Covid -19 Management Protocol - Narayana Health (25th May 2021)

For a patient with:

- RT-PCR or Trunat or CB-NAAT or Rapid Antigen Test confirmed Covid-19 infection or
- strong clinical suspicion, CT of Corads 5, in the absence of a positive RT-PCR (Covid syndrome)

Step 1:

First determine the severity of the illness using the following table.

	MILD	MODERATE	SEVERE
Clinical Criteria			
SpO2	> 94 % on Room Air	90 - 94 % on Room Air	< 90 % on Room Air PaO2/FiO2 <300 mm Hg
RR (/min)	< 24	24 – 30	> 30
Symptoms	Fever +/-	Fever plus breathing difficulty	Fever with respiratory distress
Other symptoms	Symptoms often include extra-pulmonary symptoms such as vomiting and diarrhoea, conjunctivitis, backache, neurological symptoms. A fairly constant feature is disproportionate fatigue		
Chest Xray (evaluate 3 zones in each lung upper, mid and lower zones)	Normal	Pneumonia involving 1 or two zones	Pneumonia involving more than 2 zones
CT Chest Criteria (A CT thorax is NOT needed for all patients)			
CT Severity Score (out of 25 or % lung involvement	≤ 8/25 or ≤ 25%	8-15/25 or 26-50%	> 15/25 or > 50%
Laboratory Findings			
NLR	< 3.2	3.2 - 5.5	>5.5
CRP	< 20	> 40	>40
Ferritin	<500	500-800	> 800
D-dimer	<0.5	0.5-1.0	> 1.0
LDH	<300	300 – 400	> 400
IL6	< 5.0	5 – 50	> 50, or rising
LFT	**Normal**	Slight Derangement	Moderate Derangement
Cut-offs for each of these are unclear and changing. The NLR appears less reliable during the second wave. However for all values, the greater the numerical value, the greater the risk of adverse outcomes			

<table>
<tr><th>Step 2: Choose the treatment</th><th colspan="3">TREATMENT</th></tr>
<tr><th></th><th>MILD</th><th>MODERATE</th><th>SEVERE</th></tr>
<tr><td colspan="4">Important: Apart from steroids in patients with hypoxia, all other treatments are not supported by robust evidence and not recommended in the official guidelines. They may shorten the course of illness but may offer no mortality benefit. Our group majority opinion is that the risk benefit ratio favours using the medication, if used early, but this opinion is not unanimous.</td></tr>
<tr><td rowspan="3">Symptomatic and supportive care</td><td colspan="3">T. Paracetamol 650 mg QID; in high fever not settling can give 1 gm Q8H; DO NOT exceed 3 g/day. NB: Caution in persons with liver dysfunction</td></tr>
<tr><td colspan="3">Anti-tussives SOS
Vitamin C 500 mg OD or 2 weeks
T. Zinc 50 mg BD for 2 weeks
Vit D 2000 units once daily or 60000 IU once weekly for 4-8 weeks</td></tr>
<tr><td colspan="2">Consider Sucralfate
or oral Esomeprazole 40 mg OD, if symptomatic</td><td>Inj. Pantoprazole 40 mg IV OD; titrate up or down depending on symptoms and response</td></tr>
<tr><td>Fluids</td><td colspan="2">Adequate but conservative hydration - oral or parenteral</td><td>Conservative Fluids</td></tr>
<tr><td>Antivirals

Ideally start within first 7 days <u>after symptom onset.</u>

<u>Delayed use has no benefit</u>

Consider collecting the data for a trial</td><td><u>OPTIONAL</u>

DOXYCYCLINE 100mg BD for 5 days
+
IVERMECTIN 12mg OD for 3-5 days

or
Antibody CASIRIVIMAB + IMDEVIMAB (must be started within 3 days of test or 5 days of symptom onset, whichever is earlier. Indicated only if there is no hypoxia)</td><td colspan="2">• Inj REMDESIVIR
‣ 200 mg IV on day 1 followed, by 100 mg IV daily for 4 days (total 5 days)</td></tr>
<tr><td><u>Antibiotics</u></td><td colspan="3">Avoid unless a bacterial infection is likely; can be prescribed with expert consultation</td></tr>
</table>

Step 2: Choose the treatment	TREATMENT		
	MILD	**MODERATE**	**SEVERE**
Anticoagulation Contraindicated in ESRD, active bleeding, emergency surgery, platelets < 20,000/, BP > 200/120	**If at high risk for thrombo-embolism:** Apixaban (Eliquis) 2.5 mg BD **Alternatively:** Tab Aspirin 75 mg (or clopidogrel 75/ mg)	Inj. Enoxaparin 1 mg/kg SC OD or Tab Apixaban (Eliquis) 2.5 mg BD or Tab Dabigatran 110 mg BD In ESRD, Unfractionated Heparin – 5000U SC BD	Inj. Enoxaparin 40 mg SC BD or Tab Apixaban (Eliquis) 5 mg BD or Tab Dabigatran 150 mg twice daily In ESRD, Unfractionated Heparin – 5000 U SC BD
	Atorvastatin 10 mg or rosuvastatin 5 mg once daily		
Steroids	Inhaled Budesonide 400 mcg 2 puffs twice daily (via DPI or pMDI via Spacer). Gargle after use	Inj. Dexamethasone 6 mg IV OD **or** Oral dexamethasone 6 mg OD for 5-10 days **or** inj. Methyl Prednisolone 0.5 -1 mg/kg ≈ 60mg OD x 5 -10 Days Stop or taper if significantly better	Inj. Dexamethasone 0.2 – 0.4 mg /kg ≈ 6 mg IV BD x 10 Days or Inj. Methyl Prednisolone 1.0 - 2.0 mg/kg ≈ 80 mg OD x 10 Days
JAK inhibitors (unlikely to be useful after 14 days)	No recommendation	Baricitinib 4 mg PO once daily for upto 14 days or till discharge, whichever is earlier. (or Tofacitinib 10mg administered orally twice daily for 14 days or until hospital discharge; as part of a trial, or if baricitinib is unavailable) Co-administer with remdesivir.	

Other anti inflammatory agents	• **COLCHICINE (consider if fever persists despite paracetamol)**
	  • Dosage: 0.5 mg bd for 7 to 10 days and then reduce to 0.5 mg od for 5 days (Administer OD from beginning if body weight <60 kg)
	  • Contraindicated if eGFR <30 ml/min/1.73m^2		

Oxygen Maintain Target sPO_2 of 91 to 92 %	Not Required Encourage awake proning	Awake proning ↓ Nasal Prongs (4 lit / min) ↓ Face Mask (5-10 lit / min) ↓ Non-rebreathing mask with reservoir (10 -15 lit / min) ↓ HFNC (30-35 lit / min) ↓ NIV	Maintain Target SPo2 > 90 % NRM (10 -15 lit / min) ↓ HFNC (30 - 60 lit / min) ↓ NIV ↓ MV (ARDS Protocol)

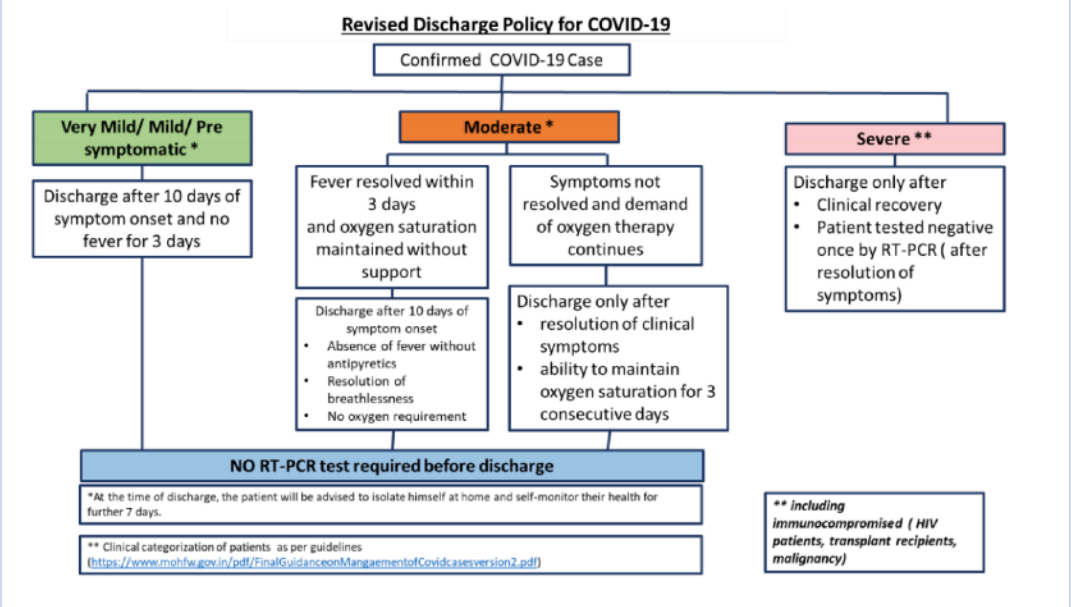
Step 2: Choose the treatment	TREATMENT		
	MILD	MODERATE	SEVERE
Anti IL6 agents (Tocilizumab or Itolizumab).	NOT INDICATED	Consider tocilizumab **or** itolizumab for any of the following: • within 24 h of requirement for NIV or MV • hospitalised patients at high risk of needing MV • who have progressed despite treatment with corticosteroids • have none of the exclusion criteria **Method of Use:** • Itolizumab- (1.6 mg/kg dose iv infusion) **slowly over 6 hours** - 25 mg in the first hour and the remaining dose over 5 hours **or** • **Inj. Toculizumab 8 mg/kg (usually 400 mg to max 800 mg) slow IV in 100 ml NS over 1 Hour.** If well tolerated and improvement in patient observed, clinician has the discretion to repeat a dose (after 1 week for itolizumab or after 12 hours for tocilizumab **only after expert opinion**) **Informed consent is mandatory**	

Exclusion Criteria for tocilizumab/ itolizumab:

- Patients >80 years of age
- Treatment with tocilizumab or itolizumab in previous 4 weeks
- Uncontrolled bacterial superinfection according to treating clinician
- History of severe allergic reaction to monoclonal antibodies
- History of diverticulitis requiring antibiotic treatment or history of colon perforation
- History of primary immunodeficiency (e.g. CVID) or progressing malignancy
- History of chronic liver disease (>Child-Pugh A)
- ALT/AST >5 X ULN
- Hemoglobin <8.0 g/dL, TLC <2000/mL, Absolute neutrophil count <1000, Platelets < 50000

COMORBIDITIES AND COMPLICATIONS			
Comorbidities and Complications	**Treat Appropriately; seek expert opinion where needed**		
MONITORING: All at baseline, then repeat based on clinical status; stated timings are only for guidance)			
BP / HR	Daily	6th Hourly	4th Hourly
RR / WOB /spO₂	6th Hourly	2nd Hourly	Continuously
CBC/RFT /LFT	If indicated	Every 2 Days	Daily
D Dimer	Repeat every 4 days	Once every 4 days	Once every 2 days
Troponin/CK-MB	Baseline, and repeat after 24 hours & 36 hours	Once every 2 days	Once everyday
ECG	Baseline	Once every 2 days	Daily
ABG	Baseline, if SpO2 not obtainable/unreliable	Guided by clinical status	
X Ray	Guided by clinical status		
	MUCOR PREVENTION STRATEGIES		
Glycemic control	Screen all patients for hyperglycaemia Seek help from Diabetes team if Fasting glucose > 110, Hba1c% > 6, Pre-meal glucose > 140, 2h post-meal or random glucose > 180		
High risk individuals	(1) severe illness (2) initiated on steroids (3) High risk individuals (CVD, Obesity, age > 50) (4) immunocompromised patients		
Monitoring	Monitor blood glucose even if initially normoglycemic if high risk individuals		
If high risk, and hypoxia is not controlled with steroids	Consider immunomodulators (anti-IL-6 agents or JAK inhibitors) early		
Mucormycosis prophylaxis	Pharmacoprophylaxis is not recommended; discuss with Infectious Diseases/ MedPulmo team in case of high risk individuals. Inform patients to seek early care if they exhibit symptoms like nasal discharge, facial pain or headache, tearing or redness of eyes If considering nasal douching with saline/ sodium bicarbonate: ensure that sterile water is used Zinc and iron may increase risk for mucormycosis in high risk individuals. Monitor along with ENT team		

DISCHARGE POLICY



DISCHARGE ADVICE		
Anticoagulation (if no contraindications)	Tab Apixaban 2.5 mg BD or Tab Dabigatran 110 mg BD or Tab Ecosprin AV 1 tablet HS Duration: 3-6 weeks	Tab Apixaban 5 mg BD or Tab Dabigatran 150 mg BD Duration: 6 weeks
Supportive therapy (unevidenced)	• Tab Zinc 50 mg 1-0-1 X 7 DAYS • Tab Vitamin C 500 mg 1-0-1 X 7 DAYS • Tab N Acetylcysteine 600mg 1-1-1 (if Patient has cough with thick sputum)	
	Isolation + Self Monitoring for 7 Days	
	Take all necessary precautions (e.g. single room with good ventilation, face-mask wear, reduced close contact with family members, separate meals, good hand sanitation, no outdoor activities, personal hygiene) in order to protect family members and the community from infection and further spread of SARS-CoV-2.	
Covid vaccination after Covid infection	Postpone Covid vaccination (Covishield or Covaxin) for 12 weeks after an infection; this may be shortened to 4-8 weeks in persons with other serious illnesses requiring hospitalisation or ICU care	

Note on anticoagulation.

The decision on anticoagulation needs to take into account the risk of thrombosis and of bleeding on anti-coagulants.
When the risk of thrombosis is high, (as assessed by the ISTH SIC score) and a high bleeding risk has been ruled out (using the HAS-BLED score), we would recommend therapeutic anticoagulation.

A high HAS-BLED score (≥3) is indicative of the need for regular clinical review and followup, but should not be used per se as a reason for stopping oral anticoagulation. All scores are available through online calculators.

Anticoagulation at discharge
Decide based on the risk of thrombosis, balanced against the bleeding risk:
1. Modified IMPROVE VTE (MIV) score ≥4
2. MIV ≥2 with a d-dimer value >2 times the upper limit of normal range
3. Age ≥75 years
4. Age >60 years with a d-dimer value >2 times the upper limit of normal range
5. Age 40–60 years with a d-dimer value >2 times the upper limit of normal range and history of VTE or with diagnosed malignancy

Modified IMPROVE VTE risk score

VTE risk factor	VTE risk score
Previous VTE	3
Known thrombophilia	2
Current lower limb paralysis or paresis	2
History of cancer	2
ICU/CCU stay	1
Complete immobilisation ≥1 day	1
Age ≥60 years	1

HAS-BLED score

Condition	Points
H - Hypertension	1
A - Abnormal renal or liver function (1 point each)	1 or 2
S - Stroke	1
B - Bleeding	1
L - Labile INRs	1
E - Elderly (> 65 years)	1
D - Drugs or alcohol (1 point each)	1 or 2

HAS-BLED score	Bleeds per 100 patient-years
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
5	12.5

Note: HAS-BLED has been validated for warfarin, but not for the new anticoagulants.

Summary of recommendations (ERS)