



CIRCULAR H158/2020

**TO: DDG: CHIEF OF OPERATIONS
CHIEF DIRECTORS; DIRECTORS AND HEADS OF INSTITUTIONS
MANAGER: CAPE MEDICAL DEPOT
HEAD OF HEALTH: CITY OF CAPE TOWN**

N.B. FOR CIRCULATION TO ALL MEDICAL, PARAMEDICAL, PHARMACEUTICAL AND NURSING PERSONNEL

RECOMMENDATIONS FOR THE USE OF DEXAMETHASONE AND PREDNISONE FOR THE TREATMENT OF COVID-19

This circular is a follow up to Circular H111/2020: The Recovery Study: Interim guidance on the use of Steroids in Covid-19 Patients.

Attached, please find:

1. National Department of Health Circular, dated 10/07/2020, ref: 2020/06/20/EDP/01: Notice: Recommendations for the use of dexamethasone for the treatment of severe COVID-19. Doses indicated in the notice are for adult patients.
2. NDOH EML Rapid Review Summary, dated 23 June 2020: Corticosteroids for COVID-19: Evidence review of the clinical benefit and harm.
The full review is available at: <http://www.health.gov.za/index.php/national-essential-medicine-list-committee-nemic/category/633-covid-19-rapid-reviews>

Steroids should only be used for patients with confirmed or high clinical likelihood of COVID-19 who are admitted to hospital and require supplemental oxygen, in the absence of existing risk factors for adverse events.

1. Steroids should not be started in the outpatient environment; they are ONLY for admitted patients on oxygen.
2. Steroids should not be started in the Emergency Centre unless discussed with a senior clinician or inpatient team.
3. Always seek senior clinical input in patient care decisions, through your usual supervisory pathways.
4. Follow usual clinical pathways regarding steroids in COVID-19 patients with chronic lung disease.

5. There are risks associated with short-term use of high dose steroids, including hyperglycaemia, electrolyte abnormalities, neuropsychiatric reactions, hypertension, fluid retention and susceptibility to co-infections. Monitor glucose, electrolytes and fluid status. Always aim to balance potential benefit and potential harm in clinical judgement.

Your co-operation in this matter is appreciated.

K Lowenherz

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DIRECTOR: PHARMACY SERVICES

DATE: 29/07/20



health

Department:
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Reference: 2020/06/20/EDP/01

NOTICE: RECOMMENDATIONS FOR THE USE OF DEXAMETHASONE FOR THE TREATMENT OF SEVERE COVID-19

On 19 June 2020, the National Department of Health released a statement titled, *Follow up statement on Dexamethasone by the Minister of Health*. The statement summarised the outcomes of the Randomised Evaluation of COVID-19 therapy (RECOVERY) Trial, which reported benefit from the use of dexamethasone in patients with severe COVID-19. The following were the key findings:

- Dexamethasone reduced deaths by one-third in ventilated patients;
- Dexamethasone reduced deaths by one-fifth in patients receiving oxygen only (but not ventilation);
- Dexamethasone did not provide a mortality benefit in patients who did not require respiratory support.

Note: the RECOVERY trial data have yet to be published in a peer-reviewed form, and only summary statements have been released by the trial chief investigators. The full study report and critical details on the outcomes (such as data on adverse effects) are needed before a considered judgment can be made.

Based on the available results of the RECOVERY Trial, dexamethasone is recommended in COVID-19 patients who require respiratory support only (i.e. those requiring ventilation or other forms of oxygen therapy) (see Table 1). In the RECOVERY Trial, prednisone 40mg daily was used in women who were pregnant or breastfeeding. Therapeutic alternatives are also provided in Table 1.

Corticosteroids are not indicated in patients who do not require oxygen or ventilator support, nor should they be used for prophylaxis.

Table 1: Corticosteroid use in patients with COVID-19 requiring respiratory support

Indication: Clinical management of COVID-19	Recommendation	Therapeutic alternatives
COVID-19 patients requiring respiratory support (ventilation or other oxygen therapy).	<ul style="list-style-type: none"> • Dexamethasone*, intravenous, 6mg daily for 10 days. • Prednisone*, oral, 40mg daily for 10 days. <p><i>Note: Pregnant and breast-feeding women were treated with prednisone in the RECOVERY trial.</i></p> <p><i>Note: dexamethasone tablets are only available via Section 21.</i></p>	<ul style="list-style-type: none"> • Betamethasone, oral or intravenous, 6mg daily for 10 days.

* Dosed according to the RECOVERY Trial

Provinces and Health Care Facilities are requested to distribute and communicate this information.

Comments may be submitted via e-mail:

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Kind regards

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DATE: 2020/07/10



South African National Department of Health
Brief Report of Rapid Review
Component: COVID-19

TITLE: CORTICOSTEROIDS FOR COVID-19: EVIDENCE REVIEW OF THE CLINICAL BENEFIT AND HARM

Date: 23 June 2020

Key findings

- ➔ We did not find any systematic reviews of controlled trials for the use of corticosteroids in patients with confirmed or suspected COVID-19.
- ➔ Based on a preliminary report, in an open-label, randomised controlled trial, low-dose corticosteroids (dexamethasone 6mg daily, orally or intravenously) reduced mortality at 28 days in hospitalised COVID-19 patients on oxygen supplementation. The absolute reduction in risk of death overall was 3.1% (95% confidence interval (CI) 0.89% to 5.25%). For every 33 hospitalised patients treated with low dose corticosteroids, 1 death would be averted (95% CI 19 to 112 patients to prevent 1 death).
- ➔ However, there was no benefit from corticosteroids in the subgroup who did not require oxygen at baseline, and it is possible that corticosteroids caused harm in that group.
- ➔ The greatest benefit was seen in patients requiring mechanical ventilation at baseline - the absolute reduction in risk of death was 11.7% (5.5% to 17.9%). For every 9 ventilated patients treated with low dose corticosteroids, 1 death would be averted (95% CI 6 to 18)
- ➔ In patients on oxygen without mechanical ventilation at baseline, absolute reduction in risk of death was 3.5% (0.7% to 6.3%). For every 29 patients on oxygen only treated with corticosteroids, 1 death would be averted (95% CI 16 to 151).
- ➔ In the same study, dexamethasone shortened duration of hospitalisation (median of 12 days vs. 13 days, respectively) and reduced the risk of progression to mechanical ventilation (absolute risk reduction 1.9%, 95% CI 0.6% to 3.3%).
- ➔ The preliminary report did not describe adverse drug reactions of corticosteroids in COVID-19 patients.
- ➔ We found no studies of the use of corticosteroids in children with severe COVID-19.
- ➔ There is insufficient evidence in HIV-infected patients and the role of corticosteroids in this group is unclear.

NEMLC THERAPEUTIC GUIDELINES SUB-COMMITTEE RECOMMENDATION:

Type of recommendation	We recommend against the option and for the alternative (strong)	We suggest not to use the option (conditional)	We suggest using either the option or the alternative (conditional)	We suggest using the option (conditional)	We recommend the option (strong)
					X

Recommendation: Based on this evidence review, the NEMLC Subcommittee recommends the use of a short duration of low-dose systemic corticosteroids in hospitalised severe COVID-19 patients receiving respiratory support (as either invasive mechanical ventilation or non-invasive oxygen supplementation). Hospitalised patients not requiring respiratory support should not routinely be administered systemic corticosteroids, unless indicated for another reason such as an acute exacerbation of asthma or chronic obstructive pulmonary disease. Systemic corticosteroids may also be considered in patients with COVID-19 with septic shock.

Rationale: In one RCT, which has not yet been peer-reviewed, low dose corticosteroids reduced 28-day mortality in hospitalised patients on respiratory support. However, in hospitalised patients on no respiratory support, there was no evidence of benefit, with a possibility of harms associated with corticosteroid use. The recommendation should be reviewed when the RECOVERY trial is published in final, peer-reviewed form.

Level of Evidence: RCT, Standard of care

(Refer to appendix 3 for the evidence to decision framework)

Therapeutic Guidelines Sub-Committee for COVID-19: Marc Blockman, Karen Cohen, Renee De Waal, Andy Gray, Tamará Kredo, Gary Maartens, Jeremy Nel, Andy Parrish (Chair), Helen Rees, Gary Reubenson (Vice-Chair).

Note: Due to the continuous emergence of new evidence, the rapid review will be updated when more relevant evidence becomes available. As of 23 June 2020, 22 clinical trials are investigating the role of corticosteroids (parenteral, oral or inhalation) treatment of COVID-19 are registered on <https://clinicaltrials.gov/>. Completed studies includes observational study, [NCT04374071](#), and [NCT04273321](#) - a prospective randomised trial (study results yet to be posted).