprepitant – see <a href="#">Liverpool</a>
Note 5	Domperidone- see <a href="#">Liverpool</a>
	Famotidine
	Loperamide
	Mesalazine
	Metoclopramide
Proton pump inhibitors	
	Ondansetron
	Ranitidine
Hepatitis C Antivirals – seek specialist advice	
	Glecaprevir with Pibrentasvir – see <a href="#">Liverpool</a>
	Ledipasvir with Sofosbuvir
	Sofosbuvir with Velpatasvir
☐	Sofosbuvir with Velpatasvir and Voxilaprevir
HIV Antiretrovirals – seek specialist advice	
	Abacavir
	Atazanavir/ritonavir
	Bictegravir
	Cabotegravir
	Darunavir/ritonavir
	Dolutegravir
	Emtricitabine
	Lamivudine
	Nevirapine
	Raltegravir
	Rilpivirine

	Tenofovir (all salts)
Immunosuppressants – seek specialist advice	
	Adalimumab
	Azathioprine
	Basiliximab
	Belatacept
	Ciclosporin – see <a href="#">Liverpool</a>
	Cyclophosphamide
	Etanercept
	Everolimus – see <a href="#">Liverpool</a>
	Leflunomide
	Methotrexate
	Mycophenolate
	Sirolimus – see <a href="#">Liverpool</a>
	Tacrolimus – see <a href="#">Liverpool</a>
Lipid lowering Drugs –	
☐ Note 6	Atorvastatin – see <a href="#">Liverpool</a>
	Evolocumab
	Ezetimibe
	Fenofibrate
	Fluvastatin
	Gemfibrozil
	Lovastatin – see <a href="#">Liverpool</a>
	Pravastatin
☐ Note 6	Rosuvastatin – see <a href="#">Liverpool</a>
Note 5	Simvastatin – see <a href="#">Liverpool</a>
Others	
	Alendronate
	Allopurinol
	Colchicine - see <a href="#">Liverpool</a>
☐	Dexamethasone ≥ 20mg/d
	Donepezil
	Ergotamine – see <a href="#">Liverpool</a>
	Finasteride
	Hydroxychloroquine
	Infliximab
	Levodopa
	Levothyroxine
	Memantine
	Methotrexate
☐	Mirabegron (no dose reduction in patients with normal renal function)
	Modafinil

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Others continued	
	Pramipexole
	Pyridostigmine
☐	Rifabutin– see <a href="#">Liverpool</a>
●	Rifampicin
Note 7	Tamsulosin
☐	Triamcinolone – see <a href="#">Liverpool</a>

#### Note 1 – Direct-acting oral anticoagulants (DOACs) inc apixaban, dabigatran and rivaroxaban

Coadministration of nirmatrelvir/ritonavir with DOACs may lead to increased DOAC concentrations and therefore to an increased risk of bleeding. If low risk of clotting (e.g., taking for AF with [CHADS-VASc](#) score of 1 or 2) consider holding DOAC for duration of nirmatrelvir/ritonavir and restarting 3 days after nirmatrelvir/ritonavir therapy is completed. For patients with a high risk of clotting consider an alternative COVID-19 therapy (i.e., molnupiravir) or seek specialist advice.

#### Note 2 – Clopidogrel

Coadministration of nirmatrelvir/ritonavir is expected to decrease the antiplatelet effect of clopidogrel. It may be acceptable to prescribe nirmatrelvir/ritonavir if the benefits of nirmatrelvir/ritonavir use outweigh the risk of reduced clopidogrel efficacy. For patients with a very high risk of thrombosis (e.g., following a recent CVA or within the first 3 months following an ACS or coronary stent), consider prescribing an alternative COVID-19 therapy (i.e., molnupiravir).

#### Note 3 – Ticagrelor

Coadministration of nirmatrelvir/ritonavir with ticagrelor may significantly increase exposure to ticagrelor and increase the risk of bleeding. For patients with a very high risk of thrombosis (e.g., following a recent CVA or within the first 3 months following an ACS or coronary stent), consider prescribing an alternative COVID-19 therapy (i.e., molnupiravir). For patients with a low risk of thrombosis and also taking aspirin, consider temporarily holding ticagrelor during nirmatrelvir/ritonavir therapy and restarting ticagrelor 3 days after nirmatrelvir/ritonavir therapy is completed. If not taking aspirin prior to presentation, then **do not** change antiplatelet therapy. Instead consider prescribing an alternative COVID-19 therapy (i.e., remain on ticagrelor monotherapy and prescribe molnupiravir).

#### Note 4 – Salmeterol

Coadministration of nirmatrelvir/ritonavir is expected to significantly increase concentrations of salmeterol. Where appropriate, consider temporarily holding salmeterol containing inhaler during nirmatrelvir/ritonavir therapy and for 3 days after the course it is completed. Where a salmeterol containing inhaler cannot be safely held for 8 days, consider switching to another long-acting beta-agonist (i.e. formoterol or indacaterol) for the duration of nirmatrelvir/ritonavir therapy and restart the salmeterol containing inhaler 3 days after nirmatrelvir/ritonavir therapy is completed.

#### Note 5 – Domperidone

Coadministration of nirmatrelvir/ritonavir may significantly increase domperidone exposure and increase the risk of cardiac adverse effects. Where appropriate, hold domperidone for the duration of nirmatrelvir/ritonavir therapy and for 3 days after the course is completed and/or prescribe an alternative anti-emetic for the duration of nirmatrelvir/ritonavir therapy and restart domperidone 3 days after nirmatrelvir/ritonavir therapy is completed.

#### Note 6 – Lipid Lowering Drugs (statins)

Coadministration of nirmatrelvir/ritonavir is expected to significantly increase exposure to simvastatin and moderately increase exposure to atorvastatin and rosuvastatin, increasing the risk of toxicity. However, fluvastatin and pravastatin exposure is not expected to change. Recommendations for patients on simvastatin, atorvastatin and rosuvastatin are as follows:

**Simvastatin** – Discontinue simvastatin at least 12 hours prior to initiation of nirmatrelvir/ritonavir and hold for duration of nirmatrelvir/ritonavir therapy. Restart simvastatin **5** days after nirmatrelvir/ritonavir therapy is completed.

**Atorvastatin and rosuvastatin** – Discontinue atorvastatin or rosuvastatin therapy for the duration of nirmatrelvir/ritonavir therapy (i.e., does not need to be held 12 hours prior to nirmatrelvir/ritonavir commencing). Restart atorvastatin or rosuvastatin 3 days after nirmatrelvir/ritonavir therapy completed.

Given the short duration of nirmatrelvir/ritonavir treatment, interacting statins should be held so nirmatrelvir/ritonavir can be prescribed. Temporarily stopping statins is acceptable considering that it will not negatively influence the therapeutic effect but can minimise the risk for adverse events related to a drug interaction.

#### Note 7 – Tamsulosin and tamsulosin/dutasteride combination

Coadministration of nirmatrelvir/ritonavir is expected to increase tamsulosin concentrations. Where appropriate, hold tamsulosin and restart 3 days after completing nirmatrelvir/ritonavir. Alternatively for patients at a heightened risk of urinary retention, hold tamsulosin or tamsulosin/dutasteride and consider alternative therapy such as low dose prazosin (0.5mg-1mg daily) for duration of nirmatrelvir/ritonavir and for 3 days after completing course. Monitor for hypotension.

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## Disease-modifying treatments for mild COVID-19 illness

### Nirmatrelvir plus Ritonavir (Paxlovid®)

**Patient consent required (verbal or written)**

Stock not available after hours in CALHN

<b>Drug Class</b>	<ul style="list-style-type: none"> <li>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.</li> </ul>
<b>Indications</b>	<ul style="list-style-type: none"> <li>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: <ul style="list-style-type: none"> <li>Meets <a href="#">PBS criteria</a> for treatment with nirmatrelvir/ritonavir</li> </ul> <b>OR</b> <ul style="list-style-type: none"> <li>Aged &lt; 50 years (or &lt; 30 years if Aboriginal or Torres Strait Islander) with TWO or more <a href="#">risk factors</a> for severe or critical illness</li> </ul> </li> <li>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.</li> </ul>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>Hypersensitivity to nirmatrelvir or ritonavir or any of the excipients listed in the product information.</li> <li>Children less than 12 years old and weighing &lt; 40kg.</li> <li><b>Severe hepatic impairment</b> – avoid due to insufficient data.</li> <li><b>Solid organ transplant recipients</b> at risk of significant adverse outcomes from drug-drug interactions if prescribed nirmatrelvir/ritonavir</li> <li><b>Drug interactions</b> <ul style="list-style-type: none"> <li><b>Contraception</b> – 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.</li> <li>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 page 5-8 for more information.</li> <li>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 page 5-8 for more information.</li> </ul> </li> </ul>
<b>Precautions</b>	<ul style="list-style-type: none"> <li>Exercise caution in patients with a history of anaphylaxis to other medicines.</li> <li><b>Pregnancy</b> – limited data. For treatment and management of COVID-19 illness in pregnancy contact closest local health network with specialist perinatal services.</li> <li><b>Breastfeeding</b> – limited data. The decision to breastfeed during treatment for COVID-19 should be evaluated as part of a shared decision-making process. Breastfeeding can continue if ritonavir-boosted nirmatrelvir is needed for the management of COVID-19. However, lactating patients with COVID-19 infection can transmit the virus through respiratory droplets and all precautions should be taken to avoid spreading the virus to the infant.</li> <li><b>Severe renal impairment</b> (eGFR &lt; 30 mL/min) – use with caution. Use is not recommended by manufacturer, however risk of toxicity is likely to be minimal with 5 day course. Dose recommendations (i.e. to dose as per eGFR &lt;60 mL/min) are from the Renal Drug Database and are based on a study from Wales with small numbers of</li> </ul>

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	<p>patients with end stage renal disease (ESRD). In this study patients with ESRD taking this dose experienced no serious adverse effects.</p> <ul style="list-style-type: none"> <li>• <b>Hepatotoxicity</b> - 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. No dose adjustments required for patients with mild or moderate hepatic impairment. Avoid use in patients with severe hepatic impairment.</li> <li>• <b>Risk of HIV-1 Resistance Development</b> - 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.</li> </ul>
<b>Storage and presentation</b>	<ul style="list-style-type: none"> <li>• This is a combination therapy. The two components are provided as individual, co-packaged medications. <b>Each package contains 30 tablets in total:</b> 20 x 150mg nirmatrelvir tablets, and 10 x 100mg ritonavir tablets. This is the supply required to complete the standard adult 5-day course.</li> <li>• Store at room temperature, less than 25°C</li> </ul>
<b>Dose</b>	<ul style="list-style-type: none"> <li>• <b>eGFR ≥ 60mL/min/1.73m<sup>2</sup>:</b> Nirmatrelvir 300mg (two 150mg tablets) with ritonavir 100mg (one 100mg tablet) taken together orally every 12 hours for 5 days.</li> <li>• <b>eGFR &lt; 30- 60 mL/min/1.73m<sup>2</sup>:</b> Nirmatrelvir 150mg (one 150mg tablet) with ritonavir 100mg (one 100mg tablet) taken together orally every 12 hours for 5 days.</li> <li>• <b>eGFR &lt;30 mL/min/1.73m<sup>2</sup> (including dialysis):</b> Nirmatrelvir 150mg (one 150mg tablet) with ritonavir 100mg (one 100mg tablet) taken together orally every 12 hours for 5 days. Use with caution – see precautions section above.</li> <li>• 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.</li> </ul>
<b>Administration</b>	<ul style="list-style-type: none"> <li>• 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).</li> <li>• Where possible swallow the tablets whole, with or without food.</li> <li>• 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: <ul style="list-style-type: none"> <li>○ For patients with swallowing difficulties: <ol style="list-style-type: none"> <li>1. Disperse the nirmatrelvir 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.</li> <li>2. Crush the ritonavir tablet and mix with water, or a spoonful of yoghurt or apple puree.</li> </ol> </li> <li>○ For patients with enteral feeding tubes: <ol style="list-style-type: none"> <li>1. Flush the tube with 30mL of water.</li> <li>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.</li> <li>3. Check carefully that the tablet(s) is completely dispersed and then give via enteral tube.</li> <li>4. Flush tube with 5mL of water.</li> <li>5. Crush the ritonavir tablet and mix with water, then draw into an enteral syringe.</li> </ol> </li> </ul> </li> </ul>

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	<p>6. Give the mixture via enteral tube ensuring all the mixture has been administered.</p> <p>7. Flush the tube with 30mL of water.</p>
<b>Monitoring</b>	<ul style="list-style-type: none"> <li>Baseline creatinine, electrolytes and urea, LFTs and complete blood exam.</li> <li>Monitor the patient for adverse effects.</li> <li>If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue and initiate appropriate medications and/or supportive care.</li> </ul>
<b>Adverse Effects</b>	<ul style="list-style-type: none"> <li>It may be difficult to distinguish between adverse effects of nirmatrelvir or ritonavir and the signs and symptoms of COVID-19.</li> <li>As a new medication, adverse reactions to nirmatrelvir continue to be investigated. Refer to the Paxlovid® <a href="#">product information</a> for a complete list of possible adverse effects.</li> <li>To date the most common adverse reactions reported include: <ul style="list-style-type: none"> <li>altered sense of taste</li> <li>headache</li> <li>diarrhoea</li> <li>vomiting</li> <li>hypertension</li> <li>myalgia</li> </ul> </li> <li>Suspected or confirmed adverse reactions should be reported via your local Incident Management System (for SA Health this is currently the Safety Learning System) and also via the Therapeutic Goods Administrations adverse effects online form: <a href="#">TGA adverse event reporting</a>.</li> </ul>
<b>Patient Information / consent forms</b>	<ul style="list-style-type: none"> <li>Refer to the Consumer Medicines Information (CMI) leaflets for <a href="#">nirmatrelvir plus ritonavir</a>.</li> <li>Nirmatrelvir plus ritonavir patient information leaflets can be found <a href="#">here</a></li> </ul>
<b>Drug Interactions</b>  <i>Refer to pages 5-8 for specific examples</i>	<ul style="list-style-type: none"> <li>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.</li> <li>Always check the <a href="#">University of Liverpool COVID-19 resource page</a> or <a href="#">Up-To-Date interaction checker</a> prior to prescribing nirmatrelvir plus ritonavir.</li> <li>Some of the more significant interactions are listed on pages 5-8 however this is not an exhaustive list and information may change over time. Where it states 'consider risk vs benefit' refer to the <a href="#">Australian Medicines Handbook</a>, the <a href="#">Liverpool resource page</a>, <a href="#">Up-to-date interaction checker</a> or the Paxlovid® <a href="#">product information</a> for more information on the mechanism of the interaction.</li> </ul>

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<b>Remdesivir<sup>1,4,13, 29,30,32</sup></b> <b>Patient consent (verbal or written) required</b>	
<b>Drug Class</b>	<ul style="list-style-type: none"> <li>Antiviral, a nucleotide analogue prodrug that binds to the viral RNA-dependent RNA polymerase and inhibits viral replication through premature termination of RNA transcription.</li> </ul>
<b>Indications</b>	<ul style="list-style-type: none"> <li>Second line treatment (when nirmatrelvir plus ritonavir is <b>contraindicated</b> or not appropriate due to <b>significant drug-drug interactions which cannot be managed</b>) of mild COVID-19 for non-pregnant adult patients who do not require supplemental oxygen and are <b>within 7 days of symptom onset</b></li> </ul> <p><b>AND</b></p> <ul style="list-style-type: none"> <li>Are highly <b>immunosuppressed</b>: including solid organ transplant recipients, patients with a haematological malignancy or patient who have received treatment with T or B cell depleting agents within previous 12 months</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>have cystic fibrosis</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>nil by mouth (and without NGT/PEG),</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>severely compromised gastrointestinal absorption (e.g. severe GVHD)</li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>currently being treated in the Intensive Care Unit</li> </ul> <p>Infectious Diseases (ID) approval is required for all patients prescribed or referred for remdesivir for mild COVID-19 illness not meeting criteria above</p>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>Known hypersensitivity to any ingredient of remdesivir product or remdesivir metabolites.</li> <li>Mechanical ventilation for &gt;48 hours at the time of commencement.</li> <li>Hepatic impairment: ALT <math>\geq</math> 5 times the upper normal limit (ULN) at baseline.</li> </ul>
<b>Precautions</b>	<ul style="list-style-type: none"> <li>Severe Renal impairment<sup>1</sup>: eGFR &lt; 30mL/min/1.73m<sup>2</sup> <ul style="list-style-type: none"> <li>Remdesivir is formulated with the excipient sulfobutyl betadex sodium (SBECD) which accumulates in renal impairment. For most patients with an eGFR &lt; 30mL/min/1.73m<sup>2</sup> 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.</li> <li>The Renal Drug Database and FDA have updated dosing recommendations for patients with eGFR &lt; 30mL/min/1.73m<sup>2</sup> and both state remdesivir can be used in patients with eGFR &lt; 30mL/min/1.73m<sup>2</sup> without need for dose adjustment.</li> </ul> </li> <li>Factors where the benefit of remdesivir is uncertain &amp; requires careful consideration before use:</li> </ul>

<sup>1</sup> 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<sup>2</sup>) and divide by 1.73 m<sup>2</sup>

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	<ul style="list-style-type: none"> <li>○ Presence of an intercurrent illness likely to lead to patient death within one year;</li> <li>○ Advanced age with limitations on activities of daily living;</li> <li>○ Need for more than a 5 day treatment course.</li> </ul>
<b>Drug Interactions</b>	<ul style="list-style-type: none"> <li>● 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.</li> <li>● Use with hydroxychloroquine or chloroquine is not recommended as it may reduce antiviral activity of remdesivir.</li> <li>● For detailed information regarding drug interactions with remdesivir please check the <a href="#">University of Liverpool COVID-19 resource page</a>.</li> </ul>
<b>Preparation</b>	<ul style="list-style-type: none"> <li>● There are 2 preparations available in Australia: <ul style="list-style-type: none"> <li>○ Powder for injection <ul style="list-style-type: none"> <li>▪ 100 mg sterile, preservative-free, white to off-white to yellow lyophilised powder vial.</li> <li>▪ Requires storage below 30°C.</li> <li>▪ Contains sulfobutyl betadex sodium (SBECD 3 g), hydrochloric acid &amp; sodium hydroxide.</li> </ul> </li> <li>○ Concentrated solution vial <ul style="list-style-type: none"> <li>▪ 100 mg/20 mL concentrate solution (clear colourless to yellow) vial; sterile preservative-free.</li> <li>▪ Requires refrigerated storage at 2–8°C.</li> <li>▪ Stable for up to 12 hours at room temperature (20–25°C) prior to dilution.</li> <li>▪ Contains sulfobutyl betadex sodium (SBECD 6 g), hydrochloric acid &amp; sodium hydroxide.</li> <li>▪ Concentrated solution not recommended in children &lt; 12 years of age or adolescents weighing &lt;40kg.</li> </ul> </li> </ul> </li> </ul>
<b>Dose</b>	<ul style="list-style-type: none"> <li>● <b>Mild illness:</b> 200mg via IV infusion on day 1, then 100mg IV daily for a further 2 days (total 3 days treatment).</li> <li>● <b>Moderate to critical illness:</b> 200mg via IV infusion on day 1, then 100mg IV daily for a further 4 days (total 5 days treatment maximum, can be ceased after 3 days if no longer requiring supplemental oxygen).</li> </ul>
<b>Administration</b>	<ul style="list-style-type: none"> <li>● There are different formulations of remdesivir available and administration instructions may vary.</li> <li>● For administration details refer to the <a href="#">Australian Injectables Drugs Handbook</a>.</li> </ul>
<b>Monitoring</b>	<ul style="list-style-type: none"> <li>● As experience with remdesivir at these doses and for this duration is limited, patients should have appropriate clinical and laboratory monitoring including: <ul style="list-style-type: none"> <li>○ Baseline creatinine, electrolytes, urea, LFTs, coagulation studies including prothrombin time and complete blood exam. Repeat every 1 to 2 days for inpatients or as clinically indicated for outpatients <ul style="list-style-type: none"> <li>▪ Discontinue remdesivir if: <ul style="list-style-type: none"> <li>● ALT ≥ 5 times ULN during treatment with remdesivir (remdesivir may be restarted when ALT is &lt; 5 times ULN), OR</li> <li>● ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or INR.</li> </ul> </li> </ul> </li> <li>○ Heart rate at baseline and as clinically indicated</li> </ul> </li> </ul>

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	<ul style="list-style-type: none"> <li>○ Observe for infusion-related reactions. If present, immediately discontinue administration of remdesivir and initiate supportive therapy if required.</li> </ul>
<b>Adverse Effects</b>	<ul style="list-style-type: none"> <li>● 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:             <ul style="list-style-type: none"> <li>○ Very common (&gt;10%): graded elevations in ALT, AST and bilirubin.</li> <li>○ Common (&gt;1%): prolonged prothrombin time, gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea), headache, rash.</li> <li>○ Rare (&lt;0.1%): hypersensitivity reactions (anaphylactic reactions are rare but are a medical emergency; stop the infusion and begin treatment immediately).</li> </ul> </li> <li>● Infusion-related reactions may include hypotension, nausea, vomiting, diaphoresis, shivering.</li> <li>● Post-marketing adverse effects reported include bradycardia (including severe bradycardia and sinus bradycardia), cardiac failure and hypotension.</li> <li>● Suspected or confirmed adverse reactions should be reported via your local Incident Management System (for SA Health this is currently the Safety Learning System) and also via the Therapeutic Goods Administrations adverse effects online form: <a href="#">TGA adverse event reporting</a>.</li> </ul>
<b>Patient information and consent forms</b>	<ul style="list-style-type: none"> <li>● Refer to the Consumer Medicines Information (CMI) leaflets for <a href="#">remdesivir</a>.</li> <li>● CALHN Remdesivir Consumer Information Leaflets can be found <a href="#">here</a>.</li> <li>●</li> </ul>

<p><b>Molnupiravir (Lagevrio®) 1,7,14,17,20</b>  <b>Patient consent (verbal or written) required</b>            Stock not available after hours</p>	
<b>Drug Class</b>	<ul style="list-style-type: none"> <li>● 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.</li> </ul>
<b>Indications</b>	<p>In 2023, The National Clinical Evidence Taskforce recommended against routine use of molnupiravir, except in specific circumstances and where all other treatment options were 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 most 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 CALHN 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 for the treatment of mild COVID-19 illness when nirmatrelvir/ritonavir is contraindicated or inappropriate.</p> <p>Consider risk versus benefits of molnupiravir as limited evidence in patients &lt;70 years old. For patients aged &lt; 70 years who are contraindicated from taking nirmatrelvir/ritonavir, prescribe molnupiravir if benefits outweigh risks AND appropriate reproductive counselling can be provided.</p> <ul style="list-style-type: none"> <li>● Second line treatment of mild COVID-19 for non-pregnant adults where nirmatrelvir plus ritonavir is 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:             <ul style="list-style-type: none"> <li>○ Meet <a href="#">PBS criteria</a> for treatment with molnupiravir</li> </ul> </li> </ul>

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	<ul style="list-style-type: none"> <li>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.</li> </ul>
<b>Contra-indications</b>	<ul style="list-style-type: none"> <li>Hypersensitivity to molnupiravir or any of the excipients in the product.</li> <li>Children less than 18 years old.</li> <li><b>Pregnancy</b> – the use of molnupiravir in pregnant patients is <b>not recommended</b> due to potential risk of reduced foetal growth and development.</li> <li><b>Breastfeeding</b> – 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 <b>not recommended</b> during AND for 4 days after treatment.</li> <li><b>Contraception</b> - 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.</li> </ul>
<b>Precautions</b>	<ul style="list-style-type: none"> <li>Exercise caution in patients with a history of anaphylaxis to other medicines.</li> <li><b>Renal Impairment</b> - Patients with eGFR &lt; 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.</li> <li><b>Hepatic impairment</b> – 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.</li> </ul>
<b>Drug Interactions</b>	<ul style="list-style-type: none"> <li>No formal interaction studies have been conducted with molnupiravir.</li> <li>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.</li> <li>While the potential for drug interactions with molnupiravir are considered unlikely, as this is a new drug, continue to check the <a href="#">University of Liverpool COVID-19 resource page</a>.</li> </ul>
<b>Presentation and storage</b>	<ul style="list-style-type: none"> <li>Available as 200mg capsules supplied as a bottle of 40 capsules.</li> <li>Store at room temperature, less than 30°C</li> </ul>
<b>Dose</b>	<ul style="list-style-type: none"> <li>800mg (4 x 200mg capsules) orally 12-hourly for 5 days.</li> <li>No dose adjustment is required for renal or hepatic impairment or the elderly (see precautions above).</li> <li>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.</li> </ul>
<b>Administration</b>	<ul style="list-style-type: none"> <li>Capsules can be taken with or without food.</li> <li>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.</li> <li>Preparation of the solution: <ul style="list-style-type: none"> <li>Open FOUR (4) capsules and transfer contents into an oral syringe. Discard empty capsule shells.</li> <li>Add approximately 40 mL of water to the oral syringe.</li> </ul> </li> </ul>

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	<ul style="list-style-type: none"> <li>○ Mix/stir the capsule contents and water for 3 minutes.             <ol style="list-style-type: none"> <li>1. Insoluble capsule contents may not dissolve completely.</li> <li>2. Reconstituted solutions prepared according to directions may have visible undissolved particulates and are acceptable for oral administration.</li> </ol> </li> <li>○ Administration should occur as soon as possible after the preparation and no later than 2 hours after the preparation.</li> <li>● For administration via enteral tube:             <ul style="list-style-type: none"> <li>○ Prior to administration redisperse the suspension by mixing or stirring the oral syringe for 1 minute prior to administration.</li> <li>○ Flush enteral tube with 5 mL of water prior to administration.</li> <li>○ Administer entire volume from the administration syringe.</li> <li>○ Flush tube with 5 mL of water TWICE (10 mL total) after administration of the suspension.</li> </ul> </li> </ul>
<b>Handling</b>	<ul style="list-style-type: none"> <li>● 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.</li> <li>● For all other staff, use standard Personal Protective Equipment (PPE) if preparation or administration of a dispersed tablet is required.</li> </ul>
<b>Monitoring</b>	<ul style="list-style-type: none"> <li>● Baseline creatinine, electrolytes and urea, LFTs and complete blood exam.</li> <li>● Monitor the patient for adverse effects.</li> <li>● If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue and initiate appropriate medications and/or supportive care.</li> </ul>
<b>Adverse Effects</b>	<ul style="list-style-type: none"> <li>● It may be difficult to distinguish between adverse effects of molnupiravir and the signs and symptoms of COVID-19.</li> <li>● 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:             <ul style="list-style-type: none"> <li>○ Common (&gt;1%): diarrhoea, nausea, dizziness, headache</li> <li>○ Uncommon (0.1-1%): rash, urticaria</li> </ul> </li> <li>● Suspected or confirmed adverse reactions should be reported via your local Incident Management System (for SA Health this is currently the Safety Learning System) and also via the Therapeutic Goods Administrations adverse effects online form: <a href="#">TGA adverse event reporting</a>.</li> </ul>
<b>Patient Information and consent forms</b>	<ul style="list-style-type: none"> <li>● Refer to the Consumer Medicines Information (CMI) leaflets for <a href="#">molnupiravir</a>.</li> <li>● Molnupiravir patient information leaflets can be found <a href="#">here</a>.</li> </ul>

## DEFINITIONS/ACRONYMS/ABBREVIATIONS

BMI	Body Mass Index
COPD	Chronic obstructive pulmonary disease
eGFR	estimated Glomerular Filtration Rate
GI	Gastrointestinal
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human Immunodeficiency Virus

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ID	Infectious Diseases
IV	Intravenous
MDI	Metered dose inhaler
NMS	National Medical Stockpile
NYHA	New York Heart Association

## APPENDICES

### [Appendix 1: Definition of COVID-19 disease severity for adults](#)

## RESOURCES

- [Australian Immunisation Handbook: COVID-19](#)
- [COVID-19 \(SARS-COV-2\) – Management Guide \(CALHN-PRC05409\)](#)
- [Anaphylaxis: Management Guidelines \(CALHN-CPA04038\)](#)
- [COVID-19: Disease-modifying therapy recommendations for hospitalised adults \(CALHN-GDE05778\)](#)
- [World Health Organisation. Therapeutics and COVID-19: Living Guideline](#)
- [Australian Technical Advisory Group on Immunisation \(ATAGI\)](#)
- [Clinical Excellence Commission: Medication Safety Updates](#)
- [COVID-19 Treatment: Nirmatrelvir-Ritonavir \(Paxlovid®\) \(IH-CIS05842\)](#)
- [COVID-19 Resources: Medicines Use in the treatment of COVID-19 – Consent Forms](#)

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## Appendix 1 – Definition of COVID-19 disease severity for adults<sup>1</sup>

<b>Mild illness (outpatient or inpatients admitted with another condition)</b>	<p>Adults not presenting any clinical features suggestive of moderate or severe disease or a complicated course of illness.</p> <ul style="list-style-type: none"> <li>• Characteristics: <ul style="list-style-type: none"> <li>○ no symptoms (only PBS eligible for patients <math>\geq 70</math> years); or</li> <li>○ mild upper respiratory tract symptoms; or</li> <li>○ cough, new myalgia or asthenia without new shortness of breath or a reduction in oxygen saturation or</li> <li>○ nausea, vomiting, diarrhea, loss of taste or loss of smell</li> <li>○ Oxygen saturations <math>&gt;95\%</math> on room air</li> </ul> </li> </ul>
<b>Moderate illness (ward based care)</b>	<p>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.</p> <ul style="list-style-type: none"> <li>• Characteristics: <ul style="list-style-type: none"> <li>○ Fatigue or persistent cough</li> <li>○ clinical or radiological signs of lung involvement</li> <li>○ no clinical or laboratory indicators of clinical severity or respiratory impairment</li> </ul> </li> </ul>
<b>Severe illness (specialised ward or ICU)</b>	<p>Adult patients meeting any of the following criteria:</p> <ul style="list-style-type: none"> <li>• respiratory rate <math>\geq 30</math> breaths/min</li> <li>• oxygen saturation <math>\leq 92\%</math> at a rest state on <math>\geq 4\text{L}/\text{min}</math> oxygen via nasal prongs</li> <li>• arterial partial pressure of oxygen (<math>\text{PaO}_2</math>) / inspired oxygen fraction (<math>\text{FiO}_2</math>) <math>\leq 300</math></li> </ul>
<b>Critical illness (ICU)</b>	<p>Adult patients meeting any of the following criteria:</p> <ul style="list-style-type: none"> <li>• Respiratory failure as defined by: <ul style="list-style-type: none"> <li>○ severe respiratory failure (<math>\text{PaO}_2/\text{FiO}_2 &lt; 200</math>), respiratory distress or acute respiratory distress syndrome</li> <li>○ deterioration despite advanced forms of respiratory support (non-invasive ventilation, high flow nasal oxygen) OR requiring mechanical ventilation</li> </ul> </li> </ul> <p><b>OR</b></p> <ul style="list-style-type: none"> <li>• Other signs of significant deterioration: <ul style="list-style-type: none"> <li>○ hypotension or shock</li> <li>○ impairment of consciousness</li> <li>○ other organ failure</li> </ul> </li> </ul>

## End of Appendix 1