MANAGEMENT OF ADULTS WITH MODERATE TO SEVERE COVID-19

NATIONAL COVID-19 CLINICAL EVIDENCE TASKFORCE

LEGEND

EBR: Evidence-Based Recommendation
CBR: Consensus-Based Recommendation
PP: Practice Point

Living guidance

Not prioritised for review

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Setting of care

ADMISSIONS

- Manage people with moderate COVID-19 in hospital, when possible. **PP** [Taskforce]
- Manage people with severe COVID-19 in hospital or another facility that can provide the necessary level of care. **PP** [Taskforce]

Consider admission of people with likely or confirmed COVID-19 if they are haemodynamically unstable, hypoxaemic ((SaO2 on room air ≤ 92%), have comorbidities, or an unsuitable home enivronment. **PP** [Taskforce]

MANAGING RISK OF INFECTION

As per the current national guidance on the use of personal protective equipment (PPE) in hospitals during the COVID-19 outbreak:

- use eye protection
- use P2/N95 respirators
- use other PPE as per NHMRC IPC recommendations

PP [Taskforce/ICEG; NHMRC]

Definition of disease severity

Moderate illness
Stable adult patient presenting with respiratory and/or systemic symptoms or signs. Able to maintain SpO_2 > 92% at rest (or above 90% for patients with chronic lung disease) with up to 4 L/min oxygen via nasal prongs.

Characteristics:

- fatigue, fever > 38° C or persistent cough
- clinical or radiological signs of lung involvement
- no clinical or laboratory indicators of clinical severity or respiratory impairment

Severe illness
Adult patients meeting any of the following criteria:

- respiratory rate ≥ 30 breaths/min
- SpO_2 < 92% at rest (note: in adults with darker skin pulse oximetry may underestimate severity of hypoxemia)
- arterial partial pressure of oxygen (PaO_2)/inspired oxygen fraction (FiO_2) ≤ 300

Testing and monitoring of inpatients

BASELINE TESTING AND DIAGNOSTIC WORK UP

In all people with suspected or confirmed COVID-19, perform haematology, biochemistry laboratory testing, a CXR and an ECG on admission. **PP** [Taskforce]

Investigate people with suspected or confirmed COVID-19 for influenza, CAP and other differential diagnoses as per usual practice. **PP** [Taskforce]

In cases of suspected COVID-19 that have not been confirmed by positive PCR, collect serum during the acute phase of the illness (preferably within the first 7 days of symptom onset); store and test the serum in parallel with convalescent sera collected 2 or more weeks after the onset of illness. **PP** [Taskforce/CDNA]

In cases where a strong clinical suspicion of COVID-19 remains after a negative SARS-CoV-2 PCR:

- continue isolation and treatment as for a provisional COVID-19 diagnosis;
- repeat SARS-CoV-2 PCR as soon as possible, adding a stool PCR if loose stool.

PP [Taskforce/ASID]

Whole genome sequencing of all COVID-19 cases should be undertaken. **PP** [CDNA]

MONITORING AND MARKERS OF CLINICAL DETERIORATION

Monitoring — CONSENSUS RECOMMENDATION
For people with COVID-19, monitor markers of clinical progression, such as rapidly progressive respiratory failure and sepsis, especially on days 5 to 10 after onset of symptoms. **CBR** [Taskforce]

In all people with suspected or confirmed COVID-19, perform ECG and haematology and biochemistry laboratory tests as clinically indicated to monitor for complications, such as acute liver injury, acute kidney injury, acute cardiac injury or shock. **PP** [Taskforce]

Only repeat CXR in people with suspected or confirmed COVID-19 if clinically indicated (e.g. in cases of clinical deterioration or recent intubation). **PP** [Taskforce/ASID]

Do not routinely perform CT scanning in people with suspected or confirmed COVID-19. **PP** [Taskforce]

Supportive care in hospital

GENERAL

In all people with suspected or confirmed COVID-19, anticipate complications such as arrhythmias, cardiac impairment, sepsis and multi-organ dysfunction, and address using existing standards of care.
PP [Taskforce/ACEM]

Corticosteroids — RECOMMENDED
Use 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).
EBR [Taskforce]

The suggested regimen of corticosteroid use is 6 mg of dexamethasone (oral or intravenous) daily for up to 10 days. In patients for whom dexamethasone is not available, acceptable alternative regimens include:
EBR [Taskforce]

- hydrocortisone: intravenous (50 mg), every 6 hours for up to 10 days
- prednisolone: oral (50 mg), daily for up to 10 days.

SUPPORTIVE ANTI-INFECTIOUS THERAPY

In people with suspected or confirmed COVID-19 with signs and symptoms consistent with bacterial pneumonia, prescribe antibiotics according to local or national pneumonia guidelines.

Consider early de-escalation or cessation of antibitoics if bacterial pneumonia is excluded. **PP** [Taskforce/ASID]

In people with suspected or confirmed COVID-19 with onset of symptoms < 48 hours, request an influenza PCR test.

If disease is severe, consider prescribing oseltamivir 75 mg BD (or a renally adjusted dose). If the influenza PCR is negative, cease oseltamivir.
PP [Taskforce/ASID]

Corticosteroids — CONDITIONAL RECOMMENDATION AGAINST

Do not routinely use dexamethasone (or other corticosteroids) to treat COVID-19 in **adults who do not require oxygen**. **EBR** [Taskforce]

Corticosteroids may still be considered for other evidence-based indications in people who have COVID-19. **PP** [Taskforce]

Remdesivir — CONDITIONAL RECOMMENDATION AGAINST

Do not start remdesivir in adults hospitalised with COVID-19 who require ventilation.

However, remdesivir should be continued with the appropriate dose and duration, **if it was started prior to requiring ventilation** (invasive or non-invasive mechanical ventilation and extracorporeal membrane oxygenation (ECMO)). **PP** [Taskforce]

Remdesivir — CONDITIONAL RECOMMENDATION FOR

Consider using remdesivir for adults hospitalised with moderate to severe COVID-19 **who require oxygen but not ventilation**. **EBR** [Taskforce]

Sotrovimab — CONDITIONAL RECOMMENDATION FOR

Consider using sotrovimab for the treatment of COVID-19 within five days of symptom onset in adults who do not require oxygen and who have one or more risk factors for disease progression. **EBR** [Taskforce]

In patients with confirmed COVID-19 who do not require oxygen, sotrovimab probably decreases the risk of hospitalisation if taken within five days of onset of symptoms. **PP** [Taskforce]

Results are based on the COMET-ICE trial, in which non-vaccinated adults were treated with a single one-hour intravenous infusion of 500 mg sotrovimab. Based on the inclusion criteria for this trial, risk factors for disease progression include the following:

- 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

Casirivimab plus imdevimab (REGEN-COV) — CONDITIONAL RECOMMENDATION FOR

Consider using casirivimab plus imdevimab **in seronegative patients hospitalised** with moderate to severe COVID-19. **EBR** [Taskforce]

OTHER IMMUNOMODULATING DRUGS — CONDITIONAL RECOMMENDATION FOR

Consider using one of:

- Baracitinib - Consider using baracitinib for adults hospitalised with COVID-19 **who require supplemental oxygen**, high-flow oxygen and/or non-invasive ventilation. **EBR** [Taskforce]
- Sarilumab - Consider using sarilumab for the treatment of COVID-19 in **adults who require high-flow oxygen, non-invasive ventilaton or invasive ventilation**. **EBR** [Taskforce]
- Tocilizumab - Consider using tocilizumab for the treatment of COVID-19 in **adults who require supplemental oxygen**, particularly where there is evidence of systemic inflammation. **EBR** [Taskforce]

Sotrovimab — CONSENSUS RECOMMENDATION

Within the patient population for which sotrovimab is conditionally recommended for use (as listed above), 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 or multiple risk factors, and COVID-19 vaccination status.

Consider using sotrovimab in unvaccinated or partially vaccinated patients and patients who are immunosuppressed regardless of vaccination status.

Do not routinely use sotrovimab in fully vaccinated patients unless immunosuppressed. **CBR** [Taskforce]

NOT RECOMMENDED

Aspirin
Azithromycin
Colchicine
Convalescent plasma
Hydroxychloroquine
Hydroxychloroquine plus azithromycin
Interferon β-1a
Interferon β-1a plus lopinavir-ritonavir
Lopinavir-ritonavir

Do not use these medications for the treatment of COVID-19. **EBR** [Taskforce]

OTHER TREATMENTS

VTE prophylaxis — CONDITIONAL RECOMMENDATION

Use prophylactic doses of anticoagulants, preferably low molecular weight heparin (LMWH) (e.g. enoxaparin 40 mg once daily or dalteparin 5000 IU once daily) in adults with moderate, severe or critical COVID-19 or other indications, unless there is a contraindication, such as risk for major bleeding. Where the estimated glomerular filtration rate (eGFR) (see below) is less than 30 mL/min/1.73m2, unfractionated heparin or clearance-adjusted doses of LMWH may be used (e.g. enoxaparin 20 mg once daily). **EBR** [Taskforce]

For body weights outside 50-90 kg or heights outside 150-180 cm, calculate the BSA and multiply the eGFR by BSA/1.73. **PP** [Taskforce]

Increased-dose VTE prophylaxis — CONDITIONAL RECOMMENDATION AGAINST

Do not routinely offer therapeutic anticoagulant dosing in adults with severe or critical COVID-19. There is no additional indication for therapeutic dosing for anticoagulants in adults with severe or critical COVID-19 beyond current standard best practice. **EBR** [Taskforce]

In all people with suspected or confirmed COVID-19, switch nebulisers to metered aerosols with spacers if possible.
PP [Taskforce/ANZICS/ASID]

In people with suspected or confirmed COVID-19, consider alternative routes of administration for intranasal medicines, recognising that in some situations administration via the intranasal route may be a safer option for affected individuals and healthcare workers.
PP [Taskforce/ACSQHC]

Oestrogen-containing therapies — CONSENSUS RECOMMENDATION

Consider stopping oral menopausal hormone therapy (MHT), also known as hormone replacement therapy (HRT), in women with mild or **moderate** COVID-19. **CBR** [Taskforce]

Before restarting oral MHT, review the indication for this. If MHT is continued, consider using a transdermal preparation.

CONSENSUS RECOMMENDATION

Stop oral menopausal hormone therapy (MHT) in women with **severe** or critical COVID-19. **CBR** [Taskforce]

Before restarting oral MHT, review the indication for this and consider transitioning to a transdermal preparation.

CONSENSUS RECOMMENDATION

In women who have COVID-19 and who are taking oestrogen-containing contraception, manage these medications as per usual care. **CBR** [Taskforce]

In women who stop or suspend contraception when they have COVID-19, restart contraception at the time of discharge or when acute symptoms have been resolved.

FLUID MANAGEMENT

In all patients with suspected or confirmed moderate to severe COVID-19, use a restrictive fluid management strategy, avoiding the use of 'maintenance' intravenous fluids, high volume enteral nutrition, and fluid bolus for hypotension. **PP** [Taskforce/ANZICS]

RESPIRATORY SUPPORT

In people with suspected or confirmed COVID-19 and a SaO_2 ≤ 92% or significantly below baseline, initiate supplemental oxygen (1-4 L/min) via nasal prongs. **PP** [Taskforce/ASID]

Supportive care in hospital (cont.)

Disease-modifying treatments not recommended outside of clinical trials — NOT RECOMMENDED

Do not use the following disease modifying treatments for the treatment of COVID-19 outside of randomised trials with appropriate ethical approval. **EBR** [Taskforce]:

- Angiotensin 2 receptor agonist (C21)
- Anakinra
- Aprepitant
- Baloxavir marboxil
- Bamlanivimab
- Bamlanivimab plus etesevimab
- Bromhexine hydrochloride
- Chloroquine
- Combined metabolic cofactor supplementation (CMCS)
- Comostat mesilate
- CT-P59 monoclonal antibody
- Darunavir-cobicistat
- Dutesteride
- Enisamium
- Favipiravir
- Fluvoxamine
- Human umbilical cord mesenchymal stem cells
- Immunoglobulin plus methylprednisolone
- Inhaled Interferon β-1a
- Interferon β-1b
- Interferon gamma
- Interferon-kappa + tff2
- Ivermectin
- Ivermectin plus doxycycline
- Intravenous Immunoglobulin
- Lenzilumab
- N-acetylcysteine
- Nitazoxanide
- Peginterferon lambda
- Recombinant human granulocyte colony-stimulating factor
- Ruxolitinib
- Sofosbuvir-daclatasvir
- Sulodexide
- Telmisartan
- Tofacitinib
- Triazavirin
- Umifenovir
- Vitamin C
- Vitamin D (calcifediol/ cholecalciferol)
- Zinc
- Other disease-modifying treatments

These disease-modifying treatments should still be considered for other evidence-based indications in people who have COVID-19. **PP** [Taskforce]

Trials are needed in special populations, including children and adolescents, pregnant and breastfeeding women, older people living with frailty and those receiving palliative care. Until further evidence is available, do not use other disease-modifying treatments in these populations unless they are eligible to be enrolled in trials. **PP** [Taskforce]

Escalation of care

HOSPITALS WITH ICU

Urgently refer people with suspected or confirmed COVID-19 to intensive care if they are haemodynamically unstable, have rapidly worsening tachypnoea or hypoxaemia, or require ≥ 40% FiO_2 to maintain SaO_2 ≥ 92% (or acceptable saturations in those with lower baselines). **PP** [Taskforce/ASID]

HOSPITALS WITHOUT ICU

Consider the need for early transfer of people with suspected or confirmed COVID-19 to a higher-level facility with an ICU. **PP** [Taskforce/ASID]

When preparing for transfer of people with suspected or confirmed COVID-19, consider infection control implications and whether intubation is required prior to transfer, as per local retrieval team policies. **PP** [Taskforce/ASID]

For details of high level respiratory support see the **RESPIRATORY SUPPORT FOR SEVERE TO CRITICAL COVID-19** Clinical Flowchart

Discharge planning

People with suspected or confirmed COVID-19 who are clinically ready for hospital discharge should stay in home isolation after discharge until:

- at least 14 days have passed since onset of symptoms; AND
- there has been resolution of fever and respiratory symptoms of the acute illness for the previous 72 hours.
- in people with a confirmed case of a SARS-CoV-2 variant of concern PCR testing should be undertaken on day 12-13. **PP** [Taskforce/CDNA]

People with suspected or confirmed COVID-19 with an incomplete resolution of symptoms but who are clinically ready for hospital discharge should stay in home isolation after discharge until:

- at least 14 days have passed since onset of symptoms; AND
- there has been substantial improvement in symptoms of the acute illness (including resolution of fever for the previous 72 hours); AND
- the person has had two consecutive respiratory specimens negative for SARS-CoV-2 by PCR taken at least 24 hours. **PP** [Taskforce/CDNA]

In patients with severe COVID-19 offer appropriate rehabilitation to optimise recovery, including early hospital rehabilitation. Plan transition of care to the community, including handover to general practice. **PP** [Taskforce]

Follow up care

- Assist people to connect to a GP if they do not have one.
- When the acute phase of the illness has resolved, and the patient is mobile, undertake a comprehensive review to assess their ongoing and rehabilitation needs.
- Review medications that were stopped or started.

PP [Taskforce]

Sources

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