

Model of care 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

APRIL 2022

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 model by which these medications will be used in NSW. This model is based on:

- changes in the evidence, including impacts of new variants on the efficacy of these medications
- availability of new medications in Australia
- access to supply
- the context of COVID-19 outbreaks in NSW.

This document should be read in conjunction with drug guidance developed by the Clinical Excellence Commission (CEC).

Methodology

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

Due to uncertainty surrounding medication supply and high case numbers, there is a need to identify the people who are at most risk and, therefore, potentially likely to benefit from the administration of these medicines. Key risk factors (based on the National Clinical Evidence Taskforce recommendations and outlined in [Table 1](#) and [Table 2](#)) will be targeted to identify people in these high-risk cohorts within NSW.³

The available evidence was considered by an expert group of NSW clinicians to inform the development of this model and identification of NSW specific key risk factors. Emerging medications are also being monitored by the CIU and will be included in this document, as required.

Updates – 13 April 2022

The following updates are included in this version:

- Advice regarding efficacy of some medications against Omicron BA.2 subvariant
- Updates to the figures to reflect advice around reduced efficacy against Omicron
- Use of available medications for off-label indications or in combination.

Who can be treated?

Clinical criteria and risk factors

The medications covered in this model of care are:

- [casirivimab and imdevimab](#)^{4,5} (see [Table 1](#))
- [molnupiravir](#)⁴ (see [Table 1](#))
- [nirmatrelvir plus ritonavir](#)⁴ (see [Table 1](#))
- [sotrovimab](#)⁴ (see [Table 1](#) and [Table 2](#))
- [tixagevimab and cilgavimab](#)⁴ (see [Table 3](#))

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 days from the onset of infection (or 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.

The currently approved oral antiviral medicines are **not approved** for use in children or adolescents aged under 18 years. Some monoclonal antibody treatments are approved for adolescents aged 12 to 17 years and weighing > 40kg.

Not everyone with COVID-19 will benefit, nor be eligible for these medicines. **They are not an alternative to vaccination.**

Vaccination remains the best way to protect vulnerable populations from the adverse outcomes of COVID-19 infection.

Although the indications for these medications are similar, they are not identical. As such, medication-specific risk factors, criteria and individual drug guidance should be reviewed.

Note: the CEC published medication guidance and NSW-specific key risk factors differ slightly due to the already mentioned need to identify and target patients most likely to benefit from these medications within the NSW context.

Criteria and medication-specific risk factors for sotrovimab, casirivimab plus imdevimab, molnupiravir, and nirmatrelvir plus ritonavir are outlined in [Table 1](#) for adults or [Table 2](#) for adolescents.^{7,8}

As the medicine-specific risk factors are different to other medications outlined in this document, the use of tixagevimab plus cilgavimab is specified in [Table 3](#).

Considerations for all medications, such as efficacy against sub variants and for patient populations, are outlined in [Table 4](#).

Prioritised cohorts in NSW

Access for patients should be considered in the context of NSW outbreaks. It is the recommendation of the clinical working group that the following cohorts are prioritised. Patients identified as part of the following groups also need to meet the criteria specified in the drug guidance.

- Patients who have acquired COVID-19 infection in high-risk settings, such as disability group homes and residential aged care facilities.
- Aboriginal and/or Torres Strait Islander communities.
- Rural, regional and remote communities.
- Patients in areas with large outbreaks.
- Patients with nosocomial infection (i.e. those who have acquired a COVID-19 infection in hospital or healthcare setting).

Data collected and analysed in NSW has indicated that there may be a higher risk of severe disease and mortality for people from Pasifika populations.

It may be prudent to plan access for patients in the groups listed above who have been exposed, but have not yet developed symptoms.

Vaccination

Routine use of these medications is not encouraged in patients who are up-to-date with their vaccinations, unless the patient may have a suboptimal response (e.g. severe immunosuppression from a medical condition or medication).³

People with up-to-date vaccinations should not require a monoclonal antibody or antiviral as they will be significantly protected against severe disease.

The [Australian Technical Advisory Group on Immunisation](#) (ATAGI) specifies the interval for vaccination. Vaccination can take up to 14 days to be effective.⁶

Due to the impact of these drugs on the SARS-CoV-2 spike protein, it may be possible that monoclonal antibodies could interfere with the development of effective immune responses to COVID-19 vaccines. As such, it is recommended that COVID-19 vaccines should not be given for at least 90 days after administration.

For oral antivirals, patients should delay vaccination until they have recovered from their acute illness (approximately 4 to 6 weeks).

Adverse events

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

Guidance for using the tables and figures

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).^{1,2} As such, it is recommended that where indicated and clinically appropriate, oral antivirals are prioritised over the monoclonal antibodies. The [National Clinical Evidence Taskforce](#) recommends, where infection from the Omicron BA.2 subvariant is likely, sotrovimab should only be used where other treatments are not suitable or available.

Further advice to support local decision making is given in [Figure 1](#) and [Table 4](#).

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 4](#)
- updated recommendations from the National Clinical Evidence Taskforce.

The National COVID-19 Clinical Evidence Taskforce has also developed a [risk classification tool](#) for adults with mild COVID-19 which assists clinicians to select the medication likely to be the most effective.¹⁰

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

The National Clinical Evidence Taskforce has made a conditional recommendation regarding the use of remdesivir and tixagevimab plus cilgavimab as treatment for non-hospitalised patients with mild to moderate disease.

These medicines are not currently approved by the TGA for this indication and therefore use would be considered off-label.

In relation to combination therapy (antivirals and monoclonal antibodies), the National Clinical Evidence Taskforce notes that the evidence is unclear. [The taskforce recommends](#) that the use of two or more monoclonal antibodies should be avoided except where co-formulated.

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 and 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.

Table 1. NSW-specific risk factors for high priority cohorts for use of sotrovimab, casirivimab and imdevimab, molnupiravir and nirmatrelvir plus ritonavir

Note: the guidance outlined in this model of care is for the use of a single medication for this indication.

Risk factors that must be met for prescription of any of the four medications
<ul style="list-style-type: none"> • Commence within 5 days of symptom onset (or 7 days for casirivimab plus imdevimab) AND • No oxygen requirement due to COVID-19 AND • Reduced immunity to COVID-19 by being: <ul style="list-style-type: none"> – unvaccinated (i.e. received no doses of a COVID-19 vaccination) OR – vaccination not up-to-date (as per ATAGI guidance)⁷ OR – immunocompromised (as per ATAGI guidance)^{*8} AND • Have at least TWO medication-specific risk factors as outlined below. <p>* patients that are immunocompromised do NOT need to meet the medication-specific risk factor criteria. They are eligible to receive an anti-SARS-CoV-2 monoclonal antibody or oral antiviral medicine on the basis of immunosuppression alone.</p>
Medication-specific risk factors
<p>Sotrovimab</p> <ul style="list-style-type: none"> • Pregnant women in their second or third trimester • Non-pregnant adults who are aged ≥ 60 years or aged ≥ 35 years if Aboriginal and/or Torres Strait Islander • Obesity (BMI $\geq 30\text{kg/m}^2$) • Serious cardiovascular disease such as heart failure, coronary artery disease, cardiomyopathies • Chronic lung disease, including COPD, severe asthma (requiring a course of oral steroids in the previous 12 months), interstitial lung disease and bronchiectasis • Type 1 or 2 diabetes mellitus requiring medication • Severe chronic kidney disease • Severe chronic liver disease • Active cancer, especially haematological malignancy • Other specific conditions outlined in the National Clinical Evidence Taskforce guidance but not in the above list³
<p>Casirivimab plus imdevimab</p> <ul style="list-style-type: none"> • Pregnant women • Non-pregnant adults who are aged ≥ 60 years or aged ≥ 35 years if Aboriginal and/or Torres Strait Islander • Obesity (BMI $\geq 30\text{kg/m}^2$) • Serious cardiovascular disease such as heart failure, coronary artery disease, cardiomyopathies • Chronic lung disease, including COPD, severe asthma (requiring a course of oral steroids in the previous 12 months), interstitial lung disease and bronchiectasis • Type 1 or 2 diabetes mellitus requiring medication • Severe chronic kidney disease • Severe chronic liver disease • Active cancer, especially haematological malignancy • Other specific conditions outlined in the National Clinical Evidence Taskforce guidance but not in the above list³

Medication-specific risk factors**Molnupiravir**

- Non-pregnant adults who are aged ≥ 60 years or aged ≥ 35 years if Aboriginal and/or Torres Strait Islander.
- Obesity (BMI $\geq 30\text{kg/m}^2$)
- Serious cardiovascular disease such as heart failure, coronary artery disease, cardiomyopathies.
- Chronic lung disease, including COPD, severe asthma (requiring a course of oral steroids in the previous 12 months), interstitial lung disease and bronchiectasis
- Type 1 or 2 diabetes mellitus requiring medication
- Severe chronic kidney disease
- Severe chronic liver disease
- Active cancer, especially haematological malignancy
- Other specific conditions outlined in the [National Clinical Evidence Taskforce guidance](#) but not in the above list³

Nirmatrelvir plus ritonavir

- Non-pregnant adults who are aged ≥ 60 years or ≥ 35 years if Aboriginal and/or Torres Strait Islander
- Obesity (BMI $\geq 30\text{kg/m}^2$)
- Serious cardiovascular disease such as heart failure, coronary artery disease, cardiomyopathies.
- Chronic lung disease, including COPD, severe asthma (requiring a course of oral steroids in the previous 12 months), interstitial lung disease and bronchiectasis
- Type 1 or 2 diabetes mellitus requiring medication
- Chronic kidney disease with eGFR 30-60mL/min (contraindicated with eGFR $< 30\text{mL/min}$) – note dose reduction required
- Chronic liver disease (Child-Pugh Class A or B)
- Active cancer, especially haematological malignancy
- Other specific conditions outlined in the [National Clinical Evidence Taskforce guidance](#) but not in the above list³

Table 2. NSW-specific risk factors for use of sotrovimab

Risk factors that must be met for prescription in adolescents
<ul style="list-style-type: none"> • Aged 12 to 17 years AND • Weighing at least 40kg AND • Within 5 days of symptom onset AND • No oxygen requirement due to COVID-19 AND • Reduced immunity to COVID-19 by: <ul style="list-style-type: none"> – unvaccinated (i.e. received no doses of a COVID-19 vaccination) OR – vaccination not up-to-date (as per ATAGI guidance) OR – immunocompromised* (as per ATAGI guidance), irrespective of vaccine status AND • Medication-specific age and risk factors outlined below
Medication-specific risk factors
<p>Sotrovimab</p> <p>AND at least two of the following risk factors:</p> <ul style="list-style-type: none"> • Paediatric complex chronic condition (PCCC): congenital and genetic, cardiovascular, gastrointestinal, malignancies, metabolic and neuromuscular • Diabetes (requiring medication) • Obesity (BMI \geq 95th centile for age) • Chronic kidney disease (GFR $<$ 15mL/min/1.73m²) • Heart failure, or congenital heart disease with persisting cyanosis or pulmonary hypertension • Chronic obstructive lung disease (e.g. chronic lung disease requiring oxygen, cystic fibrosis with reduced lung function) • Severe asthma (in the past 12 months: \geq1 exacerbation requiring ICU admission OR IV treatment OR \geq2 hospital admissions for asthma) <p><i>In other exceptional circumstances, please discuss eligibility with a paediatric infectious diseases specialist.</i></p>

* As per the [ATAGI guidance](#), immunocompromised means having a weakened immune system due to a medical condition or treatment. Consider this irrespective of age. Many conditions can cause immunocompromise, including:

- cancer, especially blood cancer (leukaemia or lymphoma) that is not in remission
- treatments for cancer (e.g. chemotherapy, targeted therapies, radiotherapy and CAR-T cell therapy) that weaken the immune system
- having a bone marrow, stem cell or solid organ transplant
- immune deficiencies
- HIV infection (particularly if the CD4 count is low)
- taking medications that weaken your immune system (called immunosuppressants or immunomodulators).

Table 3. NSW risk factors that must be met for prescription of tixagevimab and cilgavimab

<p>Reduced immunity to COVID-19 by being:</p> <ul style="list-style-type: none"> • unvaccinated due to contraindication OR • are expected to have an inadequate response to vaccination (irrespective of vaccination status) e.g. due to use of anti-CD20 antibodies in the last 6 months or demonstrated hypogammaglobulinemia in the last 6 months AND <p>Severely immunocompromised due to:</p> <ul style="list-style-type: none"> • being within six months post-bone marrow transplantation and/or CAR T-cell therapy with an extension to 12 months based on clinical need OR • post solid organ transplant (first 12 months)
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Further advice can be found in the Australia and New Zealand Transplant and Cellular Therapies (ANZTCT) Position Statement: COVID-19 Management in Haematopoietic Stem Cell Transplant and Chimeric Antigen Receptor T cell Patients¹¹ [available here](#).

Table 4. Overview of medications

Medication	Route of administration	Usage	Variant considerations	Patient populations	Clinical conditions
Sotrovimab	Intravenous infusion	Treatment	Reduced effectiveness against Omicron BA.2	Adults Pregnant women in their 2nd or 3rd trimester Adolescents (12 years or older and weighing at least 40 kg)	
Casirivimab plus imdevimab	Intravenous infusion or subcutaneous injection	Treatment Post-exposure prophylaxis	Reduced effectiveness against Omicron BA.1	Adults Pregnant women Adolescents (12 years or older and weighing at least 40 kg)	
Molnupiravir	Oral	Treatment		Adults	Note advice about breastfeeding and use of contraception for those of childbearing potential.
Nirmatrelvir plus ritonavir	Oral	Treatment		Adults	Not to be used in those with severe liver disease (Child-Pugh C) In those with severe renal disease: <ul style="list-style-type: none"> • Not to be used in those with eGFR <30mL/min • Dose reduction required in those with eGFR 30 – 60 mL/min Note advice about breastfeeding and use of contraception for those of childbearing potential.
Tixagevimab and cilgavimab	Intramuscular injection	Pre-exposure prophylaxis		Adults Pregnant people Adolescents	Caution in those with pre-existing cardiovascular disease or those with clinically significant bleeding disorders.

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

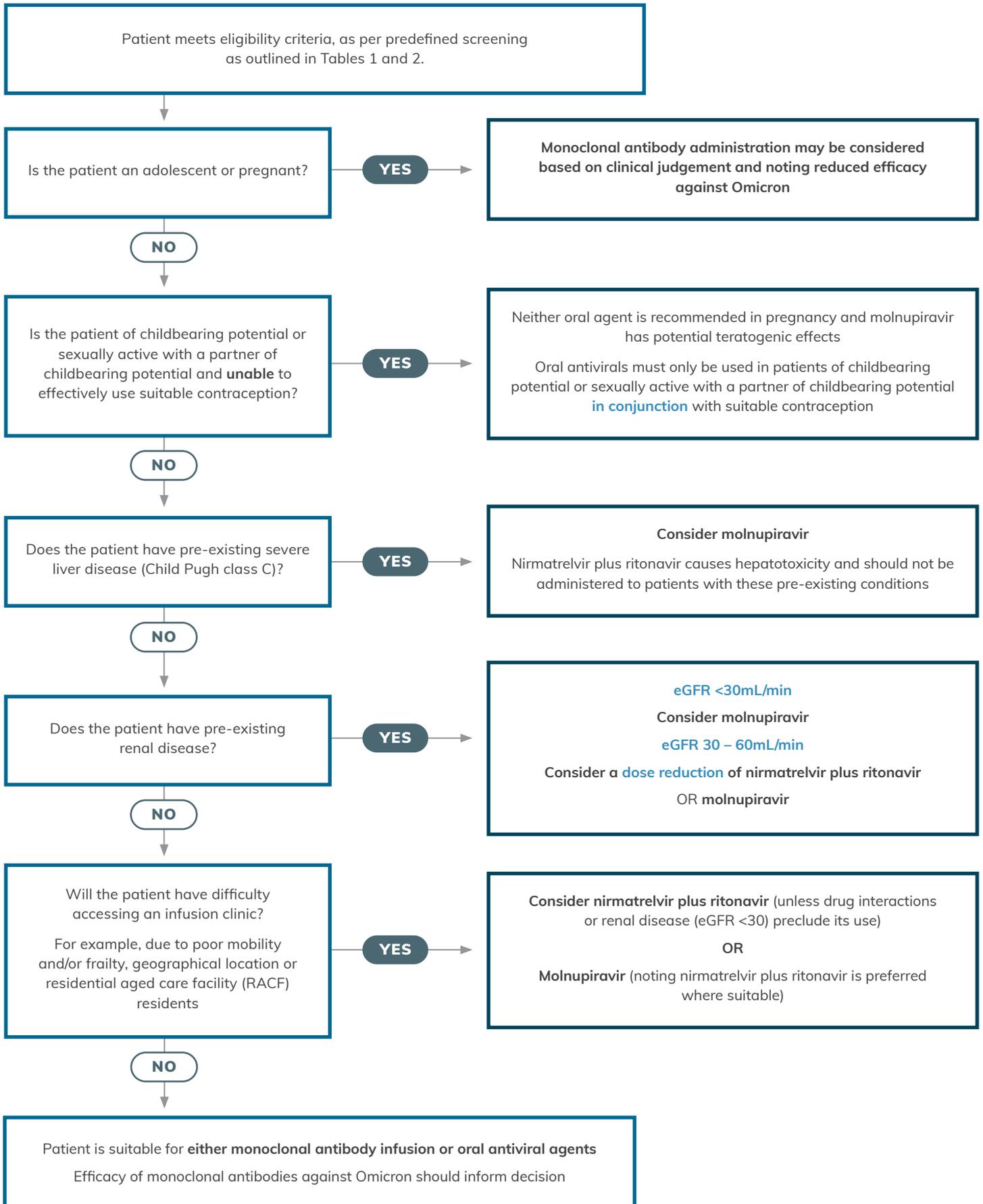
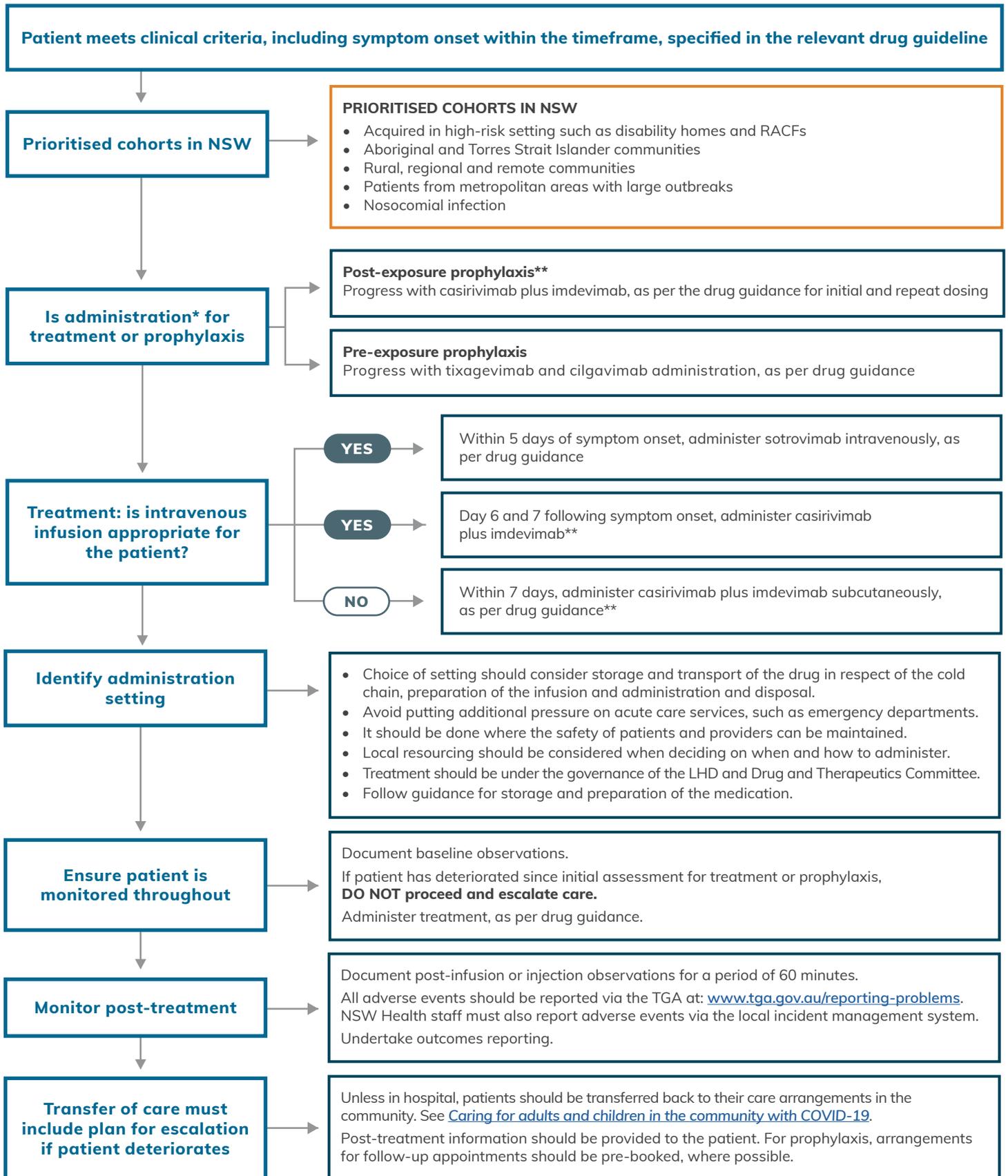


Figure 2. Flowchart for administration of sotrovimab and casirivimab and imdevimab in adults and adolescents with mild and moderate COVID-19

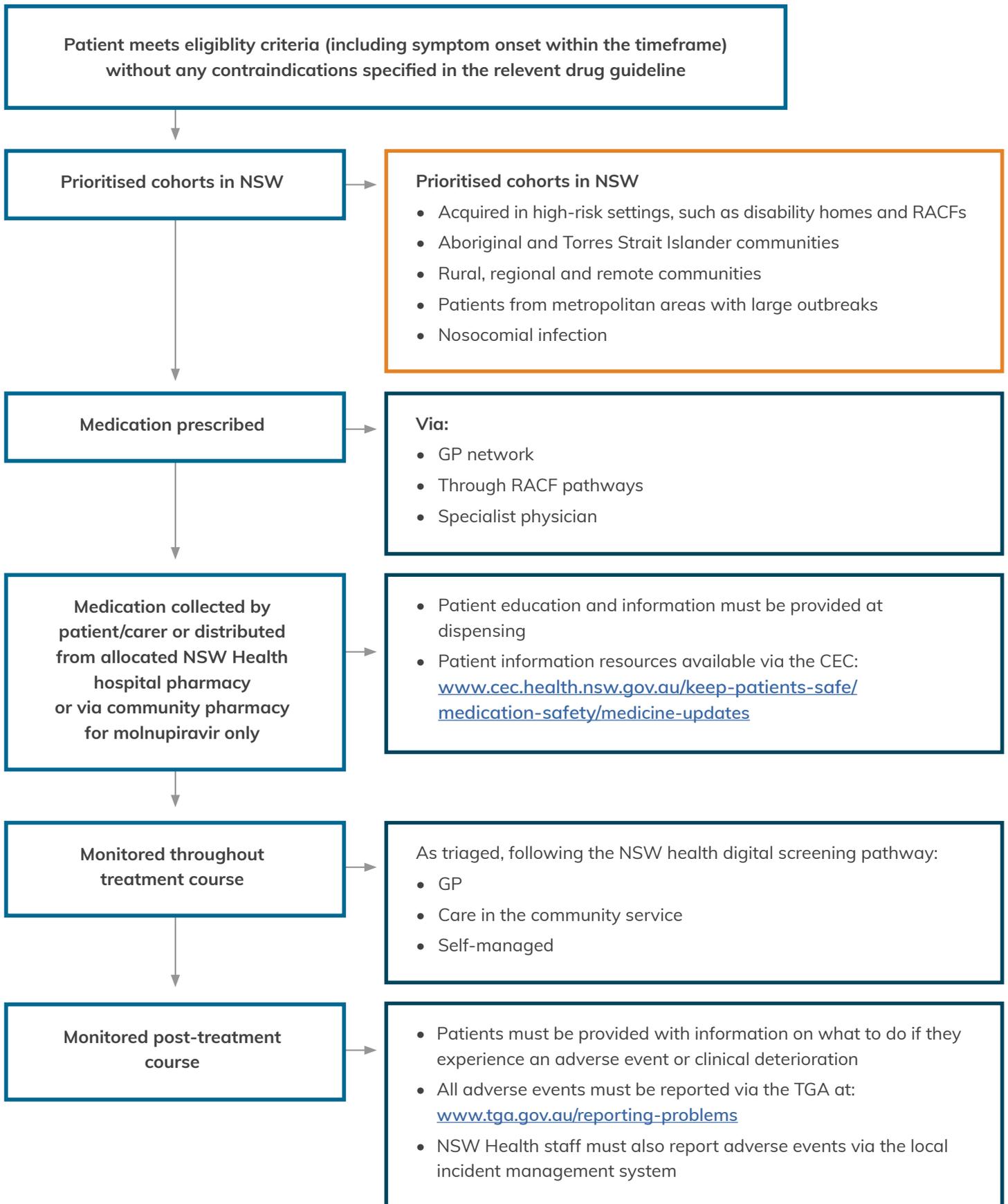


* Clinicians should consider the SARS-CoV-2 variant being targeted and the possibility of reduced sensitivity. Early evidence shows casirivimab plus imdevimab is not as effective against Omicron BA.1 and sotrovimab is not as effective against Omicron BA.2. Refer to Figure 1 and Table 4 for advice regarding use of oral antivirals versus monoclonal antibodies.

** It is recommended casirivimab plus imdevimab is NOT used for post-exposure prophylaxis where the source exposure is Omicron BA.1.

Note: these medications should not be used in patients who are asymptomatic.

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



Note: these medications should not be used in patients who are asymptomatic.

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