Clinical Guideline

Inpatient Clinical Management of COVID-19 in Adults

Due to the continuously emerging situation, this Clinical Guideline will be regularly updated

This clinical guideline applies to:	Hospitalised patients with: • **confirmed diagnosis of COVID-19** (i.e. with positive respiratory sample PCR for SARS-CoV-2), OR • **provisional diagnosis of COVID-19** (i.e. a senior clinician considers it a likely diagnosis, not only that the patient meets testing criteria)
Sites where clinical guideline applies:	All acute facilities
This Clinical Guideline applies to: • **Adults** • **Children up to 16 years** • **Neonates – less than 29 days**	 Yes No No
Target Audience	All clinicians
This document contains advice on therapeutics	Yes Approval gained from District Quality Use of Medications Council (DQUMC) on 25 January 2022
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FURTHER RESOURCES:

- COVID-19 Infection Prevention and Control Manual (see also HNE COVID19 Intranet IPC page)
- Federal CDNA Public Health guidelines
- National living COVID-19 evidence-based guidelines
- NSW Guidance on Laboratory Testing for SARS-CoV-2

Summary of key points:

1) All patients with COVID-19 symptoms should have a rapid antigen (RAT) or PCR test

2) Manage all suspected and confirmed COVID-19 patients with contact, droplet and airborne precautions (P2/N95 mask, eye protection, fluid resistant gown or apron, gloves)

3) Consider budesonide, sotrovimab or nirmatrelvir/ritonavir in patients with early disease, not requiring oxygen and risk factors for deterioration

4) Consider hospital admission if SpO_2 <94% on room air

5) Give supplemental oxygen to maintain SpO_2 > 92%. If unable to maintain target SpO_2 escalate to CPAP

6) Refer for ICU assessment if requiring >4L/min of O_2 to maintain target SpO_2 (all facilities except JHH), OR unable to maintain target SpO_2 with CPAP or NIV, or rapidly worsening tachypnoea or hypoxaemia (JHH)

7) If requiring supplemental oxygen commence dexamethasone and remdesivir

8) If, despite the above, there is an escalating oxygen requirement and severe pneumonitis, add ONE OF baricitinib, tocilizumab, or sarilumab

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1. Current Testing Criteria

- All patients with COVID-19 symptoms should have a COVID-19 rapid antigen (RAT) or PCR test
- Due to high levels of community transmission, broader SARS-CoV-2 testing including surveillance testing should be undertaken as determined by the clinical situation and risk alert level as outlined in COVID-19 Surveillance and Testing in HNELHD Facilities.

2. Diagnostic Work-up

- Consider differential diagnoses and assess as per usual practice.
- If the patient meets criteria for severe CAP and COVID-19 test pending, investigate as for severe CAP – ensure R14 swab (nose/throat sample) is attended (includes SARS-CoV-2 test). If critically unwell, include rapid Flu/RSV PCR request. Take baseline serum for storage in case paired SARS-CoV-2 serology needed later on.

- See Agency for Clinical Innovation (ACI) Care of adult patients with COVID-19 in acute inpatient wards for clinical severity and risk of deterioration tables.

3. Disease Modifying Treatments for mild early disease

- Consider disease modifying treatments for patients with symptoms of COVID-19, not-requiring oxygen and with risk factors for deterioration (e.g. age ≥65, comorbidities, immunosuppression AND unvaccinated, partially vaccinated or severely immunosuppressed regardless of vaccination status).
    - Symptom onset ≤ 5 days: ONE of the following three:
        - Sotrovimab – see Use of sotrovimab in COVID-19 patients for further guidance.
          OR
        - Casirivimab plus imdevimab (Ronapreve/REGEN-COV) – see Use of casirivimab and imdevimab injection for COVID-19 for further guidance. Note emerging data suggests that Ronapreve is ineffective against the Omicron variant, so it should not be used if Omicron is thought to be the likely causative variant.
          OR
        - Nirmatrelvir (150 mg x 2 tabs BD) + ritonavir (100 mg x 1 tab BD) (Paxlovid) for 5 days – see TGA provisional approval for further guidance
    - Symptom onset < 14 days:
        - Inhaled budesonide 800 microg BD for up to 14 days– see Budesonide for Adults for further guidance (can be used in combination with one of the above three). Note that budesonide should be ceased if the patient deteriorates and is started on dexamethasone.

4. Hospital Admission

- Patients with mild disease should be managed in the community where possible (see Caring for Adults and Children in the Community with COVID-19 Flowchart for appropriate care protocols).
- Consider admission if haemodynamically unstable, hypoxaemia (SpO_2 <94% on room air) or comorbidities.
- Discuss all provisional or confirmed COVID-19 cases requiring admission or transfer with the COVID-19 consultant for the facility.
- Consider need to transfer early to a higher-level facility (appendix 1), see section 10. If transfer required, discuss with the COVID consultant on-call for the receiving facility.
- Discuss and complete a resuscitation plan for all patients admitted with COVID-19, as soon as practicable.

5. Patient Placement and Infection Control

- Manage all patients with confirmed COVID-19 under **standard, airborne, contact and droplet additional precautions** (P2/N95 respirator, eye protection, fluid resistant gown or apron, gloves) in a locally designated COVID-19 (red) bed or area.
- Manage all suspect COVID-19 cases (awaiting test result) under **standard, airborne, contact and droplet** additional precautions in a designated separate isolation area/room to confirmed cases.
- Coordination of transferring suspected and confirmed COVID-19 patients between units must occur at a senior clinician level with a clear agreement of which specialty team will be responsible for transport. The use of a pre-planned, dedicated route is essential with the use of a “clean” runner to ensure the route is clear of bystanders and equipment, push elevator buttons and open doors. See appendix 2 for further guidance.
- Confirmed and suspect cases should not be allowed visitors, unless they are on an end of life care pathway.
- If high pre-test probability of COVID-19 and initial SARS-CoV-2 result is negative, continue to isolate and arrange repeat testing ideally on a different platform in consultation with microbiologist as soon as possible.

6. Monitoring

- Monitor CRP, FBC, EUC, LFTs, procalcitonin, D-Dimer and LDH every 1-3 days, depending on severity
- Perform baseline 12-lead ECG
- Repeat CXR only if clinically indicated (e.g. if patient is deteriorating or has been recently intubated)
- There is no need for routine CT scanning, only CT scan if clinically indicated
- If patient is critically unwell, monitor coagulation profile and troponin I

7. General Management

- All patients requiring oxygen at >4L/min to maintain SpO2>92% (or 88% where appropriate) should be encouraged to lie in the prone position for a minimum of 3 hours/day, aiming for at least 8 hours/day.
    - A recent meta-RCT found the incidence of intubation to be significantly reduced with awake prone positioning in patients requiring HFNO, for a median of 5 hours per day (hazard ratio 0.75 [0.62-0.98]). It is less clear if there is a benefit in patients not requiring HFNO, but it is recommended to trial it if tolerated in this group. The 3-8 hours per day do not need to be in continuous blocks, and we recommend spending periods of 30 minutes to 2 hours at a time prone as tolerated.
- Use restrictive fluid strategies, 1-2 litres of IV fluid per day, only if no oral intake or clinically dehydrated.
- If hypotensive, administer 250 ml fluid boluses and refer to ICU for vasopressor therapy if patient remains hypotensive after 2-3 boluses.
- Consider antibiotics for bacterial pneumonia if hypoxaemic (SpO_2 <92%), rising procalcitonin, pleural effusion or purulent sputum (treat for CAP or HAP as per HNE local guidelines).
- If awaiting influenza PCR result AND chronic comorbidities or critically ill: Prescribe oseltamivir if symptom onset <72h ago and not critically ill, or <7 days ago if critically ill. Cease if influenza PCR returns negative.
- Commence venous thromboembolism (VTE) prophylaxis as per standard protocol.
- Avoid use of nebulisers - use metered dose inhalers with spacers where possible. Check the patient is using inhaler correctly. If a nebuliser must be used, airborne infection control precautions are required.

8. Medical Therapies

Dexamethasone

- Patients requiring supplemental oxygen or ventilatory support should be prescribed dexamethasone **6 mg daily** orally or intravenously (if patient is unconscious or not tolerating oral intake) for up to 10 days or until hospital discharge, whichever occurs first.
- Systemic corticosteroids should be avoided in patients not requiring supplemental oxygen unless there is an evidence-based indication for them e.g. severe acute exacerbation of COPD or asthma.

Remdesivir

- Remdesivir is recommended in hospitalised patients with moderate to severe COVID-19 who **DO NOT** require invasive or non-invasive mechanical ventilation**.**
- Use remdesivir **200 mg intravenously on day 1, then 100 mg intravenously daily for a further 4 days (total 5 days treatment)** in patients who have O_2 saturations ≤ 92% on room air and require supplemental oxygen, but who are not intubated.
- Remdesivir is contraindicated in patients with:
    - Known hypersensitivity to any ingredient of remdesivir
    - Renal impairment (eGFR < 30mL/min/1.73m²), on dialysis or continuous veno-venous hemofiltration
    - Hepatic impairment (ALT >5 x upper limit of normal (ULN), or AST > 3x ULN and Bilirubin >2x ULN)
    - Evidence of multi-organ failure including, but not limited to, coagulopathy (significant thrombocytopenia), hepatic failure, renal failure or significant cardiomyopathy

Baricitinib / Tocilizumab

- In addition to dexamethasone +/- remdesivir, add a second immunomodulatory agent in those requiring supplemental oxygen **IF** there is evidence of systemic inflammation, escalating need for respiratory support (HFNO, BiPAP or IMV) or severe pneumonitis, despite the use of dexamethasone +/- remdesivir.
- Use **ONE** of the following depending on availability and clinician preference:
  - Baricitinib 4 mg daily orally for up to 14 days or until hospital discharge, whichever occurs first

    OR
  - Tocilizumab as a single dose IV infusion over 60 minutes
    - Patients > 90 kg: 800 mg tocilizumab
    - Patients 66–90 kg: 600 mg tocilizumab
    - Patients 41–65 kg: 400 mg tocilizumab
    - Patients ≤ 40 kg: 8 mg/kg tocilizumab

    Note additional restrictions on use of tocilizumab due to current critical supply disruption. Tocilizumab should only be used in:
    - patients where baricitinib is not suitable (e.g. can't absorb oral medications)
    - critically ill patients requiring direct admission to ICU for mechanical ventilation
    - pregnant or breastfeeding women, children and adolescents requiring supplemental oxygen
    - patients in whom administration of medications via oral/nasogastric route is not possible

    OR
  - Sarilumab as a single IV infusion of 400 mg over 60 minutes

General Guidance

- **Do not use other antivirals, antibodies or immunomodulatory agents outside the context of a randomised controlled trial**.
- See COVID-19 Resources - NSW Therapeutic Advisory Group (nswtag.org.au) for Drug Guidelines approved for local use (Sotrovimab, Dexamethasone, Baricitinib, Remdesivir, Tocilizumab), patient information and regulatory forms.
- Medications are available at the following hospital pharmacies. Refer to Pharmacy department for further advice about stock availability and access.

Medication	Locations
Baricitinib	Armidale, Belmont, CMN, JHH, Maitland, Manning, Scone, Singleton, Tamworth
Dexamethasone	Armidale, Belmont, Cessnock, CMN, JHH, Kurri Kurri, Maitland, Manning, Scone, Singleton, Tamworth
Remdesivir	Armidale, Belmont, CMN, JHH, Maitland, Manning, Scone, Singleton, Tamworth
Sotrovimab	Armidale, Belmont, CMN, JHH, Maitland, Manning, Tamworth
Tocilizumab	CMN, JHH, Maitland, Manning, Tamworth

9. Respiratory Support

Determine target oxygen saturation (SpO_2) range:

- 92-96% in most patients
- 88-92% in patients at risk of hypercapnia (e.g. severe COPD, neuromuscular weakness, known CO_2 retention)

Stepped approach to respiratory support:

1) If unable to maintain SpO_2 in target range on room air, commence supplemental O_2 with nasal prongs or venturi mask up to 4L/min.
2) If unable to maintain SpO_2 with low flow O_2 at an FiO_2 of 0.4 or flow rate of ≥ 4L/min, commence CPAP

- Discuss with ICU (if outside JHH)
- Commence CPAP at 10cmH_2O (12cmH_2O if BMI >30). Titrate oxygen up to FiO_2 0.6 (8-10L/min).
- The use of CPAP has been shown to reduce the risk of intubation and mechanical ventilation in COVID patients when compared to HFNO or conventional low flow oxygen[1].
- HFNO should be used in patients instead of CPAP if CPAP is not available, not tolerated or contraindicated
  - If HFNO is used, it should be delivered at 40L/min flow with FiO_2 at 21-40% to achieve SpO_2 within the patients target range.

3) If unable to maintain SpO_2 with CPAP at maximum FiO_2, refer for urgent ICU review and consideration of appropriateness for NIV or intubation.

The above HNELHD guidance differs slightly from ACI guidance in the application of HFNO, however is representative of local consensus on respiratory support for COVID-19 patients and aligns with clinical trials.

General

- In patients with acute hypercapnic respiratory failure/acute COVID-19 pneumonia (especially those on a background of COPD, obesity and neuromuscular disease), early use of NIV support may be indicated instead of HFNO or CPAP
- If high flow humidified nasal oxygen (HFNO) or non-invasive ventilation (NIV) are used, place patient in negative pressure isolation room where available.
  - If a negative pressure room is not available, use a single room with negative flow to outside (i.e. out of the hospital building) or a single room with the door closed.
  - Minimise the number of staff present in the room.
  - All persons in the room must wear contact, droplet and airborne precautions.
- Aim for early intubation and positive pressure ventilation in those who are deteriorating despite non-invasive respiratory support. For further information on airway management, ventilator strategies and other management see:
  - ACI – Clinical practice guide for respiratory support in adults with COVID-19
  - ANZICS COVID-19 Guideline
  - CEC – Airway Management: Respiratory Precautions
- If a suspected or confirmed COVID patient experiences cardiac or respiratory arrest, see revised COVID-19 specific Basic Life Support (BLS) and Advanced Life Support (ALS) algorithms.

10. Escalation of Care

HNELHD facilities with ICU services

- Do not refer to ICU if the patient has an advanced care directive or resuscitation plan precluding ICU care.
- Calvary Mater Newcastle, Maitland, Manning, Tamworth Hospitals - discuss with ICU if:
  - Requiring ≥ 4 L/min oxygen to maintain oxygen saturations ≥ 92% (or acceptable O_2 saturations in patients with lower baselines), or rapidly worsening tachypnoea or hypoxaemia
  - Haemodynamic instability or decreasing level of consciousness
- John Hunter Hospital - discuss with ICU if:
  - Unable to maintain target SpO_2 with CPAP or NIV, or rapidly worsening tachypnoea or hypoxaemia
  - Haemodynamic instability or decreasing level of consciousness

[1] An adaptive randomised controlled trial of non-invasive respiratory strategies in acute respiratory failure patients with COVID-19. https://www.medrxiv.org/content/medrxiv/early/2021/08/04/2021.08.02.21261379.full.pdf

HNELHD facilities without ICU services

- Do not transfer to higher level facility with intensive care services if the patient has an advanced care directive or resuscitation plan precluding ICU care.
- Consider need to transfer patient early to a higher-level facility with an ICU if:
  - Requiring ≥ 4 L/min oxygen to maintain oxygen saturations ≥ 94% (or acceptable O_2 saturations in patients with lower baselines), or rapidly worsening tachypnoea or hypoxaemia
  - Haemodynamic instability or decreasing level of consciousness
- Consider infection control implications of transfer and discuss with the retrieval service and accepting ICU regarding the safest transfer plan for both the patient and staff.

11. Palliative and End of Life Care

- If intensive medical intervention fails or is unable to be provided, ensure symptom control and end of life care is provided in line with the End of Life Toolkit.
- COVID-19 patients who are receiving end of life care should be moved to a single room if available, and be allowed to have a single visitor. Where possible, a single nominated family member/loved one/guardian should represent the family.
  - Visitation is contingent upon an exemption, further information available in the Visitors to HNELHD Facilities during COVID-19 Red Alert.
  - The visitor must be informed that they are required to use PPE which does not guarantee that they will not be infected with COVID-19.The visitor is to be supervised by staff in the donning and doffing of droplet precautions, with a mask change every 2 hours.
  - Staff should support virtual visiting for other family members (e.g. using Facetime or Skype).
- If a patient dies from COVID-19, please see Care of the Deceased – Coroners and Care of the Deceased – Non Coroners

12. Discharge Planning and Release from Isolation

To calculate the isolation period, day 0 is the day of symptom onset or the first positive test (whichever occurred first).

Patients discharged before day 7

Patients discharged before day 7 are to be advised that they can be released from isolation after day 7 if they have no symptoms. If they remain symptomatic, they are to remain in isolation until 24 hours after their symptoms have resolved.

Inpatients **with complete** resolution of acute respiratory symptoms

Inpatients who have resolution of acute respiratory symptoms on day 7 are able to be released from isolation on day 10.

Inpatients **without complete** resolution of acute respiratory symptoms

Inpatients without complete resolution of acute respiratory symptoms on day 7 or who are unable to be assessed (e.g. intubated patients) are to remain in isolation until day 14.

Inpatients who are significantly immunocompromised

Inpatients who are significantly immunocompromised must have at least two consecutive negative PCR tests collected at least 24 hours apart after day 10; OR two consecutive RAT collected at least 24 hours apart after day 14.

NOTES:

- Patients who are not significantly immunocompromised do not require repeat COVID-19 testing prior to release from isolation or within 4 weeks of release from isolation.
- Important documentation steps when inpatients are released from isolation:

- Obtain approval from relevant COVID-19 consultant
- Document the status change in the patient's healthcare record
- Notify Infection Prevention Service to enable the removal of alerts

Discharge Planning

- Patients not released from isolation who no longer require hospital-based care, are to have their care transferred to COVID Care in The Home (CCiTH) or their GP.
- If transferring patient to a Residential Aged Care Facility or Residential Disability Group home, discuss with the receiving facility or home prior to transfer and ensure clearance certificate and discharge summary are provided.
- Ensure discharge summary is completed with clear information to the general practitioner including episode of care and required follow up arrangements.

13. Revision History

Version	Date	Changes
Version 7	27 January 2022	Updates to testing criteria; addition of budesonide and nirmatrelvir/ritonavir (Paxlovid) to new disease modifying treatments section; changes to testing after negative result in patients with high pre-test probability; changes to release from isolation criteria; removal of level of care at facilities table (appendix); Updated Internal Transfer flowchart (appendix) and removal of corresponding section in guideline.
Version 6	21 December 2021	Updates to casirivimab and imdevimab (ronapreve) guidance; addition of surveillance testing information and link to guideline.
Version 5	2 December 2021	Addition of casirivimab and imdevimab (ronapreve); addition of pharmacy table; changes to release from isolation criteria and discharge planning; updates to COVID-19 consultant at facilities.
Version 4	25 October 2021	Minor changes to wording of CPAP; addition of appendix 2.
Version 3	12 October 2021	Addition of sotrovimab, intra-hospital transfers, and prone positioning; CPAP, NIV and HFNO updated.
Version 2	24 August 2021	Addition of COVID-19 Hotels; further clarity on COVID-19 Consultant, remdesivir, and tocilizumab restrictions; reinstatement of appendix 1.
Version 1	19 July 2021	Significant updates including airborne precautions, PCR rapid testing, remdesivir, baricitinib, tocilizumab and sarilumab.
HNELHD CG 20_14 versions 1 to 10	19 March 2020	Regular and significant updates throughout early stages of pandemic in 2020.

Appendix 1:

Internal Transfer of Suspected or Confirmed COVID-19

Guiding principles:

- Coordination of transferring a patient between units must occur at a senior clinician level with clear agreement of which specialty team will be responsible for transport
- The decision to transfer a patient on NIV lies with senior medical officers. If possible, consider transfer with a simple face mask or nasal prong oxygen (4-6L/min)
- A clear, pre-planned, designated route must be established with use of a 'clean' runner to ensure the route is clear of bystanders and equipment, push elevator buttons and open doors
- Staff accompanying must be restricted to essential staff only and be donned in a P2/N95 respirator, protective eyewear, gown and gloves, and minimise contact with surroundings
- The patient must wear a surgical mask including over oxygen delivery devices (with exception of NIV mask)

Plan	**Define Team/Roles** ▪ Transfer nurse ▪ "Clean" runner/s ▪ Porter / Wards person ▪ Cleaner for post transfer terminal cleans **Oxygen Delivery** ▪ Determine oxygen delivery device required for transfer ▪ Transfer on NIV or HFNO must be discussed and decided by a senior medical officer **Equipment** ▪ Full oxygen cylinder with suction ▪ Monitoring as appropriate ▪ Infusion pumps/syringes on bed pole (if applicable) ▪ Other equipment if deemed essential **Communication with Receiving Ward/Area** ▪ Estimated time of transfer + need for airborne precautions for those receiving handover ▪ Communication of equipment required to receive patient
Transfer	**Before Departure** ▪ Confirm the designated route is clear ▪ Final patient assessment (A, B, C, D) and equipment checks ▪ Apply surgical mask to patient (including over any oxygen administration device) ▪ Not required with NIV - instead optimise seal and apply viral filter to expiratory limb ▪ Confirm roles **Upon Arrival** ▪ Clinical bedside handover ▪ Transfer to ward bed and equipment ▪ Cleaning of equipment no longer required
Clean	▪ Doff PPE in doffing zone ▪ Re don PPE for cleaning of equipment ▪ All equipment used including pumps, syringe drivers, beds, lifts* must be cleaned prior to returning to usual location ▪ Doff PPE once cleaning completed and perform hand hygiene ▪ Re don PPE if required to return to clinical area *lifts must be spelled for 30 minutes with doors open prior to terminally cleaning

Acknowledgment: Tamworth Hospital Leadership Group