

COVID-19 Early Therapies

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COVID-19 early therapies

- There are a range of medications provisionally approved by the TGA available in Victoria
- Access for patients through hospitals (National Medical Stockpile) or the PBS:

Hospital medications

nirmatrelvir and ritonavir (Paxlovid™)
remdesivir (Veklury™)
molnupiravir (Lagevrio™)
sotrovimab (Xevudy™)
casirivimab plus imdevimab (Ronapreve™)

PBS medications

nirmatrelvir and ritonavir (Paxlovid™)
molnupiravir (Lagevrio™)
inhaled budesonide (not on PBS for COVID)

- Treatment goal is to prevent severe disease in high risk people with COVID-19 early in their illness

Nirmatrelvir and ritonavir (Paxlovid™)

Within 5 days of symptom onset in at risk people

89% relative risk reduction in hospitalisation and death (EPIC-HR trial). NNT 18.

Three tablets taken together twice daily for 5 days – dose reduction for eGFR 30-60ml/min

Considerations:

- Cannot use if: Severe renal impairment (eGFR < 30 ml/min)
- Severe hepatic impairment (Child-Pugh Class C)
- **Drug interactions**
- Weight < 40 kg
- Pregnancy Category B3 - do not use, avoid getting pregnant for 7 days after treatment ceases
- Do not use in breastfeeding women. Recommence 7 days after treatment ceases.
- Bitter/metallic taste

Molnupiravir (Lagevrio™)

Within 5 days of symptom onset in at risk people

30% relative risk reduction in hospitalisation and death (MOVE-OUT trial). NNT 35.

Four capsules taken twice daily for 5 days

Considerations:

- Pregnancy Category D - do not use. Women to avoid getting pregnant for 4 days after treatment ceases.
- Men should use adequate contraception during and 3 months after treatment ceases.
- Do not use in breastfeeding women. Recommence 4 days after treatment ceases.

Remdesivir (Veklury™)

Within 7 days of symptom onset in at risk

87% relative risk reduction in hospitalisation (PINETREE trial). NNT 22

IV infusion daily x 3 days

Considerations:

- Hepatic dysfunction (ALT > 5 x upper limit of normal, or ALT > 3 x upper limit of normal and bilirubin > 2 x upper limit of normal)
- Severe renal impairment (eGFR < 30 ml/min) – unless receiving dialysis treatment
- Pregnancy Category B2 - requires assessment of risks versus benefits. Being offered to some unvaccinated pregnant women with comorbidities.
- **Consider logistics of patient accessing treatment**

Sotrovimab (Xevudy™)

Within 5 days of symptom onset in at risk

79% relative risk reduction in hospitalisation and death (COMET-ICE trial). NNT 22.

Emerging evidence suggests significantly decreased viral neutralisation of sotrovimab (Xevudy™) against the BA.2 variant. Not actively being recommended, especially if alternatives.

IV infusion x single dose

Considerations:

- Weight < 40 kg
- Pregnancy Category B2 - requires assessment of risks versus benefits (2nd and 3rd trimester only).

PBS criteria: Paxlovid™ and Lagevrio™

COVID within 5 days of symptom onset

≥75 years old

One of the following



PBS Authority
code 12923

Between 65 and 74
years old

Two of the following



PBS Authority
code 12923

Aboriginal and ≥50
years old

Two of the following



PBS Authority
code 12936

- Less than two doses of the vaccine
- Living in residential aged care or residential disability care,
- Neurological conditions, including stroke and dementia,
- Respiratory compromise, including COPD, moderate or severe asthma (required inhaled steroids), and bronchiectasis,
- Congestive heart failure (NYHA Class II or greater),
- Obesity (BMI greater than 30 kg/m²),
- Diabetes Types I and II, requiring medication for glycaemic control,
- Renal failure (eGFR less than 60mL/min),
- Cirrhosis, or
- Has 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.

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PBS criteria: Paxlovid™ and Lagevrio™

Within 5 days of symptom onset

≥18 years old

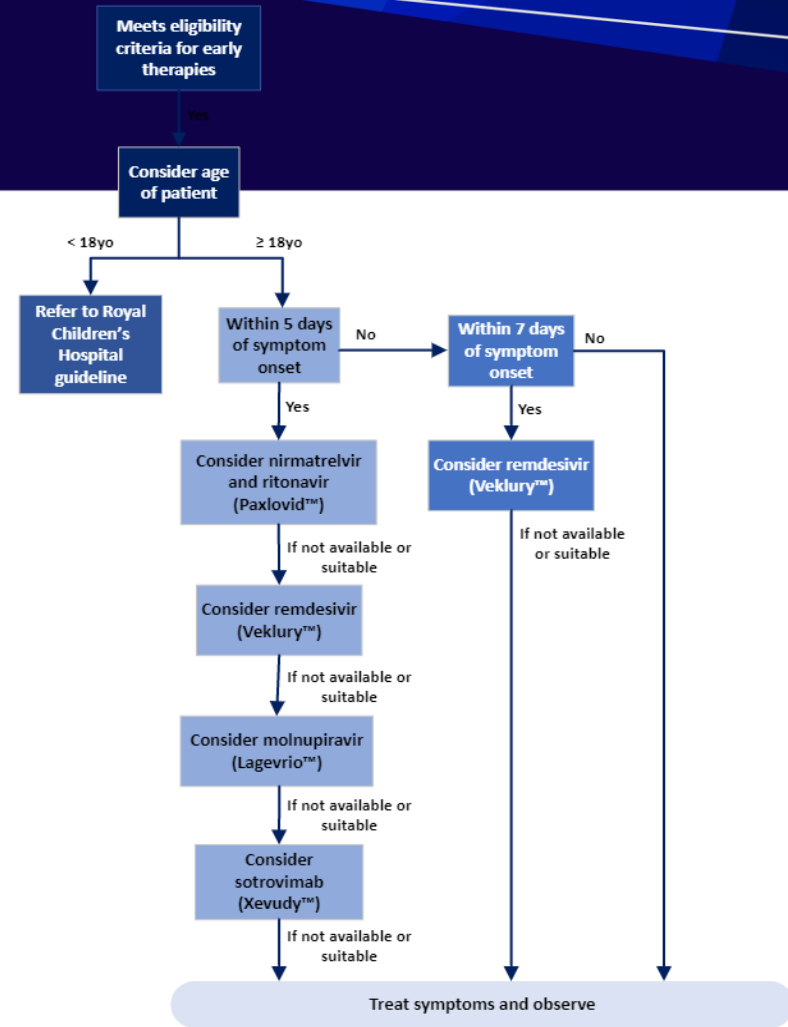


PBS Authority
code 12839

1. Any primary or acquired immunodeficiency including
 - a) Haematological neoplasms
 - b) Post-transplant- solid organ (on immunosuppressants), stem cell transplant last 12 months
 - c) primary or acquired (HIV/AIDs) immunodeficiency
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 ($\geq 20\text{mg}$ prednisolone ≥ 14 days in one month or pulse corticosteroids)
 - c) Biological agents or treatments that deplete or inhibit B cell or T cell function
 - d) Selected conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs)
3. Any significantly immunocompromising condition(s) where, in the last 12 months the patient has received rituximab
4. Others with very high risk conditions including Down Syndrome, cerebral palsy, congenital heart disease, thalassemia, sickle cell disease and other haemoglobinopathies
5. People with severe intellectual or physical disabilities requiring residential care

COVID-19 early therapies - adults

- [Clinical-decision making guide](#) published to support early therapy prescribing
- Guide includes key information on administration, timing, precautions and contraindications and links to further information



Paxlovid™ is not suitable if a patient has any of the following:

- Severe renal (eGFR < 30ml/min) or liver impairment (Child Pugh Class C)
- < 40kg
- Unable to swallow tablets
- Pregnancy
- Hypersensitive to active ingredients

Common medications which interact - coadministration not recommended:

List not exhaustive

Amiodarone	Midazolam (oral)
Bosentan	Pethidine
Carbamazepine	Phenobarbitone
Ciclosporin	Primidone
Clozapine	Phenytoin
Clonazepam	Quetiapine
Colchicine	Rifampicin
Disopyramide	Sildenafil (pulmonary hypertension)
Dronedarone	Sildenafil (pulmonary hypertension)
Enzalutamide	Sildenafil (pulmonary hypertension)
Eplerenone	St John's Wort
Flecainide	Tacrolimus
Ivabradine	Tadalafil

Take a thorough medication history:

- Check if the patient uses a compliance aid and who fills it e.g. patient, carer, pharmacy
- Gather full medication list including prescribed, over-the-counter, supplementary/herbal medications and any illicit/recreational drugs
- Check for interactions
<https://www.covid19-druginteractions.org/checker>
(or Paxlovid product info)
- Seek pharmacist advice if complex medications

Common medications with interactions - may be appropriate if withheld for 8 days or dose adjusted:

Alfuzosin	Rivaroxaban
Apixaban	Rosuvastatin
Atorvastatin	Salmeterol
Diazepam	Simvastatin
Domperidone	Ticagrelor
Lercanidipine	List not exhaustive

Medications with no known interactions:

ACE inhibitors	Inhalers (except salmeterol)
Acid reducing agents (antacids, PPIs and H2RAs)	Insulin
Aspirin	Levothyroxine
Azathioprine	Metformin
Beta Blockers	Methotrexate
Contraceptives/HRT	Monoclonal antibodies (MABs)
Corticosteroids (oral/inhaled/topical)	Mycophenolate
Flustatin	NSAIDs (except piroxicam)
Frusemide	Pravastatin
Gabapentin	Pregabalin
Immunoglobulin	List not exhaustive

Consider if the following can be done safely and is suitable based on the specific drug interaction:

- Can interacting regular medicines be safely withheld for 8 days (treatment time + 3)
- Can interacting medication be safely dose adjusted?
- Is monitoring for adverse reactions when interacting medicines are used concurrently possible?

NO

YES

Consent and prescribe

Consent patient or medical treatment decision maker and prescribe dose based on renal function

If eGFR 30-60ml/min:
Nirmatrelvir 150mg (1 x 150mg) + ritonavir 100mg
BD for 5 days

If eGFR ≥ 60ml/min:
Nirmatrelvir 300mg (2 x 150mg) + ritonavir 100mg
BD for 5 days

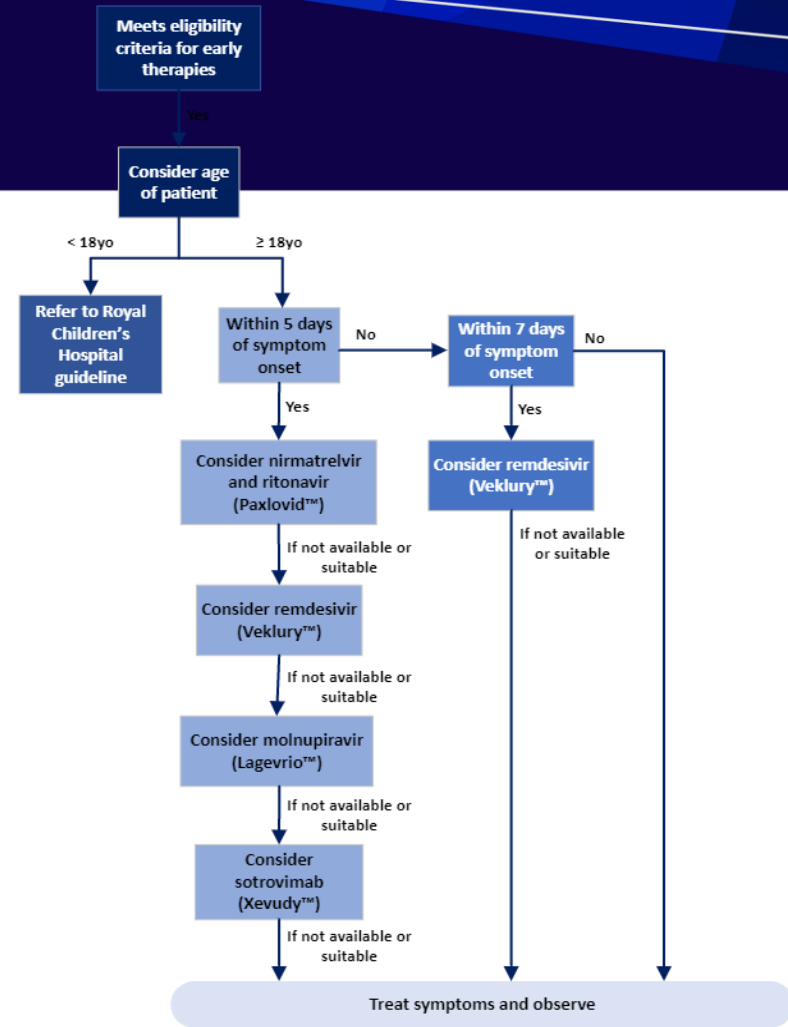
If Paxlovid™ is not suitable consider other early therapies based on precautions, contraindications, efficacy and availability

Victorian COVID Therapies PBS Prescriber Helpline

- Pharmacy helpline launched today to support GPs in the prescription of oral antivirals nirmatrelvir and ritonavir (Paxlovid™) and molnupiravir (Lagevrio™)
- Staffed by Alfred Health pharmacists experienced in prescribing COVID-19 early therapies
- 7 days a week 8am-5pm
- (03) 8290 3801

COVID-19 early therapies - adults

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Access to hospital medications

Risk factors:	Category:	Prioritisation		
	Age (years)	Priority Group 1	Priority Group 2	Priority Group 3
Immunosuppressed	≥12			
Unvaccinated	≥80			
	65-80			
	12-64			At least one high risk comorbidity
Vaccination status: Not up-to-date	≥80		At least one high risk comorbidity	
	65-80			At least one high risk comorbidity
	12-64			
Vaccination status: Up-to-date	≥80			At least one high risk comorbidity
	65-80			At least one high risk comorbidity
	18-64			
Pregnancy (>13 weeks)			Unvaccinated or Not up-to-date with at least one high risk comorbidity	Not up-to-date
Aboriginal and Torres Strait Islanders	≥50		Unvaccinated or Not up-to-date with at least one comorbidity	Not up-to-date

- [Prioritisation matrix](#) guides NMS eligibility and resource allocation
- GPs can refer to the hospitals for patient access to remdesivir (Veklury™) and sotrovimab (Xevudy™)
- [COVID-19 early therapies – factsheet for referrers](#) has statewide contact details for hospitals administering early therapies
- Service provision based on local case numbers, workforce capacity to support prescription and administration of therapies and Victorian stock availability
- The most at risk patients treated as part of the Covid Positive Pathways medium-risk pathway

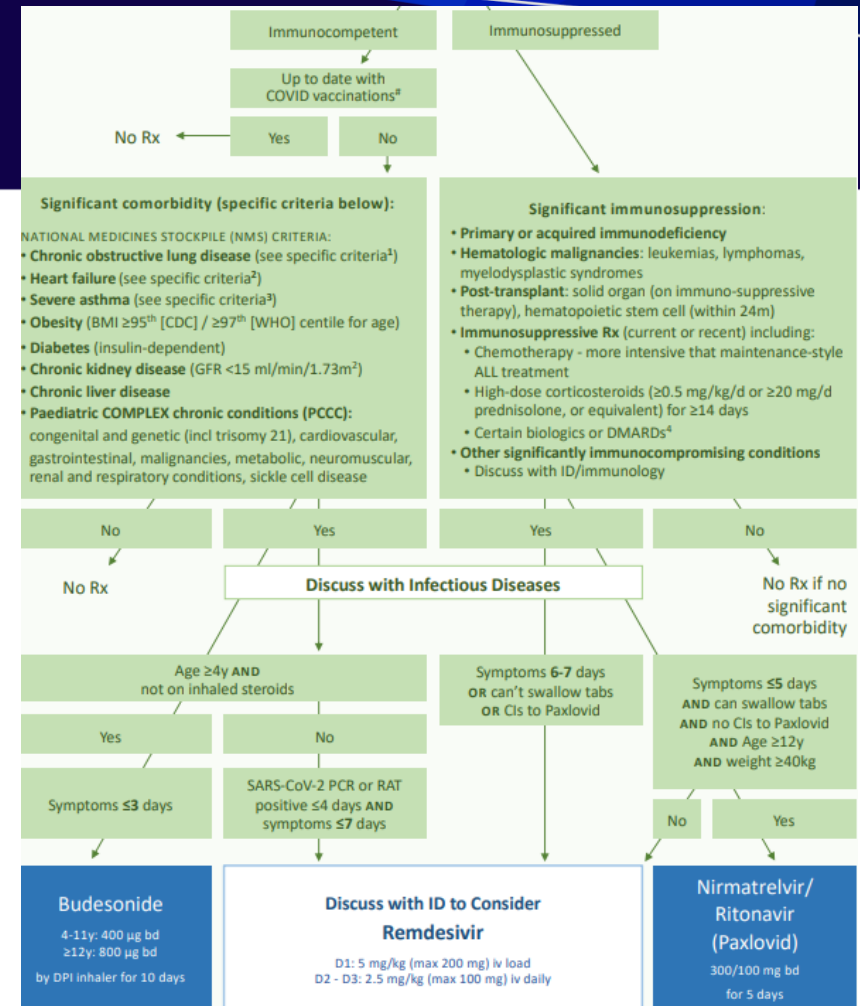
COVID-19 early therapies – for high risk people

1. Prioritise Paxlovid
2. If Paxlovid can't be used consider referral to hospital for Remdesivir if:
 - immunosuppressed
 - pregnant
 - unvaccinated and elderly
 - ATSI and not fully vaccinated with comorbidities
 - patient willing and able
3. Otherwise molnupirivir
4. Budesonide also available but conflicting evidence

COVID-19 early therapies

- children

- Clinical-decision making for children <18yo advised by [RCH guidelines](#)
- No PBS options based on current eligibility criteria
- nirmatrelvir and ritonavir (Paxlovid™) if significant immunosuppression (≥12yo)
- remdesivir (Veklury™) if significant immunosuppression OR significant comorbidities and not up-to-date with COVID vaccinations



Early therapies in primary care

- Pre-emptively identify and raise awareness among patients who fit the eligibility criteria and have an opportunistic discussion ahead of a COVID-19 diagnosis
- As part of that discussion, advise patients if they test positive through a RAT or PCR to contact the practice to get an appointment (i.e. telehealth) for a consultation and prescription
- Advise local pharmacies that as eligible patients present, GPs will be prescribing these medications so pharmacies are encouraged to hold stock

Further information

<https://www.health.vic.gov.au/covid-19/vaccines-and-medications-in-patients-with-covid-19>

<https://www.pbs.gov.au/medicine/item/12910L>

<https://www.pbs.gov.au/medicine/item/12996B>

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