

# Guidelines for the Management of Adult COVID-19 Patients

## Version 4

Issue date: 14/01/2022

Effective date: 14/01/2022

Health Policies and Standards Department

Health Regulation Sector (2022)

## INTRODUCTION

Health Regulation Sector (HRS) forms an integral part of Dubai Health Authority (DHA) and is mandated by DHA Law No. (6) of 2018 to undertake several functions including but not limited to:

- Developing regulation, policy, standards, guidelines to improve quality and patient safety and promote the growth and development of the Health Sector.
- Licensure and inspection of health facilities as well as healthcare professionals and ensuring compliance to best practice.
- Managing patient complaints and assuring patient and physician rights are upheld.
- Governing the use of narcotics, controlled and semi-controlled medications.
- Strengthening health tourism and assuring ongoing growth.
- Assuring management of health informatics, e-health and promoting innovation.

The Guidelines for the Management of Adult COVID-19 Patients aims to fulfil the following overarching DHA Strategic Priorities (2022-2026): (choose from the below)

- Pioneering Human-centered health system to promote trust, safety, quality and care for patients and their families.
- Make Dubai a lighthouse for healthcare governance, integration and regulation.
- Leading global efforts to combat epidemics and infectious diseases and prepare for disasters.
- Pioneering prevention efforts against non-communicable diseases.
- Foster healthcare education, research and innovation.

## ACKNOWLEDGMENT

This document is developed by the Subject Matter Experts panel of the COVID-19 Command and Control Center in collaboration with Health Policy and Standards Department (HPSD). HPSD would like to acknowledge and thank this panel of health professionals for their dedication toward improving quality and safety of healthcare services in the Emirate of Dubai.

### Health Regulation Sector

### Dubai Health Authority

## TABLE OF CONTENTS

INTRODUCTION .....	2
ACKNOWLEDGMENT .....	3
EXECUTIVE SUMMARY .....	6
DEFINITIONS:.....	7
ABBREVIATIONS:.....	7
1. BACKGROUND .....	8
2. SCOPE.....	8
3. PURPOSE .....	8
4. APPLICABILITY .....	8
5. RECOMMENDATION ONE: MANAGEMENT OF COVID-19 IN ASYMPTOMATIC ADULT PATIENTS.....	9
6. RECOMMENDATION TWO: MANAGEMENT OF COVID-19 IN ADULT PATIENTS WITH MILD TO MODERATE SYMPTOMS BUT NOT HOSPITALIZED.....	9
7. RECOMMENDATION THREE: MANAGEMENT OF COVID-19 IN HOSPITALIZED ADULT PATIENTS WHO DO NOT REQUIRE SUPPLEMENTAL OXYGEN.....	11
8. RECOMMENDATION FOUR: MANAGEMENT OF COVID-19 IN ADULT HOSPITALIZED PATIENTS WHO REQUIRE SUPPLEMENTAL OXYGEN (BUT NOT THROUGH A HIGH-FLOW DEVICE, NON-INVASIVE VENTILATION, INVASIVE VENTILATION OR ECMO) .....	11
9. RECOMMENDATION FIVE: MANAGEMENT OF COVID-19 IN ADULT HOSPITALIZED PATIENTS WHO REQUIRE OXYGEN DELIVERY THROUGH A HIGH-FLOW DEVICE OR NON-INVASIVE VENTILATION .....	12
10. RECOMMENDATION SIX: MANAGEMENT OF COVID-19 IN ADULT HOSPITALIZED PATIENTS WHO REQUIRE INVASIVE VENTILATION OR ECMO .....	13
11. RECOMMENDATION SEVEN: ANTIMICROBIAL AND ANTIFUNGAL THERAPY IN ADULT PATIENTS WITH COVID-19 INFECTION .....	13

<b>12. RECOMMENDATION EIGHT: VTE PROPHYLAXIS IN ADULT PATIENTS WITH COVID-19 INFECTION .....</b>	<b>13</b>
<b>13. RECOMMENDATION NINE: SUMMARY OF RECOMMENDATIONS PER CLASS OF DRUGS..</b>	<b>15</b>
<b>REFERENCES .....</b>	<b>24</b>
<b>APPENDIX: MODIFIED IMPROVE VTE RISK SCORE.....</b>	<b>27</b>

## EXECUTIVE SUMMARY

In March 2020, the World Health Organization (WHO) declared COVID-19 as a global pandemic. Clinical evidence and research indicate that COVID-19 is known to be transmitted through direct contact with respiratory droplets of an infected person through coughing and sneezing and from touching surfaces contaminated with the virus. To ensure protective and preventative measures are adopted within the community, DHA has developed this document which recommends measures to be taken to protect the patients, staff and healthcare professionals from COVID-19, as health facilities re-engage in providing routine care.

There are recommendations within the guideline, each addressing an important component to build an effective and efficient system to prevent, prepare and respond to COVID-19. The guideline seeks to adopt best practices in the Emirate of Dubai.

### Version 4 updates:

The panel has reviewed updated evidence and has amended the previous guidelines to include the new evidence. The following changes have been made:

1. Updated treatment guidelines for non-hospitalized patients with mild to moderate symptoms to include Paxlovid, IV Remdesivir and Molnupiravir for treatment of high risk patients who are at risk of disease progression/hospitalization.
2. Favipiravir has been removed from the guideline for both hospitalized and non-hospitalized patients.
3. Recent literature reference have been added.

## DEFINITIONS:

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

## ABBREVIATIONS:

<b>BID</b>	:	bis in die (Twice a day)
<b>BMI</b>	:	Body Mass Index
<b>COVID-19</b>	:	Corona Virus Disease 2019
<b>CrCl</b>	:	Creatinine Clearance
<b>CRP</b>	:	C-reactive protein
<b>CRRT</b>	:	Continuous Renal Replacement Therapy
<b>ECMO</b>	:	Extracorporeal membrane oxygenation
<b>EUA</b>	:	Emergency Use Authorization
<b>HFNC</b>	:	High Flow Nasal Cannula
<b>HIT</b>	:	Heparin Induced Thrombocytopenia
<b>IL6</b>	:	Interleukin 6
<b>IMPROVE</b>	:	International Medical Prevention Registry on Venous Thromboembolism
<b>IV</b>	:	Intravenous
<b>LMWH</b>	:	Low molecular weight heparin
<b>mg</b>	:	Milligram
<b>PO</b>	:	Per Os (Orally)
<b>VTE</b>	:	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<sup>1-4</sup> 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: MANAGEMENT OF COVID-19 IN ASYMPTOMATIC ADULT PATIENTS

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

## 6. RECOMMENDATION TWO: MANAGEMENT OF COVID-19 IN ADULT PATIENTS WITH MILD TO MODERATE SYMPTOMS BUT NOT HOSPITALIZED

6.1. Consider the following in the order of medications described below in order of priority, subject to availability, for patients who are at high risk 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.

6.1.1. Paxlovid – (nirmatrelvir 300mg plus ritonavir 100mg orally twice daily for 5 days) within 5 days of symptom onset.

**Or**

6.1.2. Molnupiravir 800mg orally twice daily for 5 days within 5 days of symptom onset.

**Or**

6.1.3. Sotrovimab 500mg administered as single intravenous infusion.

Or

- 6.1.4. Remdesivir 200mg IV on Day 1, followed by 100mg IV on days 2 and 3.
- 6.2. Bamlanivimab plus etesevimab; or Casirivimab plus imdevimab may be considered if Sotrovimab is not available in patients who are at high-risk individuals for progressing to severe COVID-19 and/or hospitalization.
- 6.3. **High-risk individuals** (with mild to moderate disease who are at-risk of progression to severe disease and/or hospitalization) as specified who meet at least one of the following criteria:
- 6.3.1. Age  $\geq$  65 years
- 6.3.2. Obesity (BMI  $\geq$ 25 kg/m<sup>2</sup>)
- 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: MANAGEMENT OF COVID-19 IN HOSPITALIZED ADULT PATIENTS WHO DO NOT REQUIRE SUPPLEMENTAL OXYGEN

- 7.1. The panel recommends against the use of dexamethasone or other form of steroids.
- 7.2. Start Remdesivir 200mg IV on day 1 followed by 100mg IV daily for 4 days for patients who are at high risk of disease progression. Remdesivir should be administered within 7 days of symptom onset PLUS VTE prophylaxis.

## 8. RECOMMENDATION FOUR: MANAGEMENT OF COVID-19 IN ADULT HOSPITALIZED PATIENTS WHO REQUIRE SUPPLEMENTAL OXYGEN (BUT NOT THROUGH A HIGH-FLOW DEVICE, NON-INVASIVE VENTILATION, INVASIVE VENTILATION OR ECMO)

- 8.1. Start Remdesivir 200mg IV on day 1 followed by 100mg IV daily for 4 days or until discharge **PLUS VTE prophylaxis.**

Or

- 8.2. 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

- 8.3. Dexamethasone 6mg IV daily for 10 days or equivalent corticosteroids **PLUS VTE prophylaxis**.
- 8.4. 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: MANAGEMENT OF COVID-19 IN ADULT HOSPITALIZED PATIENTS WHO 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**.
- 9.2. **Tocilizumab** (4- 8 mg/kg body weight [maximum dose 800 mg] once or twice) should be considered in recently hospitalized patients (within 72 hours 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  $\geq$  75).
- 9.3. 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: MANAGEMENT OF COVID-19 IN ADULT HOSPITALIZED PATIENTS WHO 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 72 hrs 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. RECOMMENDATION 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. RECOMMENDATION EIGHT: VTE PROPHYLAXIS IN ADULT PATIENTS WITH COVID-19 INFECTION

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

12.2. Enoxaparin prophylaxis doses: 40 mg subcutaneously once daily

- 12.3. Obesity BMI > 40 kg/m<sup>2</sup>: 40 mg subcutaneously every 12 hours
- 12.4. Pregnancy: 40 mg subcutaneously once daily
- 12.5. Renal impairment:
- 12.5.1. CrCl > 30 mL/minute: no adjustments required
- 12.5.2. CrCl < 30 mL/minute: 30 mg subcutaneously once daily
- 12.5.3. Hemodialysis and CRRT: Recommend monitoring anti-Xa levels frequently, as accumulation may occur with repeated doses.
- 12.6. Patients with Heparin-induced Thrombocytopenia (HIT), please follow HIT standard institutional protocol for alternative anticoagulation
- 12.7. 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:
- 12.7.1. Modified International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) VTE risk score  $\geq 4$  (Appendix)
- Or**
- 12.7.2. Modified IMPROVE VTE risk score  $\geq 2$  and D-dimer level >2 times the upper limit of normal.

### 13. RECOMMENDATION NINE: SUMMARY OF RECOMMENDATIONS PER CLASS OF DRUGS

Class	Therapy	Recommendations
Antivirals	Remdesivir	It is recommended for use in non-hospitalized patients with mild to moderate disease for a total of 3 days as EUA ( <b>BIIa</b> ) <sup>1</sup> and in hospitalized patients who require low dose supplemental oxygen ( <b>BIIa</b> ) <sup>2</sup> . 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. Treat should be initiated within 7 days of symptom onset.
	Paxlovid	In the EPIC-HR trial, ritonavir-boosted nirmatrelvir (Paxlovid) reduced the risk of hospitalization or death by 88% compared to placebo in non-hospitalized adults with laboratory-confirmed SARS-CoV-2 infection ( <b>AIIa</b> ) <sup>3</sup> . This efficacy is comparable to the efficacies reported for sotrovimab (i.e., 85% relative reduction), and remdesivir (i.e., 87% relative reduction) and greater than the efficacy reported for molnupiravir (i.e., 30% relative reduction). Currently approved by the FDA for EUA for non-hospitalized patients.
	Molnupiravir	In the MOVE-OUT trial, molnupiravir reduced the rate of hospitalization or death by 30% compared to placebo. Even though the different treatment options have not been directly compared in clinical trials, the Panel recommends using molnupiravir only when ritonavir-boosted nirmatrelvir (Paxlovid), sotrovimab, and remdesivir are not available or cannot be given ( <b>CIIa</b> ) <sup>4</sup> . Not recommended in pregnant patients in view of fetal toxicity.
	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 ( <b>AI</b> ) <sup>2,7</sup> .  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 ( <b>AI</b> ) <sup>2,7</sup> .

		The Panel recommends against the use of high-dose chloroquine (600 mg twice daily for 10 days) for the treatment of COVID-19 (AI) <sup>2,7</sup> .
	Lopinavir/Ritonavir	The Panel <b>recommends against</b> using <b>lopinavir/ritonavir (AI)</b> or other <b>HIV protease inhibitors (AIII)</b> to treat COVID-19, except in a clinical trial <sup>2,7</sup> .
	Ivermectin	There is insufficient data to recommend either for or against the use of ivermectin for the treatment of COVID-19 (AIII) <sup>2,7</sup> . 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	<p>For Hospitalized Patients With COVID-19 Who <b>Do Not Have Impaired Immunity</b></p> <p>The Panel recommends <b>against</b> the use of COVID-19 convalescent plasma for the treatment of COVID-19 in mechanically ventilated patients (AI)<sup>2,7</sup>.</p> <p>The Panel recommends <b>against</b> the use of high-titre COVID-19 convalescent plasma for the treatment of COVID-19 in hospitalized patients who do not require mechanical ventilation<sup>2,7</sup>.</p> <p>For Hospitalized Patients With COVID-19 <b>Who Have Impaired Immunity</b></p> <p>There are insufficient data for the Panel to recommend either for or against the use of high-titre COVID-19 convalescent plasma for the treatment of COVID-19<sup>1</sup>.</p> <p>The Panel recommends <b>against</b> the use of low-titre COVID-19 convalescent plasma for the treatment of COVID-19 (AIIb)<sup>2,7</sup>.</p>
	Immunoglobulins: SARS-CoV-2 Specific	There are insufficient data for the COVID-19 Treatment Guidelines Panel to recommend either for or against <b>severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoglobulins</b> for the treatment of COVID-19 <sup>2,7</sup> .
	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 <sup>2,5,7</sup> :



		<p>Sotrovimab or</p> <p>Bamlanivimab plus etesevimab (AIIa); or</p> <p>Casirivimab plus imdevimab (AIIa).</p> <p>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. Sotrovimab has been shown to retain activity against of all variants including the Omicron variant.</p>
Cell Based Therapy	Mesenchymal stem cells	The COVID-19 Treatment Guidelines Panel <b>recommends against</b> the use of <b>mesenchymal stem cells</b> for the treatment of COVID-19, except in a clinical trial <b>(AIIb)</b> <sup>2</sup> .
Immuno-modulator	Colchicine	<p>In clinical trials the effect of colchicine on COVID-19-related clinical events was not statistically significant<sup>2,7-10</sup>.</p> <p>The Panel recommends <b>against</b> the use of colchicine in hospitalized patients for the treatment of COVID-19, except in a clinical trial <b>(AIII)</b><sup>2,7-10</sup>.</p> <p>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<sup>2,7-10</sup>.</p>
	Corticosteroids	<p>The COVID-19 Treatment Guidelines Panel recommends the use of dexamethasone (or other corticosteroids) <b>(AI)</b> for hospitalized patients who require supplemental oxygen<sup>2,7</sup>.</p> <p>The COVID-19 Treatment Guidelines Panel recommends <b>against</b> the use of dexamethasone <b>(AIIa)</b> or other corticosteroids in patients who do not require supplemental oxygen therapy <sup>2,7</sup>.</p>
	Interferons	The COVID-19 Treatment Guidelines Panel <b>recommends against</b> the use of <b>interferons</b> for the treatment of patients with severe or critical COVID-19, except in a clinical trial <b>(AIII)</b> <sup>2,7</sup> .

		There are insufficient data to recommend either for or against the use of <b>interferon beta</b> for the treatment of early (i.e., <7 days from symptom onset) mild and moderate COVID-19 <sup>2,7</sup> .
	Interleukin-1 Inhibitors	There are insufficient data to recommend for or against the use of interleukin (IL)-1 inhibitors, such as <b>anakinra</b> , for the treatment of COVID-19 <sup>2</sup> .
	Interleukin-6 Inhibitors	The Panel <b>recommends</b> using <b>tocilizumab</b> (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 <sup>2</sup> . 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 FiO <sub>2</sub> /30 L/min of oxygen flow) (BIIa) <sup>2,12-13</sup> ; 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) <sup>2,12,13</sup> .
	Fluvoxamine	There are <b>insufficient</b> 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 <sup>1</sup> .
	Kinase Inhibitors	There are <b>insufficient</b> 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 <sup>1</sup> .

		<p>In the rare circumstance when corticosteroids cannot be used, the Panel recommends <b>baricitinib</b> in combination with <b>remdesivir</b> for the treatment of COVID-19 in hospitalized, non-intubated patients who require oxygen supplementation <b>(BIIa)</b><sup>2</sup>.</p> <p>The Panel recommends against the use of <b>baricitinib</b> without <b>remdesivir</b>, except in a clinical trial <b>(AIII)</b><sup>2</sup>.</p> <p>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 immunosuppressant, there is potential for an additive risk of infection.</p> <p>The Panel <b>recommends against</b> the use of <b>JAK inhibitors other than baricitinib</b> for the treatment of COVID-19, except in a clinical trial <b>(AIII)</b><sup>2</sup>.</p>
	<p>Immunoglobulins: Non-SARS-CoV-2 Specific</p>	<p>The COVID-19 Treatment Guidelines Panel <b>recommends against</b> the use of non-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-specific <b>intravenous immunoglobulin (IVIG)</b> for the treatment of COVID-19, except in a clinical trial <b>(AIII)</b><sup>2</sup>.</p> <p>This recommendation <b>should not preclude</b> the use of IVIG when otherwise indicated for the treatment of complications that arise during the course of COVID-19<sup>2</sup>.</p>
<p>Antithrombotic Therapy</p>		<p>Laboratory Testing</p> <p>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) <b>(AIII)</b><sup>2</sup>.</p> <p>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.<sup>2</sup></p> <p>Chronic Anticoagulant and Antiplatelet Therapy</p>

Patients who are receiving anticoagulant or antiplatelet therapies for underlying conditions should continue these medications if they receive a diagnosis of COVID-19 **(AIII)**<sup>2</sup>.

#### 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)**<sup>2</sup>.

Hospitalized nonpregnant adults with COVID-19 should receive prophylactic dose anticoagulation **(AIII)**<sup>2</sup> (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)**<sup>2</sup>.

There are currently insufficient data to recommend either for or against the use of thrombolytic or higher than the prophylactic dose of anticoagulation for VTE prophylaxis in hospitalized COVID-19 patients outside of a clinical trial<sup>2</sup>.

Hospitalized patients with COVID-19 should not routinely be discharged from the hospital while on VTE prophylaxis **(AIII)**<sup>2</sup>. 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)**<sup>2</sup>.

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  $\geq 4$ ; *or* Modified IMPROVE VTE risk score  $\geq 2$  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<sup>2</sup>.

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)**<sup>2</sup>.

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)**<sup>2</sup>.

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)**<sup>2</sup>.

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)**<sup>2</sup>.

Therapeutic dose heparin can be considered in patients requiring low- flow oxygen and those not admitted to intensive care unit who have a D-dimer above the upper limit of normal (ULN), and have no increased bleeding risk **(CIIa)**<sup>2</sup>.

LMWH is preferred over unfractionated heparin. The risk of bleeding is 1.7% in the treatment group vs 0.9%<sup>14</sup>.

Based on clinical trial exclusion criteria, contraindications for therapeutic anticoagulation for COVID-19 due to an increased bleeding risk are as follows: platelet count  $<50 \times 10^9/L$ , hemoglobin  $<8 \text{ g/dL}$ , need for dual antiplatelet therapy, known bleeding within the last 30 days requiring an emergency room

		<p>visit or hospitalization, known history of a bleeding disorder, or an inherited or active acquired bleeding disorder<sup>2</sup>.</p> <p>Special Considerations During Pregnancy and Lactation</p> <p>If antithrombotic therapy is prescribed during pregnancy prior to a diagnosis of COVID-19, this therapy should be continued <b>(AIII)</b><sup>2,5</sup>.</p> <p>For pregnant patients hospitalized for severe COVID-19, prophylactic dose anticoagulation is recommended if there are no contraindications to its use (see text) <b>(BIII)</b><sup>2,5</sup>.</p> <p>As for nonpregnant patients, VTE prophylaxis after hospital discharge <b>is not recommended</b> for pregnant patients <b>(AIII)</b>. Decisions to continue VTE prophylaxis in the pregnant or postpartum patient after discharge should be individualized, considering concomitant VTE risk factors.<sup>1</sup></p> <p>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 <b>(AIII)</b><sup>2,5</sup>.</p> <p>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 <b>(AIII)</b>. In contrast, direct-acting oral anticoagulants are not routinely recommended due to lack of safety data <b>(AIII)</b><sup>2,5</sup>.</p>
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 <sup>2,7</sup> .
	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 <sup>2,7</sup> .

	Zinc	<p>There are insufficient data to recommend either for or against the use of zinc for the treatment of COVID-19<sup>2,7</sup>.</p> <p>The COVID-19 Treatment Guidelines Panel <b>recommends against</b> using zinc supplementation above the recommended dietary allowance for the prevention of COVID-19, except in a clinical trial <b>(BIII)</b><sup>2,7</sup>.</p>
Miscellaneous		<p>Antimicrobial and antifungals should not be used routinely in patients with COVID-19 except in circumstances where superimposed bacterial infection is suspected</p> <p>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.</p> <p>Antipyretics: acetaminophen is preferred; however NSAIDs can be considered as a second line</p>

## REFERENCES

1. Gottlieb RL, Vaca CE, Paredes R et al. Early remdesivir to prevent progression to severe COVID 19 in outpatients. N Engl J Med 2021. Available at:  
<https://www.nejm.org/doi/full/10.1056/NEJMoa2116846>. Accessed [January 7, 2022].
2. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at <https://www.covid19treatmentguidelines.nih.gov/>. Accessed [January 5, 2022].
3. Food and Drug Administration Fact sheet for healthcare providers: emergency use authorization for Paxlovid 2021. Available at:  
<https://www.fda.gov/media/155050/download>. Accessed [January 11, 2022].
4. Bernal A, Gomes da Silva M, Musungaie D et al. Molnupiravir for oral treatment of COVID 19 in non-hospitalized patients N Engl J Med 2021. Available at: [10.1056/NEJMoa2116044](https://doi.org/10.1056/NEJMoa2116044)[external icon](#). Accessed [January 5, 2022].
5. Gupta A, Gonzalez-Rojas Y, Joarez E et al. Early treatment for COVID 19 with SARS CoV-2 neutralizing antibody Sotrovimab. N Engl J Med 2021;385(21):1941-50. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/34706189>. Accessed [January 6, 2022].
6. National Guidelines for Clinical Management and Treatment of COVID-19 18<sup>th</sup> February 2021 Version 5.1.



7. National Institute for Health and Care Excellence Guidance. COVID 19 rapid guidelines.  
Available at <https://www.nice.org.uk/guidance/published?area=cov&type=cov> Accessed [December 12, 2021].
8. Australian guidelines for clinical care of people with COVID 19. Available at <https://app.magicapp.org/#/guideline/L4Q5An/rec/ny8MYL> Accessed [June 20, 2021].
9. Deftereos SG, Giannopoulos G, Vrachatis DA, et al. Effect of Colchicine vs Standard Care on Cardiac and Inflammatory Biomarkers and Clinical Outcomes in Patients Hospitalized With Coronavirus Disease 2019: The GRECCO-19 Randomized Clinical Trial. *JAMA Netw Open*. 2020;3(6):e2013136. doi:10.1001/jamanetworkopen.2020.13136
10. Tardif et al. Colchicine for community-treated patients with COVID-19 (COLCORONA): a phase 3, randomised, double-blinded, adaptive, placebo-controlled, multicentre trial. *Lancet Respir Med* 2021. [https://doi.org/10.1016/S2213-2600\(21\)00222-8](https://doi.org/10.1016/S2213-2600(21)00222-8) Accessed [January 11, 2022].
11. REMAP-CAP Investigators, Gordon AC, Mouncey PR, et al. Interleukin-6 receptor antagonists in critically ill patients with COVID-19. *N Engl J Med*. 2021;384(16):1491-1502. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33631065>. Accessed [January 7, 2022].
12. RECOVERY Collaborative Group. Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *Lancet*.

2021;397(10285):1637-1645. Available

at: <https://www.ncbi.nlm.nih.gov/pubmed/33933206>. Accessed [January 5, 2022].

13. Rosenberg, D., Eichorn, A., Alarcon, M., McCullagh, L., McGinn, T., & Spyropoulos, A. C.

(2014). External validation of the risk assessment model of the International Medical

Prevention Registry on Venous Thromboembolism (IMPROVE) for medical patients in a

tertiary health system. *Journal of the American Heart Association*, 3(6), e001152.

<https://doi.org/10.1161/JAHA.114.001152> Accessed [January 7, 2022].

14. Sholzberg M, Tang GH, Rahhal H, et al. Effectiveness of therapeutic heparin versus

prophylactic heparin on death, mechanical ventilation, or intensive care unit admission

in moderately ill patients with COVID-19 admitted to hospital: RAPID randomised

clinical trial. *BMJ*. 2021;375:n2400. Available

at: <https://www.ncbi.nlm.nih.gov/pubmed/34649864>. Accessed [January 6, 2022].

## APPENDIX: 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 $\geq$ 1d	1
Age $\geq$ 60 years	1