## DISEASE-MODIFYING TREATMENTS FOR ADULTS WITH COVID-19

### DEFINITION OF DISEASE SEVERITY

<table>
<thead>
<tr>
<th>Not requiring oxygen WITHOUT lower respiratory tract disease</th>
<th>Not requiring oxygen WITH lower respiratory tract disease</th>
<th>Requiring oxygen WITHOUT mechanical ventilation</th>
<th>Requiring invasive mechanical ventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild</strong></td>
<td><strong>Moderate</strong></td>
<td><strong>Severe</strong></td>
<td><strong>Critical</strong></td>
</tr>
<tr>
<td>An individual with no clinical features suggestive of moderate or more severe disease:</td>
<td>A stable patient with evidence of lower respiratory tract disease:</td>
<td>A patient with signs of moderate disease who is deteriorating OR</td>
<td>A patient meeting any of the following criteria:</td>
</tr>
<tr>
<td>• no OR mild symptoms and signs (fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhoea, loss of taste and smell)</td>
<td>• during clinical assessment, such as – oxygen saturation 92-94% on room air at rest – desaturation or breathlessness with mild exertion</td>
<td>• respiratory rate ≥30 breaths/min</td>
<td>• respiratory failure (defined as any of)</td>
</tr>
<tr>
<td>• no new shortness of breath or difficulty breathing on exertion</td>
<td>• on imaging</td>
<td>• oxygen saturation &lt;92% on room air at rest or requiring oxygen</td>
<td>– severe respiratory failure (PaO₂/ FiO₂ &lt; 200)</td>
</tr>
<tr>
<td>• no evidence of lower respiratory tract disease during clinical assessment or on imaging (if performed)</td>
<td></td>
<td>• lung infiltrates &gt;50%</td>
<td>– respiratory distress or acute respiratory distress syndrome (ARDS)</td>
</tr>
<tr>
<td><strong>Note:</strong> Refer to the related consensus recommendation for additional guidance.</td>
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<td>– deteriorating despite non-invasive forms of respiratory support (i.e. non-invasive ventilation (NIV), or high-flow nasal oxygen (HFNO))</td>
</tr>
</tbody>
</table>

Consider using inhaled corticosteroids (budesonide or ciclesonide) within 14 days of symptom onset in adults with COVID-19 who do not require oxygen and have one or more risk factors* for disease progression.

Consider using one of the following:

- **Sotrovimab**
  - Within the patient population for which sotrovimab is conditionally recommended for use (see Remark), decisions about the appropriateness of treatment with sotrovimab should be based on the patient’s individual risk of severe disease, on the basis of age and multiple risk factors, COVID-19 vaccination status and time since vaccination.
  - Note: Refer to the related consensus recommendation for additional guidance.

- **Nirmatrelvir plus ritonavir (Paxlovid)**
  - 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, on the basis of age and multiple risk factors, COVID-19 vaccination status and time since vaccination.
  - Note: Refer to the related consensus recommendation for additional guidance.

- **Remdesivir**
  - Consider using in adults with COVID-19 who do not require oxygen and have one or more risk factors* for disease progression.

- **Casirivimab plus imdevimab (Ronapreve)**
  - Consider using in seronegative adults hospitalised with moderate to critical COVID-19.**

Use dexamethasone 6 mg daily intravenously or orally for up to 10 days (or acceptable alternative regimen) in adults with COVID-19 who require oxygen (including mechanically ventilated patients).

Consider using one of the following:

- **Tocilizumab**
  - For adults who require supplemental oxygen, particularly where there is evidence of systemic inflammation.

- **Baricitinib**
  - For adults hospitalised with COVID-19 who require supplemental oxygen.

- **Sarilumab**
  - For the treatment of COVID-19 in adults who require high-flow oxygen, non-invasive ventilation or invasive mechanical ventilation.**

- **Remdesivir**
  - For adults with COVID-19 who require oxygen but do not require non-invasive or invasive ventilation.

### CONDITIONAL RECOMMENDATION FOR

- **Dexamethasone**
  - 6 mg daily intravenously or orally for up to 10 days (or acceptable alternative regimen) in adults with COVID-19 who require oxygen (including mechanically ventilated patients).

- **Remdesivir**
  - Consider using in adults with COVID-19 who do not require oxygen.

- **Casirivimab plus imdevimab (Ronapreve)**
  - Consider using in seronegative adults hospitalised with moderate to critical COVID-19.**
### Conditional Recommendation for Treatment

#### Not requiring oxygen WITHOUT lower respiratory tract disease

In addition to at-risk unvaccinated adults, also consider using **sotrovimab within 5 days of symptom onset** in adults with COVID-19 who **do not require oxygen** and:
- are immunocompromised regardless of vaccination status; or
- who are not up-to-date with vaccination and are at **high risk of disease** on the basis of age and multiple risk factors.

#### Not requiring oxygen WITH lower respiratory tract disease

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 regardless of vaccination status; or
- who are not up-to-date with vaccination and are at **high risk of severe disease** on the basis of age and multiple risk factors.

#### Requiring oxygen WITHOUT mechanical ventilation

In addition to at-risk unvaccinated adults, also 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 sotrovimab or nirmatrelvir plus ritonavir) are not suitable or available.

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, on the basis of age and multiple risk factors, COVID-19 vaccination status and time since vaccination.

Consider using **molnupiravir (Lagevrio) within 5 days of symptom onset** in adults with COVID-19 who **do not require oxygen** and:
- are immunocompromised regardless of vaccination status; or
- who are not up-to-date with vaccination and are at **high risk of severe disease** on the basis of age and multiple risk factors.

**AND** where other treatments (such as sotrovimab or nirmatrelvir plus ritonavir) are not suitable or available.

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 regardless of vaccination status; or
- who are not up-to-date with vaccination and are at **high risk of severe disease** on the basis of age and multiple risk factors.

#### Requiring invasive mechanical ventilation

**DO NOT** routinely use **dexamethasone** (or other systemic corticosteroid) to treat COVID-19 in adults who **do not require oxygen**.

**DO NOT** use the following for the treatment of COVID-19:
- aspirin
- azithromycin
- colchicine
- convalescent plasma
- hydroxychloroquine
- hydroxychloroquine plus azithromycin
- interferon β-1a
- interferon β-1a plus loxapinav-ritonavir
- lopinavir-ritonavir

**DO NOT** use **casirivimab plus indemivam (Ronepreve)** in seropositive adults hospitalised with moderate to critical COVID-19.

**DO NOT** start remdesivir in adults hospitalised with COVID-19 who require non-invasive or invasive ventilation.

Do not use the following for the treatment of COVID-19 outside of randomised trials with appropriate ethical approval:
- anakinra
- azilsartan 2 receptor agonist C21
- apremilast
- baloxavir marboxil
- bamlanivimab
- bamlanivimab plus etesevimab
- bromhexine hydrochloride
- camostat mesilate
- chloroquine
- combined metabolic activators (CMA)
- darunavir-cobicistat
- doxycycline
- dutasteride
- enoximion
- favipiravir
- fluvoxamine
- human umbilical cord mesenchymal stem cells
- interferon
- interferon β-1b
- interferon gamma
- interferon kappa plus trefoil factor 2 (IFN-k plus TFF2)
- ivermectin
- ivermectin plus doxycycline
- lenzilumab
- metformin
- N-acetylcysteine
- rituximab
- peginterferon lambda
- recombinant human granulocyte colony-stimulating factor (rHuG-CSF)
- regdanavir
- ruxolitinib
- sofosbuvir-daclatasvir
- sulodexide
- telmisartan
- tocilizumab
- triazavirin
- umifenovir
- vitamin C
- vitamin D analogues (calcifediol / cholecalciferol)
- zinc
- other disease-modifying treatments
### Risk Factors for Disease Progression

#### Inhaled Corticosteroids
- Age ≥65 years or ≥50 years with one or more of the following comorbidities:
  - Diabetes (not treated with insulin)
  - Heart disease and/or hypertension
  - Asthma or lung disease
  - Weakened immune system due to a serious illness or medication (e.g., chemotherapy)
  - Mild hepatic impairment
  - Stroke or other neurological problem

Note: Risk factors are based on PRINCIPLE trial inclusion criteria.

#### Casirivimab plus Imdevimab (Ronapreve)
- Age ≥50 years
- Obesity (BMI ≥30 kg/m²)
- Cardiovascular disease (including hypertension)
- Chronic lung disease (including asthma)
- Type 1 or 2 diabetes mellitus
- Chronic kidney disease, including those that are on dialysis
- Chronic liver disease
- Immunocompromised patients (including individuals with rheumatoid arthritis, HIV/AIDS and systemic lupus erythematosus receiving immunosuppressive treatment)

Note: Risk factors are based on REGEN-COV trial inclusion criteria.

#### Molnupiravir (Lagevrio)
- Age ≥60 years
- Obesity (BMI ≥30 kg/m²)
- Chronic kidney disease (i.e. eGFR 30–60 mL/min/1.73m² by MDRD), excluding patients on dialysis
- Serious heart conditions such as heart failure, coronary artery disease or cardiomyopathies
- Chronic obstructive pulmonary disease
- Active cancer (excluding minor cancers not associated with immunosuppression, e.g. basal cell carcinomas)
- Immunocompromised state following solid organ transplant
- Sickle cell disease
- Diabetes mellitus

Note: Risk factors are based on MOVe-OUT trial inclusion criteria.

#### Nirmatrelvir plus ritonavir (Paxlovid)
- Age ≥60 years
- Diabetes (requiring medication)
- BMI ≥25 kg/m²
- Cardiovascular disease
- Hypertension
- Chronic lung disease

Note: Risk factors are based on trial inclusion criteria. Patients with the following conditions are also likely to benefit from treatment:
- Chronic kidney disease (but where the eGFR ≤30 mL/min)
- Immunosuppressed
- Medical related technological dependence (e.g., CPAP not related to COVID-19)
- HIV positive (viral load <400 copies/mL)
- Neurodevelopmental disorders (e.g. cerebral palsy, Down’s syndrome)
- Cancer (other than localised skin cancer)
- Sickle cell disease

#### Remdesivir
- Age ≥60 years
- Diabetes
- Obesity (BMI ≥30 kg/m²)
- Chronic kidney disease (any stage)
- Cardiovascular or cerebrovascular disease (coronary artery disease, congenital heart disease, heart failure, cardiomyopathy or history of stroke)
- Hypertension (systemic or pulmonary)
- Chronic liver disease
- Chronic lung disease (COPD, moderate-severe asthma, cystic or pulmonary fibrosis)
- Sickle cell disease
- Current cancer
- Immunocompromised state (no definition provided)

Note: Risk factors are based on PINETREE trial inclusion criteria.

#### Sotrovimab
- Diabetes (requiring medication)
- Obesity (BMI ≥30 kg/m²)
- Chronic kidney disease (i.e. eGFR <60 by MDRD)
- Congestive heart failure (NYHA class II or greater)
- COPD (history of chronic bronchitis, chronic obstructive lung disease, or emphysema with dyspnoea on physical exertion)
- Moderate-to-severe asthma (requiring an inhaled steroid to control symptoms or prescribed a course of oral steroids in the previous 12 months)
- Age ≥55 years

Note: Risk factors are based on COMET-ICE trial inclusion criteria.

#### Immunocompromising Conditions
- Primary or acquired immunodeficiency
  - Haematological 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 (HIV/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
- All biological disease-modifying anti-rheumatic drugs (bDMARDs) and most other (e.g. conventional synthetic) DMARDs

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

* 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.
# Efficacy is unclear in individuals who are up-to-date with vaccination or partially vaccinated.
## Casirivimab plus Imdevimab (Ronapreve) should not routinely be used where Omicron is the dominant circulating variant. Consider using casirivimab plus imdevimab in patients who are not up-to-date with vaccination. Do not routinely use casirivimab plus imdevimab in patients who are up-to-date with vaccination unless immunosuppressed.