# DRUG TREATMENTS FOR ADULTS WITH COVID-19

NATIONAL COVID-19 CLINICAL EVIDENCE TASKFORCE

**VERSION 15.1**
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| DEFINITION OF DISEASE SEVERITY | Not requiring oxygen WITHOUT lower respiratory tract disease | Not requiring oxygen WITH lower respiratory tract disease | Requiring oxygen WITHOUT mechanical ventilation | Requiring invasive mechanical ventilation |
|---|---|---|---|---|
| | **Mild**<br>An individual with no clinical features suggestive of moderate or more severe disease:<br>• no OR mild symptoms and signs (fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhoea, loss of taste and smell)<br>• no new shortness of breath or difficulty breathing on exertion<br>• no evidence of lower respiratory tract disease during clinical assessment or on imaging (if performed) | **Moderate**<br>A stable patient with evidence of lower respiratory tract disease:<br>• during clinical assessment, such as<br>– oxygen saturation 92-94% on room air at rest<br>– desaturation or breathlessness with mild exertion<br>• or on imaging | **Severe**<br>A patient with signs of moderate disease who is deteriorating<br>OR<br>A patient meeting any of the following criteria:<br>• respiratory rate ≥30 breaths/min<br>• oxygen saturation <92% on room air at rest or requiring oxygen<br>• lung infiltrates >50% | **Critical**<br>A patient meeting any of the following criteria:<br>• respiratory failure (defined as any of)<br>– severe respiratory failure ($PaO_2$/$FiO_2$ <200)<br>- respiratory distress or acute respiratory distress syndrome (ARDS)<br>– deteriorating despite non-invasive forms of respiratory support (i.e. non-invasive ventilation (NIV), or high-flow nasal oxygen (HFNO))<br>– requiring mechanical ventilation<br>• hypotension or shock<br>• impairment of consciousness<br>• other organ failure |
| **RECOMMENDED** | | | Use intravenous or oral **dexamethasone** for up to 10 days (or acceptable alternative regimen) in adults with COVID-19 ***who require oxygen*** (including mechanically ventilated patients). | |
| **CONDITIONAL RECOMMENDATION FOR** | Consider using inhaled **corticosteroids (budesonide or ciclesonide)** ***within 14 days of symptom onset*** in adults with COVID-19 who ***do not require oxygen*** and who have one or more ***risk factors***^ for disease progression. | | Consider using **tixagevimab plus cilgavimab (Evusheld)** ***within 12 days of symptom onset*** in ***unvaccinated***# adults with COVID-19 who ***require oxygen but not invasive mechanical ventilation***.*<br>*Note: Refer to the related consensus recommendation below for additional guidance.* | |
| | **Consider using one of the following:** | | Consider using **remdesivir** in adults with COVID-19 who ***require oxygen but do not require non-invasive or invasive ventilation.*** | |
| | Consider using **remdesivir** ***within 7 days of symptom onset*** in ***unvaccinated***# adults with COVID-19 who ***do not require oxygen*** and who have one or more ***risk factors***^ for disease progression.<br>Within the patient population for which remdesivir is conditionally recommended for use (see Remark), decisions about the appropriateness of treatment with remdesivir should be based on the patient's individual risk of severe disease, including their age, presence of multiple risk factors, and vaccination status (including number of doses and time since last dose / or timing of most recent infection).<br>*Note: Refer to the related consensus recommendation below for additional guidance.* | | **Consider using one of the following##:** | |
| | Consider using **nirmatrelvir plus ritonavir (Paxlovid)**** ***within 5 days of symptom onset*** in ***unvaccinated***# adults with COVID-19 who ***do not require oxygen*** and who have one or more ***risk factors***^ for disease progression.<br>Within the patient population for which nirmatrelvir plus ritonavir is conditionally recommended for use (see Remark), decisions about the appropriateness of treatment with nirmatrelvir plus ritonavir should be based on the patient's individual risk of severe disease, including their age, presence of multiple risk factors, and vaccination status (including number of doses and time since last dose/ or timing of most recent infection).<br>*Note: Refer to the related consensus recommendation below for additional guidance.* | | Consider using **tocilizumab** for the treatment of COVID-19 in adults who ***require supplemental oxygen***, particularly where there is evidence of ***systemic inflammation.*** | |
| | Consider using **tixagevimab plus cilgavimab (Evusheld)*** ***within 5 days of symptom onset*** in ***unvaccinated***# adults with COVID-19 who ***do not require oxygen*** and who have one or more ***risk factors***^ for disease progression.<br>Within the patient population for which tixagevimab plus cilgavimab is conditionally recommended for use (see Remark), decisions about the appropriateness of treatment with tixagevimab plus cilgavimab should be based on the patient's individual risk of severe disease, including their age, presence of multiple risk factors, and vaccination status (including number of doses and time since last dose/ or timing of most recent infection).<br>*Note: Refer to the related consensus recommendation below for additional guidance.* | | Consider using **baricitinib** in adults hospitalised with COVID-19 who ***require supplemental oxygen.****| | |

Note: Sotrovimab, Ronapreve (casirivimab plus imdevimab) or Regdanvimab can be used in the target population but have been omitted due to reduced effectiveness against the circulating Omicron variant.

Sarilumab can be used in adults who require high-flow oxygen, non-invasive ventilation or invasive mechanical ventilation but has been omitted because it is not easily accessible in Australia.

*Please refer to footnotes located on page 3 of this flowchart.*

| | Not requiring oxygen WITHOUT lower respiratory tract disease | Not requiring oxygen WITH lower respiratory tract disease | Requiring oxygen WITHOUT mechanical ventilation | Requiring invasive mechanical ventilation |
|---|---|---|---|---|
| CONSENSUS RECOMMENDATION FOR | In addition to at-risk unvaccinated adults, also consider using **remdesivir** ***within 7 days of symptom onset*** in adults with COVID-19 who ***do not require oxygen*** and are ***immunocompromised;*** or are at particularly ***high risk of severe disease*** on the basis of advanced age and multiple risk factors^. | | In addition to at-risk unvaccinated adults, also consider using **tixagavimab plus cilgavimab (Evusheld)** ***within 12 days of symptom onset*** in adults with COVID-19 who ***require oxygen*** and are ***immunocompromised***; or who ***require oxygen*** and are at particularly ***high risk of severe disease*** on the basis of advanced age and multiple risk factors^. | |
| | In addition to at-risk unvaccinated adults, also consider using **nirmatrelvir plus ritonavir (Paxlovid)**** ***within 5 days of symptom onset*** in adults with COVID-19 who ***do not require oxygen*** and are ***immunocompromised;*** or are at particularly ***high risk of severe disease*** on the basis of advanced age and multiple risk factors^. | | | |
| | In addition to at-risk unvaccinated adults, also consider using **tixagevimab plus cilgavimab (Evusheld)*** ***within 5 days of symptom onset*** in adults with COVID-19 who ***do not require oxygen*** and are ***immunocompromised;*** or are at particularly ***high risk of severe disease*** on the basis of advanced age and multiple risk factors^. | | | |
| | Consider using **molnupiravir (Lagevrio)** ***within 5 days of symptom onset*** in ***unvaccinated***# adults with COVID-19 who ***do not require oxygen*** and who have one or more ***risk factors***^ for disease progression, where other treatments (such as remdesivir or nirmatrelvir plus ritonavir) are not suitable or available.<br>Within the patient population for which molnupiravir is recommended for use (see Remark), decisions about the appropriateness of treatment with molnupiravir should be based on the patient's individual risk of severe disease, including their age, presence of multiple risk factors, and vaccination status (including number of doses and time since last dose/ or timing of most recent infection). | | | |
| | In addition to at-risk unvaccinated adults, also consider using **molnupiravir (Lagevrio)** ***within 5 days of symptom onset*** in adults with COVID-19 who ***do not require oxygen*** and are ***immunocompromised;*** or are at particularly ***high risk of severe disease*** on the basis of advanced age and multiple risk factors^.<br>***AND*** where other treatments (such as remdesivir or nirmatrelvir plus ritonavir) are not suitable or available. | | | |
| CONDITIONAL RECOMMENDATION AGAINST | **DO NOT** routinely use **dexamethasone** (or other systemic corticosteroid) to treat COVID-19 in adults who ***do not require oxygen***. | | | |
| NOT RECOMMENDED | **DO NOT** use the following for the treatment of COVID-19:<br>• aspirin<br>• azithromycin<br>• colchicine<br>• favipiravir<br>• hydroxychloroquine<br>• hydroxychloroquine plus azithromycin<br>• interferon β-1a<br>• interferon β-1a plus lopinavir-ritonavir<br>• ivermectin<br>• lopinavir-ritonavir | | | |
| | | | **DO NOT** use **convalescent plasma** for the treatment of COVID-19 in patients who ***require supplemental oxygen***. | |
| | | | | **DO NOT** start **remdesivir** in adults hospitalised with COVID-19 who ***require non-invasive or invasive ventilation***. |
| ONLY IN RESEARCH | Do not use **convalescent plasma** for the treatment of COVID-19 in patients who ***do not require oxygen*** outside of randomised trials with appropriate ethical approval. | | | Do not use **tixagevimab plus cilgavimab (Evusheld)** for the treatment of COVID-19 in adults who ***require mechanical ventilation*** outside of randomised trials with appropriate ethical approval. |
| | Do not use the following for the treatment of COVID-19 outside of randomised trials with appropriate ethical approval:<br>• anakinra<br>• angiotensin 2 receptor agonist C21<br>• aprepitant<br>• baloxavir marboxil<br>• bamlanivimab<br>• bamlanivimab plus etesevimab<br>• bebtelovimab<br>• bromhexine hydrochloride<br>• camostat mesilate<br>• CD24Fc<br>• chloroquine<br>• combined metabolic activators (CMA)<br>• darunavir-cobicistat<br>• doxycycline<br>• dutasteride<br>• enisamium<br>• ensovibep<br>• favipiravir<br>• fluvoxamine<br>• human umbilical cord mesenchymal stem cells<br>• immunoglobulin<br>• immunoglobulin plus methylprednisone<br>• inhaled interferon β-1a<br>• interferon β-1b<br>• interferon gamma<br>• interferon kappa plus trefoil factor 2 (IFN-k plus TFF2)<br>• ivermectin plus doxycycline<br>• lenzilumab<br>• metformin<br>• N-acetylcysteine<br>• nitazoxanide<br>• opaganib<br>• peginterferon lambda<br>• recombinant human granulocyte colony-stimulating factor (rhG-CSF)<br>• ruxolitinib<br>• sabizabulin<br>• sofosbuvir-daclatasvir<br>• sulodexide<br>• telmisartan<br>• tofacitinib<br>• triazavirin<br>• umifenovir<br>• vitamin C<br>• vitamin D analogues (calcifediol / cholecalciferol)<br>• zinc<br>• other disease-modifying treatments | | | |

*Please refer to footnotes located on page 3 of this flowchart.*

^RISK FACTORS FOR DISEASE PROGRESSION

**Immunocompromising conditions** include:

- Primary or acquired immunodeficiency
  - Haematologic neoplasms: leukaemias, lymphomas, myelodysplastic syndromes
  - Post-transplant: solid organ (on immunosuppressive therapy), haematopoietic stem cell transplant (within 24 months)
  - Immunocompromised due to primary or acquired (AIDS) immunodeficiency
  - Other significantly immunocompromising conditions
- Immunosuppressive therapy (current or recent)
  - Chemotherapy, whole body radiotherapy or total lymphoid irradiation
  - High-dose corticosteroids (≥20 mg of prednisone per day, or equivalent) for ≥14 days
  - Selected other potent immunosuppressive therapies (refer to ATAGI advice)

Refer to the **Risk Classification Tool** when making decisions about which individuals are most likely to benefit from treatment.

**Risk factors for disease progression**

- Older age (e.g. over 65 years, or over 50 years for Aboriginal and Torres Strait Islander people)
- Diabetes requiring medication
- Obesity (BMI >30 kg/m$^2$)
- Renal failure
- Cardiovascular disease, including hypertension
- Respiratory compromise, including COPD, asthma requiring steroids, or bronchiectasis
- Immunocompromising condition

*Note: This list has been simplified based on the individual risk factors for each therapy option from clinical trial evidence. Refer to the Australian guidelines for the clinical care of people with COVID-19 for further information.*

Refer to the **Decision Support Tool** for specific guidance on drug treatments for at risk adults with COVID-19 who do not require oxygen.

**Source**
National COVID-19 Clinical Evidence Taskforce – Australian guidelines for the clinical care of people with COVID-19.

Note: This flowchart does not apply to people on home oxygen due to pre-existing conditions. Use clinical judgement in these cases.

# Efficacy is unclear in individuals who have received any COVID-19 vaccine.
* Not approved for use by TGA for this indication.
** Check for common, serious drug-drug interactions before prescribing and administering nirmatrelvir plus ritonavir with other medications.
## The RECOVERY trial has demonstrated a benefit when using tocilizumab in conjunction with baricitinib, however there are limited data available to evaluate the safety of this combination. The RECOVERY trial has also demonstrated a benefit when using baricitinib in conjunction with corticosteroids, tocilizumab or remdesivir, however the Taskforce notes that the concomitant use of two or more immunomodulatory agents may increase the risk of side effects such as opportunistic infection.