DISEASE-MODIFYING TREATMENTS FOR ADULTS WITH COVID-19

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

**Mild**
An individual with no clinical features suggestive of moderate or more severe disease:
- no or mild symptoms and signs (fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhoea, loss of taste and smell)
- no new shortness of breath or difficulty breathing on exertion
- no evidence of lower respiratory tract disease during clinical assessment or on imaging (if performed)

**Consider using inhaled budesonide 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.

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

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

**Moderate**
A stable patient with evidence of lower respiratory tract disease:
- during clinical assessment, such as:
  - oxygen saturation 92-94% on room air at rest
  - desaturation or breathlessness with mild exertion
  - or on imaging

** Consider using casirivimab plus imdevimab within 7 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** sotrovimab within 5 days of symptom onset in adults with COVID-19 who do not require oxygen and have one or more risk factors** for disease progression.

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

**Requiring oxygen WITHOUT mechanical ventilation**

**Severe**
A patient with signs of moderate disease who is deteriorating OR
A patient meeting any of the following criteria:
- respiratory failure (defined as any of):
  - severe respiratory failure (PaO2/FiO2 <200)
  - respiratory distress or acute respiratory distress syndrome (ARDS)
- deteriorating despite non-invasive forms of respiratory support (i.e. non-invasive ventilation (NIV), or high-flow nasal oxygen (HFNO))
- requiring mechanical ventilation
- hypotension or shock
- impairment of consciousness
- other organ failure

**Consider using** casirivimab plus imdevimab in seronegative adults hospitalised with moderate to critical COVID-19.

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

**Consider using one of the following:**
- interferon β-1a
- interferon β-1a plus lopinavir-ritonavir
- lopinavir-ritonavir

**Critical**
A patient meeting any of the following criteria:
- respiratory failure (defined as any of):
- severe respiratory failure (PaO2/FiO2 <200)
- respiratory distress or acute respiratory distress syndrome (ARDS)
- deteriorating despite non-invasive forms of respiratory support (i.e. non-invasive ventilation (NIV), or high-flow nasal oxygen (HFNO))
- requiring mechanical ventilation
- hypotension or shock
- impairment of consciousness
- other organ failure

**Consider using** remdesivir in adults with COVID-19 who require oxygen but do not require non-invasive or invasive ventilation.

**Consider using** hydroxychloroquine plus azithromycin in adults hospitalised with COVID-19 who require oxygen.

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

**Requiring invasive mechanical ventilation**

**Severe**
A patient with signs of moderate disease who is deteriorating OR
A patient meeting any of the following criteria:
- respiratory rate ≥30 breaths/min
- oxygen saturation <92% on room air at rest or requiring oxygen
- lung infiltrates >50%

**Consider using** convalescent plasma in adults hospitalised with moderate to critical COVID-19.

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

**Consider using** tocilizumab for the treatment of COVID-19 in adults who require supplemental oxygen.

**Consider using** baricitinib in adults hospitalised with COVID-19 who require supplemental oxygen.

**Consider using** casirivimab plus imdevimab in seropositive adults hospitalised with moderate to critical COVID-19.

**NOT RECOMMENDED**
- azithromycin
- interferon β-1a
- interferon β-1a plus lopinavir-ritonavir
- lopinavir-ritonavir

**NOT RECOMMENDED**
- aspirin
- tizanidine
- colchicine
- convalescent plasma
- hydroxychloroquine
- hydroxychloroquine plus azithromycin
- interferon β-1a
- interferon β-1a plus lopinavir-ritonavir
- lopinavir-ritonavir

**DEFINITION OF DISEASE SEVERITY**

- **Mild**: An individual with no clinical features suggestive of moderate or more severe disease:
  - no or mild symptoms and signs (fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhoea, loss of taste and smell)
  - no new shortness of breath or difficulty breathing on exertion
  - no evidence of lower respiratory tract disease during clinical assessment or on imaging (if performed)

- **Moderate**: A stable patient with evidence of lower respiratory tract disease:
  - during clinical assessment, such as:
    - oxygen saturation 92-94% on room air at rest
    - desaturation or breathlessness with mild exertion
    - or on imaging

- **Severe**: A patient with signs of moderate disease who is deteriorating OR
  A patient meeting any of the following criteria:
  - respiratory rate ≥30 breaths/min
  - oxygen saturation <92% on room air at rest or requiring oxygen
  - lung infiltrates >50%

- **Critical**: A patient meeting any of the following criteria:
  - respiratory failure (defined as any of):
    - severe respiratory failure (PaO2/FiO2 <200)
    - respiratory distress or acute respiratory distress syndrome (ARDS)
  - deteriorating despite non-invasive forms of respiratory support (i.e. non-invasive ventilation (NIV), or high-flow nasal oxygen (HFNO))
  - requiring mechanical ventilation
  - hypotension or shock
  - impairment of consciousness
  - other organ failure

**CONDITIONAL RECOMMENDATION FOR**

- **Mild**
  Consider using inhaled budesonide 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.

- **Moderate**
  Consider using casirivimab plus imdevimab within 7 days of symptom onset in adults with COVID-19 who do not require oxygen and have one or more risk factors for disease progression.

- **Severe**
  Consider using casirivimab plus imdevimab in seronegative adults hospitalised with moderate to critical COVID-19.

**CONDITIONAL RECOMMENDATION AGAINST**

- **Mild**
  DO NOT use dexamethasone (or other oral or parenteral steroids) to treat COVID-19 in adults who do not require oxygen.

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

- **Severe**
  DO NOT use casirivimab plus imdevimab in seropositive adults hospitalised with moderate to critical COVID-19.

**Note:** This flowchart does not apply to people on home oxygen due to pre-existing conditions. Use clinical judgement in these cases.
**DO NOT** use the following for the treatment of COVID-19 outside of randomised trials with appropriate ethical approval:

- anakinra
- angiotensin 2 receptor agonist C21
- aprepitant
- baloxavir marboxil
- bamlanivimab
- bamlanivimab plus etesevimab
- bromhexine hydrochloride
- camostat mesilate
- chloroquine
- combined metabolic activators (CMA)
- darunavir-cobicistat
- doxycycline
- dutasteride
- favipiravir
- fluvoxamine
- human umbilical cord mesenchymal stem cells
- immunoglobulin
- immunoglobulin plus methylprednisone
- inhaled interferon β-1a
- interferon β-1b
- interferon gamma
- interferon kappa plus trefoil factor 2 (IFN-κ plus TFF2)
- ivermectin
- ivermectin plus doxycycline
- lenzilumab
- N-acetylcysteine
- nitazoxanide
- peginterferon lambda
- recombinant human granulocyte colony-stimulating factor (rhG-CSF)
- regdanvimab
- ruxolitinib
- sofosbuvir-daclatasvir
- sulodexide
- telmisartan
- tofacitinib
- triazavirin
- umifenovir
- vitamin C
- vitamin D analogues (calcifediol / cholecalciferol)
- zinc
- other disease-modifying treatments

### Risk Factors for Disease Progression

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Risk Factors</th>
</tr>
</thead>
</table>
| **Budesonide** | 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** | Outpatients with mild COVID-19  
- 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)  
Note: Risk factors are based on REGEN-COV 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)  
- Chronic obstructive pulmonary disease (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 |

**Source**