Guidelines for Management of Adult COVID-19 Patients

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DEFINITIONS

COVID-19: is a confirmed infection with SARS-CoV-2 virus.

ABBREVIATIONS

BMI	:	Body Mass Index
BID	:	bis in die (Twice a day)
COVID-19	:	Corona Virus Disease 2019
CRP	:	C-reactive protein
CrCl	:	Creatinine Clearance
CRRT	:	Continuous Renal Replacement Therapy
ECMO	:	Extracorporeal membrane oxygenation
EUA	:	Emergency Use Authorization
HFNC	:	High Flow Nasal Cannula
HIT	:	Heparin Induced Thrombocytopenia
IL6	:	Interleukin 6
IMPROVE	:	International Medical Prevention Registry on Venous Thromboembolism
IV	:	Intravenous
LMWH	:	Low molecular weight heparin
mg	:	Milligram
PO	:	Per Os (Orally)
VTE	:	Venous thromboembolism

1. BACKGROUND

Novel Corona virus (SARS-CoV-2) is a new strain of corona virus in humans, first identified in a cluster with pneumonia symptoms in Wuhan city, Hubei province of China, in December 2019. The World Health organization declared a pandemic in March 2020. The management of this novel disease has evolved since March 2020 as the results of numerous research studies have become available to the medical community. There are national and international guidelines for the management of COVID-19 that have gone through several iterations to stay up to date with the latest evidence-based literature. The authors reviewed the published national and international guidelines[1-4] and present a summary of their recommendations in this document.

2. SCOPE

2.1. To ensure the safe and efficient management of adult patients with COVID-19 in health facilities.

3. PURPOSE

3.1. Ensure safety of the adult patient with COVID-19.

3.2. Ensure that there is a standardized protocol for relevant healthcare professionals to manage adult patients, depending on the severity of the illness.

4. APPLICABILITY

4.1. DHA licensed Healthcare Professionals caring for adult patients with COVID-19 infection.

4.2. DHA licensed Health Facilities providing services or adult patients with COVID-19 infection.

5. **RECOMMENDATION ONE:** ASYMPTOMATIC COVID-19 ADULT PATIENTS

5.1. In asymptomatic patients, no specific pharmacotherapy is indicated; symptomatic management and supportive care are provided.

6. **RECOMMENDATION TWO:** COVID-19 ADULT PATIENT'S WITH MILD TO MODERATE SYMTOPMS, BUT NOT HOSPITALIZED

6.1. Consider **Favipiravir** 1600 mg PO BID X 2 doses then 600 mg PO BID (total 10 days) in high-risk individuals.

6.2. Consider **Sotrovimab; or Bamlanivimab plus Etesevimab; or Casirivimab plus imdevimab** in patients who are at high-risk individuals for progressing to severe COVID-19 and/or hospitalization. Treatment should be started as soon as possible after the patient receives a positive result on a SARS-CoV-2 test and within 10 days of symptom onset.

6.3. **High-risk individuals** as specified who meet at least one of the following criteria:

6.3.1. Age ≥ 65 years

6.3.2. Obesity (BMI ≥25 kg/m2)

6.3.3. Diabetes mellitus

6.3.4. Cardiovascular disease (including congenital heart disease) or hypertension

6.3.5. Chronic lung disease (e.g. chronic obstructive pulmonary disease, moderate-to-severe asthma, interstitial lung disease, cystic fibrosis, pulmonary hypertension)

6.3.6. An immunocompromising condition or immunosuppressive treatment

6.3.7. Chronic kidney disease

6.3.8. Pregnancy

6.3.9. Sickle cell disease.

6.3.10. Neurodevelopmental disorders (e.g. cerebral palsy) or other conditions that confer medical complexity (e.g. genetic or metabolic syndromes and severe congenital anomalies).

6.3.11. Medical-related technological dependence (e.g. tracheostomy, gastrostomy, or positive pressure ventilation [not related to COVID-19])

7. **RECOMMENDATION THREE:** COVID-19 ADULT PATIENTS WHO ARE HOSPITALIZED BUT DO NOT REQUIRE SUPPLEMENTAL OXYGEN

7.1. Start patients on **Favipiravir** 1600 mg PO BID X 2 doses then 600 mg PO BID (total 10-14 days) **PLUS VTE prophylaxis**

8. **RECOMMENDATION FOUR:** MANAGEMENT OF COVID-19 IN ADULT PATIENTS WHO ARE HOSPITALIZED AND REQUIRE SUPPLEMENTAL OXYGEN

(But do not require oxygen delivery through a high-flow device, non-invasive ventilation, invasive ventilation or ECMO)

8.1. Start patients on **Remdesivir** 200 mg intravenously (IV) for 1 day, followed by Remdesivir 100 mg IV for 4 days (total 5 days) **PLUS Dexamethasone** 6 mg IV /PO daily for 10 days or equivalent corticosteroids **PLUS VTE prophylaxis**.

OR

8.2. Start patients on **Favipiravir** 1600 mg PO BID X 2 doses then 600 mg PO BID (total 14 days) **PLUS Dexamethasone** 6 mg IV /PO daily for 10 days or equivalent Corticosteroids **PLUS VTE prophylaxis.**

8.3. The total daily dose equivalencies to dexamethasone 6 mg (oral or IV) are: Prednisone 40 mg or Methylprednisolone 32 mg or Hydrocortisone 160 mg.

9. RECOMMENDATION FIVE: COVID-19 ADULT PATIENTS WHO ARE HOSPITALIZED AND REQUIRE OXYGEN DELIVERY THROUGH A HIGH-FLOW DEVICE OR NON-INVASIVE VENTILATION

9.1. Start patients on **Remdesivir** 200 mg intravenously (IV) for 1 day, followed by Remdesivir 100 mg IV for 4 days (total 5 days) **PLUS Dexamethasone** 6 mg IV /PO daily for 10 days or equivalent corticosteroids **PLUS VTE prophylaxis**

OR

9.2. **Dexamethasone** 6 mg IV /PO daily for 10 days or equivalent corticosteroids **PLUS VTE prophylaxis**

9.3. **Tocilizumab** (4- 8 mg/kg body weight [maximum dose 800 mg] once or twice) should be considered in recently hospitalized patients (within 3 days of admission) who have rapidly increasing oxygen needs and require non-invasive ventilation or HFNC oxygen and who have significantly increased markers of inflammation (CRP ≥ 75).

9.4. The total daily dose equivalencies to dexamethasone 6 mg (oral or intravenous [IV]) are: Prednisone 40 mg or Methylprednisolone 32 mg or Hydrocortisone 160 mg).

10. RECOMMENDATION SIX: COVID-19 IN ADULT PATIENTS WHO ARE HOSPITALIZED AND REQUIRE INVASIVE VENTILATION OR ECMO

10.1. **Dexamethasone** 6 mg IV/PO daily for 10 days or equivalent corticosteroids **PLUS VTE prophylaxis**

10.2. **Tocilizumab** (4- 8 mg/kg body weight [maximum dose 800 mg] once or twice) should be considered in recently hospitalized patients (i.e., within first 3 days of admission) who have been admitted to the intensive care unit (ICU) within the prior 24 hours and who require invasive mechanical ventilation with evidence of early cytokine release syndrome (cytokine storm) with increased IL6 level, or elevated CRP of 75 or more.

11. RECOMMONDATION SEVEN: ANTIMICROBIAL AND ANTIFUNGAL THERAPY IN ADULT PATIENTS WITH COVID-19 INFECTION

11.1. **Antimicrobial and antifungals** should not be used routinely in patients with COVID-19 except in circumstances where superimposed bacterial/fungal infection is suspected.

12. RECOMMONDATION EIGHT: VTE PROPHYLAXIS IN ADULT PATIENTS WITH COVID-19 INFECTION

12.1. Therapeutic doses should not be offered because of the risk of bleeding

12.2. Thromboprophylaxis with low molecular weight heparin (LMWH) should be considered in ALL patients who require hospital admission for COVID-19 infection, in the absence of any contraindications

12.3. Enoxaparin prophylaxis doses: 40 mg subcutaneously once daily

12.4. Obesity BMI > 40 kg/m2: 40 mg subcutaneously every 12 hours

12.5. Pregnancy: 40 mg subcutaneously once daily

12.6. Renal impairment:

12.6.1. CrCl > 30 mL/minute: no adjustments required

12.6.2. CrCl < 30 mL/minute: 30 mg subcutaneously once daily

12.6.3. Hemodialysis and CRRT: Avoid use if possible but if used, anti-Xa levels should be frequently monitored, as accumulation may occur with repeated doses.

12.7. Patients with Heparin-induced Thrombocytopenia (HIT), please follow HIT standard institutional protocol for alternative anticoagulation

12.8. VTE prophylaxis after hospital discharge (Rivaroxaban 10 mg daily for 31 to 39 days) can be considered in patients who are at low risk for bleeding and high risk for VTE. High risk for VTE is defined as:

12.8.1. Modified International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) VTE risk score ≥4 (**Appendix 1**)

OR

12.8.2. Modified IMPROVE VTE risk score ≥2 and D-dimer level >2 times the upper limit of normal.

13. RECOMMONDATION NINE: SUMMARY OF RECOMMONDATIONS PER CLASS OF DRUGS

Class	Therapy	Recommendations
Antivirals	Remdesivir	It is recommended for use in hospitalized patients who require supplemental oxygen (BIIa). However, it is not routinely recommended for patients who require mechanical ventilation due to the lack of data showing benefit at this advanced stage of the disease[1]
	Hydroxychloroquine/ Chloroquine	The Panel recommends against the use of chloroquine or Hydroxychloroquine with or without azithromycin for the treatment of COVID-19 in hospitalized patients (AI)[1]. In non-hospitalized patients, the Panel recommends against the use of chloroquine or Hydroxychloroquine with or without azithromycin for the treatment of COVID-19, except in a clinical trial (AI)[1]. The Panel recommends against the use of high-dose chloroquine (600 mg twice daily for 10 days) for the treatment of COVID-19 (AI)[1].
	Favipiravir	In patients with mild to moderate disease, Favipiravir may be used to help improve clinical recovery time and viral shedding. (BIIb)[5-6].
	Lopinavir/Ritonavir	The Panel recommends against using lopinavir/ritonavir (AI) or other HIV protease inhibitors (AIII) to treat COVID-19, except in a clinical trial.[1]

	Ivermectin	There is insufficient data to recommend either for or against the use of ivermectin for the treatment of COVID-19 (AIII)[1.] Results from adequately powered, well-designed, and well-conducted clinical trials are needed to provide more specific, evidence-based guidance on the role of ivermectin in the treatment of COVID-19.
Anti-SARS-CoV-2 Antibody Products	COVID-19 convalescent plasma	For Hospitalized Patients With COVID-19 Who Do Not Have Impaired Immunity The Panel recommends against the use of COVID-19 convalescent plasma for the treatment of COVID-19 in mechanically ventilated patients (AI)[1]. The Panel recommends against the use of high-titer COVID-19 convalescent plasma for the treatment of COVID-19 in hospitalized patients who do not require mechanical ventilation[1]. For Hospitalized Patients With COVID-19 Who Have Impaired Immunity There are insufficient data for the Panel to recommend either for or against the use of high-titer COVID-19 convalescent plasma for the treatment of COVID-19[1]. The Panel recommends against the use of low-titer COVID-19 convalescent plasma for the treatment of COVID-19 (AIIb)[1].
	Immunoglobulins: SARS-CoV-2 Specific	There are insufficient data for the COVID-19 Treatment Guidelines Panel to recommend either for or against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoglobulins for the treatment of COVID-19[1].

	Anti-SARS-CoV-2 Monoclonal Antibodies	The Panel recommends using one of the following anti-SARS-CoV-2 monoclonal antibody listed below to treat outpatients with mild to moderate COVID-19 who are at high risk of clinical progression, as defined by the EUA criteria[1]: Sotrovimab or Bamlanivimab plus etesevimab (AIIa); or Casirivimab plus imdevimab (AIIa). Treatment should be started as soon as possible after the patient receives a positive result on a SARS-CoV-2 test and within 10 days of symptom onset[1].
Cell Based Therapy	Mesenchymal stem cells	The COVID-19 Treatment Guidelines Panel recommends against the use of mesenchymal stem cells for the treatment of COVID-19, except in a clinical trial (AIIb)[1].
Immunomodulators	Colchicine	In clinical trials the effect of colchicine on COVID-19-related clinical events was not statistically significant[7-8]. The Panel recommends against the use of colchicine in hospitalized patients for the treatment of COVID-19, except in a clinical trial (AIII)[1]. There are insufficient data for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of colchicine for the treatment of non-hospitalized patients with COVID-19[1].
	Corticosteroids	The COVID-19 Treatment Guidelines Panel recommends the use of dexamethasone (or other corticosteroids) (AI) for hospitalized patients who require supplemental oxygen[1]. The COVID-19 Treatment Guidelines Panel recommends against the use of dexamethasone (AIIa) or other

		corticosteroids in patients who do not require supplemental oxygen therapy[1].
	Interferons	The COVID-19 Treatment Guidelines Panel recommends against the use of interferons for the treatment of patients with severe or critical COVID-19, except in a clinical trial (AIII)[1]. There are insufficient data to recommend either for or against the use of interferon beta for the treatment of early (i.e., <7 days from symptom onset) mild and moderate COVID-19[1].
	Interleukin-1 Inhibitors	There are insufficient data to recommend for or against the use of interleukin (IL)-1 inhibitors, such as anakinra, for the treatment of COVID-19[1].
	Interleukin-6 Inhibitors	The Panel recommends using tocilizumab (single intravenous [IV] dose of tocilizumab 8 mg/kg actual body weight up to 800 mg) in combination with dexamethasone (6 mg daily for up to 10 days) in certain hospitalized patients who are exhibiting rapid respiratory decompensation due to COVID-19[1]. These patients are: Recently hospitalized patients (i.e., within first 3 days of admission) who have been admitted to the intensive care unit (ICU) within the prior 24 hours and who require invasive mechanical ventilation, non-invasive ventilation, or high-flow nasal canula (HFNC) oxygen (>0.4 FiO2/30 L/min of oxygen flow) (BIIa)[1]; or Recently hospitalized patients (i.e., within first 3 days of admission) not admitted to the ICU who have rapidly increasing oxygen needs and require non-invasive ventilation

		or HFNC oxygen and who have significantly increased markers of inflammation (CRP 75 mg/L) (BIIa)[1].
	Fluvoxamine	There are insufficient data for the Panel to recommend either for or against the use of fluvoxamine for the treatment of COVID-19. Results from adequately powered, well-designed, and well-conducted clinical trials are needed to provide more specific, evidence-based guidance on the role of fluvoxamine for the treatment of COVID-19[1].
	Kinase Inhibitors	There are insufficient data for the COVID-19 Treatment Guidelines Panel to recommend either for or against the use of baricitinib in combination with remdesivir for the treatment of COVID-19 in hospitalized patients, when corticosteroids can be used[1]. In the rare circumstance when corticosteroids cannot be used, the Panel recommends baricitinib in combination with remdesivir for the treatment of COVID-19 in hospitalized, non-intubated patients who require oxygen supplementation (BIIa)[1]. The Panel recommends against the use of baricitinib without remdesivir, except in a clinical trial (AIII)[1]. There are insufficient data for the Panel to recommend either for or against the use of baricitinib in combination with corticosteroids for the treatment of COVID-19. Because both baricitinib and corticosteroids are potent immunosuppressants, there is potential for an additive risk of infection.

		The Panel recommends against the use of JAK inhibitors other than baricitinib for the treatment of COVID-19, except in a clinical trial (AIII)[1].
	Immunoglobulins: Non-SARS-CoV-2 Specific	The COVID-19 Treatment Guidelines Panel recommends against the use of non-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-specific intravenous immunoglobulin (IVIG) for the treatment of COVID-19, except in a clinical trial (AIII)[1]. This recommendation should not preclude the use of IVIG when otherwise indicated for the treatment of complications that arise during the course of COVID-19[1].
Antithrombotic Therapy		Laboratory Testing In non-hospitalized patients with COVID-19, there are currently no data to support the measurement of coagulation markers (e.g., D-dimers, prothrombin time, platelet count, fibrinogen) (AIII).[1] In hospitalized patients with COVID-19, hematologic and coagulation parameters are commonly measured, although there are currently insufficient data to recommend for or against using this data to guide management decisions.[1] Chronic Anticoagulant and Antiplatelet Therapy Patients who are receiving anticoagulant or antiplatelet therapies for underlying conditions should continue these medications if they receive a diagnosis of COVID-19 (AIII)[1]. Venous Thromboembolism Prophylaxis and Screening For non-hospitalized patients with COVID-19, anticoagulants and antiplatelet therapy should not be initiated for the

	prevention of venous thromboembolism (VTE) or arterial thrombosis unless the patient has other indications for the therapy or is participating in a clinical trial (AIII)[1]. Hospitalized nonpregnant adults with COVID-19 should receive prophylactic dose anticoagulation (AIII)[1] (see the recommendations for pregnant individuals below). Anticoagulant or antiplatelet therapy should not be used to prevent arterial thrombosis outside of the usual standard of care for patients without COVID-19 (AIII)[1]. There are currently insufficient data to recommend either for or against the use of thrombolytics or higher than the prophylactic dose of anticoagulation for VTE prophylaxis in hospitalized COVID-19 patients outside of a clinical tria[1]. Hospitalized patients with COVID-19 should not routinely be discharged from the hospital while on VTE prophylaxis (AIII)[1]. Continuing anticoagulation with a Food and Drug Administration-approved regimen for extended VTE prophylaxis after hospital discharge can be considered in patients who are at low risk for bleeding and high risk for VTE, as per the protocols for patients without COVID-19 (see text below for details on defining at-risk patients) (BI)[1]. The Food and Drug Administration approved the use of rivaroxaban 10 mg daily for 31 to 39 days in these patients. Inclusion criteria for the trials that studied post-discharge VTE prophylaxis included:

	Modified International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) (see appendix 2) VTE risk score ≥4; *or* Modified IMPROVE VTE risk score ≥2 and D-dimer level >2 times the upper limit of normal. There are currently insufficient data to recommend either for or against routine deep vein thrombosis screening in COVID-19 patients without signs or symptoms of VTE, regardless of the status of their coagulation markers[1]. For hospitalized COVID-19 patients who experience rapid deterioration of pulmonary, cardiac or neurological function, or of sudden, localized loss of peripheral perfusion, the possibility of thromboembolic disease should be evaluated (AIII)[1]. Hospitalized Children With COVID-19 For hospitalized children with COVID-19, indications for VTE prophylaxis should be the same as those for children without COVID-19 (BIII)[1]. Treatment When diagnostic imaging is not possible, patients with COVID-19 who experience an incident thromboembolic event or who are highly suspected to have thromboembolic disease should be managed with therapeutic doses of anticoagulant therapy (AIII).[1] Patients with COVID-19 who require extracorporeal membrane oxygenation or continuous renal replacement therapy or who have thrombosis of catheters or

	extracorporeal filters should be treated with antithrombotic therapy as per the standard institutional protocols for those without COVID-19 (AIII)[1]. Special Considerations During Pregnancy and Lactation If antithrombotic therapy is prescribed during pregnancy prior to a diagnosis of COVID-19, this therapy should be continued (AIII)[1]. For pregnant patients hospitalized for severe COVID-19, prophylactic dose anticoagulation is recommended if there are no contraindications to its use (see text) (BIII)[1]. As for nonpregnant patients, VTE prophylaxis after hospital discharge is not recommended for pregnant patients (AIII). Decisions to continue VTE prophylaxis in the pregnant or postpartum patient after discharge should be individualized, considering concomitant VTE risk factors.[1] Anticoagulation therapy use during labor and delivery requires specialized care and planning. It should be managed in pregnant patients with COVID-19 in a similar way as in pregnant patients with other conditions that require anticoagulation in pregnancy (AIII)[1]. Unfractionated heparin, low molecular weight heparin, and warfarin do not accumulate in breast milk and do not induce an anticoagulant effect in the newborn; therefore, they can be used in breastfeeding individuals with or without COVID-19 who require VTE prophylaxis or treatment (AIII). In contrast, direct-acting oral anticoagulants are not routinely recommended due to lack of safety data (AIII)[1].

Adjunct Therapy	Vitamin C	There are insufficient data for the Panel to recommend either for or against the use of vitamin C for the treatment of COVID-19 in non-critically ill patients[1].
	Vitamin D	There are insufficient data to recommend either for or against the use of vitamin D for the prevention or treatment of COVID-19[1].
	Zinc	There are insufficient data to recommend either for or against the use of zinc for the treatment of COVID-19[1]. The COVID-19 Treatment Guidelines Panel recommends against using zinc supplementation above the recommended dietary allowance for the prevention of COVID-19, except in a clinical trial (BIII)[1].
Miscellaneous		Antimicrobial and antifungals should not be used routinely in patients with COVID-19 except in circumstances where superimposed bacterial infection is suspected In COVID-19 infection should not preclude from testing for other viral infections (such as influenza). In case the patient with COVID-19 tested positive for influenza, appropriate influenza therapy is indicated. Antipyretics: acetaminophen is preferred however NSAIDs can be considered as a second line

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APPENDIX 1: 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 Immobilization ≥ 1d	1
Age ≥ 60 years	1