



National Guidelines for Clinical Management and Treatment of COVID-19

15th July, 2020

Version 4.3

Prepared and Reviewed by	National Clinical Committee for COVID-19 Management
Approved by	Technical team for Pandemic Control



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Summary of Updates as of Version 4.3, 15th July, 2020:

- Asymptomatic and mild cases can be isolated at home if meet the criteria
- Treatment to be considered with currently available regimen
- Pediatric Multisystem Inflammatory Syndrome temporally associated with SARS-CoV-2



Objectives

The objectives of this document are:

- To provide guidance on clinical management of the COVID-19 infection
- To provide a protocol on the practical steps to deal with COVID-19 cases
- To detail the measures necessary to protect hospital staff, patients and visitors
- Disclaimer added
- This guideline is **not intended to override the clinical decisions** that will be made by clinicians providing individualized patient care.
- **This guideline will be updated as more information becomes available**

Introduction to Coronaviruses (CoV)

- Corona virus is a large family of viruses that cause illness in humans and animals
- In people, Corona virus can cause illness ranging in severity from the common cold to Pneumonia and Severe Acute Respiratory Illness
- Corona virus is one of seven types of known human coronaviruses. SARS COV2 like the MERS and SARS coronaviruses, likely evolved from a virus previously found in animals
- The estimated **incubation period** is unknown and currently considered to be **up to 14 days** post exposure.

Case Definition:

Suspected COVID-19 case is defined as:

1. Please refer to the local health authority websites for updated information on local case definition. MOHAP, DoH, SEHA and DHA

Confirmed COVID-19 is defined as:

A person with confirmed positive COVID-19 test positive (SARS COV2 PCR), or positive Ag test by an approved laboratory.

Probable COVID19 is defined as:

A person with clinical and radiological picture compatible with COVID19 infection awaiting PCR result or repeatedly Negative PCR tests collected from different sites with no microbiological evidence of another Infectious etiology.

Clinical Findings and Complications

Some patients with initially mild symptoms may progress over the course 5-7 days from symptom onset.

Clinical Symptoms: Signs and symptoms include:

- Fever
- Cough
- Myalgia or fatigue
- Shortness of breath
- Sore throat
- Runny nose
- Diarrhoea and nausea
- Muscle ache
- Headache
- Pneumonia and ARDS
- Loss of sense of smell
- Renal failure, pericarditis and Disseminated Intravascular Coagulation

Complications:

- Severe Pneumonia
- Acute Respiratory Failure and ARDS
- Acute Renal failure
- Disseminated intravascular coagulation
- Sepsis or septic shock

High-risk group

- Age above 60 years old
- Smoker
- Cardiovascular disease
- Diabetes
- Hypertension
- Obesity (BMI>30 or If Height not available, weight >100kg)
- Immune deficiency and or suppression (HIV/AIDS, long-term steroid therapy, post- transplant cases, chemotherapy, immune modulator therapy)
- Pre-existing pulmonary disease (uncontrolled Asthma, COPD, bronchiectasis)
- Other chronic disease such as chronic kidney disease, Chronic Respiratory disease, Sick cell...etc.



Minimum baseline Investigations for a confirmed or probable COVID19

A set of minimum required baseline work up to be conducted for clinically stable patients when evaluating them in Isolation facilities, field hospitals, PHC Clinics or Emergency Departments to allow decision on required level of care and treatment Initiation:

1. Complete blood count
2. Renal function and Electrolytes
3. Random Glucose
4. Liver function test including ALT/AST
5. ECG if available
6. CRP if available
7. Chest X ray

Investigations for confirmed or probable COVID19 patients admitted to hospitals

Chemistry and Haematology:

1. Complete blood count and differential
2. Renal function and Electrolytes
3. Serum Glucose (HbA1C if diabetic)
4. Liver Function test including Liver enzymes
5. CRP
6. procalcitonin
7. G6PD (if treatment with chloroquine is being considered)
8. LDH
9. Coagulation profile
10. Ferritin
11. D-dimer
12. fibrinogen
13. Troponin & creatinine kinase (CK)
14. Pro BNP
15. HIV Ag/Ab
16. Pregnancy test in women of child-bearing age
17. Blood group

Microbiology:

SARS COV2 PCR on following samples

1. Deep respiratory samples (sputum or deep tracheal aspirate) if lower respiratory tract infection
2. Nasopharyngeal Aspirate/Swab and oropharyngeal swab (should use non-cotton flocked swab) if upper respiratory tract infection

Staff should be trained on Sample collection.



Health care workers collecting NP and OP swab specimens from suspected or confirmed COVID-19 patients should wear a clean, non-sterile, long-sleeve gown, a medical mask, eye protection (i.e., goggles or face shield), and gloves. Procedure should be conducted in a separate/isolation room, and during NP specimen collection health care workers should request the patients to cover their mouth with a medical mask or tissue. ³⁵

3. For intubated patients, obtain deep tracheal aspirate for:

- a) SARS-CoV2 PCR
- b) Atypical PCR panel if available (Mycoplasma, chlamydia, legionella)
- c) Respiratory viral panel
- d) Other investigations to consider if the aetiology of the severe pneumonia is not identified:
 - i. Legionella urinary antigen
 - ii. Mycoplasma titres
 - iii. AFB stain/culture Tuberculosis culture and PCR
 - iv. Opportunistic pathogens in immunocompromised patients

All specimens should be regarded as potentially infectious, and HCWs who collect, or transport clinical specimens should adhere rigorously to standard precautions to minimize the possibility of exposure to pathogens.

Radiology

Ensure infection control measure are taken if patient is transferred to radiology or any other department outside the isolation room

1. CXR
 2. Chest CT scan (HRCT or non-contrasted CT scan) is mandatory for all high-risk group patients admitted to hospitals and for patients with rapidly progressing illness. Consider CT scan chest while waiting COVID19 PCR report as a diagnostic modality to guide early treatment and in patients with clinical features of pneumonia and normal chest X ray.
- (When mobilising patient ensure infection control measures are followed during and after transport)

Cardiac investigations:

3. ECG
4. Transthoracic Echocardiogram, pro-BNP, Troponin T and CK-MB if clinically indicated

Other tests If and when clinically indicated as per clinical condition and judgment of managing physician.

Requesting COVID19 PCR test:

Fill notification form and patient under investigation (PUI) form
Governmental Facilities:
Send the samples to their dedicated virology laboratory.
Private Facilities:
Fill appropriate documents e.g. "Infectious Disease Reference Laboratory Request Form" <u>or</u> "Miscellaneous Request Form" accompanied by copy of Emirate ID <u>or</u> passport copy



Send samples after informing the laboratory in each district
Abu Dhabi: Sheikh Khalifa Medical City
Dubai: Latifa Hospital
Northern Emirates: Al Qassimi Hospital, Sharjah
Approved private laboratories

Transport of Respiratory Secretions Samples

Transport of the respiratory secretions sample to the reference laboratory of your district, using double packing system at 2-8°C temperature.

Trained personnel following safe handling practices should transport specimen

Medical Care for Patients with confirmed COVID-19 infection

- **All suspected or confirmed cases should have the appropriate forms for public health filled and submitted to concerned Public Health Authority**
- All confirmed cases should be screened for eligibility for treatment, as per UAE Health Authorities' recommendation.
- All positive cases to be assessed, if fitting criteria for institutional isolation, can be isolated at designated isolation building, with full instructions and to inform PH/PHC/OPD for follow up. If patient's condition deteriorates, they will be transferred to the nearest healthcare facility for further assessment and management.
- **Asymptomatic and mild cases can be isolated at home if meet the criteria as per the public health guidelines.**
- Admit patients with stable moderate illness and patients with mild illness and risk factors to hospitals/ field hospital /isolation facilities and follow active treatment pathway according to the clinical data.
- If patient's condition deteriorates, upgrade level of care, with immediate arrangement for transfer to hospital if elsewhere with proper communication with receiving facility
- Admit all severe and critically ill patients to hospitals and once their condition stabilizes, they can be transferred to lower levels of care areas.
- Admit all patients with COVID19 infection to single rooms with good ventilation and separate toilet, unless aerosol generating procedures is anticipated then in a room with Negative Pressure Ventilation.
- If hospital capacity is full, positive COVID 19 cases can be cohorted in the same room, provided there is 6 feet distance between the patients.
- Implement standard, contact and droplet precautions whenever coming in contact with positive cases. (Appendix I). Unless aerosol generating procedure then, airborne precaution.
- Consider recommended active management plan for patients with moderate to severe illness.
- Avoid un-necessary use of Antibiotics in patients with COVID-19 infection and adhere to Antimicrobial Stewardship Principles.



Dealing with Patients attending Primary Health Care (PHC) or Accident and Emergency (AE)

***Suspected cases if admitted need to be in a single room with droplet precaution unless aerosol generating procedure then, airborne precaution.**

Clinical Scenario	Decision
No symptoms Not meeting case definition	<ul style="list-style-type: none"> • COVID19 testing is not indicated • Reassure and discharge
Meeting case definition	<ul style="list-style-type: none"> • Collect sample for lab-based SARS CoV2 PCR on Respiratory samples • Fill required notification forms • Respiratory Panel test if available • Baseline work up and chest X ray are indicated • If there is evidence of an alternate diagnosis and the patient is stable; less likely to be COVID19, and manage accordingly, however, it does not rule out coinfection with COVID-19 • Admission, discharge or transfer decision should be based on clinical stability and baseline work up results. • If discharged, quarantine at home/institution pending PCR results • If first COVID19 test is Positive, follow Positive cases management pathway • If first COVID19 test is Negative, and clinical presentation and investigation is suggestive of COVID-19, repeat SARS CoV2 PCR

Clinical Management and Treatment for confirmed COVID 19 cases

Disclaimer:

1. This document is a guideline and NOT a substitute for good clinical practice and judgment of clinician for individual cases
 2. Literature is rapidly evolving & this document may not necessarily reflect all the updated day to day information.
 3. Guidelines will be reviewed by National Committee can be modified/updated if National committee deems it necessary in case of significant, high quality substantial evidence emerge against or in favor of any of the pharmacological options.
- **In view of the lack of specific antiCOVID-19 medication, consider treatment with currently available regimen.**



- **Treat all positive cases of COVID-19 when indicated as early as possible.**
- Apply Standard Precautions, Contact Precautions, and Droplet Precautions with eye protection should always be used when caring for the patient
- If asymptomatic or mild symptoms can be cared for in single room with good ventilation and droplet precaution. Negative pressure rooms are not required unless aerosol generating procedures or anticipating these procedures.
- Clinical management includes prompt implementation of recommended infection prevention and control measures and supportive management of complications, including advanced organ support if indicated.
- There is no specific approved treatment for COVID19 infection to date. However, FDA has issued emergency use authorization for Chloroquine and Hydroxychloroquine. FDA has also published recommendations for investigational COVID19 Convalescent Plasma. See table below
 - Give low flow oxygen therapy to mild pneumonia cases regardless of their saturations. For moderate and severe cases, oxygen to be given as per their clinical requirements.
 - Consider awake proning for eligible patient regardless of level of care. (see appendix II)
 - Use conservative fluid management, whenever possible.
 - Only use empiric antimicrobials if evidence of super added bacterial infection, and preferably narrow spectrum, if clinically indicated.
 - Closely monitor patients for signs of clinical deterioration.
 - Use prophylaxis low molecular weight heparin if no contraindications.
 - Address co-morbid condition(s).
 - Do not administer empirical antibiotic therapy to all patients upon admission unless clinically indicated for reasons other than pure COVID-19 pneumonia. Only patients with severe Pneumonia and unstable vital signs on admission will need empirical broad spectrum antimicrobial therapy pending culture and lab reports. Antibiotics can be stopped or de-escalated if there is no evidence of an active bacterial infection.

Pharmacological options : (Based on limited available information's, expert's opinion & in view of regional and/ or international dynamics of practice)

1. National committee strongly encourage clinicians to maximize the efforts to start, participate in clinical trials to bring maximum patients in context of clinical trials.
 2. Strict monitoring patient for drug induced potential harms and timely intervention in case of any early signals of possible treatment related potential harm
- If the patient is admitted to a private hospital and Active treatment is indicated, but not available, Public Health and Health Regulations in concerned Emirate/Health Authority to be contacted.



Laboratory and Radiological Monitoring

- Baseline tests should be done prior to treatment initiation for all patients.
- Repeat PCR test after 5 days of positive swab collection date.
- Thereafter, repeat blood tests every 72 hours and imaging every week, unless clinically indicated earlier, while on treatment.
- Repeat more frequently in critically ill patients if indicated

Recommended monitoring parameters for Drug Therapy management

- CBC, Renal Profile and extended electrolytes (Na⁺, K⁺, Mg⁺⁺, Ca⁺⁺, Phosphate), Uric Acid, Hepatic Profile, Serum Amylase, Serum Lipase, Coagulation profile,
- G6PD test baseline
- Blood glucose in patients with **Chloroquine or hydroxychloroquine**, frequent **blood glucose monitoring** is required in **diabetic patients** as risk of hypoglycaemia is high ((may require **adjusting Insulin** or other diabetic medications dosing)

ECG Monitoring:

Perform Baseline ECG on **every patient** and may repeat every 24 to 48 hours for patients suspected to have QT prolongation, or high risk for QT prolongation i.e.

- Elderly, female gender, patients with electrolytes imbalance (Hypokalaemia, Hypomagnesemia, Hypophosphatemia, Hypocalcaemia etc.) if low level of any these electrolytes, immediately replace it, keep serum K⁺ > 4mmol/L
- History of cardiac arrhythmia, Bradycardia, Heart disease (Myocarditis, pericarditis, and cardiomyopathy may increase risk for arrhythmia)
- On concurrent QTc prolonging drugs or in the recent past patient has taken QT prolonging drugs with long half-life e.g Amiodarone, Azithromycin, Fluoxetine etc for other QT prolonging drugs check Pharmacokinetic i.e. half-life for the specific drug
- Following are just few examples of QT prolonging drug classes (Fluoroquinolones, Macrolides, Azoles antifungals, Ivabradine, Anti-emetics, Anti-depressants, Antipsychotics, Antiarrhythmic etc) **(Avoid these and any other QT prolonging drugs in patient on COVID-19 treatment)** for more details check on following link
www.qtdrugs.org
<https://www.mdcalc.com/tisdale-risk-score-qt-prolongation> (QT risk calculator)



If a COVID-19 patient needs antibiotic to cover for atypical micro-organism in case of concurrent community acquired bacterial pneumonia, then **Doxycycline** should be choice in view relative safety of Doxycycline on QT prolongation, can be used with Chloroquine/Hydroxychloroquine

Doxycycline can be as an alternative to Macrolides & Fluroquinolones if indicated in patients with QT issues

Prognostic Factors & Markers for Severe COVID-19 Disease

Epidemiological- Category 1	Vital signs- Category 2	Labs-Category 3
Age > 55	Respiratory rate>24 breaths/min	D-dimer>1000 ng/mL
Pre-existing pulmonary disease	Heart rate > 125 beats/min	CPK>twice upper limit of normal
Chronic kidney disease	SpO2 <90% on ambient air	CRP>100
Diabetes with A1c>7.6%		LDH>245 U/L
History of hypertension		Elevated troponin
History of Cardiovascular disease		Admission absolute lymphocyte count<0.8
Use of biologics		Ferritin>300 ug/L
Obesity (BMI>30 or If Height not available, weight >100kg)		
History of transplant or other immunosuppression		
All patients with HIV (regardless of CD4 count)		

Treatment Options:

- The various treatment options including regimens are provided in table 1
- Any drug-induced side effect to be managed accordingly
- Rule out pregnancy before starting Favipiravir, Ribavirin etc**
- Favipiravir, Ribavirin are absolutely contraindicated in pregnancy**
- Check details in Medication safety information section regarding Favipiravir, Ribavirin before prescribing any of these drug for women with child bearing age & and male patients who female**



partner is already pregnant or can be pregnant during & 7 days after end of treatment with Favipiravir, and during or up to 6 months after end of treatment with Ribavirin

- Get Informed consent from patient for treatment of COVID19, if patient can't provide consent then his family member /guardian

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Table 1: Therapeutic Regimens for Adults

- There is no approved therapy for COVID19 to date. Medications used are off label or experimental, based on best available data.
- Chloroquine dose is according to Chloroquine Phosphate salt NOT on Chloroquine Base
- For patients having renal or hepatic impairment, consult individual drug monograph for additional monitoring or dose adjustment.
- **Baseline Monitoring parameters and early initiation of treatment is highly advisable**

Chloroquine Serious Warnings: Potential serious risk of QT prolongation & fatal arrhythmia Torsades de pointes, ventricular fibrillation, cardiac arrest.

1. Careful use & strict screening, monitoring of patient risk factors for QT prolongation (for details see ECG monitoring section)
2. Avoid QT prolonging drug during & even after 3 to 5 days of stopping Chloroquine ^[26] and 6-8 weeks after stopping Hydroxychloroquine (Half life 40 days) in patients with high risk for QT prolongation (If use of significantly QT prolonging drugs after stopping of Chloroquine & Hydroxychloroquine during this wash out period then, strict monitoring of ECG and correction of electrolytes and close monitoring of patient condition by clinicians)
3. Do Not use Chloroquine, Hydroxychloroquine before at least 3-5 days period after stopping Azithromycin, if not possible, strictly monitor ECG and patient condition
4. Should avoid use of Hydroxychloroquine, chloroquine concurrently or within 8-10 weeks of stopping Amiodarone as half life of Amiodarone is very long (average 58 days) ,do not start Amiodarone with in 6-8 weeks of stopping Hydroxychloroquine if possible (If use of significantly QT prolonging drugs after stopping of Chloroquine & Hydroxychloroquine during this wash out period is unavoidable, then strict monitoring of ECG and correction of electrolytes and close monitoring of patient condition by clinicians)
5. For other QT prolonging drugs avoid overlap period depending upon medication pharmacokinetic parameters.
6. Check Cardiac risk management for Hydroxychloroquine in COVID-19 <https://www.acc.org/latest-in-cardiology/articles/2020/03/27/14/00/ventricular-arrhythmia-risk-due-to-hydroxychloroquine-azithromycin-treatment-for-covid-19#inpatient>

Clinical Presentation	Suggested Medications
Clinical presentation	<p>Dosing & frequency mentioned is for normal Renal & Hepatic Functions</p> <p>For Moderate to severe Hepatic Impairment & or severe Renal impairment, Drug interaction etc.</p> <p>(Consult individual drug monograph for additional monitoring or dose adjustment)</p>



Contact	No Post exposure Prophylaxis is indicated for the time being
Probable case of COVID-19 URTI without pneumonia	Please follow the confirmed case management
Probable case of COVID-19 Pneumonia (see Probable case definition above)	Please follow the confirmed case management
Confirmed COVID19 Asymptomatic	<p>No treatment,</p> <p>High risk: Age above 60 years old, Cardiovascular disease, hypertension, Diabetics, Pre-existing lung disease, or Immunocompromised / cancer patients, (Obesity (BMI>30 or If Height not available, weight >100kg)</p> <p>If high risk:</p> <p>Chloroquine Phosphate 500 mg PO BID X 2 doses then 250 mg PO BID (total 5days) OR Hydroxychloroquine 400mg PO BID X 2 doses then 200mg PO BID (total 5days) ⁽⁴⁹⁾</p> <p>If radiological evidence of pneumonia, follow pneumonia recommendation</p>
Confirmed COVID19 URTI without Pneumonia For 5 Days	<p>Hydroxychloroquine 400mg PO BID then 200 mg PO BID (total 5 days) OR Chloroquine Phosphate 500 mg PO BID X 2 doses then 250 mg PO BID (total 5 days) OR Favipiravir 1600 mg PO BID X 2 doses then 600 mg PO BID (total 5 days) OR Lopinavir-Ritonavir (200/ 50 mg) 2 tablets PO BID ^[7] ⁴⁸ (Total 5 days)</p> <ul style="list-style-type: none"> Addition of Camostat 200 mg PO TID X 5 days optional on case by case basis as per treating physician choice (if available)
Confirmed COVID19 Pneumonia For 7 days [Interferon therapy can be a possible add on option on case by case basis in patient with moderate disease]	<p>Favipiravir 1600 mg PO BID X 2 doses then 600 mg PO BID (total 7 days) ^[8,13] +Hydroxychloroquine 400mg PO BID X 2 doses then 200mg PO BID (total 5 to 7 days) ± Camostat 200 mg PO TID for 5 to 7 days (if available and optional) OR Favipiravir 1600 mg PO BID X 2 doses then 600 mg po BID from day2 (total 7 days) +Chloroquine Phosphate 500 mg PO BID X 2 doses then 250 mg PO BID (total 5 to 7 days) ± Camostat 200 mg PO TID for 5 to 7 days (if available and optional) OR Lopinavir-Ritonavir (200/ 50 mg) 2 tablets PO BID (total 7 days) ^[7] + Hydroxychloroquine 400 mg PO BID X 2 doses, then 200 mg PO BID (total 5 to 7 days) (alternatively Chloroquine 500 mg PO BID X 2 doses, then 250 mg PO BID) (5 to 7 days) ±Camostat 200 mg PO TID (5 to 7 days) (if available and optional) OR Remdesivir 200 mg IV on day 1, followed by 100 mg IV daily ^[8,15,40]</p>



<p>Confirmed COVID19</p> <p>Severe Pneumonia /Critically ILL patients</p> <p><u>For 10 days</u></p>	<p>Favipiravir 1600 mg PO BID X 2 doses then 600 mg PO BID +Camostat 200 mg PO TID ± nebulized Interferon Alpha or Interferon Beta (for 5 days) through Nebulizer creating fine mist (ultrasonic nebuliser) e.g. Aerogen Nebulizer (Do NOT use Pegasys or any other pegylated interferon for Nebulization)</p> <p>OR</p> <p>Lopinavir-Ritonavir (200/ 50 mg) 2 tablets PO BID +Ribavirin* 400 m PO BID for 7 days PLUS Interferon ^[40] through Nebulizer creating fine mist e.g. Aerogen Nebulizer (Do NOT use Pegasys or any other pegylated interferon for nebulization)</p> <p>Interferon Formulations & dosing for nebulization: No specific dosing established for COVID-19 through nebulization for both formulations, dosing frequency, duration mentioned below are based on suggestion of National committee Physician members from MOH, DHA in view of their limited experience Depending upon Availability:</p> <p>Interferon Alpha 2b 5 million units /ampule (Bioferon) dilute 2 ampules with 4 ml of normal saline, use BID X 5 days via ultrasonic nebulization</p> <p>Interferon beta 1b (Betaferon) Interferon beta 1b 8 million units (250 microgram) Sub-cutaneous on alternative days for 3 doses or use through Nebulization 8 million units (250 microgram)/vial, mix reconstituted solution of 1 vial of Betaferon with 2 ml of normal saline BID X 5 days</p> <p>*= Contra-Indications for Ribavirin ^[41] Hypersensitivity, Pregnancy, males whose wives are pregnant, concomitant use with didanosine, autoimmune hepatitis, fatal hepatic failure, pancreatitis, hemoglobinopathy (thalassemia major, sickle cell anaemia), CrCL <50 ml/minute (for pregnancy & teratogenic risk check medication safety information section)</p> <p>OR</p> <p>Remdesivir 200 mg IV on day 1, followed by 100 mg IV daily ^[8,15 41]</p> <p>For ICU patients consider empirical antibiotics if bacterial co-infection is suspected according to individual hospital protocol/guideline</p> <p>Anticoagulation (see details below)</p> <p>Steroids (see details below)</p> <p>Tocilizumab to be considered in case of cytokine storm (see details below)</p> <p>Convalescent plasma to be considered as experimental therapy (see details below)</p>
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Camostat Mesylate

Camostat Mesylate^[14,]Is approved drug for medical use in Japan for more than 10 years in other indications like: **Chronic Pancreatitis, Post surgery reflux esophagitis** (Specific dosing regimen information for COVID-19 Not yet available the doses suggested in the guidelines are based on extrapolation from approved dosing regimens for above mentioned other indications.)

- According to research in Germany on SARS-2 Virus of COVID-19 attack on Lung cells in laboratory setting showed that Camostat Mesylate inhibited TMPRSS 2 partially & resulted in ~ 50 % blockage of

attack through ACE2 receptors pathway. “Hoffmann et al., SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor”, Cell (2020),

<https://doi.org/10.1016/j.cell.2020.02.052>. [14]

- As per their recommendation the drug should be tried in clinical studies

Clinical Studies/Trials:[36]

To date 5 clinical trials registered with clinicaltrials.gov (2 in USA,1 in Denmark,1 in Germany,1 in Israel) to evaluate the efficacy of Camostat in RCT ,so far no published information's /findings, however expectations from the drug to show efficacy in early course of disease to prevent or minimize progression of disease into severe form.

Safety profile: Overall safe drug, rarely Hyperkalaemia, Eosinophilia with pneumonitis, urticaria etc.

Favipiravir:

Dose may need adjustment based on clinical scenario, **Patient is elderly or any patient with other risk factors for CKD and develops AKI** i.e 50% rise in serum creatinine from baseline during course of Favipiravir and the rise is persistent

Persistent rise in serum creatinine without any other possible obvious medical reason i.e

- No other nephrotoxic drugs,
- No hypotension or hypertensive emergency
- No sepsis,
- No dehydration
- No other medical cause of rise in serum creatinine (i.e no recent exposure to contrast).

In these patients strict intake/output monitoring with daily serum urea & creatinine and correct any other reason i.e. dehydration, hypotension..etc. If rise is persistent despite all corrective actions then can modify dose and/or minimize duration or stop/hold to avoid permanent renal injury in high risk patients for renal toxicity i.e. elderly ,diabetic ,HTN, Heart diseases ,other nephrotoxic medications.

For individual case it is advised to consult Nephrologist & clinical pharmacist for their input to advise based on risks vs benefits

Remdesivir: [7,13,40]

Remdesivir has Emergency use authorization from FDA. Explain risks vs benefits to patient's, strict monitoring of patient clinical condition, documentation & reporting of significant or serious adverse drug reactions is required.

Low dose corticosteroids

Low dose corticosteroids in early Course of disease have been shown to have benefit in patients requiring oxygen or ventilation. However, has no benefit in mild cases where oxygen is not required



Dexamethasone

As per the Recovery trial, 6mg (IV or Oral) once per day for 10 days for patients on oxygen or ventilated, to be given early in the disease, showed reduction in death by one third in ventilated patients and by one fifth in other patients receiving oxygen⁴⁷

Methylprednisolone

Addition of Low Dose Early corticosteroids in moderate to severe COVID-19 Pneumonia ^[38]: As per the pre-print of Quasi Experimental pre-test (81 pts), post-test (132 pts) study at Henry ford hospital USA. In post test Early use of short course of IV Methylprednisolone 0.5-1 mg/kg in 2 divided dose X3 days in Non ICU & 5-7 days in ICU patients reduced composite end points (hospital length of stay, reduced progression of disease ,all-cause mortality)in post-test group [Raef Fadel, Austin Morrison, Amit Vahia, Zachary R Smith, Zohra Chaudhry et al
<https://www.medrxiv.org/content/10.1101/2020.05.04.20074609v1>

Addition of Multivitamins/supplements ^[45, 46]

Vitamin C 1000 mg PO BID , Vitamin-D 50000 units weekly for 2 weeks (currently being investigated in clinical trials) may have possible add on benefit

Addition of Elemental Zinc ^[39,42,43,44]: Addition of Elemental Zinc 50 mg PO daily for 5 to 7 days in patients with Hydroxychloroquine therapy may be beneficial according to one retrospective study Philip Carlucci, Tania Ahuja et al ,doi: <https://doi.org/10.1101/2020.05.02.2008003> (also currently being investigated in clinical trials) ,the similar benefits is expected from chloroquine as well because it acts as Zinc Ionophore[42,43] (increase zinc transport into cells hence zinc in high concentration can possibly inhibit virus replication)

Anakinra:

Anakinra can be a possible alternative to Tocilizumab in case of shortage of Tocilizumab or contra-indications, the decision to use Tocilizumab or Anakinra should be in consultation with hospital rheumatologist (if available) and MRP as an multidisciplinary team decision

VTE Thromboprophylaxis & Anticoagulants use in COVID-19 patients:

Use according to institutional protocol/policy, use prophylactic anticoagulant in all admitted COVID 19 patients irrespective of VTE risk if no contra-indications to use of anticoagulant Intermittent pneumatic compression devices should be considered if there is a contra-indication to the use of prophylactic anticoagulation.

Interferons

Use being investigated in different clinical studies, Interferon beta 1 b used as 8 million units Sub-Q on alternative days for 3 doses in triple therapy in phase 2 trial in Hongkong by Prof Ivan Fan Ngai Hung et al DOI :[https://doi.org/10.1016/S0140-6736\(20\)31042-4](https://doi.org/10.1016/S0140-6736(20)31042-4)

Interferon Alpha 2B and other interferon of Alpha group also being evaluated for COVID-19



Non-Pharmacological Options

Convalescent plasma (In context of clinical trial):

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has several therapies which are undergoing investigation, but the efficacy of these drugs is yet to be established, furthermore, the use of convalescent plasma was recommended as treatment during former viral infections, therefore, there is a hypothesis that convalescent plasma might be efficacious in the treatment of patients infected with COVID-19. However, there is limited evidence from a few, very small studies that its use is beneficial in these patients, and more recent studies demonstrated its potential benefit when administered to non-intubated patients.

Therefore, COVID-19 convalescent plasma is recommended as follow:

Cases in the serious category with COVID pneumonia and oxygen requirements are the preferred candidates and we recommend to introduce COVID-19 convalescent plasma (CCP) treatment early in the admission process, patients should have their cardiac enzyme, ECG, renal function and Pro-BNP performed and patient should not demonstrate any cardiac or renal compromise prior to administration of CCP.

CCP is not recommended for the life-threatening intubated patients' category unless it's for compassionate use and in a case by case basis.

Two doses that are 48 hours apart is recommended, exception to the second dose are patients who either demonstrates a dramatic improvement or deterioration in their cardiac and/or renal status

Extra Corporeal Blood purification therapies in Cytokine Release syndrome in critically ill COVID-19 patients (In context of clinical trial):

COVID 19 patients can present with a cytokine release syndrome (CRS) and severe acute respiratory failure induced by high level of circulating cytokines levels. Currently there are limited options for patients who deteriorate requiring Intensive care. In view of the complexity of the immune response in response to COVID 19, and the resulting CRS, it is likely that a specific therapy directed against a single cytokine, may not be completely effective in modulating a very dysregulated inflammatory response.

Current therapeutic options in context of COVID 19 related CRS have been limited to experimental antibody-based therapies (e.g. tocilizumab, intravenous immunoglobulins (IVIgG) and convalescent plasma administration.

Extra Corporeal Blood purification (ECBP) has been proposed to remove cytokines in patients with sepsis and systematic inflammatory (1, 2, 3, 4). The rationale for use of these ECBP is that these extracorporeal adsorption membranes are used in cytokine removal, and potentially could improve immune homeostasis and perhaps might help prevent CRS-induced organ damage (2, 6). In addition neither haemodialysis nor hemadsorption appear to remove molecules such as IgG and Tocilizumab as their size (e.g., 150 kDa for IgG, Tocilizumab 148 kDa) exceeds the upper size of molecules mainly being removed these therapies (around 60 kDa) (7). Hence these ECBP therapies will not preclude the use of the other experimental therapies on a compassionate use.

The U.S. Food and Drug Administration have recently provided an emergency use authorization of 4 Extra Corporeal Blood purification devices to treat acute respiratory failure in COVID 19 in context of clinical trials.

1. Oxiris Set device <https://www.fda.gov/media/137267/download>
2. Seraph 100 Microbind Affinity Blood Filter <https://www.fda.gov/media/137101/download>

3. Depuro D2000 Adsorption Cartridge <https://www.fda.gov/media/136834/download>
4. CytoSorb device <https://www.fda.gov/media/136867/download>

There are multiple clinical trials underway in assess effectiveness of this approach.

ClinicalTrials.gov Identifier: NCT04358003, NCT04344080, NCT04385771, NCT04324528

These devices such as Cytosorb, HA330, Depuro D200 have theoretical value in the management of COVID-19 disease and some anecdotal evidence; however, actual clinical trial data that establish true efficacy are lacking even as the body of anecdotal evidence of benefits expands rapidly. **For these reasons, among patients who have been admitted to Intensive Care Unit with COVID-19 related acute respiratory failure, the U.A.E COVID guideline writing panel recommends that “Extra Corporeal Blood purification therapies may be offered to patients with acute respiratory failure in the context of a clinical trial to improve patient access to these devices and to increase clinical knowledge”**

Adults Tocilizumab Protocol for critically ill patients with COVID-19 Pneumonia ^[7,13,24,37]

(Do Not Use Sub-Q formulation pre-filled syringes, autoinjectors to prepare IV Solutions) Use only Commercial product specific for IV use

The decision to use Tocilizumab or Anakinra should be in consultation with ID or Rheumatologist and MRP as a multidisciplinary team decision

Tocilizumab for Cytokine Release syndrome (CRS):

It is FDA approved drug for treatment of CRS due to (Chimeric antigenic T-Cell therapy): Chimeric antigenic T-Cell therapy that works as an IL-6 receptor inhibitor; It is FDA approved drug for treatment of cytokine storm syndrome following Chimeric Antigen Receptor T cell (CAR-T) therapy for B cell malignancies and in Macrophage Activation Syndrome, conditions that share several immune features with COVID-19.

- **Tocilizumab For severely ill ICU patients with COVID-19 Pneumonia remains investigational and off-label.** Therefore, caution in prescribing it is warranted.

Severe Form of Disease: Adults who meet any one of the following:

1. Shortness of breath, RR > 30 breaths/minute;
2. Oxygen saturation < 93% at rest
3. Arterial oxygen partial pressure (PaO₂)/ fraction of inspired oxygen (FiO₂) < 300mmHg (1mmHg = 0.133 kPa)

Determine severity and intervention of Cytokine release syndrome

Grade	Definition	Intervention
Grade 1	Mild reaction	No treatment with tocilizumab
Grade 2	Moderate reaction, fever, need for IV fluid (not hypotension), mild oxygen requirement	Send for serum IL-6

Grade 3	Severe, liver test dysfunction, kidney injury, IVF for resuscitation, low dose vasopressor, supplemental oxygen (high flow, BiPAP, CPAP)	<ol style="list-style-type: none"> 1. Send for serum IL-6, and screening tests (hepatitis B surface Antigen and antibody, hepatitis B core antibody, hepatitis C, quantiferon) 2. Consider tocilizumab after sending screening tests. If no response, consider low dose corticosteroids
Grade 4	Life-threatening, mechanical ventilation, high dose vasopressors	<ol style="list-style-type: none"> 1. Send for serum IL-6 2. Consider tocilizumab as Grade 3; consider corticosteroids

Indication criteria for Use of Tocilizumab ^[7, 15]

- ◇ Extensive and bilateral lung disease and severely ill patients with elevated IL-6 level alternatively High levels of d-dimer and / or CRP/ or ferritin and / or fibrinogen progressively increasing.
- ◇ Worsening of respiratory exchanges such as to require non-invasive or invasive support from ventilation

Laboratory Parameters also supportive of cytokine storm ^[26]

- Serum IL-6 $\geq 10\times$ upper normal limit
- Ferritin >300 ug/L (or surrogate) with doubling within 24 hours
- Ferritin >600 ug/L at presentation
- and LDH >250 U/L
- Elevated D-dimer (>1 mg/L)
- High CRP

Tocilizumab Exclusion Criteria of Patients: ^[7, 15, 24]

- Active TB
- AST /ALT values higher than 5 times the normal levels.
- Neutrophil value lower than 500 cells / mm^3
- Platelets value lower than $50,000$ cells / mm^3
- Complicated diverticulitis or intestinal perforation
- Confirmed systemic bacterial & or fungal infection (i.e. Bacteraemia with pathogenic bacteria, fungemia)
- Pregnant women (there are insufficient data about its safety in pregnancy)
- Skin infection in progress (e.g. dermohypodermatitis not controlled by antibiotic therapy)
- Immunosuppressive anti-rejection therapy

Adult Tocilizumab Dosing Regimen ^[24,41]

(Need to Send IL-6 level prior to giving first dose of Tocilizumab)

- The suggested dose is 4- 8 mg/kg body weight (maximum dose 800 mg) X Once only

Administration: Dilute in 100 ml of 0.9 % saline, allow diluted solution to reach room temperature, infuse over more > 60 minutes using **dedicated line** (Do Not infuse if opaque particles or discoloration visible same)



If partial or incomplete clinical response POSSIBLE second infusion maybe given 8-12 hrs after the first dose (Maximum 2 doses)

Pediatric Patients COVID-19 treatment options

Due to the limited data at this point in time, the current approach is on different protocols from some countries, ongoing investigations for some of the drugs in adults & extrapolated from available evidence from adult based studies

- Treatment in Paediatric patients on case by case basis after consultation with ID Physician and concerned speciality
- Get Informed consent from patient for treatment of COVID19, If patient can't provide consent then his family member /guardian
- * Chloroquine dose is according to Chloroquine Phosphate salt NOT on Chloroquine Base
 - Consideration of antiviral therapy in combination with Hydroxychloroquine or Chloroquine should be based on patient condition, safety profile and preference of the patient and primary team in consultation with Paediatric infectious diseases physician
 - Total duration of treatment with Chloroquine /Hydroxychloroquine should not be more than 5-7 days
 - Nebulized interferon alpha 2b, Interferon Beta 1b may be a possible option in addition to Kaletra (Lopinavir-Ritonavir), chloroquine, Hydroxychloroquine in critically ill paediatric patients
- **Interferon should not be routine option for all PICU patients**, in very rare cases **based on thorough evaluation of serious risks vs benefits** by MRP with ID, may be used. (For Interferon dosing check Lexicomp & or product leaflet/prescribing informations for general dosing according to individual patient need, if need any adjustment or not).

- **If patient is already on Interferon discontinue it** (If considering use of Tocilizumab)
- At least 24-48 hrs gap after last dose of regular interferon, and
- At least 3-5 days gap after 'Pegylated Interferon (taking into consideration average half-life) " before starting Tocilizumab.
- Do Not use or restart systemic Interferon therapy in patient who **received Tocilizumab**

Clinical Presentation	Suggested Medications (for paediatrics)
Confirmed COVID 19	Follow the below recommendations
Asymptomatic	No treatment
Drug	General dosing (Avoid Hydroxychloroquine/Chloroquine in critically ill/PICU patients)
Hydroxychloroquine Sulfate ^[10,20,21] (Per Oral)	Loading Dose: 6.5 mg/kg PO (Maximum 400 mg per dose) BID X 2 doses Maintenance: 3.25 mg/kg PO (maximum 200 mg per dose) BID X 4 days (total duration 5 days)

Chloroquine Phosphate ^[10,11] Dose based on Chloroquine Phosphate salt NOT on Chloroquine Base	Chloroquine Loading dose Day One: 8.3 mg/kg Once (Maximum 500 mg per dose) Maintenance dose from day two: 5 mg/kg once daily (250 mg per day) X 4 Days (total duration 5 days)
Lopinavir/Ritonavir [7,10]	Weight-directed dosing (Children and Adolescents) (Per oral) <15 kg: Lopinavir 12 mg/3 mg /kg/dose PO twice daily 15 to 40 kg: Lopinavir 10 mg/2.5 mg/kg/dose PO twice daily >40 kg: Lopinavir 400 mg/100 mg PO twice daily

Favipiravir dosing is in patients ≥ 12 months of Age & body weight ≥ 10 kg

(There is no data regarding use & dosing in COVID-19, doses in below table derived & modified from **Ebola study in 12 children**)

Body weight	Favipiravir 200 mg Tablet
10-15 kg	Loading Dose: One tablet PO BID for One day (maximum 400 mg/day) Maintenance from Day2: Half tablet (100 mg) PO BID (maximum 200 mg/day)
16-21 kg	Loading Dose: Two tablets PO BID One day (maximum 800 mg/day) Maintenance from Day2: One Tablet PO BID (maximum 400 mg/day)
22-35 kg	Loading Dose: 3 Tablets PO BID for One day (maximum 1200 mg/day) Maintenance from Day2: One tablet PO TID (maximum 600 mg/day)
36-45 kg	Loading Dose: Four tablets PO BID for One day (maximum 1600mg/day) Maintenance from Day2: Two tablets PO BID (maximum 800 mg/day)
46-55 kg	Loading Dose: Five tablets PO BID for One day (maximum 2000 mg/day) Maintenance from Day2: Two tablets qAM, three Tablets qPM (maximum 1000 mg/day)
For >55 kg	Can use adult dosing if age ≥ 16 years, if age <16years use dosing of 46-55 kg range

Pediatrics Tocilizumab Protocol for use in PICU patients ^[26] ≥ 2 years

Currently under investigation for use in the treatment of COVID-19 associated pulmonary complications with elevated IL-6 levels (see [ClinicalTrials.gov](https://clinicaltrials.gov)). **Safety & efficacy is not yet established for COVID-19 at this time point in time. (use only IV commercial formulation, Do Not use Sub-Q prefilled syringes/pens)**

Use restricted to Intensivist & ID only AND COVID-19 positive patients with severe ARDS after failing or not qualifying for first line treatments

- ◇ Risks of serious toxicity including serious hepatotoxicity leading to fulminant liver failure & cases of liver transplant in past, life threatening secondary infection & or other side effects vs benefits need to be assessed and discussed with patient guardian/family & clearly explained & informed consent to be signed by father/ guardian

Need to send for IL-6 Level before starting therapy with Tocilizumab ideally

Grade	Definition	Intervention
Grade 1	mild reaction	No treatment with Tocilizumab

Grade 2	moderate reaction, fever, need for IV fluid (not hypotension), mild oxygen requirement	Send for serum IL-6
Grade 3	severe, liver test dysfunction, kidney injury, IVF for resuscitation, low dose vasopressor, supplemental oxygen (high flow, BiPAP, CPAP)	Send for serum IL-6, and screening tests (hepatitis B surface Antigen and antibody, hepatitis B core antibody, hepatitis C, QuantiFERON) Consider tocilizumab after sending screening tests. If no response, consider low dose corticosteroids
Grade 4	Life-threatening, mechanical ventilation, high dose vasopressors	Send for serum IL-6 Consider tocilizumab as Grade 3; consider corticosteroids

Severe Form of Disease in Children [7]: Children who meet any one of the following:

- Show shortness of breath (<2 months old, $RR > 60$ times/min;
- 2~12 months old, $RR > 50$ times/min;
- 1~5 years old, $RR > 40$ times/min; except the effects of fever and crying;
- Oxygen saturation $<92\%$ at rest.

Laboured breathing (wheezing, flaring of nostrils, three concave sign), cyanosis, intermittent apnoea.

- Lethargy, convulsions.
- Refusal to eat or difficulty feeding; signs of dehydration.

Critical form of Disease: Meeting any of the following criteria:

- ◇ Respiratory failure occurs and mechanical ventilation is required, Shock,
- ◇ Combined failure of other organs that requires ICU monitoring

In Paediatric ICU if patient is **in early ARDS and Possible Cytokine Storm** as per criteria set in Tocilizumab protocol and may be a candidate for Tocilizumab, **THEN Do-Not Start Interferon** as high risk of potential serious side effects concurrently with two Immune modulating drugs (i.e. Tocilizumab, Interferon).

Indication criteria for Use of Tocilizumab [7, 15, 23, 25]

- ◇ Extensive and bilateral lung disease and severely ill patients with elevated IL-6 level
- ◇ Alternatively, High levels of d-dimer and / or CRP/ or ferritin and / or fibrinogen progressively increasing.
- ◇ Worsening of respiratory exchanges such as to require non-invasive or invasive support from ventilation

Laboratory Parameters also supportive of cytokine storm [25]

The inflammatory markers criteria should be in context of IL-6 along with other markers mentioned below

- Serum IL-6 > 10 x upper normal limit
- Ferritin >300 ug/L (or surrogate) with doubling within 24 hours
- Ferritin >600 ug/L at presentation
- and LDH >250 U/L
- Elevated D-dimer (>1 mg/L)
- High CRP

Tocilizumab Exclusion Criteria of Patient: [7, 15, 24]

- Active TB
- AST / ALT values higher than 5 times the normal levels.
- Neutrophil value lower than 500 cells / mm³
- Platelets value lower than 50,000 cells /mm³
- Complicated diverticulitis or intestinal perforation
- Skin infection in progress (e.g. dermohypodermatitis not controlled by antibiotic therapy)
- Immunosuppressive anti-rejection therapy
- Confirmed systemic bacterial & or fungal infection (i.e. Bacteraemia with pathogenic bacteria, fungemia)

Tocilizumab dosing in Pediatrics ≥ 2 years [24]:

- IV: 8 mg/kg/dose (maximum 400 mg per dose) X Once
- **Administration:** Dilute in 100 ml of 0.9 % saline, allow diluted solution to reach room temperature, infuse over 60 minutes using **dedicated line** (Do Not infuse if opaque particles or discoloration visible same)
- **Administration:** Dilute in 100 ml of 0.9 % saline, allow diluted solution to reach room temperature, infuse over 60 minutes using **dedicated line** (Do Not infuse if opaque particles or discoloration visible same)

Explanation for Calculation of “Favipiravir dosing” for COVID-19 in paediatrics

Use of Favipiravir [19,20] **(Avigan) In Paediatrics’ ≥ 12 months of Age & body weight ≥10kg.** As such no dosing information data available from any ongoing or proposed trial or study in Paediatrics’ in COVID-19.

Dosing regimens were derived dosing from the doses used in Ebola **Trial [19]** in 12 children **≥ 12 months of Age & body weight ≥10kg** [19] (dosing regimen derived on almost similar scale used in adults from Ebola to COVID-19 regimen)

For Adult patients Favipiravir (Avigan) COVID-19 Dosing is less than Ebola dosing i.e.(COVID-19 Loading dose is 50% less ,maintenance dose 25%-50% less compared to Ebola dosing) based on almost similar scale it is plausible to adopt the same strategy in children for dose reduction as well for the safety reasons and hence COVID-19 dosing were adopted for “Paediatrics”

In children of lower body weight range i.e. 10-15 & 16-21 kg range more conservative dosing approach adopted due to safety concerns.

Pediatric Multisystem Inflammatory Syndrome temporally associated with SARS-CoV-2

The Covid-19 pandemic has been temporally associated with the emergence of a pediatric presentation of severe inflammation and shock. This syndrome has some clinical similarities to Kawasaki shock and toxic shock. Patients have presented with mild to severe illness. In the majority of patients, coronavirus has not been detected by PCR on nasal swabs, however serological evidence of SARS-CoV-2 infection is present in some. The likeliest mechanism is a delayed antibody-mediated dysregulated host immune response.

- **Pediatric Multisystem Inflammatory Syndrome associated with SARS-CoV-2 should be reported to the authorities as part of COVID 19 case reports.**

<p style="text-align: center;">Clinical features</p> <p>May include one or more of the following:</p> <ul style="list-style-type: none"> • Persistent Fever > 39 C • Neurocognitive symptoms: Lethargy, Headache and confusion • Abdominal Pain, Diarrhoea and Vomiting • Rash/Conjunctivitis/mucous membranes involvement • Hypotension (Wide pulse pressure), tachycardia +/- Shock 	<p style="text-align: center;">Laboratory features</p> <p>Raised CRP and ESR Raised LDH Raised Ferritin (>500) Raised Troponin and B-NP Raised Fibrinogen Lymphopenia / neutrophilia Raised D-Dimer Platelets initially low or normal Renal dysfunction</p>
<p>Significant similarity in presentation with other pediatric conditions Septic shock - may require higher volume fluid resuscitation and source control Peritonitis -negative laparotomy reported in some cases: Needs surgical review with appropriate radiology</p>	
<p style="text-align: center;">Initial management</p> <p>Examination:</p> <ul style="list-style-type: none"> • Exclude potential septic foci and careful cardiac assessment (liver, JVP, cardiac / thoracic ratio on CXR) <p>Resuscitation:</p> <ul style="list-style-type: none"> • If signs of shock – fluid resuscitation (10ml/kg NS) with re- evaluation after each bolus and discuss with PICU • If no improvement with fluid, start inotropes: Dopamine@ 5 - 10mcg/kg/min, until central access (consider Epinephrine) 	<p style="text-align: center;">Investigations</p> <p>Core investigations:</p> <ul style="list-style-type: none"> • CBC/Diff, Renal function, LFT • CRP, PCT, ESR • Ferritin, Triglycerides, Trop-T, D-Dimers, CK, NT-proBNP, LDH • Serum IL-6 level • Coagulation profile (Including Fibrinogen) • Blood / Urine culture • Immunoglobulins levels • Save serum & EDTA sample • Chest X-ray • Consider abdominal imaging to exclude abdominal pathology



<ul style="list-style-type: none"> Ceftriaxone and Clindamycin as sepsis impossible to exclude. Add broader spectrum antibiotics (e.g. Vancomycin) if hospital acquired or concern of infections due to resistant pathogens, keep clindamycin to reverse toxins release Early IVIG 2g/kg (once over 10-12 hours), Max 100 gram <p>Severe myocardial dysfunction common:</p> <ul style="list-style-type: none"> If intubation required: cardio-stable induction (ketamine+ prepare emergency drugs) 	<p>Additional investigations (PICU admission)</p> <ul style="list-style-type: none"> Vitamin D, amylase Type and screen (cross match if considering ECMO) Blood smear Virology for SARS-CoV-2 PCR on Stool, NPA, blood serology for SARS-CoV-2 Standard Respiratory Viral panel Viral serology blood PCR: EBV, CMV, Adeno, Enterovirus Pneumonia panel if intubated
<p>PICU management</p> <p>Patient to be managed as COVID+ (even if PCR negative for SARS- CoV-2) – full PPE and management in appropriate area</p> <ul style="list-style-type: none"> Central access: awake femoral line preferable in self ventilating patients-most require Epinephrine Temperature control – regular paracetamol, active cooling if ventilated Ensure IVIG was administered otherwise give a dose as above, monitor for fluid overload during infusion. Methylprednisolone as per clinical severity table Proton pump inhibitors (esomeprazole 1 mg/kg/day, max 40 mg/day) Aspirin/Anticoagulation as detailed in the third page. <p>Monitoring:</p> <ul style="list-style-type: none"> Urgent Echo upon admission to PICU. Repeat as clinically indicated. 12 lead ECG at admission, repeat daily or if clinical concerns. If oxygen requirement repeat CXR Regular blood gas – measure lactate Repeat <i>core investigations</i> 12 hourly – if rising inflammatory markers discuss with ID team. 	<p>Cardiac Manifestations and Management</p> <p>Pancarditis may include: bi-ventricular impairment, mitral/ tricuspid valve regurgitation, diastolic dysfunction, pericardial effusion, coronary artery dilatation / aneurysm (may be better visualized on CT)</p> <ul style="list-style-type: none"> Clinical course unpredictable with rapid deterioration observed in some. 12 lead ECG – arrhythmias reported Urgent Echocardiogram Low threshold for Milrinone infusion Severe cases consider levosimendan VA ECMO for refractory shock – Discuss with SKMC <p>Response to treatment</p> <ul style="list-style-type: none"> Defined as the normalization of vital signs, CRP, and blood test, and the resolution of symptoms and signs <p>Therapy Complications</p> <ul style="list-style-type: none"> Fluid overload risk with IVIG infusion – consider diuretics Hypertension: high dose methyl prednisolone associated with severe hypertension and PRES. Treatment with Ca channel blockade or SNP if severe cardiac dysfunction. Hyperglycemia: – may require insulin infusion. Gastritis: patients should all receive high dose PPI. Salicylate complications: AKI, Respiratory alkalosis



Classification of Clinical Severity

- **Mild:** No vasoactive requirement, minimal/no respiratory support, minimal organ injury
- **Moderate:** Vasoactive-Inotropic Score* (VIS) ≤ 10 , significant supplemental oxygen requirement, mild or isolated organ injury
- **Severe:** Vasoactive-Inotropic Score > 10 , non-invasive or invasive ventilatory support, moderate or severe organ injury including moderate to severe ventricular dysfunction

Vasoactive-Inotropic Score (VIS)* below

Management by Clinical Severity

Therapeutic Category	Mild	Moderate	Severe
Steroid Initial Dosing For 2 mg/kg/day dosing: max 60 mg/day For pulse dosing: max 1 g/day	Methylprednisolone 2 mg/kg/day	Methylprednisolone 10 mg/kg X 1, then 2 mg/kg/day	Methylprednisolone 30mg/kg/day (max 1000 mg/day) for 1-3 days, then 2 mg/kg/day
Other Immunomodulation	Consider pulse Methylprednisolone or Anakinra if refractory course * Consult Rheumatology	Consider 1-3 days pulse Methylprednisolone, consider Anakinra if refractory to steroids * Consult Rheumatology	Consider Anakinra if refractory to steroids, consider other biologics if refractory to Anakinra * Consult Rheumatology
GI prophylaxis with proton pump inhibitor	Yes	Yes	Yes
Broad-spectrum antibiotics	Yes	Yes	Yes
Steroid Taper	2-3 weeks	6-8 weeks	Steroid taper with subspecialty consultation

Further immunomodulation poor response may include:

- Repeat IVIG dose
- Pulse Steroid
- Anakinra (IL-1 receptor antagonist)
- Infliximab (monoclonal antibody)
- Tocilizumab (IL-6 receptor antibody)
- Details on second page

Adapted from Morgan Stanley children's Hospital

INTRAVENOUS IMMUNOGLOBULINS

- All patients with MIS-C should receive IVIG 2g/kg up to 100g. A second dose of IVIG should be considered in refractory cases. Obtain serum quantitative immunoglobulins and necessary serum serologies before administration of IVIG.



Recommended doses for BIOLOGICS (following discussion with Pediatric rheumatology)

- Anakinra 2-4 mg/kg/dose (max 100mg/dose) SQ twice daily (may increase to 3 times daily) for 3 days
 - * doses up to 10 mg/kg/dose SQ q6hr have been utilized
- Infliximab 10mg/kg/dose IV once
- Tocilizumab <30kg: 12mg/kg IV; >30kg 8mg/kg IV, max 800mg
 - * An additional dose may be given 12 hours after the first dose if clinical symptoms worsen or show no improvement.

* **VIS** = Dopamine dose (mcg/kg/minute) +
Dobutamine dose (mcg/kg/minute) +
100 X Epinephrine dose (mcg/kg/minute) +
100 X Norepinephrine dose (mcg/kg/minute) +
10 X Milrinone dose (mcg/kg/minute) +
10,000 X Vasopressin dose (U/kg/minute)

Aspirin/Anticoagulation Protocol

- **All Patients regardless of coronary artery abnormalities**
 - < 60 kg: enoxaparin 0.5 mg/kg/dose Q12hr, Max 30 mg/dose [Prophylaxis]
 - > 60 kg: enoxaparin 30 mg Q12hr (Prophylaxis).
 - Change Frequency to q24h If Cr Clearance < 30/min/1.73 m²
- **Patients with coronary ectasia or dilation**
 - Enoxaparin as above
 - AND
 - Low-dose ASA (3-5 mg/kg/day, max 81 mg)

- **Exceptions to low-dose ASA:** Platelets less than 100,000
 - Consult cardiology to review anticoagulation/antiplatelet recommendations, on case-by-case basis
- **Patients with moderate or severe systolic dysfunction (e.g., EF < 30%), rapidly expanding aneurysms, or giant aneurysms:**
 - LMWH (Therapeutic) for all patients in consultation with cardiology
 - Usual dosing is 1 mg/kg/dose Q12h, with anti-Xa target of 0.5-1.0
 - Cardiology will determine need for additional antiplatelet therapy with aspirin
- **Duration of treatment with aspirin:**
 - In patients prescribed ASA as inpatients, low-dose ASA should be continued through at minimum the time of cardiology/rheumatology follow up with ultimate duration to be determined at the outpatient visit.
- **Duration of treatment with LMWH:**
 - LMWH should be discontinued when the patient no longer meets high-risk criteria for VTE prophylaxis, or at the time of hospital discharge.
 - After LMWH is discontinued, patients should be transitioned to low-dose ASA, with duration as described above. Duration of LMWH for children with moderate or severe cardiac dysfunction should be discussed with cardiology team.
- **Special Considerations for Aspirin:**
 - Avoid ibuprofen or other NSAID (antagonizes anti-platelet effect of aspirin)
 - Adverse effects (rare): GI bleed, tinnitus, Reye's syndrome
 - Reye's syndrome – rare, but increased risk with aspirin and viral infection.
 - Consider inactivated influenza vaccine (avoid live vaccines (e.g. varicella) until off aspirin or discuss risk benefit when on low-dose aspirin).

Pregnant patients:

- In Pregnant Patients management of COVID-19 Case by case basis with ID Consultation and obstetrician.
- Nebulized interferon alpha 2b, Interferon Beta 1b can be a possible option in addition to Kaletra (Lopinavir-Ritonavir), chloroquine, Hydroxychloroquine in pregnant women for details of specific formulations dosing, method, duration, check treatment section for severe pneumonia/ critically ill adult patients (page 11-12)



Medications Safety Information

For more details about the suggested medications, refer to Appendix VII-COVID -19 Treatment Options Index

Drug Use Management of COVID-19 Patients

Follow the basic principle of Medicine" First **Do No Harm**"

COVID -19 patients are often with underlying diseases receiving multiple types of drugs, at risk for adverse effects.

The following is expected from every healthcare giver to ensure safety of treatment options

- **Strict compliance** to Labs, ECG monitoring Parameters (mentioned in this guideline)
- Side Effects Monitoring, prompt action accordingly
- Check for Drug interaction & if dose adjustment required when patient is on COVID-19 drugs

Nursing monitoring Parameters:

- ◇ For any potential side effects and inform MD on Duty “
- ◇ Strict Monitoring of Glucose, Hypoglycaemia especially in diabetic or NPO, Insulin & Diabetic medications dose adjustment may be required case on cases basis
- ◇ Monitor sign of arrhythmia, immediately inform MD

Pregnancy Warning with “Avigan” (Favipiravir)

Avigan is **contra-indicated in pregnancy**

When administering AVIGAN® (Favipiravir) to women of child-bearing potential, **rule out pregnancy before starting the treatment**. Explain fully the risks and instruct thoroughly to use most effective contraceptive methods with her partner during and for 7 days after the end of the treatment. If pregnancy is suspected during the treatment, instruct to discontinue the treatment immediately and to consult a doctor.

Advice for Male patient

AVIGAN (Favipiravir) is distributed in sperm. When administering the drug to male patients, explain fully the risks and instruct thoroughly to use most effective contraceptive methods in sexual intercourse during and for 7 days after the end of the treatment (men must wear a condom). In addition, instruct not to have sexual intercourse with pregnant women during & for 7 days after the end of the treatment.

- ◇ **Favipiravir in Breastfeeding /Lactation:** When administering Favipiravir to lactating women, instruct to stop lactating (The major metabolite of Favipiravir, a hydroxylated form, was found to be distributed in breast milk.)

Pregnancy Warning with Ribavirin: Teratogenic, serious foetal abnormalities **absolutely Contra-indicated**



Significant teratogenic and/or embryonal effects have been demonstrated in all animal species exposed to ribavirin. In addition, ribavirin has a multiple dose half-life of 12 days, and it may persist in non-plasma compartments for as long as 6 months.

Therefore, ribavirin, is **contraindicated** in **women who are pregnant** and in the **male partners of women who are pregnant**.

Extreme care must be taken to avoid pregnancy during therapy and for 6 months after completion of therapy in both female patients and in female partners of male patients who are taking ribavirin therapy. **At least two reliable forms of effective contraception** must be utilized **during treatment** and **during the 6-month post treatment** follow-up period

Rule out pregnancy before starting treatment whenever applicable

- Check for any potential drug interaction if patient is on any other medication or being started while on COVID-19 treatment
- Avoid concurrent use of Macrolides, and other QT prolonging drugs in patient with chloroquine, Hydroxychloroquine therapy
- Keep monitoring patient clinically for any early sign of potential drug adverse effect and take prompt action to assess the patient regimen and manage accordingly

Hydroxychloroquine & G6PD Concerns:

- " In Lexicomp Drug information source: It mentions as precaution not Contra-indication for G6PD deficiency: Although the manufacturer's labelling recommends hydroxychloroquine be used with caution in patients with G6PD deficiency due to a potential for haemolytic anaemia, there is limited data to support this risk. Many experts consider hydroxychloroquine, when given in usual therapeutic doses to WHO Class II and III G6PD deficient patients, to probably be safe (Cappellini 2008; Glader 2017; Luzzatto 2016; Youngster 2010). Safety in Class I G6PD deficiency (ie, severe form of the deficiency associated with chronic hemolytic anemia) is generally unknown (Glader 2017). In a retrospective chart review, no incidence of hemolytic anemia was found among the 11 patients identified with G6PD deficiency receiving hydroxychloroquine therapy, despite >700 months of exposure (all patients were African American and located in the US) (Mohammad 2017). In addition, the ACR Rheumatology guidelines do not mention the need to evaluate G6PD levels prior to initiation of therapy (Singh 2016).
- So, if used, exercise cautions and monitor closely for any early sign of Hemolytic anemia & manage accordingly



Discharge Criteria for COVID19 confirmed cases

- if COVID19 PCR test from nasopharyngeal sample or lower respiratory sample is positive, repeat samples after 5 days from the positive swab and every 72 hours thereafter.
- Once a sample becomes negative, collect after 24 hours
- for De-isolation of COVID-19 Patients, please refer to:

Interim Guidance for De-isolation of COVID-19 Patients Version 1.0 (26 May 2020)

Please ensure that you follow the latest version of the guidance, above is current version upon publishing

For Asymptomatic and Mild symptomatic COVID-19 positive patients, please refer to the guidance above.

For Moderate, severe, and critical symptomatic hospitalized COVID-19 positive patients (as per guidance above):

• **Test-based strategy:**

Patient can be discharged once they have:

- o Two consecutive respiratory specimens negative tests for COVID 19 that are ≥ 24 hours apart
and
 - o Patient is afebrile for more than 3 days without the use of fever-reducing medications
and
 - o Patient has improved/minimal respiratory symptoms
and
 - o Pulmonary imaging (CXR/ HRCT) shows significant improvement
- All patients after discharge should be self-isolated at home for 7 days from discharge date and to have a sick leave documented in medical record
 - Discharged patients to be followed in the clinic in the hospital after 2 weeks, unless patient develops respiratory symptoms to attend earlier.
 - If asymptomatic at 2 weeks, no more follow up
 - Notify Public health/Preventive medicine at discharge.



Infection Control Measures for Suspected or Confirmed COVID19 Cases in Healthcare Facilities

Early Recognition

Enhance early recognition of suspected cases by:

- Visual triage at the entry point of the healthcare facility, for early identification of all patients with acute respiratory illness (ARI).
- Visual triage station should be placed at the entry point of the AE and any entry point
- Attended by a trained nurse or nurse assistant. Staff should be trained on appropriate questions to ask as well as actions based on findings and updated case definition
- Post visual alert signage to enhance self-reporting by symptomatic patients.
- Provide enough supply of surgical masks & hand hygiene sanitizers in the AE room.
- All identified acute respiratory infection (ARI) patients should be offered to
- Wear a surgical mask, if they can tolerate it, and should be asked to perform hand hygiene.
- All contacts of suspected patients should also be offered to wear a surgical mask and should be asked to perform hand hygiene.
- Do not allow suspected COVID19 into common areas with other patients.
- Place suspected COVID19 in a dedicated waiting area with at least 3 feet and preferably 6 feet distance between them.
- Screen all patients walking into the ED for symptoms of acute respiratory illness (ARI) using the COVID-19 visual triage form below.
- Perform Infection Control Risk Assessment in triage.

Infection Control Practices in Healthcare Facilities:

Training

- All healthcare workers entering these rooms should be trained on proper use of PPE and fit tested in order to use N95. (Appendix I)
- Ensure that patients and visitors receive education about the precautions being used; the duration of precautions; the prevention of transmission of infection to others; and use of appropriate PPE.
- Ensure that front line staff as well as other staff at risks i.e. radiology, respiratory therapist; cleaning staff receive training on COVID19 preventative strategies.

The mode of transmission of COVID 19 remains unknown.



General recommendations:

Implement Standard Precautions for all patients at all times focusing on

- Hand hygiene: adherence to WHO steps and moments
- Ensure availability and Proper use of PPE.
- Follow Respiratory Hygiene Practices:
 - Offer a medical mask for suspected cases of COVID 19 for those who can tolerate it.
 - Educate patient and relatives about cough and sneeze etiquette ie. Cover nose and mouth during coughing or sneezing with tissue or flexed elbow for others.
 - Avoid touching your eyes, mouth or nose.
 - Post visual aid for cough etiquette, hand hygiene and symptoms to report early.
- Risk assessment is critical for all activities, i.e. assess each health care activity and determine the personal protective equipment (PPE) that is needed for adequate protection.

Practice droplet and contact Precaution when dealing with Suspected Cases (Appendix I)

For suspected cases:

Patients to be placed in a single room with its own toilet.

Practise droplet and contact precautions for suspected cases:

- Wear a surgical mask, eye protection i.e. goggles or a face shield, gloves and impermeable gown.
- Practice airborne precautions for aerosol-generating procedures (wear fit tested N95 mask) as (bronchoscopy, open suction, nebulization, sputum induction, ambu-bagging intubation and extubation, BiPAP, CPR, and autopsy)

Practice droplet and contact Precaution when dealing with Confirmed Cases

For confirmed cases:

- Place patient in a single room with good ventilation and with its own toilet, with the door closed.
Airborne infection isolation room is only required if aerosol generating procedure is anticipated.
- If a negative pressure, room is needed for aerosol generation procedures but not available, put the patient in a single room, well ventilated, and place air disinfectant (Plasma air filter or Portable HEPA filter) in the room, next to patient's head.
- Practise droplet and contact precautions for confirmed cases unless aerosol generating procedure.
- HCP should wear respiratory protection equivalent to a fitted N95 filtering facepiece respirator or equivalent N95 respirator during aerosol-generating procedures.



- Unprotected HCP should not be allowed in a room where an aerosol-generating procedure has been conducted until sufficient time has elapsed to remove potentially infectious particles as per room air exchange per hour
- Conduct environmental surface cleaning following procedures (see section on environmental infection control).
- Avoid the presence of unnecessary individuals in the room.
- Practice airborne precautions for aerosol-generating procedures
- Note that high risk patients may present with mild symptoms but are at high risk of deterioration.

Personal Protective Equipment (PPE) for confirmed cases of COVID 19

PPE should be available where and when it is indicated in the correct size and sufficient quantity

- Ensure all staff wear surgical mask, eye protection i.e. goggles or a face shield, gloves, head cover and impermeable gown in the usual setting, however, if aerosol generating procedure or prolonged stay in patient's room then use a fit-tested N95 or equivalent.
- Designate staff who will be responsible for caring for suspected or known COVID-19 patients. Ensure they are trained on the infection prevention and control recommendations for COVID-19 and proper use of personal protective equipment.
- All health care provider should wear and remove the PPE safely.
- If there is concern and/or breach of PPE during patient care, leave the patient care area when safe to do so and properly remove and change the PPE and report it to your direct line manager and infection control Practitioner/unit
- Minimize the time spent and entry to the patient room by cohorting the task together
- All PPE should be used for certain task with certain patient and should be removed and discarded before leaving the patient room except N95 will be removed immediately outside patient room
- In case of shortage of PPE, refer to WHO and CDC guidelines for extended use/reuse of PPE

Patient Care Equipment

- When possible use disposable devices or equipment.
- If disposables devices and equipment not an option, dedicate devices or equipment to a single patient
- If dedicated devices or equipment is not available, clean and disinfect the shared equipment before using it for other patients with approved disinfectant maintaining product contact time



- Approved disinfectant for COVID 19: quaternary ammonium compounds, sodium hypochlorite and 70% alcohol wipes

Patient Transport in the hospital

- Avoid the movement and transport of patients out of the isolation room or area unless medically necessary.
- The use of designated portable X-ray, ultrasound, echocardiogram and other important diagnostic machines is recommended when possible.
- If transport is unavoidable, the following should be observed:
 - Patients should wear a surgical mask during movement to contain secretions.
 - Use routes of transport that minimize exposures of staff, other patients, and visitors.
 - Notify the receiving area of the patient's diagnosis and necessary precautions before the patient's arrival.
 - Ensure that healthcare workers (HCWs) who are transporting patients wear appropriate PPE if they will participate in direct patient care and perform hand hygiene afterward.
 - Area used by the patient/wheelchair to be cleaned appropriately after patient's transfer.

Patient Transport to another facility:

- Inform the other facility about referring a suspected/confirmed case
- Call ambulance and inform about the case being suspected/confirmed COVID 19, which will be transferred in designated ambulance
- If hospital ambulance used ensure that ambulance will be cleaned and disinfected based on hospital guide
- If ambulance personnel will come in contact with the patient, they should wear appropriate PPE.

Additional Measures

- Dedicate HCWs and limit the number of persons present in the room to the absolute minimum required for the patient's care and support
- Limit visitors entering the room to the minimum necessary.
- Keep log sheet of all persons coming in contact with the suspected/confirmed COVID 19 patients
- Exclude immunocompromised, pregnant, non-competent staff from the care of suspected/confirmed COVID 19 patients



Aerosol- generating procedures

Below are most common Aerosol- generating procedures:

- Cardiopulmonary resuscitation
- Intubation
- Extubation
- High flow nasal oxygen
- Non-Invasive ventilation: BiPAP/CPAP
- Open suction
- Ambu Bagging
- Bronchoscopy
- Tracheostomy
- Upper GI endoscopy
- Dental Procedures
- Nebulizer therapy
- Sputum induction

Environmental cleaning in isolation rooms/areas

- Ensure that environmental cleaning and disinfection procedures are followed consistently and correctly
- Increase frequency of cleaning by housekeeping in patient care areas especially high touch surfaces (door handle, call bell, patient side rails ...etc.)
- Isolation areas should have their own cleaning supplies that are separate from clean patient care areas and are kept in or near isolation area
- Responsible housekeeping staff should be trained and educated with regard to cleaning method and technique, donning and doffing of PPE, spill management, dealing with occupational exposure ...etc.)
- Cleaners/housekeeping should wear appropriate PPE when cleaning an isolation room or area
- All waste from the isolation area is considered contaminated and should be disposed of following your facilities methods for contaminated waste use Virkon or sodium hypochlorite for regular cleaning while patient is in the isolation room.
- After patient is discharged, use terminal cleaning with fumigation with accelerated hydrogen peroxide 6% or use UVC, time and cycles adjusted per room size and shape.

Linen and laundry management, food service utensils and waste management, related to COVID19 case

Refer to the facility guideline/ protocol for waste management, to be dealt with as infectious material



Managing Suspected /Confirmed case in Operation Theater

- Postpone elective operations immediately.
- Only emergency or medically necessary surgery should be performed
- Designate a specific operating theater for all COVID-19 cases. This room should be out of high-traffic areas and be completely emptied of all non-essential materials. When an anteroom is available, this should be used as an area for donning and doffing of personal protective equipment and exchange of equipment, medications and materials for the case.
- Use of personal protective equipment is recommended by the Centers for Disease Control for every operative procedure performed on a patient with confirmed COVID-19 infection or a patient where there is suspicion for infection.
- N95 respirators or respirators that offer a higher level of protection should be used when Performing, or present for, an aerosol-generating procedure (e.g. OR patient intubation) in COVID-19 or suspected infected patient.
- All traffic in and out of the operating theater should be minimized. A runner or support staff should be dedicated to the Operating Theater to provide all materials needed throughout the case with exchanges performed using a material exchange cart placed immediately outside of the room or in the anteroom.
- Procedures should be performed by senior and experienced staff to minimize procedure time.

Performing intubation and/or extubation in Operating Room (OR):

- Ideally intubate patients in an Airborne Infection Isolation Room (All) room and then transfer them to the positive pressure OR (once intubated they are considered low risk because it is a closed system). Also consider transferring the patient to an All room for extubation.
- If not possible, a portable high-efficiency particulate air (HEPA) filtration unit may be used by positioning the unit near the patient's breathing zone.
- Switching the portable unit off during the surgical procedure.
- Only essential personnel wearing respiratory protection, such as an N95 respirator or PAPR, should be in the OR when intubation and extubation occur
- A bacterial filter that filters particles 0.3 μm in size and has a filter efficiency of >95 percent should be placed on the patient's anesthesia breathing circuit at the endotracheal tube or expiratory side of the circuit. The entire circuit should be changed after the surgery is completed

After the procedure:

- The patient should be recovered in the operating theatre with dedicated staff until they can be transferred to an isolation room on the ward or in the intensive care unit.
- Adequate air exchanges should occur before environmental services enters the room for cleaning. With 15-20 air exchanges it will be around 30 minutes.



Managing bodies in the Mortuary

- Although no post-mortem transmission of COVID 19 has been documented, deceased bodies theoretically may pose a risk when handled by untrained personnel.

Preparing and packing the body for transfer from a patient room to mortuary

- The health worker attending to the dead body should follow standard precaution such as perform hand hygiene, ensure proper use of PPE (water resistant apron, goggles, N95 mask, gloves).
- All tubes, drains, and catheters on the dead body should be removed. Any puncture holes or wounds (resulting from removal of catheter, drains, tubes, or otherwise) should be contained with dressing.
- Keep both the movement and handling of the body to a minimum;
- There is no need to disinfect the body before transfer to the mortuary area
- Place patient in leak-proof plastic body bag (Cadaver bags) and those handling the body at this point should use PPE (surgical mask, clean gloves, and isolation gown).
- If the family of the patient wishes to view the body at the time of removal from the isolation room or area, they may be allowed to do so with the application of **Standard Precautions and should wash hands thoroughly with soap and water after the viewing.**
- **Give the family clear instructions not to touch, kiss or hug the body, Adults >60 years and immunosuppressed persons should not directly interact with the body**
- Morgue's staff should be informed about infectious status of the deceased, risk of infection and appropriate precautions required before transferring the patient to mortuary and should be well trained on standard precaution and infection control measure.
- Limit the number of Mortuary staff handling COVID dead body to limit the exposure
- No special transport equipment or vehicle is required. The trolley carrying the body must be disinfected after transmission with approved disinfectant (with 1% Hypochlorite solution, quarterly ammonium chloride ...etc)
- Dead bodies should be stored in cold chambers maintained at approximately **4°C**
- The mortuary must be kept clean. Environmental surfaces, instruments and transport trolleys should be properly disinfected

Preparing and transferring the body from mortuary to Graveyard



- The body is prepared for burial in mortuary department of the healthcare facility as its forbidden to transport it to the home and it is only allowed to move it to public washing places with trained and competent people with appropriate equipment to deal with the dead bodies of infectious diseases.
- Limit the number of people washing the body
- All personal performing the body wash should be competent and should wear appropriate PPE (gloves, mask, gown and face shield) and should thoroughly wash their hands with soap and water when finished
- Instruct the family to avoid large gathering at the burial ground it should limited to close family contacts
- The belongings of the deceased person do not need to be burned or otherwise disposed of. However, they should be handled with gloves and cleaned with a detergent followed by disinfection with a solution of at least 70% ethanol or 0.1% (1000 ppm) bleach, Clothing and other fabric belonging to the deceased should be machine washed with warm water at 60–90°C (140–194°F) and laundry detergent
- After removing the body, the mortuary fridge, door, handles and floor should be cleaned with approved disinfectant such as 1% Hypochlorite solution
- The vehicle, after the transfer of the body must be decontaminate

Surveillance

- Develop a database containing information for all suspected/confirmed case who were/are assessed at your facility.
- Develop a database containing information for all healthcare workers and visitors that were in contact /caring for the confirmed cases of COVID 19

Surge capacity

- Develop an emergency response plans to provide surge capacity, the plan should include human resources; staffed beds, ICU and non-ICU beds; critical equipment, supplies and other resources, including extra quantities of personal protective equipment, ventilators, ECMO machines, etc...).



Guidance for Extended Use, Limited Reuse and decontamination of N95 Respirators during Pandemic

Disposable filtering facepiece respirators (FFRs) are not approved for routine decontamination and reuse as standard of care. However, FFR decontamination and reuse may need to be considered as a crisis capacity strategy to ensure continued availability.

As supplies of N95 respirators can become depleted during a pandemic or wide-spread outbreak of other infectious respiratory illnesses. Combination of approaches to conserve supplies are recommended, while safeguarding health care workers in such circumstances. These existing guidelines recommend that health care institutions:

- Prioritize the use of N95 respirators for **aerosol generating procedure only** and
- Minimize the number of individuals who need to use respiratory protection through the preferential use of engineering and administrative controls (**limit number of personal dealing with patient, cohorting the task of patient care Assigning designated teams of HCP...etc.**)
- Prioritize the use of N95 respirators for those personnel at the highest risk of contracting or experiencing complications of infection.
- Use alternatives to N95 respirators (e.g., other classes of filtering facepiece respirators, elastomeric half-mask and full facepiece air purifying respirators, powered air purifying respirators) where feasible;
- N95 respirators must only be used by a single wearer, prevent inadvertent sharing of respirators.
- All staff should be trained in proper technique of extended use of the mask such as (**removing, storing and re-wearing it**)

1. Definitions

1.1 Extended use: - refers to the practice of wearing the same N95 respirator for repeated close contact encounters with several patients, without removing the respirator between patient encounters. Extended use may be implemented when multiple patients are infected with the same respiratory pathogen and patients are placed together in dedicated waiting rooms or hospital wards.

1.2 Reuse: - refers to the practice of using the same N95 respirator for multiple encounters with patients but removing it ('doffing') after each encounter. The respirator is stored in between encounters to be put on again ('donned') prior to the next encounter with a patient.



2. Respirator Extended Use Recommendations

2.1 Discard N95 respirators

If contaminated with blood, respiratory or nasal secretions, or other bodily fluids from patients

- If used during aerosol generating procedures without face shield
- close contact with, or exit from, the care area of any patient co-infected with an infectious disease requiring contact precautions
- Obviously damaged or becomes hard to breathe through.

2.2 Consider use of a cleanable face shield (preferred) over an N95 respirator and/or other steps (e.g., masking patients, use of engineering controls), Or surgical mask if face shield is not available, when feasible, to reduce surface contamination of the respirator

2.3 Minimize unnecessary contact with the respirator surface, strict adherence to hand hygiene practices, and proper PPE donning and doffing technique, including physical inspection and performing a user seal check.

2.4 Mask can be **re-use up to 5 times, no longer than 8 hours** and **decontaminated not more than** manufactural recommendation and sterilization method

2.5 Ensure that the mask maintains its **fitness after decontamination**.

2.6 All supplies of N95 respirators should be stored in locked or secured, designated areas (ex. Unit Manager) and will be issued to staff with an appropriately handled paper bag or container that allows breathability.

2.7 N95 respirators **must only** be used by a single wearer, prevent inadvertent sharing of respirators.

3. Instruction of reuse the N95 Mask

3.1 Keep used respirators in a designated storage area or keep them in a clean, breathable container such as a paper bag between uses. To minimize potential cross-contamination, store respirators so that they do not touch each other and the person using the respirator is clearly identified. Storage containers should be disposed of or cleaned regularly.

3.2 Pack or store respirators between uses so that they do not become damaged or deformed.

3.3 Avoid touching the inside of the respirator. If inadvertent contact is made with the inside of the respirator, discard the respirator and perform hand hygiene.

3.4 Use a pair of clean (non-sterile) gloves when donning a used N95 respirator and performing a user seal check. Discard gloves after the N95 respirator is donned and any adjustments are made to ensure the respirator is sitting comfortably on your face with a good seal.

3.5 Strictly adhere to proper hand hygiene practices, and proper PPE donning and doffing technique.

4. Decontamination of N95 mask

4.1 In Department Procedures

4.1.1 Collect Plasma Sterilization pouch from CSSD.

4.1.2 Before use label the N95 respirator and paper storage bag with the **user's name, department, number of use and date** to prevent reuse by another individual. Write name on mask where straps are attachment or on elastic straps of N95 mask and on plasma CSSD pouch



4.1.3 **Do not** decontaminate mask more than 2 times with STERRAD sterilizer or 10 times with Steris sterilizer or more frequent based on manufacture recommendation

4.1.4 You must wear full face shield over N95 mask to reduce risk of contamination especially if patient require Airborne and contact precaution such as COVID-19, varicella, etc.

4.1.5 Perform hand hygiene with soap and water or an alcohol-based hand sanitizer before and after touching or adjusting the respirator (if necessary, for comfort or to maintain fit).

4.1.6 Remove N95 mask carefully the front is potentially contaminated, so remove carefully by bending forward and using the elastic band.

4.1.7 After removing N-95, visually inspect for contamination, distortion in shape/form. If contaminated /wet, creased or bent, N95 should be discarded.



- 4.1.8** If the facemask is not visibly contaminated or distorted, carefully store in prepared CSSD pouch and seal with sterilization indicating tape to avoid destroying the shape of the mask place the pouch in designated CSSD container that with led cover in dirty utility room
- 4.1.9** Send it to CSSD decontamination Room.
- 4.1.10** Clean and disinfect the storage box.

5. In CSSD Department

- 5.1** Wear appropriate PPE (mask, gloves)
- 5.2** Receive N95 Mask boxes by the CSSD staff and keep in dedicated trolley.
- 5.3** inspect receiving mask of visible damage and soil/contamination (e.g. blood, dried sputum, soil, bodily fluids).
- 5.4** Any N95 respirator whose traceability was lost or number of decontamination cycles not able to be identified should be discarded.
- 5.5** Decontaminated the mask based on manufactural recommendation of your N95 mask.



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45. <https://clinicaltrials.gov/ct2/results?cond=COVID&term=vitamin+C&cntry=&state=&city=&dist=>
46. <https://clinicaltrials.gov/ct2/results?cond=covid19&term=vitamin+D&cntry=&state=&city=&dist=>
47. <https://www.recoverytrial.net/news/low-cost-dexamethasone-reduces-death-by-up-to-one-third-in-hospitalised-patients-with-severe-respiratory-complications-of-covid-19>
48. <https://www.recoverytrial.net/news/no-clinical-benefit-from-use-of-lopinavir-ritonavir-in-hospitalised-covid-19-patients-studied-in-recovery>
49. [https://www.ijidonline.com/article/S1201-9712\(20\)30534-8/fulltext](https://www.ijidonline.com/article/S1201-9712(20)30534-8/fulltext)

Appendix I: Proper Use of PPE

COVID-19 Personal Protective Equipment (PPE) for Healthcare Personnel

Preferred PPE – Use N95 or Higher Respirator



Acceptable Alternative PPE – Use Facemask

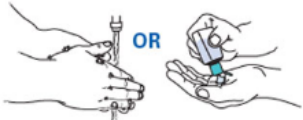
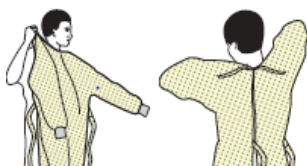





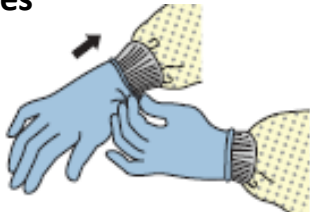
CS 110618-C, 06/25/2020

cdc.gov/COVID19

Donning Personal Protective Equipment (PPE)

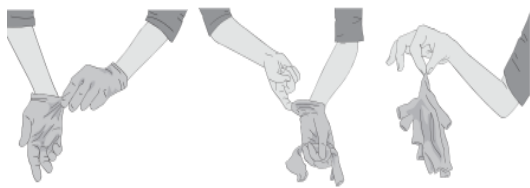
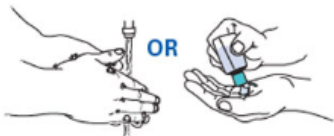

The following PPE sequence is specific to the situation requiring **Standard, Contact, and Airborne precautions.**

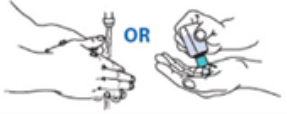



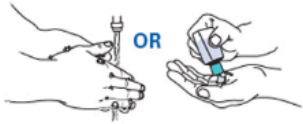

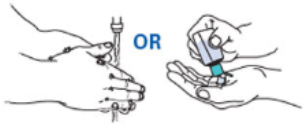
Step	Coaching Sequence	Observed
1. Hand Hygiene 	1. Perform hand hygiene following WHO steps.	<input type="checkbox"/>
2. Gown 	1. Fully cover torso from neck to knees, arms to end of wrists, and wrap around the back. 2. Fasten gown by tying at the waist.	<input type="checkbox"/> <input type="checkbox"/>
3. Put the Head Cover 	1. Caps coverings must cover all hair, and jewellery must be removed or contained within the head.	<input type="checkbox"/>
4. N95 Mask  <p>Perform a user seal Check</p>	2. Cup the respirator in your hand with the nosepiece at fingertips, allowing the head straps to hang freely below hand. 3. Position the respirator under your chin with the nosepiece up while holding the respirator in place, pull the top strap over your head. 4. While continuing to hold the respirator firmly in place, pull the bottom strap over your head and position it below your ears. Untwist the straps. Position the respirator low on your nose. 5. Using both hands, mold the nosepiece to the shape of your nose by pushing inward while moving your fingertips down both sides of the nosepiece. 6. <u>PERFORM A USER SEAL CHECK:</u> Place both hands completely over the respirator, being careful not to disturb the position, and exhale sharply. If air leaks around your nose, adjust the nosepiece as described in step 5. If air	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>

	leaks at respirator edges, adjust the straps back along the sides of your head.	
5. Face Shield 	1. Place over face and eyes and adjust to fit.	<input type="checkbox"/>
6. Wear Gloves 	1. Wear the appropriate size. Extend to cover wrist of isolation gown.	<input type="checkbox"/>

Doffing Personal Protective Equipment (PPE)

Standard, Contact, and Airborne precautions. Always assume that the outside of your gloves, mask, and face shield and the front and sleeves of your gown are contaminated. Use particular caution when maneuvering near your face. Remove all your PPE inside the patient room except N95 mask, it will be removed outside.

Step	Coaching Sequence	Observed
1. Removing the Gloves 	1. Inspect the gloves for any torn, tears or holes. 2. Using a gloved hand, grasp the palm area of the other gloved hand and peel off first glove. 3. Hold removed glove in gloved hand. 4. Slide fingers of ungloved hand under remaining glove at wrist and peel off second glove over first glove. 5. Discard gloves in a waste container.	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
2. Perform Hand Hygiene 	1. Perform hand hygiene following WHO steps and adhere to proper timing (count for 5 for each step)	<input type="checkbox"/>
3. Removing the Face Shield/googles 	1. Remove goggles or face shield from the back by lifting head band or ear pieces. 2. Discard face shield in an infectious waste container. 3. Decontaminate hands with alcohol-based hand sanitizer.	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>

<p>4. Perform Hand Hygiene</p> 	<p>1. Perform hand hygiene following WHO steps and adhere to proper timing (count for 5 for each step)</p>	<input type="checkbox"/>
<p>5. Safely remove contaminated personal protective gowns</p> 	<p>1. Unfasten ties 2. Pull away from neck and shoulders, touching inside of gown only 3. Turn gown inside out 4. Fold or roll into a bundle and discard</p>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
<p>6. Perform Hand Hygiene</p> 	<p>1. Perform hand hygiene following WHO steps and adhere to proper timing (count for 5 for each step)</p>	<input type="checkbox"/>
<p>7. Removing N95 Mask</p> 	<p>1. If anti room is available remove your N95 mask in anteroom if not available then discard immediately outside patient room. 2. Without touching the respirator, slowly lift the bottom strap from around your neck up and over your head. 3. Lift off the top strap. Do not touch the respirator 4. Discard the Mask in infectious Waste.</p>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
<p>8. Perform Hand Hygiene</p> 	<p>1. Perform hand hygiene following WHO steps and adhere to proper timing (count for 5 for each step).</p>	<input type="checkbox"/>
<p>9. Remove the head cover</p> 	<p>1. Remove the head cover from behind the head to front</p>	<input type="checkbox"/>
<p>10. Perform Hand Hygiene</p> 	<p>1. Perform hand hygiene following WHO steps and adhere to proper timing (count for 5 for each step).</p>	<input type="checkbox"/>

Appendix II: Flow diagram decision tool for conscious proning process



Figure 1 – Flow diagram decision tool for Conscious Proning process

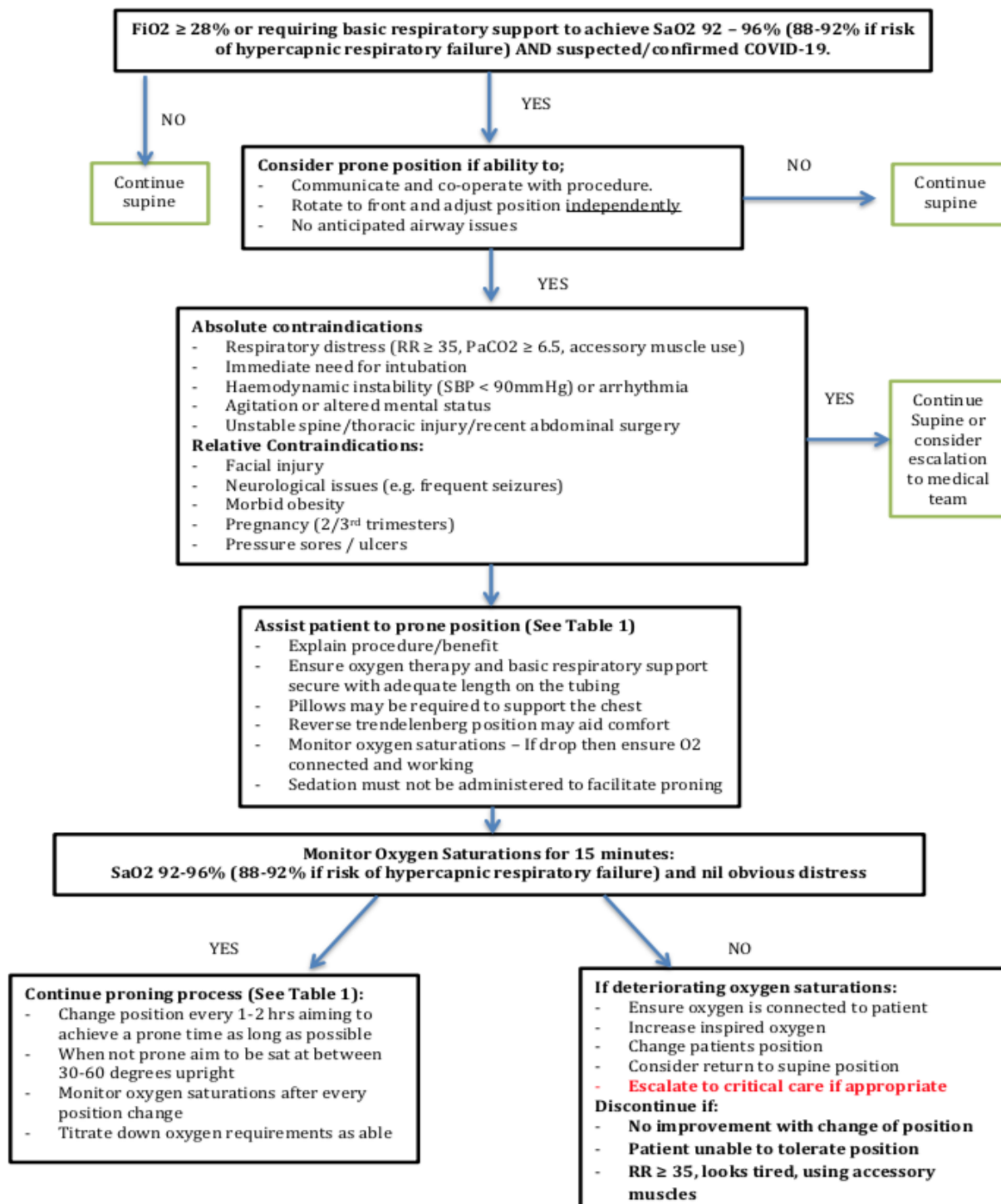


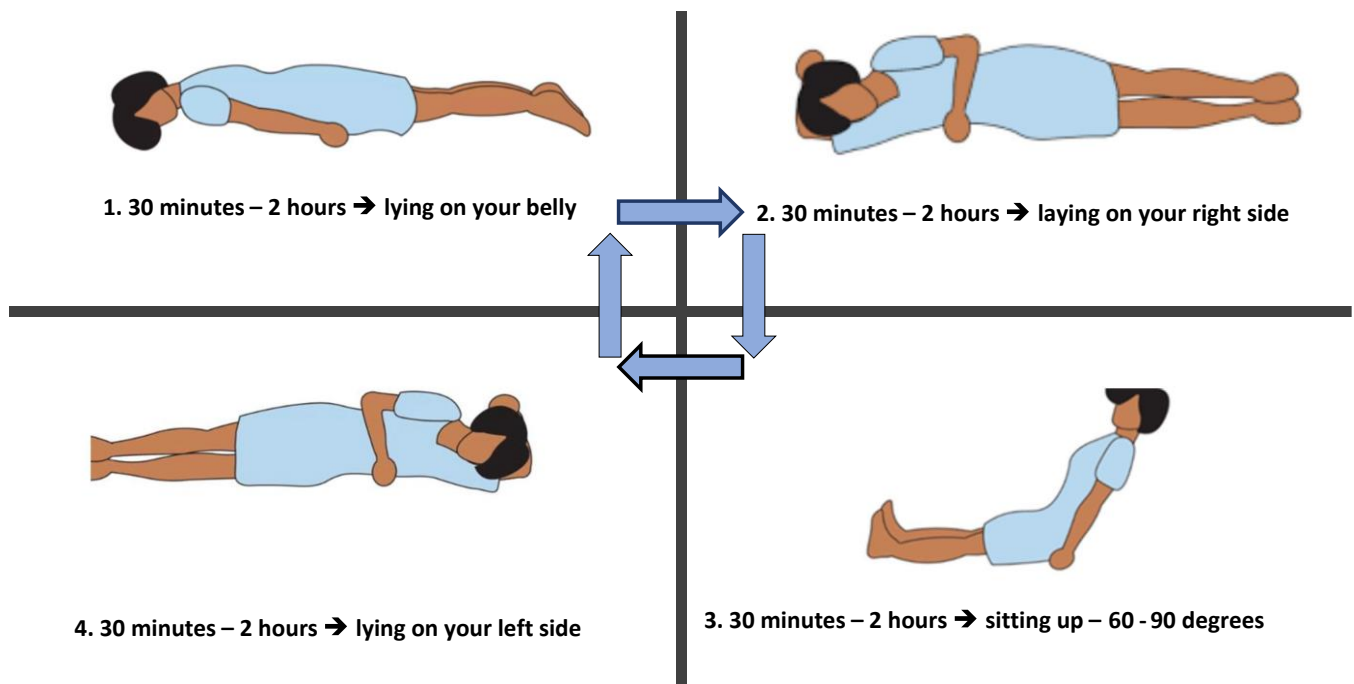
Table: Timed position changes for patients undergoing conscious proning process

Main prone position is lying on the belly, however, sometimes difficult to achieve so the other positions can help.

If patient fulfils criteria for proning ask the patient to switch positions as follows. Monitor oxygen saturations 15 minutes after each position change to ensure oxygen saturation has not decreased. Continue to monitor oxygen saturations as per the National Early Warning Score (NEWS)

- 30 minutes to 3 hours lying fully prone (bed flat)
- 30 minutes to 2 hours lying on right side (bed flat)
- 30 minutes to 2 hours sitting up (30-60 degrees) by adjusting head of the bed
- 30 minutes to 2 hours lying on left side (bed flat)
- 30 minutes to 3 hours lying prone again
- Continue to repeat the cycle

COVID Awake Repositioning/ Proning Protocol (CARP)





Appendix III:

Informed consent to treatment with INVESTIGATIONAL medication

This is a consent form. Its purpose is to inform you about risks and benefits when using a new INVESTIGATIONAL drug in the management of your condition (COVID- 19)

Treatment regimen could include one or more of the following drugs:

Treatment duration:

I, _____, understand that there is no approved FDA treatment yet for the treatment of my current Infectious Illness (COVID19 infection).

In view of the current lack of other safe and effective alternatives, I give my consent for being treated with above mentioned investigational drug/drugs by my managing team.

I acknowledge that possible common drug-related side effects have been explained to me.

Hospital name: -----

Physician name: _____ staff number: _____ signature: _____

Witness name: _____ staff number: _____ signature: _____

Patient's name (next of kin) name and signature: _____

Date/time: _____



الموافقة المسبقة على العلاج بالأدوية التجريبية

هذا نموذج موافقة. الغرض منه هو إبلاغك بالمخاطر والفوائد عند استخدام دواء تحقيقي جديد في إدارة حالتك (كوفيد-19).

يمكن أن يشمل نظام العلاج واحدًا أو أكثر من الأدوية التالية:

مدة العلاج:

أنا، _____، أفهم أنه لا يوجد علاج معتمد من إدارة الغذاء والدواء حتى الآن لعلاج مرضي المعدي الحالي (كوفيد-19).

في ضوء النقص الحالي في البدائل الأخرى الآمنة والفعالة، أُمِنح موافقتي على العلاج بالعقار/العقاقير التجريبية المذكورة أعلاه من قبل الفريق الطبي.

أقر بأن الأعراض الجانبية الشائعة المتعلقة بالعقاقير قد تم شرحها لي.

اسم المستشفى: _____

اسم الطبيب: _____ رقم الموظف: _____ التوقيع: _____

اسم الشاهد: _____ رقم الموظف: _____ التوقيع: _____

اسم المريض (أقرب الأقرباء) وتوقيعه: _____

التاريخ / الوقت: _____



Appendix: IV

Informed consent to treatment with OFF-LABEL medications

This is a consent form. Its purpose is to inform you about risks and benefits when using an OFF-LABEL drug in the management plan of your condition, covid-19 (SARS coV2 Infection)

Any of the following treatment regimen:

Hydroxychloroquine/chloroquine

Lopinavir-Ritonavir 2 tablets per oral daily every 12 hours

Interferon 1-B 180 microgram Subcutaneous once per week

Favipiravir 1600 mg twice a day for 1 day then 600 mg twice a day

Other treatment as indicated

Treatment duration:

5-10 days

I _____, understand that medication listed above are all FDA approved for other medical indications with proven safety and efficacy, and they are not approved yet for the treatment of my acute infectious illness (2019 Novel Corona Virus Infection).

In view of the current lack of other safe and effective alternatives, I give my consent for being treated with one or a combination of above drugs by my managing team.

I acknowledge that possible drug-related side effects have been explained to me (drug allergy, skin rash, mild anaemia, loose motions)

Hospital name:

Physician name:

staff number

signature:

Witness name:

staff number:

signature:

Patient's name (next of kin):

signature:

Date:

Time:



الموافقة المسبقة على العلاج بالأدوية لغير استخدامها المعتمد

هذا نموذج موافقة. الغرض منه هو إبلاغك بالمخاطر والفوائد عند استخدام دواء لغير استخدامها المعتمد في خطة إدارة حالتك (كوفيد – 19).

نظام العلاج:

Hydroxychloroquine/chloroquine

Lopinavir-Ritonavir حبة يومياً عن طريق الفم كل 12 ساعة

Interferon 1-B 180 ميكروغرام تحت الجلد مرة واحدة في الأسبوع

Favipiravir 1600 ملغ في اليوم الأول ثم 600 ملغ يومياً

أي علاج آخر تستدعيه حالتي

مدة العلاج:

10-5 يوم

أنا _____ ، أفهم أن الأدوية المذكورة أعلاه معتمدة من قبل هيئة الغذاء والدواء لمؤشرات طبية أخرى ذات سلامة وفعالية مثبتة، ولم تتم الموافقة عليها بعد لعلاج مرضي المعدي الحاد (كوفيد – 19).

في ضوء النقص الحالي في البدائل الأخرى الآمنة والفعالة، فأنا أعطي موافقتي على العلاج بواحد أو مجموعة من الأدوية المذكورة أعلاه من قبل الفريق الطبي.

أقر بأن الأعراض الجانبية المحتملة المتعلقة بالأدوية قد تم شرحها لي (حساسية، طفح جلدي، فقر دم خفيف، اسهال)

اسم المستشفى: _____

اسم الطبيب: _____ رقم الموظف: _____ التوقيع: _____

اسم الشاهد: _____ رقم الموظف: _____ التوقيع: _____

اسم المريض (أقرب الأقرباء): _____ التوقيع: _____

التاريخ: _____ الوقت: _____



Appendix: V- Home Quarantine Consent

Undertaken to implement the home quarantine procedure

I the under-designed, declare that I was notified about the health procedures and the medical advices that I should follow, and that I am aware of the risks that could happen to the society in case I am not committed to them, so for the sake of the public health and to avoid the legal accountability I hereby declare that I will not leave the house and I will consider not to get in contact with others as much as I can until the required health measures end , and the duration of the quarantine is --- days starting from _____ (decided by health authority)

This is my acknowledgment that I have been notified of the above mentioned.

Name: _____

Passport / ID No.: _____

Mobile number: _____

Home address: _____

Number of friend/sponsor/next of kin: _____

Email address: _____

Signature: _____

Date: ____/____/____

اقرار وتعهد بتنفيذ اجراءات الحجر الصحي

انا الموقع ادناه اتعهد بانه تم إبلاغي بالإجراءات الصحية والنصائح الطبية الواجب اتباعها، وإنني أدرك المخاطر التي من الممكن ان تلحق بالمجتمع في حال عدم التزامي، لذا حرصا على الصحة العامة وتجنب المسائلة القانونية اتعهد بعدم مغادرة المنزل مع مراعاة تجنب مخالطة الآخرين قدر الامكان حتى نهاية الاجراءات الصحية المطلوبة وفترة الحجر الصحي لمدة 7 يوما اعتبارا من تاريخ _____ (تحدده الجهة الصحية)

وذلك اقرارا مني بانه تم إخطاري بما ذكر اعلاه

الاسم: رقم الجواز / الهوية الوطنية:

رقم الهاتف المتحرك: عنوان المنزل:

رقم أحد الأقارب أو الكفيل: البريد الالكتروني:

التوقيع: التاريخ: / /



Appendix: VI

Instructions for HOME Quarantine for (COVID-19)	تعليمات الحجر الصحي المنزلي ل (كوفيد - 19)
<p>Self- isolation for the next --- days from the date of discharge from the hospital/clinic</p> <ol style="list-style-type: none"> Stay at home in a single room with separate washroom and separate yourself from other people in your home. If you share any facility at home, please make sure you disinfect it thoroughly after every use with warm water and detergent then dry your items with a separate towel that only you would use Don't go outside your room, unless its unavoidable and then wear a facemask Cover your mouth and nose when you cough or sneeze with tissue then dispose of it immediately in a sealed plastic bag Wash your hands frequently with soap and water for 20 seconds at least then dry them well and avoid touching your eyes, nose and mouth if you haven't washed your hands Avoid sharing household items Monitor your symptoms (Breathing difficulty, Fever, Sore throat, Cough, Runny nose, Headache) and check your temperature daily. (or the person you are caring for, as appropriate) Do not have visitors in your home If you have pets in the household, try to keep away from your pets. If this is unavoidable, wash your hands before and after contact. Waste management: All waste that has been in contact with the individual, including used tissues, and masks if used, should be put in a plastic rubbish bag and tied when full. The plastic bag should then be placed in a second bin bag and tied. If you need to visit your doctor, call ahead before visiting. 	<p>العزلة الذاتية للأيام الـ --- القادمة من تاريخ الخروج من المستشفى/ العيادة</p> <ol style="list-style-type: none"> ابق في المنزل في غرفة واحدة مع دورة مياه منفصلة وافصل نفسك عن الآخرين في منزلك إذا كنت تشارك أي مرفق في المنزل، يرجى التأكد من تطهيره جيداً بعد كل استخدام بالماء الدافئ والمنظف، ثم جفف أغراضك بمنشفة منفصلة تستخدمها أنت فقط لا تخرج خارج غرفتك، إلا إذا كان ذلك لا مفر منه ثم ارتدِ كمامة غط فمك وأنفك عند السعال أو العطس بالمنديل ثم تخلص منه فوراً في كيس بلاستيكي محكم الغلق اغسل يديك بشكل متكرر بالماء والصابون لمدة 20 ثانية على الأقل ثم جففها جيداً وتجنب لمس عينيك وأنفك وفمك إذا لم تغسل يديك تجنب مشاركة الأدوات المنزلية مع الآخرين راقب أعراضك (صعوبة التنفس، الحمى، التهاب الحلق، السعال، سيلان الأنف، الصداع) وافحص درجة حرارتك يومياً. (أو الشخص الذي تعتني به، حسب الاقتضاء) لا تستقبل الزوار في منزلك إذا كان لديك حيوانات أليفة في المنزل، حاول الابتعاد عن حيواناتك الأليفة. إذا كان ذلك لا مفر منه، اغسل يديك قبل وبعد الاتصال إدارة النفايات: يجب وضع جميع النفايات التي كانت على اتصال مع الفرد، بما في ذلك المناديل الورقية المستخدمة والأقنعة في حالة استخدامها، في كيس قمامة بلاستيكي وربطها عند امتلائها. يجب بعد ذلك وضع الكيس البلاستيكي في كيس آخر وربطه. إذا كنت بحاجة إلى زيارة طبيبك، اتصل مسبقاً قبل الزيارة.

If you develop any active complaints (fever, body aches, headache, cough, throat pain or shortness of breath) during home quarantine period, please contact one of the following numbers for advice:

- **8001717: The Operation Center, Department Of Health**
- **80011111: Ministry Of Health And Prevention**
- **800342: Dubai Health Authority**



Dosing & frequency mentioned is for normal renal & hepatic functions

For moderate to severe hepatic or renal impairment dosing, other drug interactions etc.

(Please consult the on-call pharmacist)

For further information on these medications please refer to the clinical pharmacist/pharmacist at your facility

Lopinavir/Ritonavir:

Lopinavir was shown to have in vitro activity against both SARS-CoV-1 and MERS-CoV in some studies.

A recent randomized, controlled, open-label trial assessed lopinavir-ritonavir (n=99) vs. standard of care (n=100) in SARS-CoV-2 patients showed that:

- Treatment with LPV/r was not associated with a difference in time to clinical improvement or mortality
- Randomization didn't occur until a median of 13 days after symptom onset however, so the window for benefit may have already closed.

Therefore, Lopinavir/Ritonavir should not be used as a monotherapy and to be used in mild to moderate confirmed cases not in severe cases.

Although all the protease inhibitors have precautions about worsening or causing liver toxicity, **Tipranavir** is the **only** protease inhibitor that carry a black box warning for potentially fatal hepatotoxicity and fatal and nonfatal intracranial hemorrhage.

Abnormal fat redistribution syndrome is a big concern, it consists of two distinct syndromes:

- 1- Lipohypertrophy, or central body fat accumulation characterized by a "dorsal fat pad," increased abdominal girth, and increased breast size in women, and
- 2- Lipoatrophy, or peripheral wasting of face, buttocks, and extremities.

Dosage Recommendations:

Adult: 800 mg lopinavir /200 mg ritonavir once daily.

Pediatric:

Weight: 15 to 20 kg 200 mg /50 mg bid

>20 to 30 kg 300 mg / 75 mg bid

>30 kg 400 mg / 100 mg bid

Dose adjustment:

Once daily is not recommended for pregnant women , children below 18 years of age, hemodialysis or patient taking enzyme inducing anticonvulsants (e.g., phenytoin, phenobarbital, carbamazepine). (Dividing the dose every 12 hours is preferred).

No dose adjustment requires for renal or hepatic impairment (Some degree of serum aminotransferase elevations may occur, could reach >5 times the upper limit of normal), however, it is a transient elevation, discontinuation of therapy is not required, as most patients recover spontaneously with continued treatment.

Administration:

Take the tablet with food swallow whole without crushing chewing or break. (Food can decrease GI side effects and increase

Tolerability).

Monitoring:

- A baseline of:
 1. Hepatitis B screening (surface antigen or antibody) and hepatitis C antibody.
 2. Fasting blood glucose or HbA1c. (Patients with a family history of diabetes mellitus may be at a greater risk, and demand a close monitoring).
 3. Fasting lipid profile. (For patient with cardiovascular risk or on estrogens or atypical antipsychotics or interferon alpha).
 4. ALT, AST, and total bilirubin. (Repeat after 2 weeks).
- Pregnancy test.

Common Side effects:

- Dyslipidemias and Lipodystrophy.
- Elevated liver enzymes. (Found in 3% to 10% of patients, although rates may be higher in patients with HIV or HCV coinfections).
- Increase blood glucose level.
- Gastrointestinal disturbances including: diarrhea, nausea and vomiting. (Before starting prescriber should take into his consideration manifestation of the disease (accompanied digestive symptoms) and rule out liver insufficiency).
- Headache
- QT prolongation $\leq 2\%$ of patients. (QT interval should be observed when is taken with other drugs that might induce QT prolongation).

Drug-Drug Interactions with other anti-covid-19:

Drug	Interaction	Recommendation
Chloroquine	Co-administration has not been studied. Lopinavir/ritonavir could potentially increase chloroquine exposure to a moderate extent due to the multiple elimination pathways.	No dosage adjustment is recommended for Chloroquine but monitor toxicity. Caution is advised when prescribing Lopinavir/ritonavir and medicinal products known to induce QT interval prolongation such as Chloroquine.

Chloroquine OR Hydroxychloroquine:

Chloroquine has a modest effect by itself but has synergistic effect when combined with selected antiretrovirals (such as: zidovudine and didanosine). These in-vitro results warrant in-vivo confirmation.

An expert consensus group out of China suggests that chloroquine improved lung imaging and shortened disease course.

Hydroxychloroquine was found to be more potent than chloroquine in inhibiting SARS-CoV-2 in vitro.

Dosage Recommendations:

The concentration of chloroquine in the plasma reached 10 μ M when a daily intake of 500 mg was prescribed. Researchers found that to inhibit SARS-CoV replication by 99% three days postinfection, 16 μ M chloroquine was needed, therefore the required daily dose is **500 mg bid chloroquine phosphate**.

Hydroxychloroquine sulfate a loading dose of 400 mg twice daily day 1, followed by a maintenance dose of 200 mg twice daily for 5-7 days.

Administration:

Administer with meals to decrease GI upset.

Monitoring:

- A baseline of:

1. Discontinue and avoid all other non-critical QT prolonging agents.
2. Assess a baseline ECG, renal function, hepatic function, serum potassium and serum magnesium.
3. When possible, have an experienced cardiologist/electrophysiologist measure QTc, and seek pharmacist input in the setting of acute renal or hepatic failure.
4. CBC
5. G6PD level

- **Ongoing:**

1. Place on telemetry prior to start of therapy
2. Monitor and optimize serum potassium daily.
3. Acquire an ECG 2-3 hours after the second dose of hydroxychloroquine, and daily thereafter.
4. If QTc increases by >60 msec or absolute QTc >500msec (or >530-550 msec if QRS >120 msec), discontinue azithromycin (if used) and/or reduce dose of hydroxychloroquine and repeat ECG daily.
5. If QTc remains increased >60 msec and/or absolute QTc >500 msec (or >530-550 msec if QRS >120 msec), reevaluate the risk/benefit of ongoing therapy, consider consultation with an electrophysiologist, and consider discontinuation of hydroxychloroquine.

Common Side effects:

Cardiovascular: Atrioventricular block, bundle branch block, cardiac arrhythmia, cardiomyopathy (mostly with prolonged use), ECG changes (including prolonged QRS and QTc intervals) if administered in combination with other QTc-prolonging agents such as azithromycin, metoclopramide, ondansetron, haloperidol, quetiapine ...etc)

Endocrine metabolic: Hypoglycemia

Gastrointestinal: Abdominal cramps, anorexia, diarrhea, nausea, vomiting.

Central nervous system: Agitation, anxiety, confusion, decreased deep tendon reflex, delirium, depression, extrapyramidal reaction.

Ophthalmic: Disorder of macula of retina, Retinal disorder.

Drug-Drug Interactions with other anti-covid-19:

Drug	Interaction	Recommendation
Lopinavir/Ritonavir	Co-administration has not been studied. Lopinavir/ritonavir could potentially increase chloroquine exposure to a moderate extent due to the multiple elimination pathways.	No dosage adjustment is recommended for Chloroquine but monitor toxicity. Caution is advised when prescribing Lopinavir/ritonavir and medicinal products known to induce QT interval prolongation such as Chloroquine.

Remdesivir:

It is an experimental broad-spectrum antiviral agent, which was synthesized and developed in 2017 as a treatment for Ebola virus infection.

In-vitro studies showed that remdesivir can inhibit coronaviruses such as SARS-CoV and MERS-CoV replication, and against SARS-CoV-2.

Preclinical randomized, controlled, double blind trials are conducted to evaluate the efficacy and safety of remdesivir in patients with moderate and severe COVID-19 respiratory disease.

Dosage Recommendations:

The dose which is used in these trials is 200 mg loading dose on day 1 followed by 100 mg once-daily for 9 days. Which is the same dose which was used before in Ebola Virus 2019 trial.

Administration:

IV infusion.

Monitoring:

- A baseline of:
 1. CBC
 2. Renal and liver functions

Common Side effects:

- Hypotension, anaphylactic shock, diarrhea, constipation, nausea and vomiting.
- Elevated liver function tests (AST, ALT), phlebitis and headache.
- Remdesivir is co-formulated with sulfobutyl ether β -cyclodextrin (SBECD), so there is a theoretical risk of accumulation in renal failure promoting further renal injury, similar to intravenous voriconazole. Especially if creatinine clearance is < 50 ml/minute

Drug-Drug Interactions with other anti-covid-19:

No interaction documented so far.

Favipiravir

A novel pyrazine derivative, an inhibitor of influenza RNA dependent RNA polymerase that is active against influenza A, B, and C viruses, including oseltamivir-resistant variants.

A prospective study was conducted in 2019 to compare the clinical effectiveness of combined favipiravir and oseltamivir therapy versus oseltamivir monotherapy in critically ill patients with influenza virus infection.

In this small study the results showed that the combination therapy can accelerate the recovery compared to oseltamivir alone.

In Vitro Favipiravir showed significant activity against a huge range of RNA viruses including rabies and influenza viruses.

A study of Ebolavirus-infected mice showed that favipiravir treatment reduced viral loads and improved survival. A clinical trial in which all patients with Ebolavirus infection were given favipiravir (6 g initially; then 2.4 g daily) showed a decrease in Ebolavirus RNA by 0.3 log₁₀/day. **QT interval prolongation is a concern with this high dose** ,furthermore, the dose of 6 g loading requires 30 tablets which deems difficult to swallow.

Dosage Recommendations:

The dose regimens assessed in the combination trial were based on the approved favipiravir regimen in Japan (two 1600 mg oral loading doses on day 1, followed by 600 mg twice daily (BID) on days 2–5) and on the higher one (1800 mg BID on day 1 followed by 800 mg BID thereafter) tested in randomized, placebo-controlled phase 3 treatment trials outside of Japan.

Clinical use of up to 3.6g on first day followed by 800mg twice daily can be considered safe according to the WHO guidelines for ebola treatment.

The recommended dose by WHO for covid-19 is 1600 mg BID loading then 600 mg TID for 5-7 days.

Administration:

Orally.

Monitoring:

- A baseline of:
Liver functions. (Repeat after 1 week).

Common Side effects:

Transient elevation in serum alanine aminotransferase.

QT prolongation with high doses or if administered in combination with other QTc-prolonging agents such as chloroquine, hydroxychloroquine, azithromycin, metoclopramide, ondansetron, haloperidol, quetiapine ...etc)

Drug-Drug Interactions with other anti-covid-19:

Drug	Interaction	Recommendation
Paracetamol	Potential increase of paracetamol level by 14-16%	Observe liver function closely, if elevated reduce paracetamol dose.

Interferon alpha

In a 2013 systematic review there was only one randomized controlled trial compared ribavirin with interferon-1a which showed no advantage of ribavirin over interferon in patients with SARS. In addition, there were observational studies comparing Interferon-1a with untreated controls. Interferon led to improvements in clinical and laboratory parameters compared with control patients.

However, there was no standard regime used and adverse events were not well documented.

Dosage Recommendations:

Adults: Starting with 9mcg/daily for at least 2 days, then 15 mcg/daily if no response for 8-13 days. (subcutaneously).

Pediatric: 2–4 mcg/kg in 2 mL sterile water, twice daily for 5–7 days (Nebulization).

Administration:

Subcutaneous injection

Nebulization

Monitoring:

- A baseline of:

(Repeat during therapy if clinically indicated): Chest x-ray, serum creatinine, albumin, prothrombin time, triglycerides.

CBC, liver function, renal function, electrolytes and TSH, ophthalmic exam, ECG (in patients with pre-existing cardiac abnormalities or in advanced stages of cancer). (repeat liver function after 2 weeks).

Common Side effects:

- Central nervous system: Fatigue, headache, chills, rigors, depression, drowsiness, dizziness, vertigo, irritability.
- Gastrointestinal disturbances including: diarrhea, nausea and vomiting.
- Hematology: Neutropenia, granulocytopenia, leukopenia, anemia, thrombocytopenia.
- Elevated liver enzymes
- Neuromuscular & skeletal: Myalgia
- Flu-like symptoms

Drug-Drug Interactions with other anti-covid-19:

Drug	Interaction	Recommendation
Tocilizumab and Sarilumab	Bone marrow suppression	Avoid these drugs for at least 3 day after INF administration

Tocilizumab and Sarilumab

IL-6 inhibitors are FDA approved for cytokine release syndrome complications related.

IL-6 and ferritin levels elevation is reported to correlate with severe COVID-19 cases.

Retrospective reviews in patients with rheumatological disease suggest a possible increase in serious bacterial infection, so use caution if secondary infection is clinically suspected.

Dosage Recommendations:

Tocilizumab: 4-8mg/kg (suggested dose 400 mg) IV x1. Dose may be repeated 12 hours later if inadequate response to the first dose. The total dose should be no more than 800 mg per dose. Tocilizumab should not be administered more than twice.

Sarilumab 200 – 400 mg single dose.

Administration:

Intravenous infusion. (To be infused over 60 minutes). (For further details about IV preparation please call the pharmacist).

Monitoring:

- A baseline of:
 1. Latent TB
 2. CBC
 3. Liver enzymes.
 4. Lipid profile.
 5. Ferritin, IL-6 & CRP

Common Side effects:

- Elevated liver enzymes.
- Infusion reaction.
- Hypercholesterolemia.
- Neutropenia.

Drug-Drug Interactions with other anti-covid-19:

No interaction documented so far.

Camostat

A serine protease inhibitor which was displayed antiviral activity in a pathogenic animal model for SARS-CoV1 infection.



It inhibits the enzymatic activity of cell-surface proteases involved in coronavirus activation. and the resultant production of inflammatory cytokines possibly through inhibition of transmembrane proteases activities.

Dosage Recommendations:

200 mg TID and adjust upon response

Administration:

Oral with meal.

Monitoring:

- A baseline of:
 1. CBC
 2. Liver enzymes.
 3. Electrolytes.
 4. Ferritin & CRP

Side effects:

- Rarely GI disturbances & elevated liver enzymes

Drug-Drug Interactions with other anti-covid-19:

No interaction documented so far.

Zinc

Multiple meta-analyses and pooled analyses of randomized controlled trials (RCTs) have shown that oral zinc supplementation reduces the incidence rate of acute respiratory infections by 35%, shortens the duration of flu-like symptoms by approximately 2 days, and improves the rate of recovery.

The mechanisms by which zinc alters human susceptibility to acute lower respiratory infection likely include the regulation of pro-inflammatory cytokine secretion, lymphocyte proliferation, T lymphocyte function and protection of the integrity of respiratory epithelial cells in the setting of acute inflammatory lung injury.

Dosage Recommendations:

100 mg elemental zinc daily.

Administration:

Administer 1 hour after meal.



Side effects:

- Rarely GI disturbances & elevated liver enzymes

Drug-Drug Interactions with other anti-covid-19:

No interaction documented so far.

Vitamin C (Ascorbic acid)

It acts as an antioxidant, limiting inflammation and tissue damage associated with immune response.

In six trials, orally administered vitamin C in doses of 1–3 g/day reduced the length of ICU stay by 8.6% and in three trials shortened the duration of mechanical ventilation by 18.2%.

Currently a trial using for high-dose IV vitamin C in COVID-19 patients in China is conducted and slated to be complete in the fall of 2020.

Dosage Recommendations:

Oral or IV 1-3 g daily. (For more details about IV preparation please call the pharmacist).

Administration:

Administer orally with food.

Common Side effects:

Hyperoxaluria (with high dose)

Drug-Drug Interactions with other anti-covid-19:

No interaction documented so far.

APPENDIX VIII

WHO case definition for SARS-COV-2 related multisystem inflammation

Children and adolescents 0 – 19 years of age with fever > 3 days AND two of the following:

1. Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).
2. Hypotension or shock.
3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
4. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
5. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

AND

Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin.

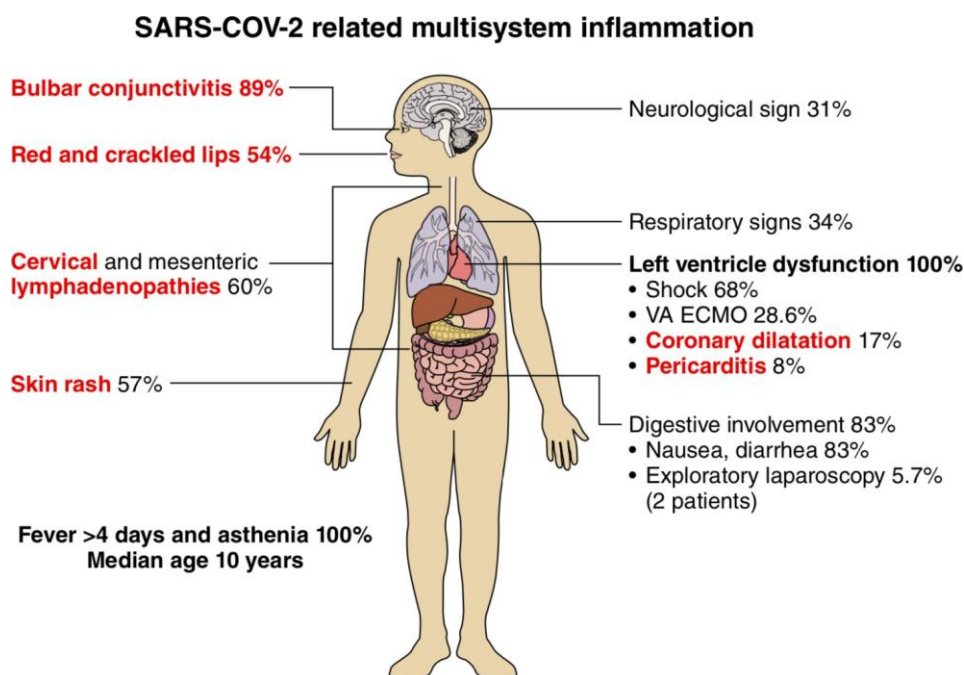
AND

No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.

AND

Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19

Schematic representation



Adapted from Belhadjer et al. Circulation.