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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

MARCH 2023

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 Clinical Evidence Taskforce (NCET) 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).[2-7]

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).[8]

Updates – March 2023

Inclusion of advice to reflect:

- the reduced effectiveness of monoclonal antibodies against current variants
- clarification of advice for the use of tixagevimab and cilgavimab.

Who can be treated?

Clinical criteria and risk factors

The medications covered in this model of care are:

- casirivimab plus imdevimab
- molnupiravir
- nirmatrelvir plus ritonavir
- remdesivir
- sotrovimab
- tixagevimab plus cilgavimab.

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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.

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, NCET 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 and Table 2.

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.[9]

The Australian Technical Advisory Group on Immunisation (ATAGI) specifies the interval for vaccination. Vaccination can take up to 14 days to be effective.[9]

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.[10]

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 NCET 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 30 years or older 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 patients prescribed tixagevimab plus cilgavimab by their community-based GP or medical specialist (only if the patient does not have an existing link to a NSW Health facility or private hospital)
- 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 NCET but are ineligible for PBS supply.

Evidence indicates that there is reduced efficacy of monoclonal antibodies against Omicron (including all subvariants).[2,3,11,12] Therefore, it is recommended that use of these medications is generally avoided for people with Omicron subvariants.

Patients who receive monoclonal antibodies for prophylaxis should be informed of the potential for breakthrough infections to occur due to the development of viral variants that are resistant to these medicines.

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 NCET.

The NCET 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.[13]

There is no supporting evidence for combination therapy (antivirals plus monoclonal antibodies). The NCET recommends that the use of two or more monoclonal antibodies should be avoided except where co-formulated.[14]

Where a clinician believes that a patient may benefit from the use of an available medication that is not recommended for routine use in this guidance, 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 PD2022_056) 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. Recommended 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. The medications in Table 1 are listed in order of recommended priority. Also see Figure 1 for more information.

Medication	Usage	NSW criteria for administration	Variant considerations	Route of administration
Nirmatrelvir plus ritonavir (Paxlovid)	Treatment	As per PBS criteria and NCET recommendations for adults (with the Aboriginal and Torres Strait Islander age threshold of 30 years)*[19,20]		Oral
Remdesivir (Veklury)	Treatment (early treatment only, within 7 days of symptom onset)	As per NCET recommendations (with the Aboriginal and Torres Strait Islander age threshold of 30 years)§ for: Adults[22] Pregnant or breastfeeding women[27] Children and adolescents 12 years or older and weighing at least 40 kg[28]		Intravenous infusion
Molnupiravir (Lagevrio)	Treatment	The NCET has made a conditional recommendation against use for routine treatment. Note that molnupiravir should only be used for treatment where other treatments are contraindicated, not practical or available. Criteria remain as per PBS and NCET		Oral

* 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 patients prescribed tixagevimab plus cilgavimab by their community-based GP or medical specialist (only if the patient does not have an existing link to a NSW Health facility or private hospital)
- 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 NCET but are ineligible for PBS supply. (NCET requires only one risk factor to trigger treatment and has a lower age threshold than the PBS.)

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

§ Between days 5 to 7 following symptom onset remdesivir may be suitable for high-risk patients. Where GPs believe remdesivir use is indicated, patients may be referred to their specialist (if available) or otherwise via HealthPathways and local referral pathways, as prescription cannot occur through the PBS.

Table 2. Not routinely recommended for use

The following medications have reduced efficacy against Omicron (including all subvariants) and are not routinely recommended for use.

Medication	Usage	NSW criteria for administration	Variant considerations	Route of administration
Sotrovimab (Xevudy)	Treatment	As per NCET recommendations (with the Aboriginal and Torres Strait Islander age threshold of 30 years) for: Adults[7] Pregnant women in their 2nd or 3rd trimester[23] Children and adolescents 12 years or older and weighing at least 40 kg[24]	Reduced effectiveness against Omicron BA.5, BR.2, BA2.75, BQ.1 and XBB	Intravenous infusion
Casirivimab plus imdevimab (Ronapreve)	Treatment Post-exposure prophylaxis	As per NCET recommendations (with the Aboriginal and Torres Strait Islander age threshold of 30 years) for: Adults (treatment)[12] Adults (post-exposure prophylaxis)[16] Pregnant or breastfeeding women (treatment)[25] Children and adolescents 12 years or older and weighing at least 40 kg (treatment)[26]	Reduced effectiveness against Omicron BA.5, BR.2, BA2.75, BQ.1 and XBB	Intravenous infusion or subcutaneous injection
Tixagevimab plus cilgavimab (Evusheld)	Treatment	NCET (treatment) TGA (treatment)	Waning effectiveness against Omicron BA.5, BR.2, BA2.75, BQ.1 and XBB	Intramuscular injection
Tixagevimab plus cilgavimab (Evusheld)	Pre-exposure prophylaxis‡	As per the following: NCET (pre-exposure prophylaxis and repeat doses) TGA (pre-exposure prophylaxis and repeat doses)	Waning effectiveness against Omicron BA.5, BR.2, BA2.75, BQ.1 and XBB‡	Intramuscular injection

‡ Patients who receive tixagevimab plus cilgavimab for pre-exposure prophylaxis should be informed of the potential for breakthrough infections to occur due to the development of viral variants that are resistant to the medicine. Patients should be instructed to promptly seek medical advice if signs or symptoms of COVID-19 occur.

Figure 1. Recommended treatment pathway

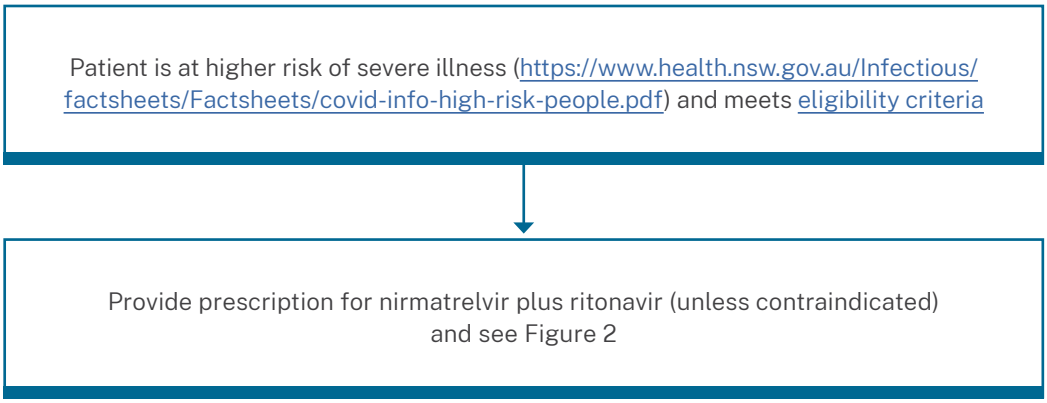
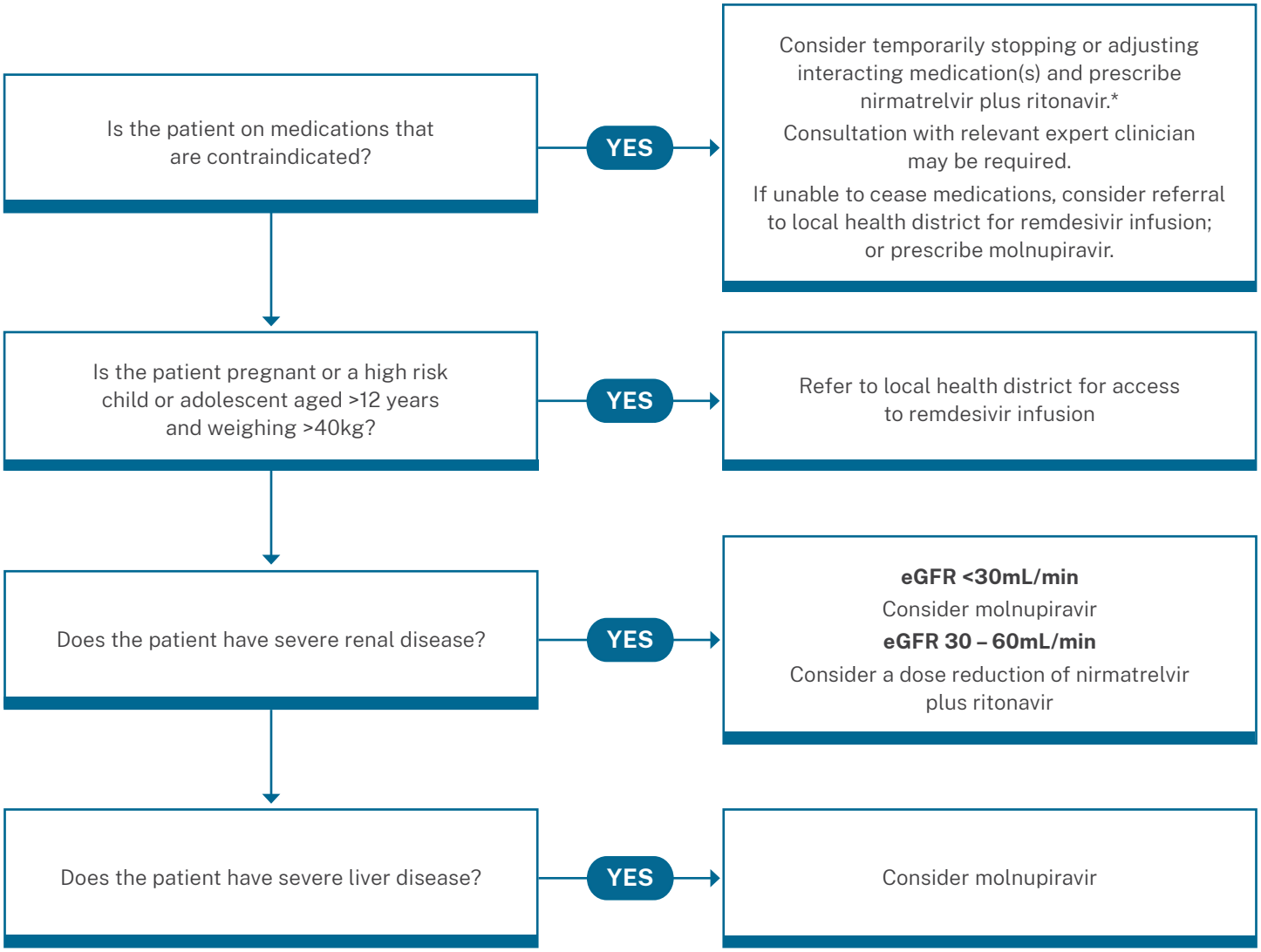


Figure 2. Decision pathway for contraindication to nirmatrelvir plus ritonavir



*The University of Liverpool COVID-19 Drug Interactions checker may be a helper and is available at https://www.covid19-druginteractions.org/checker

References

1. National Clinical Evidence Taskforce Living Guidelines [internet]. NCET: Melbourne; 2021 [cited 7 February 2022]. Available from: https://covid19evidence.net.au/#living-guidelines
2. NSW Agency for Clinical Innovation. COVID-19 Critical Intelligence Unit: Monoclonal antibodies - in brief [internet]. ACI: Sydney; 2021 [cited 7 February 2022]. Available from: https://aci.health.nsw.gov.au/__data/assets/pdf_file/0006/696948/Evidence-Check-Monoclonal-antibodies.pdf
3. NSW Agency for Clinical Innovation. COVID-19 Critical Intelligence Unit: Omicron (B.1.1.529) [internet]. ACI: Sydney; 2021 [cited 7 February 2022]. Available from: https://aci.health.nsw.gov.au/__data/assets/pdf_file/0008/696743/Evidence-Check-Omicron.pdf
4. NSW Agency for Clinical Innovation. COVID-19 Critical Intelligence Unit: Paxlovid - in brief [internet]. ACI: Sydney; 2022 [cited 11 November 2022] Available from: https://aci.health.nsw.gov.au/__data/assets/pdf_file/0009/746523/Evidence-Check-Paxlovid.pdf
5. NSW Agency for Clinical Innovation. COVID-19 Critical Intelligence Unit: Disease modifying treatments for COVID-19 in children – in brief [internet]. ACI: Sydney; 2022 [cited 11 November 2022] Available from: https://aci.health.nsw.gov.au/__data/assets/pdf_file/0010/702973/Evidence-Check-Disease-modifying-treatments-for-COVID-19-in-children.pdf
6. NSW Agency for Clinical Innovation. COVID-19 Critical Intelligence Unit: Sotrovimab – in brief [internet]. ACI: Sydney; 2022 [cited 11 November 2022] Available from: https://aci.health.nsw.gov.au/__data/assets/pdf_file/0012/695982/Evidence-Check-Sotrovimab.pdf
7. NSW Agency for Clinical Innovation. COVID-19 Critical Intelligence Unit: Molnupiravir – in brief [internet]. ACI: Sydney; 2022 [cited 11 November 2022] Available from: https://aci.health.nsw.gov.au/__data/assets/pdf_file/0009/686466/Evidence-Check-Molnupiravir.pdf
8. Clinical Excellence Commission. Medication safety updates [internet]. CEC: Sydney; last updated 11 May 2022 [cited 16 May 2022]. Available from: https://www.cec.health.nsw.gov.au/keep-patients-safe/medication-safety/medicine-updates
9. Australian Government Department of Health. ATAGI statement on defining 'up-to-date' status for COVID-19 vaccination [internet]. Department of Health: Canberra; 2022 [cited 3 Mar 2022]. Available from: https://www.health.gov.au/news/atagi-statement-on-defining-up-to-date-status-for-covid-19-vaccination
10. Australian Government Department of Health. Clinical recommendations for COVID-19 vaccines [internet]. Department of Health: Canberra; 2022 [cited 16 May 2022]. Available from: https://www.health.gov.au/initiatives-and-programs/covid-19-vaccines/advice-for-providers/clinical-guidance/clinical-recommendations
11. National Clinical Evidence Taskforce. Living guidelines 6.1.8.1 Sotrovimab for adults [internet]. NCET: Melbourne; 2022 [cited 16 May 2022]. Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/EvAXkn
12. National Clinical Evidence Taskforce. Living guidelines 6.1.1.1 Casirivimab plus imdevimab (Ronapreve) for adults [internet]. NCET: Melbourne; 2022 [cited 16 May 2022]. Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/EPxpqE
13. National Clinical Evidence Taskforce. Risk classification tool for adults with mild COVID-19 [internet]. NCET: Melbourne; 2022 [cited 24 Mar 2022]. Available from: https://clinicalevidence.net.au/wp-content/uploads/RISK-CLASSIFICATION-TOOL.pdf?=221027-43702
14. National Clinical Evidence Taskforce. Living guidelines 6.1.9.1 Tixagevimab plus cilgavimab (Evusheld) for adults [internet]. NCET: Melbourne; 2022 [cited 16 May 2022]. Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/jmY6gP
15. National Clinical Evidence Taskforce. Living guidelines 6.1.5.3 Nirmatrelvir plus ritonavir (Paxlovid) for children and adolescents [internet]. NCET: Melbourne; 2022 [cited 16 May 2022]. Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/LA6RlV
16. National Clinical Evidence Taskforce. Living guidelines 7.1 Casirivimab plus imdevimab (Ronapreve) for post-exposure prophylaxis [internet]. NCET: Melbourne; 2022 [cited 16 May 2022]. Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/nYO14j

17. Australian Government Department of Health. The Pharmaceutical Benefits Scheme, Molnupiravir [internet]. Department of Health: Canberra; 2022 [cited 16 May 2022]. Available from: https://www.pbs.gov.au/medicine/item/12910L

18. National Clinical Evidence Taskforce. Living guidelines 6.1.4.1 Molnupiravir (Lagevrio) for adults [internet]. NCET: Melbourne; 2-22 [cited 16 May 2022]. Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/Lql2q4

19. Australian Government Department of Health. The Pharmaceutical Benefits Scheme, Nirmatrelvir (&) Ritonavir [internet]. Department of Health: Canberra; 20-2022 [cited 16 May 2022]. Available from: https://www.pbs.gov.au/medicine/item/12996B

20. National Clinical Evidence Taskforce. Living guidelines 6.1.5.1 Nirmatrelvir plus ritonavir (Paxlovid) for adults [internet]. NCET: Melbourne; 2022 [cited 16 May 2022]. Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/Evwm1a

21. Australian Government Department of Health, Therapeutic Good Administration. Australian Product Information, Evusheld™ (tixagevimab and cilgavimab) [internet]. Department of Health: Canberra; 2022 [cited 20 December 2022]. Available from: https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent=&id=CP-2022-PI-01156-1&d=20221215172310101&d=20221216172310101&d=20221220172310101

22. National Clinical Evidence Taskforce. Living guidelines 6.1.7.1 Remdesivir for adults [internet]. NCET: Melbourne; 2022 [cited 16 May 2022]. Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/EQlPrn

23. National Clinical Evidence Taskforce. Living guidelines 6.1.8.2 Sotrovimab for pregnant women [internet]. NCET: Melbourne; 2022 [cited 26 May 2022]. Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/jNkX8L

24. National Clinical Evidence Taskforce. Living guidelines 6.1.8.3 Sotrovimab for children and adolescents [internet]. NCET: Melbourne; 2022 [cited 26 May 2022]. Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/jXxakY

25. National Clinical Evidence Taskforce. Living guidelines 6.1.1.2 Casirivimab plus imdevimab (Ronapreve) for pregnant or breastfeeding women [internet]. NCET: Melbourne; 2022 [cited 26 May 2022]. Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/EeYoKE

26. National Clinical Evidence Taskforce. Living guidelines 6.1.1.3 Casirivimab plus imdevimab (Ronapreve) for children and adolescents [internet]. NCET: Melbourne; 2022 [cited 26 May 2022]. Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/n32oVy

27. National Clinical Evidence Taskforce. Living guidelines 6.1.7.2 Remdesivir for pregnant or breastfeeding women [internet]. NCET: Melbourne; 2022 [cited 26 May 2022]. Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/EZ5m2n

28. National Clinical Evidence Taskforce. Living guidelines 6.1.7.3 Remdesivir for children and adolescents [internet]. NCET: Melbourne; 2022 [cited 26 May 2022]. Available from: https://app.magicapp.org/#/guideline/L4Q5An/section/LqkQbE

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