Disease-modifying treatments for mild COVID-19

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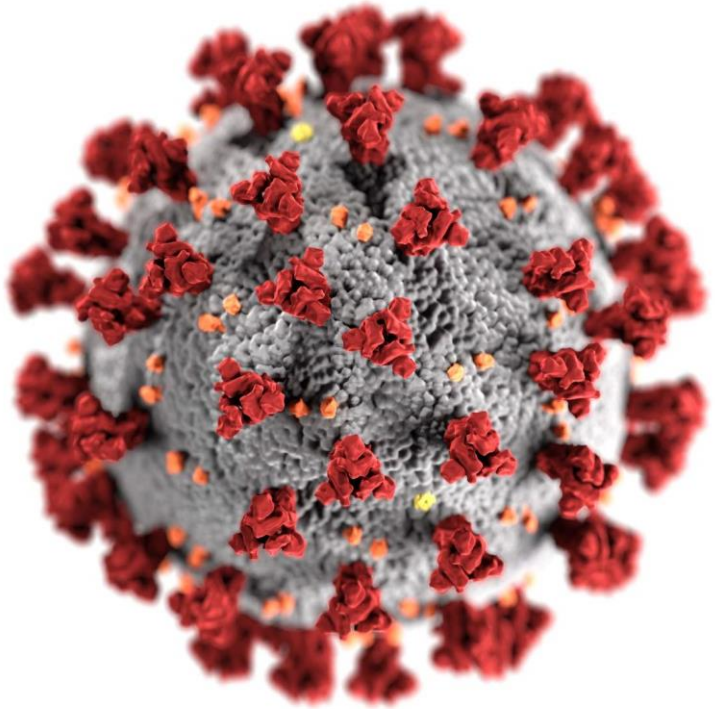
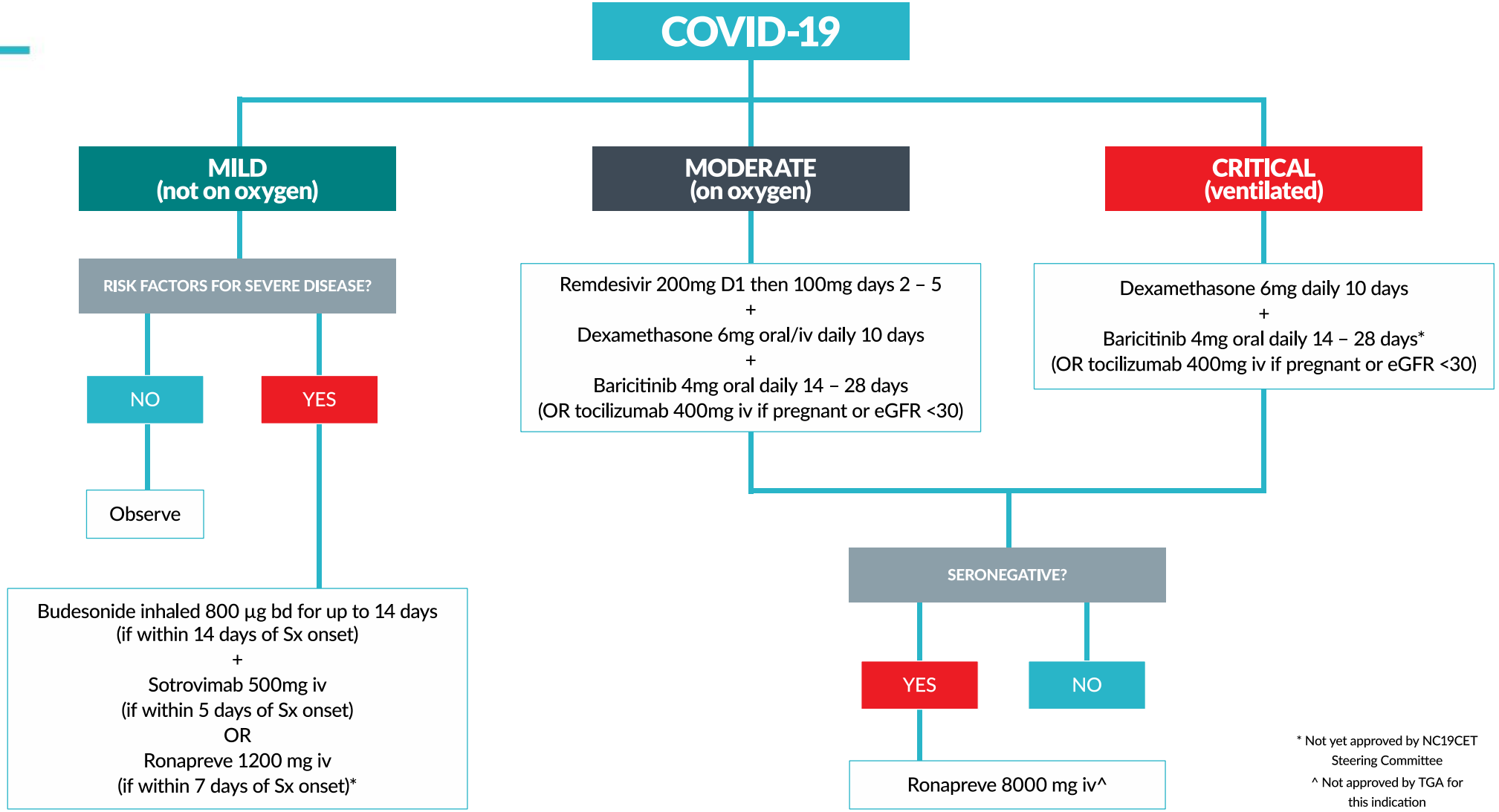
November 2021



Drug treatments by disease severity

NATIONAL COVID-19 CLINICAL EVIDENCE TASKFORCE



* Not yet approved by NC19CET Steering Committee

^ Not approved by TGA for this indication

Sotrovimab

Monoclonal antibody directed against SARS-CoV-2 spike protein

If given early to people with risk factors, decreases risk of severe disease

In COMET-ICE RCT (n=1057), decreased risk of hospital admission or death from 5.7% to 1.1 %

- Inclusion: NOT VACCINATED; Within 5 days of symptom onset. Age >55 OR >18 with >=1 risk factor (obesity, diabetes, CKD, CCF, COPD, asthma)

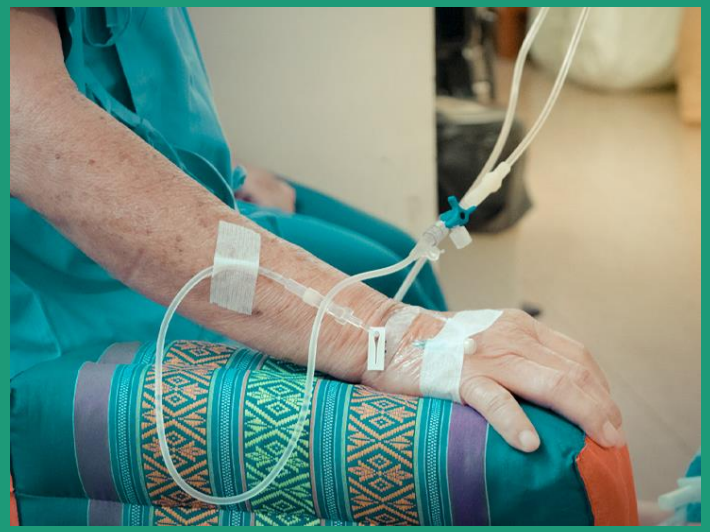
Single IV infusion over 30 minutes

Approved by TGA, recommended by national guidelines

For above patients plus immunosuppressed. Limited national supply

Ronapreve (Casirivimab/imdevimab)

- 2 monoclonal antibodies directed against SARS-CoV-2 spike protein
- If given early to people with risk factors, decreases risk of severe disease
- In 1 RCT (n=4,057), decreased risk of hospital admission or death from 4.6% to 1.3 %.
  - Inclusion: Within 7 days of symptom onset. Age >50 OR >18 with >=1 risk factor (obesity, diabetes, CKD, CCF, COPD, immunocompromise)
- Single IV infusion over 30 minutes
- Conditionally approved by TGA, recommended by national guidelines
- Limited national supply



Sotrovimab versus Ronapreve

No head to head trials. Similar effect size and target populations

Both available via national medicines stockpile

Both probably cost $2,000-$3,000 per dose – but “free” currently

Both need to be given by IV infusion, and need 30-60 minutes observation afterwards

- Thus done in hospital COVID wards or specially set up infusion centres
- ~50 doses Sotro used in HNE with excellent efficacy

Molnupiravir

Induces errors in viral RNA, leading to “lethal error catastrophe”

Pharma RCT, not even in pre-print yet (press release only)

- 762 patients, <=5 days symptoms, >=1 RF for severe disease
- Hospital admission or death 7.3% versus 14.1%

Australian DoH has 300,000 doses on order (pending TGA approval)

Approved in UK, currently before TGA

Not yet in Australian guidelines (but likely will be soon)

Paxlovid

Protease inhibitor oral antiviral drug (ritonavir boosted)

1 pharma RCT, press-release only

- 774 adult outpatients with mild, early COVID-19
- <=5 days from symptom onset and >=1 RF for severe disease
- 1% versus 8.3% hospital admission or death

Not yet approved anywhere, but is before the FDA

	Molnupiravir (Merck)	Paxlovid (Pfizer)
Efficacy in high-risk patients, reduction of hospitalizations/deaths at 28 days Deaths in placebo vs drug	50% 14.1 vs 7.3% 8 vs 0	89% 8.2 vs 0.7% 7 vs 0
Duration of therapy (twice daily)	5 days	5 days
Given with co-drug to promote half-life	No	Yes, ritonavir
Drug interactions (CYP3A4)	Minimal	Yes, many statins, blood thinners
Repurposed	Yes, Equine encephalitis Planned to test for RSV, influenza, redirected	No, Covid specific New chemical entity adapted from an anti-SARS molecule
Mechanism	Nucleoside analog; Induces mutations	Inhibits Mpro, not mutagenic
Active against all variants tested	Yes	Yes
Cost	~$700	~$700

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NATIONAL COVID-19 CLINICAL EVIDENCE TASKFORCE

Inhaled budesonide

- If given early to mild COVID-19 patients with risk factors, decreases risk of severe disease
- PRINCIPLE trial (UK), n=787 budesonide, 1069 usual care
- Age >=65 or >=50 with comorbidities
- W/i 14 days of symptom onset (i.e. symptomatic), NOT requiring O_2
- High dose (800mcg BD)
- Faster self-reported recovery (11.8 vs 14.7 days)
- Lower chance of hospital admission (12.5% vs 5.6%)
- Added to national guidelines this week

Summary – recommended treatments

- Prophylaxis in non-vaccinated close contacts with risk factors
  - REGN-COV (Casirivimab/imdevimab)
- Treatment of early mild disease with risk factors
  - Sotrovimab single dose OR Ronapreve single dose
  - Budesonide 800mcg BD for up to 14 days
- Needing O_2 but not HFNO/BiPAP/IMV
  - Dexamethasone 6mg, remdesivir
- Severe pneumonitis, needing HFNO/BiPAP/IMV
  - Remdesivir if not yet intubated
  - Dexamethasone plus ONE OF baricitinib, tocilizumab, sarilumab