

Guidance for the use of anti-SARS-CoV-2 monoclonal antibodies and antiviral agents as prophylaxis or to prevent severe infection from COVID-19 in NSW

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A range of anti-SARS-CoV-2 monoclonal antibodies and antiviral medications have been provisionally approved by the Therapeutic Goods Administration.

These medications are for prophylaxis or for the treatment of patients in the early phase of infection with COVID-19 who are at risk of progression to severe disease. This guidance outlines the use of these medications in NSW.

Methodology

The National COVID-19 Clinical Evidence Taskforce (NCCET) Guidelines specify recommendations for the use of anti-SARS-CoV-2 monoclonal antibodies and antivirals in adults, and children and adolescents (aged over 12 years) in Australia based on available evidence.¹ This guidance is based on these recommendations and the evidence checks undertaken by the [NSW Critical Intelligence Unit](#) (CIU).^{2,3}

The available evidence was considered by an expert group of NSW clinicians to inform the development of this guidance. Emerging medications are also being monitored by the CIU and will be included in this document, as required. This document should be read in conjunction with drug guidance developed by the Clinical Excellence Commission (CEC).⁴

Updates – 27 May 2022

The following updates are included in this version:

- Alignment to NCCET, Pharmaceutical Benefits Scheme (PBS) or the Therapeutic Goods Administration (TGA) eligibility criteria for monoclonal antibodies and antiviral agents (please see [Table 1](#) for details)
- Updates to the decision pathway figure to reflect recommendation from NCCET for nirmatrelvir plus ritonavir to be prescribed for children and adolescents if appropriate
- Inclusion of the PBS prescription pathway for oral antiviral medications
- Addition of remdesivir for treatment of those who do not require supplemental oxygen and who are at high risk of progressing to severe COVID-19.

Who can be treated?

Clinical criteria and risk factors

The medications covered in this model of care are:

- [casirivimab and imdevimab](#)
- [molnupiravir](#)
- [nirmatrelvir plus ritonavir](#)
- [remdesivir](#)
- [sotrovimab](#)
- [tixagevimab and cilgavimab](#).

The drug guidelines for these medications are available on the [CEC website](#).

Generally, these drugs are for use early in the course of the disease before significant symptoms or severe disease have developed, and within a window of 5 to 7 days from the onset of infection (preferably as early as possible). These agents prevent the replication and spread of the virus and are likely to work best soon after infection has occurred. This limits the spread of the virus beyond the respiratory tract and before a severe systemic immune response has been initiated. The guidance outlined in this document is for the use of a single medication for this indication.

Note: Tixagevimab plus cilgavimab can be used for pre-exposure prophylaxis and casirivimab plus imdevimab for post-exposure prophylaxis.

Currently only some of these medications are approved for children and adolescents aged 12 to 17 years who weigh >40kg.

Only specific patient groups are expected to benefit from, and hence be eligible for, these medicines. They are not an alternative to COVID-19 vaccination, which remains the best way to protect vulnerable populations from severe outcomes of COVID-19 infection.

Although the indications for these medications are similar, they are not identical. As such, NCCET eligibility criteria recommendations and individual drug guidelines should be reviewed, particularly with respect to the COVID-19 variants likely to be present.

Considerations for all medications are outlined in [Table 1](#).

Vaccination

Routine use of these medications is not encouraged in patients who are up to date with their COVID-19 vaccinations, unless a suboptimal response is predicted (e.g. severe immunosuppression from a medical condition or medication) or if the patient has multiple co-morbidities that increase their risk of disease progression.⁵

The [Australian Technical Advisory Group on Immunisation](#) (ATAGI) specifies the interval for vaccination. Vaccination can take up to 14 days to be effective.⁵

ATAGI does not recommend a minimum time frame to defer vaccination due to monoclonal antibody medicine or antiviral administration. However, it is recommended to follow guidance to defer vaccination for 3 months following infection.⁶

Adverse events

All adverse events should be reported to the TGA at www.tga.gov.au/reporting-problems. NSW Health staff must also report adverse events via the local incident management system (IIMS+).

Criteria for prescription in NSW

The criteria for prescribing monoclonal antibody treatments and antiviral medicines in NSW align to the NCCET recommendations (for TGA-approved indications) or PBS criteria, with some additions, as summarised in [Table 1](#).

Where Aboriginal or Torres Strait Islander status appears as a risk factor, an age of >35 years should be applied.

Wherever possible, prescribing of the oral antivirals (molnupiravir and nirmatrelvir plus ritonavir) must occur via the Pharmaceutical Benefits Scheme. However, in the following circumstances dispensing by a NSW Health Pharmacy Department may continue to occur:

- where the patient is an inpatient in an NSW health facility
- for patients presenting to emergency departments
- for virtual care or COVID Care in the Community patients

- for patients identified by general practitioners or community-based medical specialists who meet the criteria outlined by the NCCET but are ineligible for PBS supply.

Currently, there is a high prevalence of Omicron BA.2 subvariant circulating in NSW. Evidence indicates that there is reduced efficacy of sotrovimab against Omicron (BA.2 subvariant) and casirivimab plus imdevimab against Omicron (and in particular BA.1 subvariant).^{2,3} As such, it is recommended that where indicated and clinically appropriate, oral antivirals are prioritised over the monoclonal antibodies.

The NCCET recommends, where infection from the Omicron BA.2 subvariant is likely, sotrovimab should only be used where other treatments are not suitable or available.⁷ In addition, where Omicron is likely to be the dominant circulating variant, use of casirivimab plus imdevimab should only be considered where other treatments are not suitable or available.⁸

To support ongoing use of this document all medications within scope have been retained. However, clinicians and services should note:

- the information provided regarding efficacy against current variants
- the most current decision advice in [Figure 1](#)
- the considerations outlined in [Table 1](#)
- updated recommendations from the NCCET.

The NCCET has also developed a [risk classification tool](#) for adults with mild COVID-19 that assists clinicians to select the medication likely to be the most effective.⁹

Use of available medications for off-label indications or in combination

The NCCET has made:

- a conditional recommendation regarding the use of tixagevimab plus cilgavimab as treatment for non-hospitalised patients with mild to moderate disease¹⁰
- a consensus recommendation regarding the use of nirmatrelvir plus ritonavir in children and adolescents aged 12 years and over and weighing at least 40 kg who do not require oxygen and who are at high risk of deterioration.¹¹

These medicines are not currently approved by the TGA for these indications and therefore, use is off-label.

There is no supporting evidence for combination therapy (antivirals plus monoclonal antibodies). The NCCET recommends that the use of two or more monoclonal antibodies should be avoided except where co-formulated.¹⁰

Where a clinician believes that a patient may benefit from the use of an available medication for an off-label indication or combination therapy (antivirals plus monoclonal antibodies), approval must be sought from the local Drug and Therapeutics Committee (via the Individual Patient Use process, see [PD2016_033](#)) prior to commencing therapy. An independent peer-review process is also encouraged. Primary care practitioners should flag the patient through their local LHD escalation pathways.

Table 1. Overview of medications

The medications listed for treatment are for administration in the first 5 -7 days of symptom onset, for patients who do not require oxygen and are at high risk of disease progression.

Medication	Usage	NSW criteria for administration	Variant considerations	Route of administration
Sotrovimab (Xevudy)	Treatment	As per NCCET recommendations (with the Aboriginal and Torres Strait Islander age threshold of 35 years) for: Adults ⁷ Pregnant women in their 2nd or 3rd trimester ¹⁹ Children and adolescents 12 years or older and weighing at least 40 kg ²⁰	Reduced effectiveness against Omicron BA.2	Intravenous infusion
Casirivimab plus imdevimab (Ronapreve)	Treatment Post-exposure prophylaxis	As per NCCET recommendations (with the Aboriginal and Torres Strait Islander age threshold of 35 years) for: Adults (treatment) ⁸ Adults (post-exposure prophylaxis) ¹² Pregnant or breastfeeding women (treatment) ²¹ Children and adolescents 12 years or older and weighing at least 40 kg (treatment) ²²	Reduced effectiveness against Omicron BA.1 and BA.2	Intravenous infusion or subcutaneous injection
Molnupiravir (Lagevrio)	Treatment	As per PBS criteria and NCCET recommendations for adults (with the Aboriginal and Torres Strait Islander age threshold of 35 years) ^{*13,14}		Oral
Nirmatrelvir plus ritonavir (Paxlovid)	Treatment	As per PBS criteria and NCCET recommendations for adults (with the Aboriginal and Torres Strait Islander age threshold of 35 years) ^{*15,16}		Oral
Tixagevimab plus cilgavimab (Evusheld)	Pre-exposure prophylaxis	As per TGA approved product information for adults, pregnant women, and children and adolescents 12 years or older and weighing at least 40 kg (pre-exposure prophylaxis) ¹⁷		Intramuscular injection
Remdesivir (Veklury)	Treatment (early treatment only, within 7 days of symptom onset)	As per NCCET recommendations (with the Aboriginal and Torres Strait Islander age threshold of 35 years) ⁵ for: Adults ¹⁸ Pregnant or breastfeeding women ²³ Children and adolescents 12 years or older and weighing at least 40 kg ²⁴		Intravenous infusion

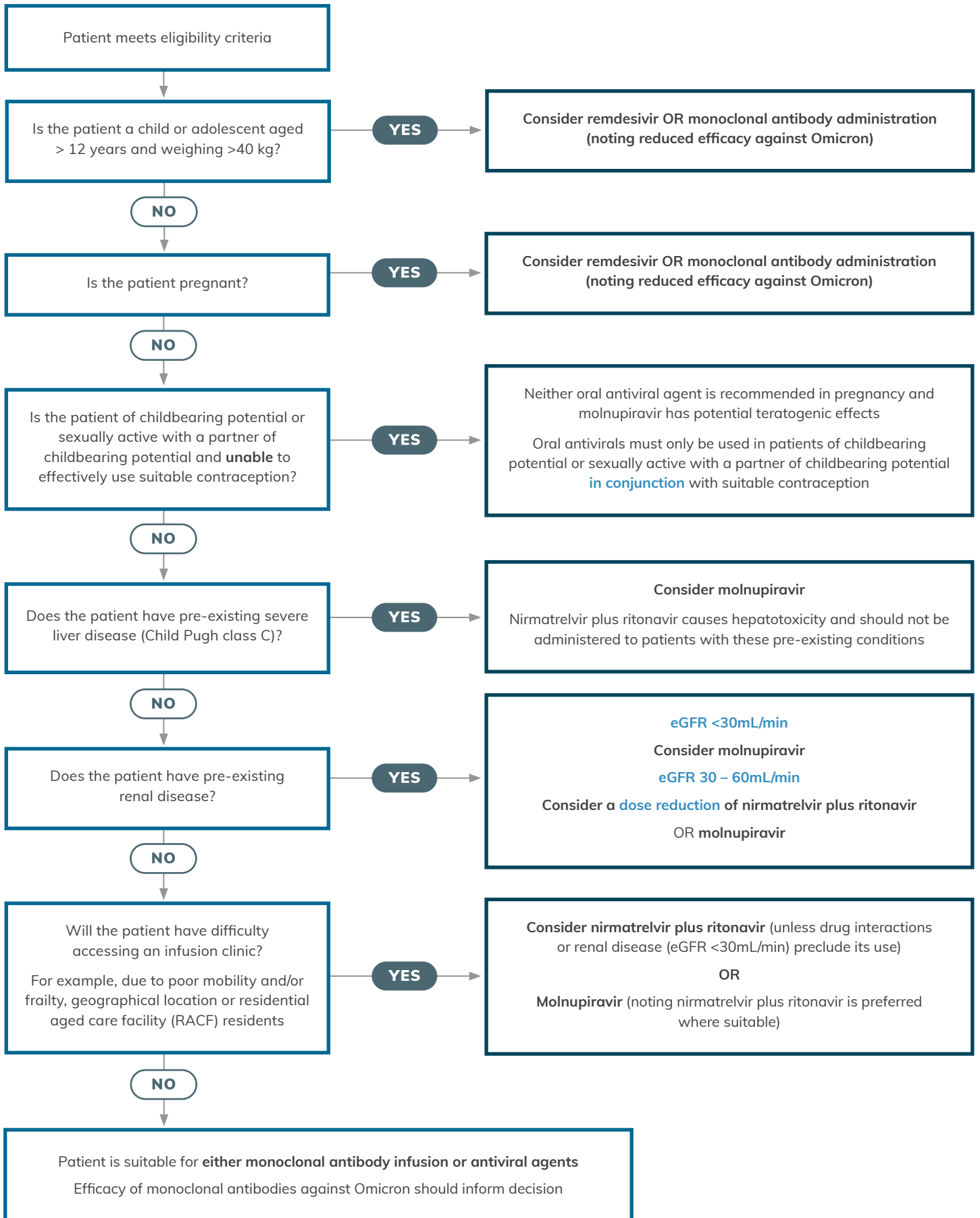
* Wherever possible, prescribing of the oral antivirals (molnupiravir and nirmatrelvir plus ritonavir) must occur via the PBS. However, in the following circumstances dispensing by a NSW Health Pharmacy Department may continue to occur:

- where the patient is an inpatient in an NSW health facility
- for patients presenting to Emergency Departments
- for virtual care or COVID Care in the Community patients
- for patients identified by general practitioners or community-based medical specialists that meet the criteria outlined by the NCCET but are ineligible for PBS supply. (NCCET requires only one risk factor to trigger treatment and has a lower age threshold than the PBS.)

¹ Where uncertainty exists regarding vaccine response in an individual, anti-SARS-CoV-2 spike antibody testing may be useful.

⁵ Between days 5 to 7 following symptom onset remdesivir may be suitable for high-risk patients. Where GPs believe this is indicated, this should be escalated to the local LHD lead via the HealthPathways escalation line as prescription cannot occur through the PBS.

Figure 1. Decision pathway: suitability for sotrovimab, casirivimab plus imdevimab, molnupiravir, nirmatrelvir plus ritonavir and remdesivir



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