Decision Pathway: treatment of mild-to-moderate COVID-19 infection in Adults - Queensland

Positive RAT/PCR within 5 days of symptom onset (NB. Up to 7 days for remdesivir)
NOT requiring supplemental oxygen (if O_2 required, refer to recommendations in NCCET)
NOT pregnant/breastfeeding (in pregnancy/breastfeeding, refer to recommendations in NCCET)
NOT < 18 years (for COVID management in children, refer to CHQ-GDL- 63327)

NOT Immunocompromised

Age <50 (or <30 if ATSI)

NOT eligible

CONSIDER

Patients who are **not up to date with COVID-19 vaccination with additional risk factors** may be considered for therapy through NMS stock. Risk factors include:

- Obesity (BMI ≥ 30 kg/m²)
- Renal impairment (eGFR < 60 mL/min)
- Heart failure, CAD, Cardiomyopathies, Hypertension
- Respiratory compromise (e.g. COPD, mod-severe asthma, bronchiectasis)
- Diabetes (Type I or II requiring medication)
- Medical related technologic dependence (BiPAP, other ventilation not related to COVID-19)
- Neurodevelopment disorders (including cerebral palsy, Down's syndrome etc)
- Sickle cell disease
- Patients with neuromuscular disease **with** respiratory muscle involvement

Age ≥50 years (or ≥ 30 years if ATSI)

Presence of 2 or more risk factors (or 1 risk factor if ATSI) from:

- Patient in RACF
- Disability with multiple comorbidities or frailty
- Neurological condition (e.g. stroke, dementia, demyelinating condition)
- Respiratory compromise (e.g. COPD, mod-severe asthma, bronchiectasis)
- Heart failure, CAD, Cardiomyopathies, Hypertension
- Obesity (BMI greater than 30kg/m²
- Diabetes (Type I or II requiring medication)
- Renal impairment (eGFR less than 60mL/min)
- Cirrhosis
- Lack of access to higher level healthcare or remote (MMM Cat 5 or above)

NO

NOT eligible

Contact COVID-19 specialist if therapy required

CONSIDER

YES

Age ≥ 70 years

Nirmatrelvir/ritonavir (Paxlovid®) NOTE1

OR

Molnupiravir (alternative)

OR

Remdesivir IV x 3 days NOTE2

Immunocompromised (see page 2)

Age ≥18 years

Consider antiviral and/or monoclonal Antibody therapy regardless of vaccination status based on degree of immunosuppression (page 2 and 3), age and patient comorbidities, including:

- Obesity (BMI ≥ 30 kg/m²)
- Renal impairment (eGFR < 60 mL/min)
- Heart failure, CAD, Cardiomyopathies, Hypertension
- Respiratory compromise (e.g. COPD, mod-severe asthma, bronchiectasis)
- Diabetes (Type I or II requiring medication)
- Medical related technologic dependence (BiPAP, other ventilation not related to COVID-19)
- Neurodevelopment disorders (including cerebral palsy, Down's syndrome etc)
- Sickle cell disease
- Patients with neuromuscular disease **with** respiratory muscle involvement

The effectiveness of combination therapy is unclear but may be considered for high risk patients. Patients who have previously received tixagevimab/cilgavimab (Evusheld®) for pre-exposure prophylaxis (PrEP) may benefit from antiviral therapy and/or additional administration tixagevimab/cilgavimab (Evusheld®) in keeping with tixagevimab/cilgavimab (Evusheld®) treatment dose recommendations.

Nirmatrelvir/ritonavir (Paxlovid®) NOTE1 **OR** Molnupiravir (alternative)

OR

Remdesivir IV x 3 days NOTE2

OR

Tixagevimab/cilgavimab (Evusheld®) NOTE3,NOTE4

NOTE1: ALWAYS check contraindications and drug-drug interactions for nirmatrelvir/ritonavir (Paxlovid®). See information in prescribing guideline. The drug-drug interactions website https://www.covid19-druginteractions.org/checker should be used.
NOTE2: Check precautions as well as renal and liver function as per the remdesivir guidelines prior to prescribing.
NOTE3: Please contact usual treating team AND obtain advice/authorisation from Infectious Diseases or appropriate COVID delegate.
NOTE4: In unvaccinated patients who are not severely immunosuppressed, sole therapy with an oral antiviral is recommended. Tixagevimab/cilgavimab may be considered second line where patients are unable to receive oral antivirals.

V2: October2022

A patient is considered **severely immunocompromised** as per below[1]:

- B or T cell depleting therapy within previous 12 months (rituximab, ocrelizumab, obinutuzumab, ofatumumab, alemtuzumab) or planned to receive B or T cell depleting therapy within two weeks of tixagevimab and cilgavimab administration
- High dose (> 1 g/m^2) cyclophosphamide within previous 12 months
- Receiving Bruton's tyrosine kinase (BTK) inhibitors (zanubrutinib, ibrutinib, acalabrutinib)
- Receiving JAK inhibitors, Sphingosine 1-phosphate receptor modulators , anti-complement antibodies and anti-thymocyte globulin.
- CAR-T/NK cell immunotherapy within previous 24 months
- Stem cell transplant (SCT) – autologous SCT within previous 12 months, allogeneic SCT within previous 24 months, allogeneic SCT with chronic GvHD
- Haematologic malignancy on active therapy
- Non-haematological malignancy with current active treatment (e.g. chemotherapy, whole body irradiation)
- Solid organ transplant on immunosuppressive therapy
- HIV with CD4 cell count < 250 cells/mm^3 or unable to be established on effective antiretroviral therapy
- Combined primary immunodeficiency syndromes (including SCID)
- Common variable immunodeficiency (CVID) with additional T-cell defects, past opportunistic infection or requiring immunosuppressive therapy
- Newly diagnosed humoral immunodeficiency with baseline IgG < 3 g/L

A patient is considered **moderately immunocompromised** as per below[1]:

- Primary immunodeficiency including combined immunodeficiency and syndromes, major antibody deficiency (e.g. common variable immune deficiency (CVID) or agammaglobulinemia), defects of innate immunity (including phagocytic cells), defects of immune regulation, complement deficiencies and phenocopies of primary immunodeficiencies.
- Long term haemodialysis or peritoneal dialysis
- Patients on immunosuppressive therapy listed in table 1 (page 3), outside of severely immunosuppressed criteria

Patients who are moderately immunocompromised are less likely to derive clinical benefit from tixagevimab + cilgavimab (Evusheld®) unless they have other significant risk factors, or the patient has not seroconverted post vaccination

Other considerations for oral antivirals[2] :

- Very high-risk conditions including
  - Down Syndrome
  - cerebral palsy
  - congenital heart disease
  - Thalassemia
  - sickle cell disease and other haemoglobinopathies
- People with disability with multiple comorbidities and/or frailty.

References

1. ATAGI, Recommendations on the use of a 3rd primary dose of COVID-19 vaccine in individuals who are severely compromised. V2.5, July 2022.
2. PBS, Population criteria "moderately to severely immunocompromised". Available at: https://www.pbs.gov.au/medicine/item/12910L OR https://www.pbs.gov.au/medicine/item/12996B

Table 1: Immunosuppressive therapies*

Class	Examples	Therapy timeframe (If not specified: therapy received within the previous 3 months[2]).
Anti-CD20 antibodies	rituximab, obinutuzumab, ocrelizumab, ofatumumab	Within 12 months
BITE antibodies		Within 12 months
BTK inhibitors	ibrutinib, acalabrutinib, zanubrutinib	Within 6 months
JAK inhibitors	tofacitinib, baricitinib, ruxolitinib, upadacitinib	
Sphingosine 1-phosphate receptor modulators	fingolimod, siponimod	
Anti-CD52 antibodies	alemtuzumab	Within 12 months
Anti-complement antibodies	eculizumab	
Anti-thymocyte globulin	anti-thymocyte globulin	Within 12 months
Other immunomodulators	• Venetoclax • Daratumumab • Ruxolitinib • Borezomib, carfilzomib • Lenalidomide, pomalidomide • Belimumab • Abatacept	• Within 6 months • Within 6 months • Within 6 months
TKIs and other targeted therapies	Dasatinib,nilotinib, imatinib, osimertinib, erlotinib, crizotinib, alectinib, lorlatinib	
Corticosteroids (high dose)	Prednisolone >20mg/day (or equivalent) for ≥14 days in a month, or pulse corticosteroid therapy	
Selected conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDS) (excluding hydroxychloroquine or sulfasalazine when used as monotherapy)	• mycophenolate • methotrexate (≥10 mg/week) • Leflunomide (>10mg/day) • azathioprine (≥ 1mg/kg day) • 6-mercaptopurine (≥0.5mg/kg/day) • alkylating agents (e.g. cyclophosphamide, chlorambucil) • systemic calcineurin inhibitors (e.g. cyclosporin, tacrolimus)	• High dose cyclophosphamide(>1g/m^2) - within 12 months
Anti-TNF or Anti-IL-6 when used in combination with other DMARDs	• infliximab, adalimumab, etanercept, golimumab, certolizumab • tocilizumab	
Other immunosuppressive agents	mTOR inhibitors (sirolimus, everolimus)	

Table 2: Immunosuppressive therapies NOT considered to affect immunity status to COVID-19 when administered as monotherapy*

Class	Examples
Anti-integrins	Natalizumab, vedolizumab
Anti-TNF-α antibodies	Infliximab, adalimumab, etanercept, golimumab, certolizumab
Anti-IL1 antibodies	Anakinra
Anti-IL-6 antibodies	Tocilizumab
Anti-IL-17 antibodies	Secukinumab, ixekizumab
Anti-IL-4 antibodies	Dupilimab
Anti-IL-23 antibodies	Ustekinumab
Immune checkpoint inhibitors	Nivolumab, Pembrolizumab, Ipilimumab, Atezolizumab

** Tables 1 and 2 have been developed from recommendations as per ATAGI[1] as well as expert consensus in consultation with CTWG. These lists are not exhaustive, and clinicians may use their judgement for immunosuppressive medications which are not listed.*