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Model of care for the use of anti-SARS-CoV-2 monoclonal antibodies

for adults with mild and moderate COVID-19

There are a range of anti-SARS-CoV-2 monoclonal antibodies (Mab) and antiviral medications that have been approved, or are under consideration, by the Therapeutic Goods Administration. These medications are for the treatment of patients with mild to moderate COVID-19 who are at risk of progression to severe disease.

The purpose of this guidance is to outline the model by which these medications will be used in NSW. This model will be updated as required and 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 outbreaks of COVID-19 in NSW.

Local access to these medications will be through the usual Drug and Therapeutic Committee processes at the local health district (LHD) and specialty health network (SHN) level. This document should be read in conjunction with the drug guidance developed for NSW use by the Clinical Excellence Commission (CEC) and the NSW Therapeutic Advisory Group (NSW TAG).

Methodology

The model is based on recommendations from the National Clinical Evidence Taskforce guidelines and the evidence checks undertaken by the NSW Agency for Clinical Innovation's Critical Intelligence Unit (CIU).

The evidence checks are:

- COVID-19 Critical Intelligence Unit: Monoclonal antibodies – in brief
- COVID-19 Critical Intelligence Unit: Omicron (B.1.1.529)

The evidence was considered by an expert group of NSW clinicians to inform the development of this model. This included subject matter experts in:

- infectious diseases
- hospital in the home
- aged care
- respiratory
- medication safety
- drug and therapeutics
- oncology.

Emerging medications are also being monitored by the CIU and will be included in this document as required.

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Who can be treated?

Clinical criteria

The National Clinical Evidence Taskforce Guidelines outline the clinical criteria for the use of these medications in adults and children. These are further specified in NSW guidance developed by the NSW TAG and CEC.

Generally, these drugs are for use in the disease course before significant symptoms have occurred. This is especially important for pulmonary involvement and the need for oxygen and in people who have one or more risk factors as specified in the drug guidance.[3,5]

Although the indications for these medications are similar, they are not identical. As such, individual drug guidance should be reviewed at the links below.

The medications covered in this model of care currently include:

- sotrovimab
- casirivimab and imdevimab

Risk factors

The following additional risk factors should also be considered:

- patients who are immunosuppressed, even if they are partially or fully vaccinated
- Aboriginal and Torres Strait Islander patients over 35 years old.

Clinical judgement should be used when assessing the severity of specific risk factors. This may include other significant chronic health conditions including, but not limited to, cardiac failure, chronic lung disease, immunosuppression and active malignancy.

Eligibility for patients who are asymptomatic should be assessed based on their risk of progression to severe disease.

Rapid antigen testing

A positive rapid antigen test (RAT) is sufficient to establish indication for the use of sotrovimab in the appropriate population. The positive RAT should be confirmed via PCR/rapid PCR prior to treatment. However, treatment should not be withheld if there is a delay in receiving the PCR result.

Vaccination

Routine use of these medications is not encouraged in those patients who are fully vaccinated unless the patient may have a suboptimal response to a primary course of COVID-19 vaccination (e.g. severe immunosuppression from a medical condition or medication)[4,5]

People who are adequately vaccinated should not require a monoclonal antibody as they will be significantly protected against severe disease.

The Australian Technical Advisory Group on Immunisation (ATAGI) specifies the interval for booster doses.[6]

Monoclonal antibody treatment may be considered for those who are due, but have not yet received their booster dose, where they:

- are aged over 70 years old
- have multiple comorbidities or severe comorbidities assessed against the medication criteria
- are pregnant.

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.

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 clinical criteria specified in the drug guidance.

- Aboriginal and/or Torres Strait Islander communities.
- Rural, regional and remote communities:
  a. where there is a significant outbreak impacting the community.
  b. for patients who have been brought to a regional centre (from a remote location) for monitoring due to their risk of acquiring severe disease.

c. for patients who are in a remote location and prefer to remain in their community and/or on country.

- To support the public health response in areas with large outbreaks.
- Patients with nosocomial infection – those who have acquired a COVID-19 infection in hospital or healthcare setting.
- Patients who have acquired COVID-19 infection in high-risk settings such as disability group homes and residential aged care facilities.

Data collected and monitored in NSW has indicated that there may also 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 above groups who have been exposed but have not yet developed symptoms.

Principles for settings for administration

- An intravenous (IV) infusion may be delivered in a range of settings, depending on local requirements. Choice of setting should consider storage and transport of the drug (such as cold chain), preparation of the infusion and administration and disposal.
- Currently the preferred mode of administration is via IV infusion. Consider subcutaneous injection only (for casirivimab and imdevimab) when intravenous access is not feasible or possible.
- As much as possible, the administration setting should avoid putting additional pressure on acute care services such as emergency departments.
- It should be done where the safety of patients and providers can be maintained. This includes the requirements to observe the patient receiving an infusion for a period of up to 90 minutes (30 minutes during administration and 60 minutes post-infusion) and managing any adverse events safely.
- Local resourcing should be considered when deciding on when and how to administer.
- Irrespective of the setting, use of monoclonal antibody treatment should be under the governance of the local Drug and Therapeutic Committee and approved protocols.

Medication guidance

Specifications for administration are available at the following links:

- sotrovimab[5]
- casirivimab and imdevimab[9,10]

The NSW Safety Notice 024/21 outlines risks associated with the use of casirivimab and imdevimab with the aim of ensuring its safe and appropriate use.

Clinicians should consider the SARS-CoV-2 variant being targeted and the possibility of reduced sensitivity. Early evidence shows casirivimab and imdevimab is not as effective against Omicron as against other variants. As such, sotrovimab is the preferred medication for treatment of the omicron variant of concern.[2]

It is further recommended that casirivimab and imdevimab is NOT used for post exposure prophylaxis where the source exposure is Omicron.

Specific notes for the community and rural setting:

Many patients with COVID-19 are receiving care in the community as outlined in the guidance Caring for adults with COVID-19 in the community.

Adverse events

- Patients should be monitored for adverse events during and post infusion.
- Following the observation period, patients should be provided with advice regarding post infusion requirements, including adverse effects and who to contact for more information.
- All adverse events should be reported via:
  - the local incident management system; AND
  - the Therapeutic Goods Administration (TGA) at www.tga.gov.au/reporting-problems.

Patient consent

- Informed consent should be obtained from the patient (or responsible person) prior to initiating treatment with monoclonal antibodies. Information leaflets for patients, family and carers and patient consent forms are available at:
  - sotrovimab
  - casirivimab and imdevimab

- The prescriber should conduct a detailed discussion about the benefits and potential harms associated with use of the medicine with the patient or responsible person prior to them signing the form.

Documentation

- Prescribers should complete a Prescribing Declaration/Individual Patient Usage Application Form for each patient they intend to treat and submit this to their local Drug and Therapeutics Committee for approval. Contact the local pharmacy department for more information, if required. The forms are available at:
  - sotrovimab
  - casirivimab and imdevimab
- The Individual Patient Use Application Form should clearly indicate their patient's eligibility criteria. The completed form will need to be submitted to HealthShare NSW with medication orders prior to the release of stock.

Monitoring of outcomes

- The use of monoclonal antibody treatment requires reporting and monitoring of outcomes.
- To assist in monitoring outcomes of treatment, it is suggested that the following information is also collected:
  - Collect one Serum Separator Tube (SST) and request anti-SARS-CoV-2 spike antibody testing. This should be documented in the clinical notes as 'COVID-19, baseline prior to monoclonal antibody treatment'.
  - Collect combined nasopharyngeal and throat swabs and request SARS-COV-2 PCR, culture and whole genome sequencing – refer to Institute of Clinical Pathology and Medical Research (ICPMR) Westmead. This should be documented in the clinical notes as 'COVID-19, baseline prior to monoclonal antibody treatment'.
- For recipients who are subsequently hospitalised (or who progress to require oxygen, for those who were inpatients at the time of monoclonal antibody administration, or otherwise have repeat swabs collected for any reason after monoclonal antibody treatment) also:
  - Collect combined nasopharyngeal and throat swabs and request SARS-COV-2 PCR, culture and whole genome sequencing – refer to ICPMR, Westmead. This should be documented in the clinical notes as 'COVID-19, given xxx monoclonal antibody on ##/##/####. ?resistance mutations'.

Access and supply

The access and supply of these medications are managed by HealthShare and is aligned to the processes for other COVID-19 medications.

Flowchart for administration of monoclonal antibodies in adults with mild and moderate COVID-19

Patient meets clinical criteria, including symptom onset within the timeframe, specified in the relevant drug guideline

Prioritised cohorts in NSW

PRIORITISED COHORTS IN NSW
- Aboriginal and Torres Strait Islander communities
- Rural, regional and remote communities
- To support the public health response in metropolitan areas with large outbreaks
- Nosocomial infection
- Acquired in high-risk setting such disability homes and RACFs

Is administration* for treatment or prophylaxis

Prophylaxis:** Progress with casirivimab and imdevimab, as per the drug guidance for initial and repeat dosing

Treatment: Is intravenous infusion appropriate for the patient?

YES → Within 5 days of symptom onset administer sotrovimab intravenously, as per drug guidance

YES → Day 6 and 7 post symptom onset and not Omicron variant administer casirivimab and imdevimab

NO → Within 7 days, administer casirivimab and imdevimab subcutaneously (not Omicron variant), as per drug guidance

Identify administration setting

- Choice of setting should consider storage and transport of the drug in respect of the cold chain, preparation of the infusion and administration and disposal.
- Avoid putting additional pressure on acute care services such as emergency departments.
- It should be done where the safety of patients and providers can be maintained.
- Local resourcing should be considered when deciding on when and how to administer.
- Treatment should be under the governance of the LHD and Drug and Therapeutics Committee.
- Follow guidance for storage and preparation of the medication.

Ensure patient is monitored throughout

Document baseline observations.

If patient has deteriorated since initial assessment for treatment or prophylaxis, **DO NOT proceed and escalate care.**

Administer treatment as per drug guidance.

Monitor post-treatment

Document post infusion or injection observations for a period of 60 minutes
All adverse events should be reported via:
- local incident management system AND
- TGA at www.tga.gov.au/reporting-problems

Undertake outcomes reporting.

Transfer of care must include plan for escalation if patient deteriorates

Unless in hospital, patients should be transferred back to their care arrangements in the community. See Caring for adults with COVID-19 in the community.

Post treatment information should be provided to the patient. For prophylaxis, arrangements for follow up appointments should be pre-booked where possible.

* Clinicians should consider the SARS-CoV-2 variant being targeted and the possibility of reduced sensitivity. Early evidence shows casirivimab and imdevimab is not as effective against Omicron as against other variants. As such sotrovimab is the preferred medication for treatment of Omicron.

** It is recommended casirivimab and imdevimab is NOT used for post exposure prophylaxis where the source exposure is Omicron.

Prescription, governance and settings for administration

Operationalisation of models of care for use of medications for treatment of COVID-19 should be determined in consultation with local clinicians and the local Drug and Therapeutics Committee (DTC).

Use in community setting and hospital in the home

The clinical working group has recommended that monoclonal antibodies requiring an infusion are not delivered in hospital in the home (HITH) or community care settings.

This is in recognition that these are new treatments and require monitoring during and after infusion.

It is acknowledged that some LHDs may adopt a HITH approach for the administration of anti-SARS-CoV-2 monoclonal antibodies locally where they can address the considerations below and feel it meets the needs of their local community.

As staff need to be on site for a period of up to two hours, local health districts will need to manage processes for extended COVID-19 exposure.

Staff need to have competency in monitoring for infusion reactions, managing adverse events and resuscitation skills in the event of anaphylaxis.

Principles

- Depending on the medication, the indication for administration is within five to seven days of symptom onset. Treatment can be planned and will rarely need to occur after hours.
- Administration of monoclonal antibody treatment should occur in a health care facility, which may be in an inpatient or outpatient setting. The setting within the facility must meet patient flow, infection prevention and control and adverse event management requirements.
- Confirm communication processes with primary care and care-in-the-community pathways.
- LHDs and SHNs should establish local processes to:
  - Proactively identify eligible patients based on the clinical criteria and priority populations outlined in the model of care.
  - Define governance arrangements for authorised prescribers. In addition to infectious disease and respiratory physicians, these arrangements should outline any oversight, approval and stewardship requirements for other medical staff caring for COVID-19 positive patients who are seeking to prescribe this treatment.
  - Establish a communication process with the pharmacy department to confirm supply of stock before booking patients.
  - Ensure access to the medication through outreach settings is done under usual LHD and DTC arrangements for prescribers in these settings.
  - Coordinate the service model including the outpatient location, staffing and infection control procedures.
- A prescribing declaration/individual patient use (IPU) application should be completed prior to prescription of monoclonal antibody treatment and approved by the local DTC to ensure appropriate and safe administration of the medication. The local DTC should confirm local governance arrangements.
- LHDs and SHNs should establish a booking process for patient treatment including:
  - Provide information on the treatment via phone and email with the patient or carer and then obtain consent via phone prior to attendance at the facility for infusion. Depending on the local staffing and coordination model, booking and consent may be undertaken via a multi-step process and involve multiple communications with the patient or carer. (See information leaflets and consent forms for sotrovimab and casirivimab and imdevimab).
  - Whether informed consent is verbally obtained by the prescriber or is provided using written consent form, it should be documented in the medical record prior to administration.
  - Ensure patients are provided with information on:
    i. Personal protective equipment requirements for attending their infusion

ii. how to find the treatment area to expedite access and minimise access to other parts of the facility and exposure to other patients and staff

iii. confirmation of the appointment to support patients leaving isolation to attend the health care facility

iv. transport arrangements (where required).

- Confirm follow up arrangements after treatment, including who to contact for more information and advice around timelines for vaccination. See information for sotrovimab and casirivimab and imdevimab.
- Provision of printed information should be available for patients including information about the treatment and post treatment care. See information for sotrovimab and casirivimab and imdevimab. It is preferable to provide this information at the time of booking at the infusion clinic. Consider access to interpreter services as required.

- Ensure staff, such as emergency department, site managers, screening station and security staff, are aware of the location and arrangements for the treatment to assist patients to find their way. Where practical, temporary signage should be posted to assist patients and staff.
- Ensure reporting requirements are communicated, documented and submitted, including adverse events. This needs to be done via the local incident management system and the TGA.
- Ensure appropriate equipment and medicines to deal with an adverse event including anaphylaxis are readily available.
- Arrangements for patient follow up should be defined and may be supported by the treatment service or community care, virtual care or HITH services, depending on local resources and need.

Administration in the inpatient setting

- Patients who fulfil the priority eligibility criteria who are already admitted to a healthcare facility may be given this treatment in a ward setting provided the monitoring requirements can be met. This may be appropriate for patients already admitted to a COVID-19 ward, or who have nosocomial infection.
- This will prevent patient transfer to the nominated outpatient area, minimising movement for the patient and potential exposure to other areas of the hospital.

Administration in the outpatient setting

- A hub and spoke model may be appropriate where one site within the LHD is identified for the administration of monoclonal antibodies.
- There needs to be a dedicated and physically appropriate location at the health facility for the treatment, that:
  - offers pathways to access this location, as patients must not pass through other patient areas
  - ensures infection prevention and control requirements for administration, ventilation and cleaning
  - enables line of sight to support clinicians monitoring patients during the observation period.
- If different to usual local clinical emergency response system protocols, agree, document and communicate arrangements for escalation in the event of clinical deterioration. This should also include access to a resuscitation trolley.
- Confirm transport options to enable patient access as part of the booking process. LHDs and SHNs should implement a patient self-transport approach wherever possible.
  - Identify an accessible car park for patient use as close to the treatment location as possible.
  - Provide instructions for patients on locating the car park and directions on how to access the treatment area via a ‘hot entrance’.
  - Provide information to patients regarding their appointment if they are stopped by authorities for leaving isolation.

  - Consider informing local authorities regarding the provision of this service and that patients will need to self-transport for treatment.
  - Where patients are not able to self-transport, arrangements should be made with HealthShare for access via the Patient Transport Service (PTS). Given the demand on these services, requests should be planned and notified to PTS with as much notice and flexibility around appointment times as possible.
- Ensure the appropriate level of nursing coverage and competency is available including:
  - infusion preparation, cannulation and administration of intravenous medication
  - preparation and administration of subcutaneous medication
  - monitoring for adverse events including initial management of anaphylaxis.
- Access to medical advice and review should be readily available for adverse events.

Administration in the outreach setting

- Access to monoclonal antibody treatment via outreach should be established by LHDs and SHNs based on a local assessment of need.
- Identification of eligible patients should occur as early as possible to enable planning for the outreach service including travel requirements and time.
- As with outpatient settings, the outreach service should be provided in an appropriate health care setting which meets patient flow, infection prevention and control and resuscitation equipment requirements, for example, a multipurpose service or a general practice.
- Depending on local resources and requirements, it may be appropriate to provide access outside of health care facility utilising specialist medical and nursing workforce. For example, these could be the Rural Flying Doctor Service and Justice Health or correctional services. This should be locally determined based on patient needs and resources and must be comply with usual LHD, DTC prescriber arrangements.
- Medical and nursing workforce with the appropriate skills and competency will need to be mobilised, including staff with skills such as these:
  - infusion preparation cannulation and administration of intravenous medication
  - preparation and administration of subcutaneous medication
  - monitoring for adverse events including management of anaphylaxis.
- Workforce planning should also consider appropriate rostering to support travel requirements over long distances.
- Establish equipment and medication requirements for the outreach team, including arrangements for access and re-supply of the medication and resuscitation equipment.
- Consider escalation processes for ambulance and retrieval services in the event of adverse events requiring ongoing management or admission to hospital.
- Consider storage and transport requirements for monoclonal antibodies in respect of maintenance of cold chain.

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