

MEDICATION INFORMATION

COVID-19 TREATMENT OPTIONS

Background

This document is aimed at providing general information around possible treatment options for COVID-19 infections caused by the SARS-CoV-2 Virus. There is currently little evidence-based information available and the document will evolve as new information and research becomes available.

This document does not intend to replace the use of manufacturers package inserts or other relevant references nor the clinical judgement of the prescribing medical practitioner.

Abbreviations and acronyms

Term	Definition
COPD	Chronic Obstructive Pulmonary Disease
CAP	Community acquired pneumonia
PJP	Pneumocystis Jiroveci Pneumonia
RCT	Randomised Control Trial
SARI	Severe Acute Respiratory Infection

Version 2: What's New?

- **Lopinavir/ ritonavir:** No benefit was seen in RCT with respect to viral load, time to clinical improvement or mortality in severe hospitalised adults
- **Chloroquine:**
 - National out of stock situation
 - Reserve treatment for confirmed severe hospitalised patients only
- **Hydroxychloroquine:** – May be available on Section 21
 - Reserve treatment for confirmed severe hospitalised patients only
- Limited data on the effectiveness of Acetylcysteine
- General editing

Treatment options

There is currently no registered treatment for COVID-19 and treatment is generally supportive.

Antiviral or immunomodulatory therapies are not yet proven effective for the treatment of COVID-19. There are currently clinical trials underway of supportive or targeted therapies¹. Research into experimental and other treatments will continue as they become evident as effective treatment.

Please refer to the following clinical treatment guideline for detailed information:

Reference guideline:

- NDoH: Clinical management of a suspected or confirmed COVID-19 Disease V2 (19 March 2020)

Other relevant guidelines:

- NICD: Clinical management of suspected or confirmed COVID-19 disease
- WHO: Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected
- WHO: Home care for patients with COVID-19 presenting with mild symptoms and management of their contacts
- South African Guideline for the management of community acquired pneumonia in adults

Early Symptomatic treatment^{1,2}

- Supplemental oxygen for patients with low oxygen saturation. Refer to NDoH guideline¹.
- Conservative fluid management in patients with SARI with no evidence of shock
- If clinical suspicion for co-infection exists, consider empirical antimicrobials –
 - Conventional community-acquired pneumonia pathogens (or hospital-acquired pneumonia pathogens if appropriate) – e.g. amoxicillin-clavulanate [SA community-acquired pneumonia guidelines⁴]
 - Atypical pneumonia pathogens – e.g. azithromycin [SA community-acquired pneumonia guidelines⁴]
 - Influenza (if influenza epidemiology fits and the patient has severe illness) – oseltamivir [NICD influenza guidelines⁵]
 - PJP (if appropriate risk factors present, e.g. HIV with low CD4 count)
 - Empiric therapy should be de-escalated on the basis of microbiology results and clinical judgment.
- Antipyretics e.g. paracetamol

Other supportive therapy that are discussed in the literature

- Bronchodilator Metered dose inhalers
- Acetylcysteine preparations as mucolytic (limited data about the benefit)
- Ascorbic acid

Closely monitor patients with SARI for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis, and apply supportive care interventions immediately.

Experimental treatment of an acute respiratory syndrome coronavirus 2 (SARS-CoV-2) COVID-19

Where possible please enrol patients in randomised control trials

<p>Chloroquine - Reserved for severe hospitalised patients only (International supply issues – currently out of stock in SA)</p>	
<p>Strong antiviral effects on SARS-CoV of primate cells. Prevent the spread of SARS CoV in the cell structure. Display treatment and prophylactic properties.</p>	
<p>Current NDOH and NICD recommendation¹</p>	
<p>Severe disease</p> <ul style="list-style-type: none"> •Consider chloroquine treatment 	
<p>Mild disease with risk factor for severe disease*</p> <ul style="list-style-type: none"> •Consider chloroquine treatment 	
<p>Mild disease without risk factors for severe disease</p> <ul style="list-style-type: none"> •No treatment recommended 	
<p>*Risk factors for severe disease are age >65years, underlying cardiac or pulmonary disease</p>	
<p>Chloroquine sulphate 200mg = 150mg base</p>	<p>Hydroxychloroquine (Only available on Section 21) 200 mg = base 155 mg base.</p>
<p>Recommended dose: 10 mg/kg base daily for 2 days, then 5 mg/kg base daily for 1 day</p>	<p>Recommended dose: 400 mg 12h for 1 day then 200 mg 12h for 4 days</p>
<p>Important drug interactions:</p> <p>Avoid combination of chloroquine with Lopinavir/ritonavir</p> <p>Combination of chloroquine with co-trimoxazole increase risk for hypoglycaemia</p>	
<p>Potential side effects and contra-indications:</p> <p>Cardiovascular effects: Cardiomyopathy resulting in cardiac failure, QT prolongation, <i>torsade de pointes</i>, and ventricular arrhythmias.</p> <p>Use with caution in patients with cardiac disease.</p> <p>Hypoglycemia: Severe hypoglycemia, including loss of consciousness, has been reported in patients treated with or without antidiabetic agents.</p>	

<p>Neuromuscular effects: Skeletal muscle myopathy or neuromyopathy,</p> <p>Common adverse reactions: Nausea/vomiting, diarrhoea, abdominal pain, visual disturbances, headache.</p> <p>Monitor: QT interval and full blood count (FBC)</p>
<p>Lopinavir and Ritonavir (Kaletra® / Aluvia®)</p> <p>Antiretroviral agent, blocks viral replication.</p> <p>No current evidence from RCT to recommend treatment for patients with suspected COVID-19 infection. No benefit was seen with respect to viral load, time to clinical improvement, or mortality³.</p> <p>Potential side effects and contra-indications: Precaution in patients with cardiac risk or other risk for prolonged QT prolongation.</p> <p>Important drug interactions: <i>Avoid combination with Chloroquine</i></p>
<p>Ribavirin (Copegus®)</p> <p>Appears to work better in combination with lopinavir/ritonavir</p> <ul style="list-style-type: none"> • Only oral drug available in very limited quantities • Contra-indicated in pregnancy • Avoid use in unstable cardiac disease
<p>Remdesivir</p> <p>Currently not available in South Africa</p> <ul style="list-style-type: none"> • Patient needs to be enrolled in study to access medication, available only from manufacturer. • Designed for Ebola • Phase 3 trials in process
<p>Vaccine development</p> <p>Currently no vaccine available but multiple trials are in process</p>

Treatment not routinely indicated in COVID-19 (NDoH)

Medication	Reasoning
Corticosteroids	Given lack of effectiveness and possible harm, routine corticosteroids should be avoided unless they are indicated for another reason
Anti-virals e.g. Tamiflu and Relenza	Not indicated for SARS-CoV-2, only use when a clinical suspicion of co-infection with Influenza exists

Antibiotics	Not indicated for SARS-CoV-2, only use when a clinical suspicion of a bacterial co-infection exists. Consider use of first line agents for community acquired pneumonia as per the South Africa Guidelines ³
NSAIDS	Preliminary reports suggest that these agents may exacerbate symptoms resulting in a prolonged or more severe illness and an increased incidence of complications likely due to a weakened immune response. Short-term fever or pain relief: Avoid this class of agents where possible and use paracetamol. For patients requiring NSAIDs for chronic comorbidities: The evidence is not conclusive enough to recommend discontinuation
Angiotensin converting enzyme (ACE) inhibitors or angiotensin-receptor blocker (ARB)	The binding site for SARS-CoV-2, within tissues including the lung and heart, prompting concern that this might place patients at risk of worse outcomes with COVID-19. Pending further evidence we therefore do not recommend switching patients off ACEi or ARBs unless there are other medical reasons to do so.
Nebulisation	Avoid of nebulisation due to the generating of aerosol particles and a cough response in the patient which might increase the transmission risk.

References

1. National Department of Health. Clinical management of a suspected COVID-19 V2 19 March 2020.
2. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected March 2020. Available from: [https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\(ncov\)-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected)
3. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, et al. A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19. New England Journal of Medicine. 2020.
4. Boyles TH, Brink A, Calligaro GL, Cohen C, Dheda K, Maartens G, Richards GA, van Zyl Smit R, Smith C, Wasserman S, Whitelaw AC, Feldman C; South African Thoracic Society, Federation of Infectious Diseases Societies of Southern Africa. South African guideline for the management of community-acquired pneumonia in adults. Thorac Dis 2017;9(6):1469-1502. Available from: <https://www.fidssa.co.za/Content/Documents/Boyles-et-al-SA-CAP-Guideline-J-Thoracic-Diseases-2017.pdf>
5. NICD Influenza guidelines 2020. Available from http://www.nicd.ac.za/wp-content/uploads/2019/06/Influenza-guidelines-rev_-6-June-2019clean.pdf