

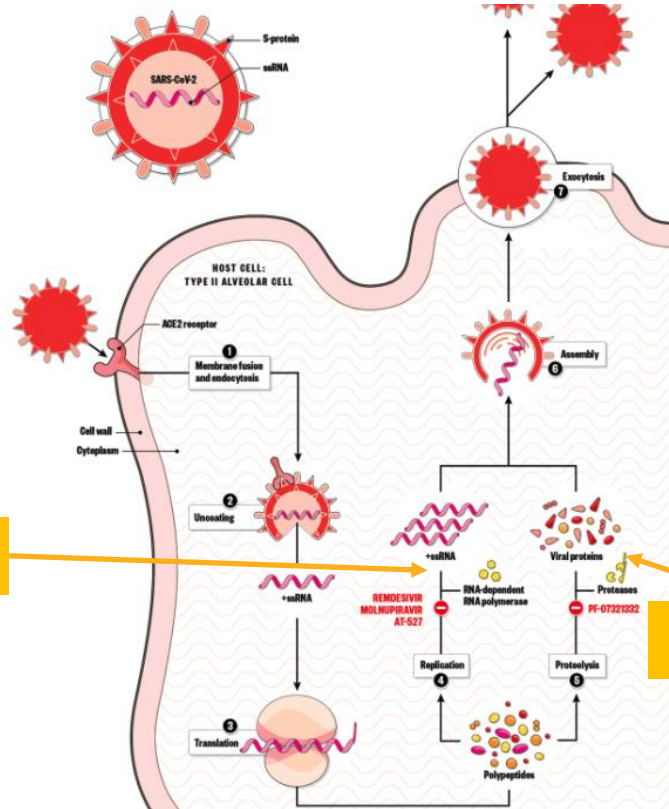
# Oral antiviral agents for SARS-CoV2

Prof Peter Wark, ACI NSW Health



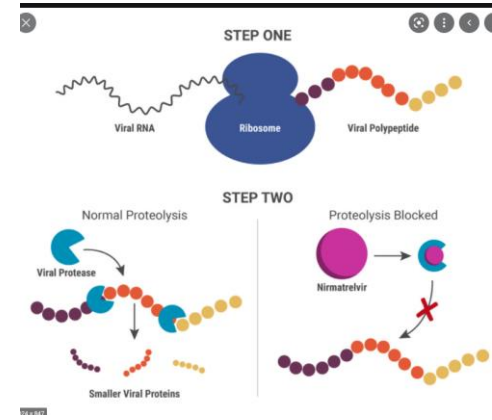
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# Antiviral mechanisms of action



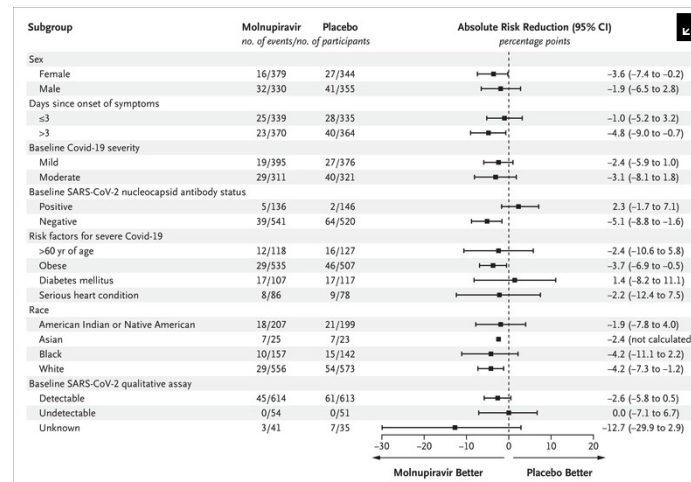
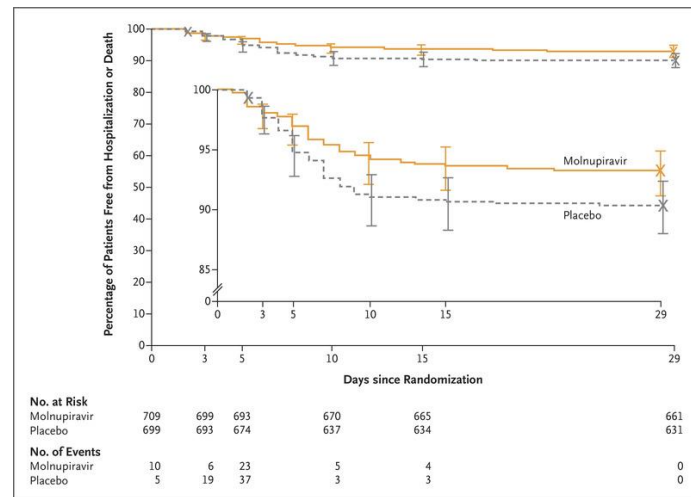
Molnupirivir

Nirmatrelvir



# Molnupirivir or Lagevrio

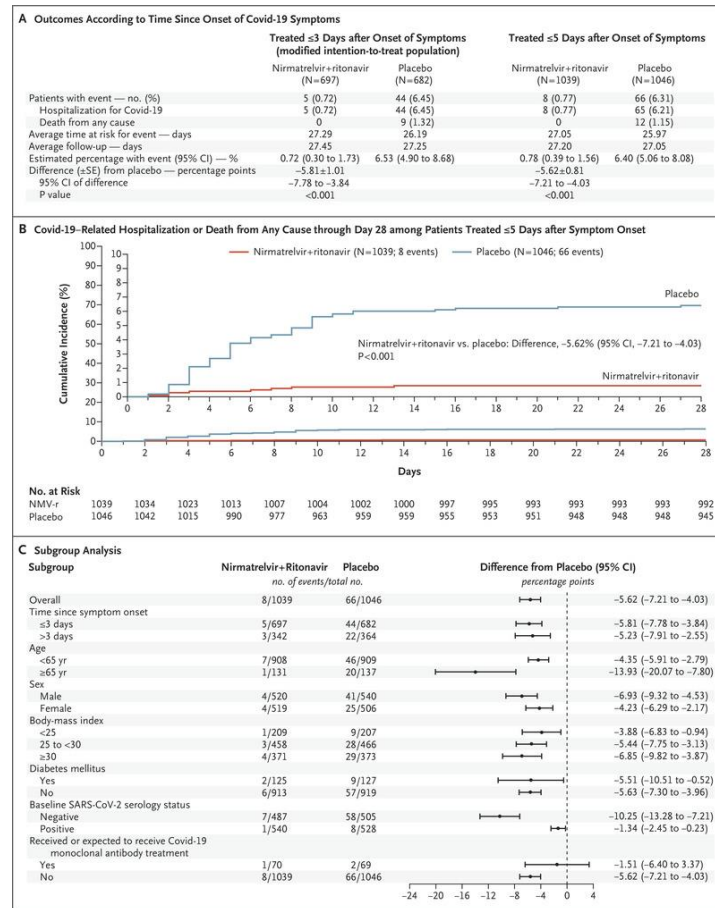
- RCT 1433
  - >18yrs
  - all unvaccinated
  - At least 1 risk factor severe COVID-19
  - Within 5 days of infection
- Randomised Molnupirivir 800mg BD or placebo for 5 days
- molnupiravir (28 of 385 participants [7.3%]) than with placebo (53 of 377 [14.1%]) (difference, -6.8 percentage points; 95% confidence interval, -11.3 to -2.4; P=0.001)
- Relative risk reduction, 48%, NNT 15
- no serious side-effects



# Nirmaltrevir/Ritonavir or Paxlovid

- RCT 2246 people
  - >18yrs
  - all unvaccinated
  - At least 1 risk factor severe COVID-19
  - Within 5 days of infection
- Hospitalization or death by d28 lower in the nirmatrelvir group vs placebo by 6.32 % (95%CI; -9.04 to -3.59; P<0.001
- relative risk reduction, 89.1%, NNT 16
- The viral load lower with at day 5 of treatment, adjusted mean difference of  $-0.868 \log_{10}$

Hammond et al NEJM 2021;

<https://www.nejm.org/doi/full/10.1056/NEJMoa2118542>


## Contraindications

### Molnupiravir (LAGEVRIO)

- not recommended in pregnancy and breastfeeding. It is recommended that sexually active women of childbearing potential use contraception and men also use contraception during and 3 months after treatment with LAGEVRIO.

## Contraindications

### Nirmaltrevir-Ritonavir (PAXLOVID)

- not recommended in pregnancy or breastfeeding, and in women of childbearing potential. It is recommended that sexually active women of childbearing potential use contraception.
- Not in severe renal disease eGFR<30ml/min (dose reduction 30-60ml/min)
- Not is severe liver disease

Medicinal product class	Medicinal products within class
<b>Interactions that result in an increase or decrease in concentrations of concomitant medicine</b>	
Alpha 1-adrenoreceptor antagonist	alfuzosin
Antianginal	ranolazine
Antiarrhythmics	amiodarone, flecainide
Anticancer	neratinib, venetoclax
Anti-gout	colchicine
Antipsychotics	lurasidone, clozapine
Ergot derivatives	ergometrine
Lipid-modifying agents HMG-CoA reductase inhibitors	simvastatin
Nonsteroidal anti-inflammatory drugs (NSAIDs)	piroxicam
Opioid analgesic	pethidine
PDE5 inhibitor	avanafil, sildenafil, vardenafil, tadalafil
Sedative/hypnotics	diazepam

# Anti-SARS-CoV-2 Monoclonal antibodies & antivirals

Expanding the model of care

Care in Community CoP | 10 February 2022

Ellen Rawstron



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## Overview

- NSW Monoclonal antibody model of care – updated for oral antivirals
- Defines eligibility & priority cohorts
  - Clinical consensus
  - Considerations = those most at risk & supply
- Recommendations for adults and adolescents (Table 1 and Table 2)
- Decision Flow Charts (Figures 1, 2, 3)
- To be used with CEC & NSW Health Care in Community Guidance
- Available via NSW Health and ACI websites at <https://aci.health.nsw.gov.au/covid-19/communities-of-practice>



## Eligibility in NSW

- Within 5 days of symptom onset **AND**
- No oxygen requirement due to COVID-19 **AND**
- Reduced immunity to COVID-19 by being:
  - unvaccinated (i.e. received no doses of a COVID-19 vaccination) **OR**
  - not fully vaccinated (i.e. has not completed their primary course of COVID-19 vaccination) **OR**
  - overdue for booster (as per **ATAGI guidance**) **OR**
  - Immunocompromised\* (irrespective of age and vaccine status) **AND**
- Medicine-specific age and risk factors (as outlined in Table 1 or Table 2).

\*Immunocompromised defined as per ATAGI guidance.  
NSW Agency for Clinical Innovation

**Table 1. NSW-specific risk factors for high priority cohorts in adults****Risk factors that must be met for prescription of any of the four medications**

- Within 5 days of symptom onset **AND**
- No oxygen requirement due to COVID-19 **AND**
- Reduced immunity to COVID-19 by being:
  - unvaccinated (i.e. received no doses of a COVID-19 vaccination) **OR**
  - not fully vaccinated (i.e. has not completed their primary course of COVID-19 vaccination) **OR**
  - overdue for booster (as per [ATAGI guidance](#)) **OR**
  - immunocompromised\* **AND**
- Medicine-specific age and risk factors outlined below

**Medication-specific risk factor/s****Sotrovimab**

- Pregnant women in their second or third trimester **OR**
- Age  $\geq$  65 years or  $\geq$ 35 years if Aboriginal and/or Torres Strait Islander (excluding pregnant women)

**AND one** of the following risk factors:

- Obesity (BMI  $\geq$  30 kg/m<sup>2</sup>)
- Severe cardiovascular disease (including hypertension)
- Severe chronic lung disease; including severe asthma (requiring a course of oral steroids in the previous 12 months), COPD and interstitial lung disease
- Type 1 or 2 diabetes mellitus
- Severe chronic kidney disease, including those that are on dialysis
- Severe chronic liver disease
- Immunocompromised\*

**Medication-specific risk factor/s****Nirmatrelvir plus ritonavir**

- Non-pregnant adults who are aged  $\geq 65$  years or  $\geq 35$  years if Aboriginal and/or Torres Strait Islander

**AND one** of the following risk factors:

- Obesity (BMI  $\geq 30$  kg/m<sup>2</sup>)
- Severe cardiovascular disease (including hypertension)
- Severe chronic lung disease; including severe asthma (requiring a course of oral steroids in the previous 12 months), COPD and interstitial lung disease
- Type 1 or 2 diabetes mellitus

**OR** aged  $\geq 18$  years if immunocompromised\*

**Molnupiravir**

- Non-pregnant adults who are aged  $\geq 65$  years or  $\geq 35$  years if Aboriginal and/or Torres Strait Islander

**AND one** of the following risk factors:

- Obesity (BMI  $\geq 30$  kg/m<sup>2</sup>)
- Severe cardiovascular disease (including hypertension)
- Severe chronic lung disease; including severe asthma (requiring a course of oral steroids in the previous 12 months), COPD and interstitial lung disease
- Type 1 or 2 diabetes mellitus
- Severe chronic kidney disease, including those who are on dialysis and unable to receive monoclonal antibody treatment
- Severe chronic liver disease

**OR** aged  $\geq 18$  years if immunocompromised\*

Table 2. NSW-specific risk factors for adolescents

Risk factors that must be met for prescription in adolescents
<ul style="list-style-type: none"> <li>• Aged 12 to 17 years <b>AND</b></li> <li>• Weighing at least 40kg <b>AND</b></li> <li>• Within 5 days of symptom onset <b>AND</b></li> <li>• No oxygen requirement due to COVID-19 <b>AND</b></li> <li>• Reduced immunity to COVID-19 by:               <ul style="list-style-type: none"> <li>– unvaccinated (i.e. received no doses of a COVID-19 vaccination) <b>OR</b></li> <li>– partially vaccinated (i.e. only 1 dose of COVID-19 vaccine) <b>OR</b></li> <li>– immunocompromised (as per ATAGI guidance), irrespective of vaccine status <b>AND</b></li> </ul> </li> <li>• Medication-specific age and risk factors outlined below</li> </ul>
Medication-specific risk factors
<p><b>Sotrovimab</b></p> <p>AND at least <b>two</b> of the following risk factors:</p> <ul style="list-style-type: none"> <li>• Paediatric complex chronic condition (PCCC): congenital and genetic, cardiovascular, gastrointestinal, malignancies, metabolic and neuromuscular</li> <li>• Diabetes (requiring medication) and pre-gestational diabetes (requiring medication) in pregnant women</li> <li>• Obesity (BMI <math>\geq</math> 95th centile for age)</li> <li>• Chronic kidney disease (GFR <math>&lt;15</math> mL/min/1.73m<sup>2</sup>)</li> <li>• Heart failure, or Congenital Heart Disease with persisting cyanosis or pulmonary hypertension</li> <li>• Chronic obstructive lung disease (e.g. chronic lung disease requiring oxygen, cystic fibrosis with reduced lung function)</li> <li>• Severe asthma (in the past 12 months: <math>\geq 1</math> exacerbation requiring ICU admission OR IV treatment OR <math>\geq 2</math> hospital admissions for asthma)</li> </ul> <p><i>In other exceptional circumstances, please discuss eligibility with a paediatric infectious diseases specialist.</i></p>

Figure 1. Decision pathway: outpatient suitability for monoclonal antibodies or oral antivirals

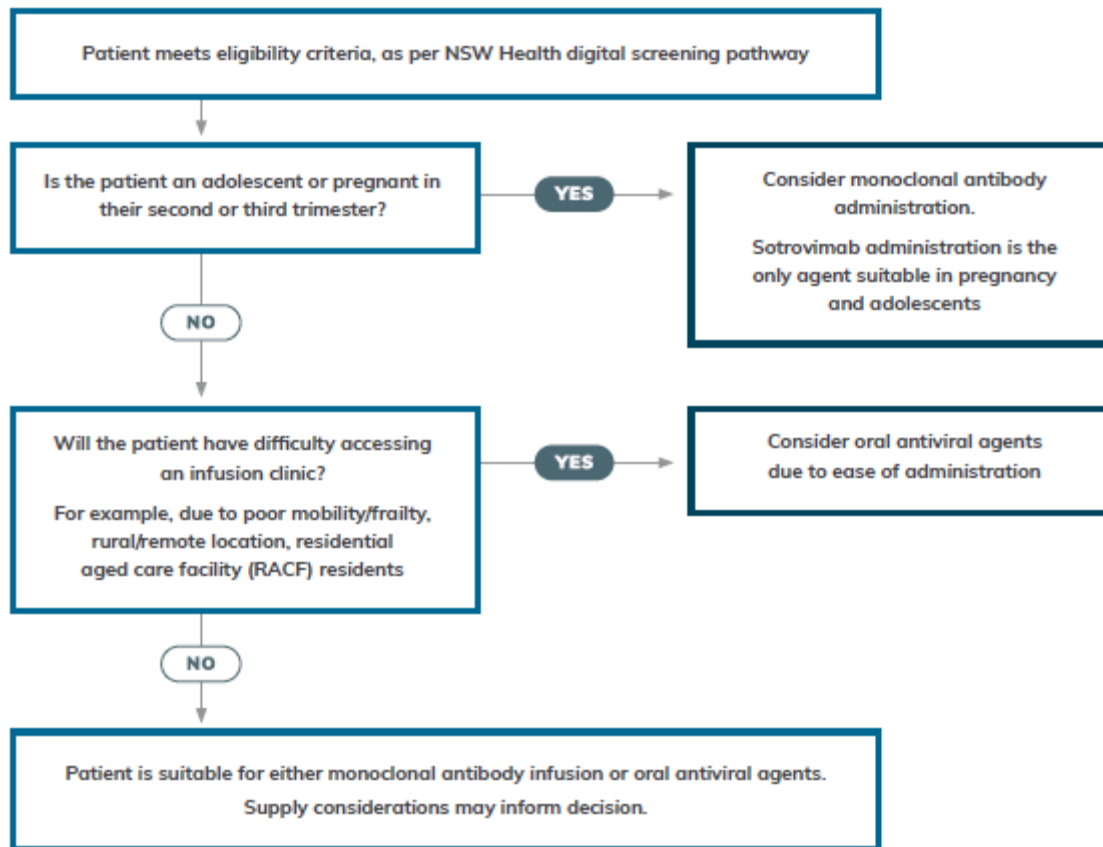
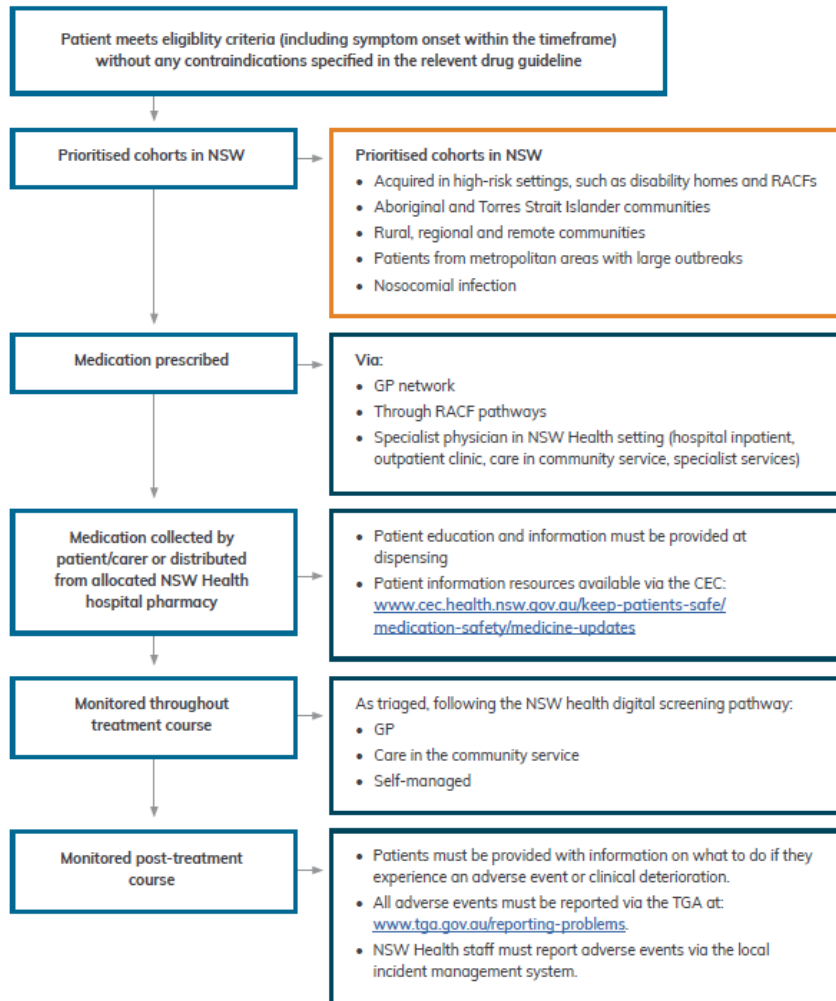


Figure 3: Flowchart for administration of oral antivirals in adults with mild and moderate COVID-19





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