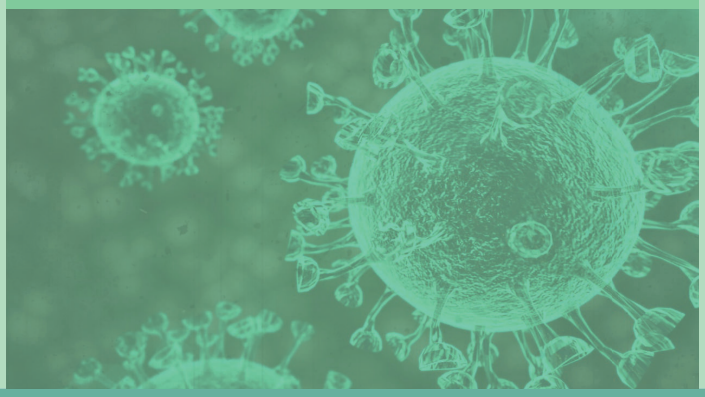
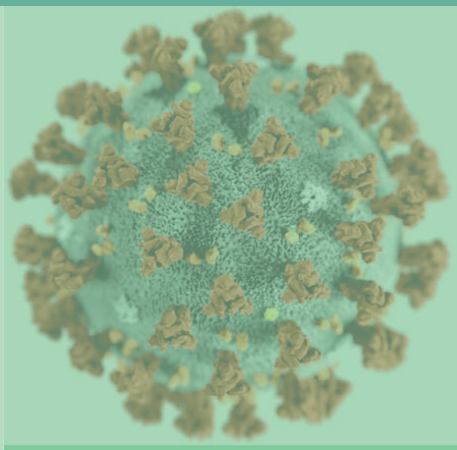
Healthy Lung
Easy Breath



Treatment Recommendations Of COVID-19 For Adults



ASTHMA ASSOCIATION BANGLADESH

National Institute Of Diseases Of The Chest And Hospital
Mohakhali, Dhaka-1212, Bangladesh, www.asthmabd.net

প্রশান্তি ভরা শ্বাস
আমাদের প্রয়াস

Treatment Recommendations Of COVID-19 For Adults

Version 1.0
May 2021

Published By:
Asthma Association Bangladesh

First Published:
May, 2021

Printed By:
Asian Colour Printing
130, DIT Extension Road
Fakirerpool, Dhaka-1000
Mobile: 01835180135
E-mail: asianclr@gmail.com

Treatment Recommendations Of COVID-19 For Adults

Editorial Board

Treatment Recommendations Of COVID-19 For Adults

Advisory Board

Professor Dr. Mahmud Hasan

Professor Dr. M Iqbal Arslan

Professor Dr. Abul Kalam Azad

Professor Shah Md. Keramat Ali

Professor Dr. Md. Sofiullah

Professor KMHS Serajul Haque

Professor Md. Shahidullah

Professor Dr. Md. Abul Kashem Khandaker

Professor Dr. Md. M. Jalaluddin

Professor Dr. Md. A. P. M. Sohrabuzzaman

Professor Dr. AKM Razzaque

Professor Dr. Md. Enamul Karim

Professor Dr. SM Mostafa Kamal

Professor Dr. Shamsul Arefin Khan

Professor Dr. Chowdhury Yakub Jamal

Professor Dr. Mujibur Rahman

Professor Dr. Uttam Kumar Barua

Asthma Association Bangladesh

Executive Committee

President	:	Professor Dr. Bashir Ahmed
Vice-President	:	Professor Dr. Md. Khairul Hassan Jessy Professor Dr. Biswas Akhtar Hossain Dr. Md. Wahiduzzaman Akhanda
Secretary General	:	Professor Dr. Md. Shahedur Rahman Khan
Treasurer	:	Professor Dr. Krishna Chandra Ganguly
Joint Secretary	:	Dr. Md. Zakir Hossain Sarker Dr. Shah Md. Saifur Rahman
Organizing Secretary	:	Dr. Barkat Ullah
Scientific & Research Secretary	:	Dr. Syed Rezaul Huq
Press & Publication Secretary	:	Dr. Jalal Mohsin Uddin
Information & Public Relation Secretary	:	Dr. Adnan Yusuf Choudhury
Office Secretary	:	Dr. AKM Akramul Haque
Members	:	Professor Dr. Md. Ali Hossain Professor Dr. Md. Mostafizur Rahman Professor Dr. Md. Rashidul Hassan Professor Dr. AKM Razzaque Professor Dr. Md. Abdul Qayyum Dr. Anowara Khatun Dr. Md. Serazul Islam Professor Dr. Md. Mohiuddin Ahmad Professor Dr. Md. Mazharul Hoque Tapan Dr. Md. Sayedul Islam

Contributing Authors (Not According To Seniority)

1. Dr. Sheikh Shahinur Hossain, Associate Professor Of Respiratory Medicine, National Institute Of Diseases Of The Chest And Hospital (NIDCH), Mohakhali, Dhaka.
2. Dr. K. M. Monjurul Alom, Assistant Professor Of Respiratory Medicine, Shaheed Ziaur Rahman Medical College, Bogura.
3. Dr. Md. Ferdous Wahid, Assistant Professor Of Respiratory Medicine, NIDCH, Mohakhali, Dhaka.
4. Dr. Titop Kumar Bala, Registrar, NIDCH, Mohakhali, Dhaka.
5. Dr. Md. Mofazzal Haider Siddique, Assistant Registrar, Medicine, Mugda Medical College And Hospital, Dhaka.
6. Dr. Md. Sanwar Nawaz Khan, Medical Officer, Chest Disease Hospital, Pabna.
7. Dr Sheikh Shamsuzzaman, Medical Officer, NIDCH, Mohakhali, Dhaka.
8. Dr. Arjuman Sharmin, Assistant Professor Of Pulmonology, Enam Medical College And Hospital, Savar, Dhaka.
9. Dr. Safayat Ahmed, Assistant Professor Of Respiratory Medicine, Khwaja Yunus Ali Medical College And Hospital, Sirajgonj.
10. Dr. Muhammad Billal Hossain, Deputy Civil Surgeon, Dhaka.
11. Dr. Muhammad Rashedul Islam, Deputy Program Manager, Medical Education and Health Manpower Development, Directorate General Of Medical Education, DGHS, Dhaka.
12. Dr. Nibir Sarkar, Medical Officer, NIDCH, Mohakhali, Dhaka.
13. Dr. Aminul Islam, Medical Officer, NIDCH, Mohakhali, Dhaka.
14. Dr. Tazrin Farhana, Medical Officer, NIDCH, Mohakhali, Dhaka.
15. Dr. Ashik Imran, Medical Officer, NIDCH, Mohakhali, Dhaka.
16. Dr. Aminur Rashid Mishu, Medical Officer, NIDCH, Mohakhali, Dhaka.
17. Dr. Zannatul Rayhan, Medical Officer, NIDCH, Mohakhali, Dhaka.
18. Dr. Habibur Rahman, MD Resident (Phase B), Pulmonology, NIDCH, Mohakhali, Dhaka.
19. Dr. Naeem Hossain, MD Resident (Phase B), Pulmonology, NIDCH, Mohakhali, Dhaka.
20. Dr. Ashok Bhowmick, MD Resident (Phase B), Pulmonology, NIDCH, Mohakhali, Dhaka.
21. Dr. Imran Hossain, MD Resident (Phase B), Pulmonology, NIDCH, Mohakhali, Dhaka.
22. Dr. Shamima Nasrin Sumi, MD Resident (Phase B), Pulmonology, NIDCH, Mohakhali, Dhaka.
23. Dr. S.M. Ashrafuzzaman Shojib, MD Resident (Phase B), Pulmonology, NIDCH, Mohakhali, Dhaka.
24. Dr. Ashraful Alam Khan, Medical Officer, NIDCH, Mohakhali, Dhaka.
25. Dr. Salauddin Anach, MD Resident (Phase B), Pulmonology, NIDCH, Mohakhali, Dhaka.
26. Dr. Lipi Debnath, Junior Consultant, Department Of Cardiology, National Institute Of Cardiovascular Diseases (NICVD), Dhaka.
27. Dr. Reaz Mahmud Huda, Assistant Professor Of Cardiology, NICVD, Dhaka.
28. Dr. Timir Kumar Debnath, Associate Consultant, National Center For Hearing And Speech For Children (SAHIC), Dhaka.
29. Dr. Dilruba Yeasmin, MD (Chest Diseases), Final Part, NIDCH, Mohakhali, Dhaka.

30. Dr. Leema Saha, MD Resident (Phase B), Pulmonology, NIDCH, Mohakhali, Dhaka.
31. Dr. Mohammad Sana Ullah Sarkar, Specialist, Respiratory Medicine, Square Hospital, Dhaka.
32. Dr. Md. Mehedi Hasan, Registrar, Medicine, Shaheed Ziaur Rahman Medical College Hospital, Bogura.
33. Dr. Md. Sarower Islam, MD Resident (Phase B), Gastroenterology, BSMMU, Dhaka.
34. Dr. Abdullah Al Masud Shamim, Medical Officer, NIDCH, Mohakhali, Dhaka.
35. Dr. Rowshan Arif, Medical Officer, NIDCH, Mohakhali, Dhaka.
36. Dr. Md. Didarul Alam, Medical Officer, NIDCH, Mohakhali, Dhaka.
37. Dr. Tanveer Kamal, MD Resident (Phase B), Pulmonology, NIDCH, Mohakhali, Dhaka.
38. Dr. Md. Ahsanul Islam, Medical Officer, Medicine OPD, Sylhet MAG Osmani Medical College Hospital (SOMCH), Sylhet.
39. Dr. Chitta Ranjan Paul, MD (Chest Diseases), Final Part, NIDCH, Mohakhali, Dhaka.
40. Dr. Suman Barua, MD (Internal Medicine) Final Part, NIDCH, Mohakhali, Dhaka.
41. Dr. Md. Delwar Hossain, MD (Chest Diseases), NIDCH, Mohakhali, Dhaka.
42. Dr. Faquir Walid Shah, OSD, Directorate General Of Health Services (DGHS), Dhaka.
43. Dr. A.F.M Abdul Hoque, Assistant Professor Of Respiratory Medicine, Abdul Malek Ukil Medical College (AMUMC), Noakhali.
44. Dr. Miraz Mahmud, Medical Officer, NIDCH, Mohakhali, Dhaka.
45. Dr. Tanveer Chowdhury, Medical Officer, NIDCH, Mohakhali, Dhaka.
46. Dr. Mohammad Mostafizur Rahman, Assistant Surgeon, Satarkul Union Health Center, Tejgaon Thana Health Complex, Dhaka.
47. Dr. Md. Shahjada Tabrez, Medical Officer, NIDCH, Mohakhali, Dhaka.
48. Dr. Selina Akter, Professor Of Obstetrics And Gynaecology, United Hospital, Dhaka.
49. Dr. Rezwana Ashraf, Assistant Professor Of Paediatric Nephrology, National Institute Of Kidney Diseases And Urology (NIKDU), Dhaka.
50. Dr. Fariha Hassan, Intern Doctor, Chattogram Medical College And Hospital (CMCH), Chattogram.
51. Dr. Md. Jahedul Islam, MD (Chest Diseases) Final Part, NIDCH, Mohakhali, Dhaka.
52. Dr. Merazul Alam, Emergency Medical Officer, NIDCH, Mohakhali, Dhaka.
53. Dr. Mohammed Kamrul Hasan, Junior Consultant, 250 Bed TB Hospital, Shyamoli, Dhaka.
54. Dr. A.K.M Fahmid Noman, Medical Officer, 250 Bed TB Hospital, Shyamoli, Dhaka.
55. Dr. Golam Hossen Tauhid, Medical Officer, NIDCH, Mohakhali, Dhaka.
56. Dr. Mohammad Shahjahan Siddike Shakil, Medical Officer, NIDCH, Mohakhali, Dhaka.
57. Dr. Ruhul Alam Tarek, Assistant Professor, NIDCH, Mohakhali, Dhaka.
58. Dr. Mehedi Khan, UH&FPO, Lauhajang Upazilla Health Complex, Munshiganj.
59. Dr. Sadia Sultana Reshma, MD Resident (Phase B), Pulmonology, NIDCH, Mohakhali, Dhaka.

International Contributors

1. Dr. Sayeda Kamrun Naher, Medical Oncologist, Liverpool Hospital, New South Wales, Australia.
2. Dr. Salma Hasan, GP Registrar, Health Education England, NHS, UK.

Preface

All praises for the Almighty Allah, the most merciful and beneficent, for giving me sufficient opportunity and courage and providing me enough energy and patience to initiate and carry on this updated treatment recommendations of COVID-19.

It is a great pleasure to acknowledge a deep sense of gratitude and indebtedness to the President, Secretary General, Treasurer, Board of Editors, Board of Advisors, Associate Editors, Officials of Asthma Association Bangladesh and Contributing Authors from home and abroad for their valuable suggestions, constructive criticisms and encouragement during the work.

I acknowledge Dr. Syed Nesar Ahmed and Dr. Romal Chowdhury for their wholehearted contribution in this work. Without their sincere and untiring cooperation, it was impossible for me to publish this work. Indeed both Dr. Syed Nesar Ahmed and Dr. Romal Chowdhury have done an excellent effort to make this feasible even in this pandemic situation. So again I am deeply indebted to both of them for their brilliant job.

I appreciate the keen interest taken by my colleagues and students in making useful suggestions, critical revisions and correcting the proofs throughout the work. Although it is not possible to name individually each and everyone associated with the task but it is my bounded duty to acknowledge and remember their contribution always.

Coronavirus Disease-2019 (COVID-19) outbreak, which started in Wuhan, China, in December 2019, have turned into a pandemic. There is constantly changing treatment protocol of COVID-19 and thousands of studies going on.

We will update the treatment recommendations from time to time to incorporate latest evidences and recommendations by WHO and various established guidelines. We welcome every suggestion and feedback in this work.

May the Almighty bless all of us with His Mercy and Forgiveness.

Professor Dr. Md. Khairul Hassan Jessy
Professor Of Respiratory Medicine
And Editor-In-Chief
Bangladesh Journal Of Pulmonology
Asthma Association Bangladesh
National Institute Of Diseases Of The Chest And Hospital (NIDCH)
Mohakhali, Dhaka-1212

Abbreviations

ACS	Acute Coronary Syndrome
AF	Atrial Fibrillation
AST/ALT	Aspartate Aminotransferase/Alanine Amino Transferase
CBC	Complete Blood Count
COVID-19	Coronavirus Disease 2019
CRRT	Continuous Renal Replacement Therapy
CRP	C-Reactive Protein
DIC	Disseminated Intravascular Coagulation
DOAC	Direct Oral Anticoagulant
ECMO	Extracorporeal Membrane Oxygenation
EUA	Emergency Use Authorization
ICU	Intensive Care Unit
IVIG	Intravenous Immunoglobulins
LDH	Lactate Dehydrogenase
LFT	Liver Function Tests
LMWH	Low Molecular Weight Heparin
MAP	Mean Arterial Pressure
NIPPV	Non-Invasive Positive Pressure Ventilation
PPE	Personal Protective Equipment
RT-PCR	Real time- Polymerase Chain Reaction
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SC	Subcutaneous
UFH	Unfractionated Heparin
VV	Venovenous
VTE	Venous Thromboembolism

Contents

Introduction

Novel coronavirus disease 2019 (COVID-19) is an infectious disease caused by the newly discovered severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Since its identification in December 2019, COVID-19 has spread around the world and was declared a Public Health Emergency of International Concern by the World Health Organization (WHO) on 30 January 2020 [1].

Early diagnosis, recognition, rapid isolation and quarantine are essential to prevent transmission and provide appropriate care in time frame. High index of clinical suspicion is needed for diagnosing COVID-19 patients and evaluation should be performed according to pneumonia severity indexes and sepsis guidelines (if sepsis is suspected) in all patients with severe illness [2].

There is no specific treatment found to be unequivocally effective for COVID-19, therefore, the mainstay of management is early diagnosis and optimum supportive care to relieve symptoms and to support organ function in more severe illness. Patients should be managed in a hospital setting when possible; however, home care may be suitable for selected patients; asymptomatic and cases with mild illness (without comorbidity) unless there is concern about rapid deterioration or an inability to prompt transfer to hospital if necessary. Even for those suitable for home care, if self-isolation at home is not possible because of lack of care giver, overcrowding at home or for any other cause, patient should be brought to the hospital for institutional isolation in a designated area. Designated isolation centers with necessary facilities should be developed across the country [2]. In Bangladesh, COVID-19 infections are being reported from Directorate General of Health Services on daily basis.

The reason of this booklet is the constantly changing treatment option for COVID-19. Here we follow different updated treatment guidelines for COVID-19 [2-4].

The Recommendation

Recommendation For [3]

A strong recommendation is given when there is high-certainty evidence showing that the overall benefits of the intervention are clearly greater than the disadvantages. This means that all, or nearly all, patients will want the recommended intervention.

Recommendation Against [3]

A strong recommendation against the intervention is given when there is high-certainty evidence showing that the overall disadvantages of the intervention are clearly greater than the benefits. A strong recommendation is also used when the examination of the evidence shows that an intervention is not safe.

Conditional Recommendation For [3]

A conditional recommendation is given when it is considered that the benefits of the intervention are greater than the disadvantages, or the available evidence cannot rule out a significant benefit of the intervention while assessing that the adverse effects are few or absent. This recommendation is also used when patient preferences vary.

Conditional Recommendation Against [3]

A conditional recommendation is given against the intervention when it is judged that the disadvantages of the intervention are greater than the benefits, but where this is not substantiated by strong evidence. This recommendation is also used where there is strong evidence of both beneficial and harmful effects, but where the balance between them is difficult to determine. Likewise, it is also used when patient preferences vary.

Consensus Recommendation [3]

A consensus recommendation can be given for or against the intervention. This type of recommendation is used when there is not enough evidence to give an evidence-based recommendation, but the panel still regards it as important to give a recommendation.

Rating Of Recommendation [4]

A= Strong
B= Moderate
C= Optional

Rating Of Evidence [4]

I = One or more randomized trials without major limitations

IIa = Other randomized trials or subgroup analysis of randomized trials

IIb = Nonrandomized trials or observational cohort studies

III = Expert opinion

Definition Of Disease Severity For Adults

Consensus Recommendation [3]

Asymptomatic	No symptoms but test positive for SARS - CoV-2
Mild illness	Adults not presenting any clinical features suggestive of moderate or severe disease or a complicated course of illness. Characteristics: • No symptoms • or mild upper respiratory tract symptoms • or cough, new myalgia or asthenia without new shortness of breath or a reduction in oxygen saturation
Moderate illness	Stable adult patient presenting with respiratory and/or systemic symptoms or signs. Able to maintain oxygen saturation above 92% (or above 90% for patients with chronic lung disease) with up to 4 L/min oxygen via nasal prongs. Characteristics: • Prostration, severe asthenia, fever > 38^{o}C or persistent cough • Clinical or radiological signs of lung involvement • No clinical or laboratory indicators of clinical severity or respiratory impairment
Severe illness	Adult patients meeting any of the following criteria: • Respiratory rate ≥ 30 breaths/min • Oxygen saturation ≤ 92% at a rest state • Arterial partial pressure of oxygen (PaO_2)/ inspired oxygen fraction (FiO_2) ≤ 300
Critical illness	Adult patient meeting any of the following criteria: Respiratory failure • Occurrence of severe respiratory failure (PaO_2/FiO_2 < 200), respiratory distress or acute respiratory distress syndrome (ARDS). This includes patients deteriorating despite advanced forms of respiratory support (non-invasive ventilation (NIV), high-flow nasal oxygen (HFNO)) OR patients requiring mechanical ventilation. OR other signs of significant deterioration • Hypotension or shock • Impairment of consciousness • Other organ failure

Figure 1: Pharmacologic Management Of Patients With COVID-19 Based On Disease Severity

[a] See the Anti-SARS-CoV-2 Monoclonal Antibodies section for more information on using bamlanivimab plus etesevimab or casirivimab plus imdevimab in patients with mild to moderate COVID-19.

[b] Patient who are receiving corticosteroids for other indications should continue therapy for their underlying conditions as directed by their health care providers.

[c] **The remdesivir dose** is 200 mg IV for one dose, followed by remdesivir 100 mg IV once daily for 4 days or until hospital discharge (unless the patient is in a health care setting that can provide acute care that is similar to inpatient hospital care). Treatment duration may be extended to up to 10 days if there is no substantial clinical improvement by day 5.

[d] For patients who are receiving remdesivir but progress to requiring oxygen through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or ECMO, remdesivir should be continued until the treatment course is completed.

[e] **The dexamethasone dose** is 6 mg IV or PO once daily for 10 days or until hospital discharge.

[f] The combination of dexamethasone and remdesivir has not been studied in clinical trails.

[g] In the rare circumstances where corticosteroids cannot be used, baricitinib plus remdesivir can be used **(BIIa**). The FDA has issued an EUA for baricitinib use in combination with remdesivir . The dose for baricitinib is 4 mg PO once daily for 14 days or until hospital discharge.

[h] The combination of dexamethasone and remdesivir may be considered for patients who have recently been intubated (**CIII**). The Panel **recommends against** the use of remdesivir monotherapy in these patients.

Key:

ECMO	=	Extracorporeal Membrane Oxygenation
EUA	=	Emergency Use Authorization
FDA	=	Food And Drug Administration
IV	=	Intravenous
PO	=	Orally
SARS-CoV-2	=	Severe acute respiratory syndrome coronavirus-2

Treatment Protocol For COVID-19 Cases [2]

- Mild cases can be managed at home through telephone/telemedicine service.
- Mild case with risk factor, Moderate, Severe and Critical patients should receive hospital care after appropriate triage.

Laboratory Investigations [2]

- To be chosen based on availability.
- The most important investigations are initial CBC and Chest X-ray (may require to be repeated).
- HRCT scans have high sensitivity for diagnosis even in PCR negatives. Not advised routinely but if available, will be better than Chest X-ray.
- Any clinically defined case should be tested with RT-PCR.

Mild Cases:

- CBC with CRP, Chest X-ray, ECG (>50 yr age).

Moderate Cases:

- CBC with CRP, D-dimer, Chest Xray (P-A view) (preferably portable), LFT, RFT, ECG (>50 yr age)
- **HRCT chest is more sensitive** than chest Xray for early diagnosis and also for follow up.

Severe Cases:

- CBC with CRP, Serum electrolytes, ABG, Coagulation profile (D-dimer especially), LDH, Ferritin, LFT, RFT, Blood culture, Procalcitonin, Lactate, Echocardiogram, Troponin I and Pro-BNP, ECG.
- **HRCT chest is more sensitive** than chest X ray for early diagnosis and also for follow up.

Critical Cases:

- All investigations for severe cases with additional ICU investigations as deemed necessary.

General Management [2]

- Bed rest and strengthening support therapy.
- Ensuring sufficient calorie intake.
- Monitoring vital signs and oxygen saturation.
- Timely initiation of effective oxygen therapy.
- Treatment venue will be determined according to severity of the disease:
  - Suspected and confirmed cases should be isolated and preferably treated at designated hospitals with effective isolation, protection and infection prevention conditions in place.
  - A mild case may be treated in isolation in a single room at home. (Home isolation protocol should be followed).
  - Mild cases with comorbidity/risk factor, Moderate and Severe cases should be treated in hospital.
  - Critical cases should be admitted to ICU as soon as possible.

Admission Criteria [2]

All suspected/ confirrmed cases of COVID-19 presenting as:

- Moderate case- clinical or radiological evidence of pneumonia
- Severe Pneumonia- clinical or radiological evidence of pneumonia with signs of severe pneumonia (RR > 30 /min or oxygen saturation <90%)
- Critical COVID-19: ARDS, Sepsis, Septic shock
- Hypoxia (SPO2 <93%) even in the absence of any clinical signs
- Patient with multiple uncontrolled comorbidities or prothrombotic state such as high-risk pregnancy, active malignancy, DVT irrespective of severity etc.

Pharmacological And Supportive Treatment

A. Asymptomatic Patients [2]

Supportive care + Isolation protocol (either home or institutional depending on national strategy).

Advice For Cases In Home Isolation:

- Rest at home in self-isolation (If self-isolation at home is not possible because of lack of care giver, overcrowding at home or for any other cause, patient should be brought to the hospital for institutional isolation in a designated area.)
- Physical distancing with family members (If possible, remain in a separate single room)
- No visitor
- Hand wash (20 seconds each time) (Repeated hand wash is beneficial)
- Cough etiquette (use tissue paper or elbow followed by hand wash)
- Medical mask (both patient and caregiver)

B. Mild Cases

- Mild case without comorbidities- Only symptomatic management and home isolation in a single room. (above mentioned home isolation protocol should be strictly followed).
- Mild case with controlled comorbidities- such as DM, HTN, IHD, Asthma/COPD/ILD, CKD, CLD, Malignancy, Pregnancy, Obesity can be managed at home. However, patient should be carefully monitored at home with finger pulse oximetry and be watchful about danger signs.
- Mild case with multiple uncontrolled comorbid conditions such as HTN, DM, IHD, CKD, CLD, COPD/Asthma/ILD and prothrombotic state such as high risk-pregnancy and active malignancy etc. should receive thromboprophylaxis along with symptomatic management and should be admitted.

Management of Mild Cases

- For fever: Tab Paracetamol (500mg) 1-2 tablet 3-4 times daily.
- For Rhinorrhea: Antihistamine.
- For cough: Antitussive for dry cough, inhaled budesonide 200mcg 2 puff 12 hourly.

- **Thromboprophylaxis:** Thromboprophylaxis is not routinely indicated for mild cases except for Mild COVID 19 cases with multiple uncontrolled comorbidities and prothrombotic conditions: Enoxaparin 40 mg, SC, once daily (OD) [for obese patients (BMI>40), 40 mg BID]. When CrCl< 30ml/min: Enoxaparin 20 mg SC OD for both obese and non-obese patient. or Unfractionated Heparin 5000 unit SC/BID.
- Monitor oxygen saturation at rest and minimum exertion such as walking for 3-6 minutes.
- Look for any danger signs of COVID as for example- Breathing difficulties, chest pain, light headedness, disorientation, extreme weakness which results in even difficulties in walking and drop in oxygen saturation to or <93% etc.
- Investigations: No routine investigations are required for mild cases.

N.B There is no role of systemic steroid in mild cases. Rather it may be harmful if given during the viremic phase of the disease especially in the first 7 days.

C. Patients With Mild To Moderate COVID-19 Who Are Not Hospitalized

Recommendations

- There are insufficient data for the Panel to recommend either for or against the use of any specific antiviral or antibody therapy in these patients [4].
- The Panel **recommends the use of SARS-CoV-2-neutralizing antibodies bamlanivimab 700 mg plus etesevimab 1,400 mg** or **casirivimab plus imdevimab** for the treatment of outpatients with mild to moderate COVID-19 who are at high risk of clinical progression as defined by the EUA criteria [4] **(BIIa)**.
- The Panel **recommends against** the use of **dexamethasone** or **other corticosteroids (AIII)** [4].
- Patients who are receiving dexamethasone or another corticosteroid for other indications should continue therapy for their underlying conditions as directed by their health care provider [4].

D. Patients Who Are Hospitalized With Moderate COVID-19 But Who Do Not Require Supplemental Oxygen

Recommendations

- The Panel **recommends against** the use of **dexamethasone** or **other corticosteroids (AIIa)** [4].
- Patients w ho are receiving dexamethasone or another corticosteroid for other indications should continue therapy for their underlying conditions as directed by their health care provider [4].
- **Do not routinely use dexamethasone (or other corticosteroids) to treat COVID-19** in **adults who do not require oxygen** [3]. **(Conditional recommendation against)**
- There are **insufficient data to recommend either for or against the routine use of remdesivir** in these patients [4].
- The use of remdesivir may be appropriate in patients who have a high risk of disease progression [4].
- **Use prophylactic doses of anticoagulants**, preferably low molecular weight heparin (LMWH) (e.g**. enoxaparin 40 mg once daily or dalteparin 5000 IU once daily**) in adults with moderate COVID-19 or other indications, unless there is a contraindication, such as risk for major bleeding [3]. **(Consensus recommendation)**

- Where the estimated glomerular filtration rate (eGFR) is less than 30 mL/min/1.73m^2, **unfractionated heparin (UFH) 60U/kg bolus+12units/kg/hr infusion-for ACS and 80U/Kg bolus +18units/kg/hr infusion-for VTE and AF or clearance-adjusted doses of LMWH may be used (e.g. enoxaparin 20 mg once daily or dalteparin 2500 IU once daily)** [3]. **(Consensus recommendation)**

E. For Hospitalized Patients With COVID-19 Who Require Supplemental Oxygen But Who Do Not Require Oxygen Delivery Through A High-Flow Device, Noninvasive Ventilation, Invasive Mechanical Ventilation, Or Extracorporeal Membrane Oxygenation

Recommendations

The Panel **recommends one of the following** options for these patients:

- **Remdesivir** (e.g., for patients who require minimal supplemental oxygen) **(BIIa)**; or
  - Dosage of Remdesivir: 200 mg IV infusion (within 30 min-2 hours) on Day 1 followed by 100 mg infusion (within 30 min to 2 hours) from Day 2 to Day 5 [2,3] .
- **Dexamethasone plus remdesivir** (e.g., for patients who require increasing amounts of oxygen) [4] **(BIII)**; *or*
- **Dexamethasone** (e.g., when combination therapy with remdesivir cannot be used or is not available) [4] **(BI)**.
- **Consider using tocilizumab in combination with dexamethasone** for the treatment of COVID-19 in adults **who require supplemental oxygen, particularly where there is evidence of systemic inflammation** [3]. **(Conditional recommendation)**
- For adults with COVID-19 and respiratory symptoms who are receiving any form of supplemental oxygen therapy and have not yet been intubated, consider **prone positioning for at least 3 hours per day** as tolerated [3].
- When positioning a patient in prone, ensure it is used with caution and accompanied by close monitoring of the patient [3].
- Use of prone positioning should not delay endotracheal intubation and mechanical ventilation in patients with COVID-19 who are deteriorating despite optimised less invasive respiratory therapies [3]. **(Consensus recommendation)**
- **Use prophylactic doses of anticoagulants**, preferably low molecular weight heparin (LMWH) (e.g. **enoxaparin 40 mg once daily or dalteparin 5000 IU once daily**) in adults with moderate COVID-19 or other indications, unless there is a contraindication, such as risk for major bleeding [3].
- Where the estimated glomerular filtration rate (eGFR) is less than 30 mL/min/1.73m^2, **unfractionated heparin (UFH) 60U/kg bolus+12units/kg/hr infusion-for ACS and 80U/Kg bolus +18units/kg/hr infusion-for VTE and AF or clearance-adjusted doses of LMWH may be used (e.g. enoxaparin 20 mg once daily or dalteparin 2500 IU once daily)** [3]. **(Consensus recommendation)**

Additional Considerations

- If dexamethasone is not available, an alternative corticosteroid such as **prednisone**, **methylprednisolone**, or **hydrocortisone** can be used [4] **(BIII)**.

- The suggested regimen of corticosteroid use is 6 mg of dexamethasone (oral or intravenous) daily for up to 10 days. In patients for whom dexamethasone is not available, acceptable alternative regimens include [3]:
  - Hydrocortisone: intravenous (50 mg), every 6 hours for up to 10 days
  - Prednisolone: oral (50 mg), daily for up to 10 days
  - Methylprednisolone may also be an acceptable alternative, however the most appropriate dosage is uncertain
- In the rare circumstances when corticosteroids cannot be used, **baricitinib (4mg once daily PO for 14 days) plus remdesivir** can be used **(BIIa)**. **Baricitinib should not be used** without **remdesivir** [4].
- There is insufficient evidence to identify which patients would benefit from the addition of baricitinib or tocilizumab to dexamethasone (with or without remdesivir). Some Panel members would add either baricitinib or tocilizumab to patients who are exhibiting signs of systemic inflammation and rapidly increasing oxygen needs while on dexamethasone, but who do not yet require high-flow oxygen or noninvasive ventilation.

F. For Hospitalized Patients With COVID-19 Who Require Delivery Of Oxygen Through A High-Flow Device Or Noninvasive Ventilation But Not Invasive Mechanical Ventilation Or Extracorporeal Membrane Oxygenation

Recommendations

The Panel **recommends one of the following** options for these patients:

- **Dexamethasone** alone [4] **(AI)**; *or*
- A combination of **dexamethasone plus remdesivir [4] (BIII)**
- **Tocilizumab [4] (BIIa)**
- The Panel recommends using either baricitinib (BIIa) or tocilizumab (BIIa) (listed alphabetically) in combination with dexamethasone alone or dexamethasone plus remdesivir for the treatment of COVID-19 in hospitalized patients on high-flow oxygen or noninvasive ventilation who have evidence of clinical progression or increased markers of inflammation.
- **Consider using increased prophylactic dosing of anticoagulants, preferably LMWH (e.g. enoxaparin 40 mg twice daily or dalteparin 5000 IU twice daily**) in **adults with severe or critical COVID-19 or other indications**, unless there is a contraindication, such as risk for major bleeding or platelet count < 30 x 10^9/L [3].
- Where eGFR (see below) is less than 30 mL/min/1.73m^2, **unfractionated heparin (UFH) 60U/kg bolus+12units/kg/hr infusion-for ACS and 80U/Kg bolus +18units/kg/hr infusion-for VTE and AF or clearance-adjusted doses of LMWH may be used (e.g. enoxaparin 40 mg once daily or dalteparin 5000 IU once daily**) [3]. **(Consensus recommendation)**
- For adults with COVID-19 and respiratory symptoms who are receiving any form of supplemental oxygen therapy and have not yet been intubated, consider **prone positioning for at least 3 hours per day** as tolerated [3].
- When positioning a patient in prone, ensure it is used with caution and accompanied by close monitoring of the patient. Use of prone positioning should not delay endotracheal intubation and mechanical ventilation in patients with COVID-19 who are deteriorating despite optimised less invasive respiratory therapies [3]. **(Consensus recommendation)**

Additional Considerations [4]

- The combination of dexamethasone and remdesivir has not been rigorously studied in clinical trials. Because there are theoretical reasons for combining these drugs, the Panel considers both dexamethasone alone and the combination of remdesivir and dexamethasone to be acceptable options for treating COVID-19 in this group of patients.
- The Panel **recommends against** the use of **remdesivir alone** because it is not clear whether remdesivir confers a clinical benefit in this group of patients **(AIIa)**.
- For patients who initially received remdesivir monotherapy and progressed to requiring high-flow oxygen or noninvasive ventilation, dexamethasone should be initiated and remdesivir should be continued until the treatment course is completed.
- If dexamethasone is not available, equivalent doses of other corticosteroids such as **prednisone, methylprednisolone**, or **hydrocortisone** may be used **(BIII)**.
- The Panel recommends against the use of baricitinib in combination with tocilizumab for the treatment of COVID-19, except in a clinical trial (AIII). Because both baricitinib and tocilizumab are potent immunosuppressants, there is the potential for an additive risk of infection.

G. For Hospitalized Patients With COVID-19 Who Require Invasive Mechanical Ventilation Or Extracorporeal Membrane Oxygenation

Recommendations

- The Panel **recommends the use of dexamethasone** in hospitalized patients with COVID-19 who require invasive mechanical ventilation or ECMO [4] **(AI)**.
- **Tocilizumab [4] (BIIa)**
- There is insufficient evidence for the Panel to recommend either for or against the use of baricitinib in combination with dexamethasone for the treatment of COVID-19 in hospitalized patients who require invasive mechanical ventilation.
- For mechanically ventilated adults with COVID-19 and hypoxaemia despite optimising ventilation, consider prone positioning for **more than 12 hours a day**[3]
- Current reports suggest prone ventilation is effective in improving hypoxia associated with COVID-19. This should be done in the context of a hospital guideline that includes suitable personal protective equipment (PPE) for staff and which minimises the risk of adverse events, e.g. accidental extubation [3].
- **Consider using increased prophylactic dosing of anticoagulants, preferably LMWH (e.g. enoxaparin 40 mg twice daily or dalteparin 5000 IU twice daily) in adults with severe or critical COVID-19 or other indications**, unless there is a contraindication, such as risk for major bleeding or platelet count < 30 x 10^9/L [3].
- Where eGFR is less than 30 mL/min/1.73m^2, unfractionated heparin 60U/kg bolus+12units/kg/hr infusion-for ACS and 80U/Kg bolus +18units/kg/hr infusion-for VTE and AF or clearance-adjusted doses of LMWH may be used (e.g. enoxaparin 40 mg once daily or dalteparin 5000 IU once daily) [3]. **(Consensus recommendation)**

Additional Considerations [4]

- If dexamethasone is not available, equivalent doses of alternative corticosteroids such as **prednisone**, **methylprednisolone**, or **hydrocortisone** may be used **(BIII)**.
- For patients who initially received remdesivir monotherapy and progressed to requiring invasive mechanical ventilation or ECMO, dexamethasone should be initiated and remdesivir should be continued until the treatment course is completed.
- The Panel recommends against the use of remdesivir monotherapy **(AIIa)**.

H. Care Of Critically ill Patients With COVID-19

Summary Recommendations

Infection Control

- For health care workers who are performing aerosol-generating procedures on patients with COVID-19, the COVID-19 Treatment Guidelines Panel (the Panel) recommends using an N95 respirator (or equivalent or higher-level respirator) rather than surgical masks, in addition to other personal protective equipment (PPE) (i.e., gloves, gown, and eye protection such as a face shield or safety goggles) [4] **(AIII)**.
- The Panel recommends minimizing the use of aerosol-generating procedures on intensive care unit patients with COVID-19 and carrying out any necessary aerosol-generating procedures in a negative-pressure room, also known as an airborne infection isolation room, when available [4] **(AIII)**.
- For health care workers who are providing usual care for nonventilated patients with COVID-19, the Panel recommends using an N95 respirator (or equivalent or higher-level respirator) or a surgical mask in addition to other PPE (i.e., gloves, gown, and eye protection such as a face shield or safety goggles) [4] **(AIIa)**.
- For health care workers who are performing non-aerosol-generating procedures on patients with COVID-19 who are on closed-circuit mechanical ventilation, the Panel recommends using an N95 respirator (or equivalent or higher-level respirator) in addition to other PPE (i.e., gloves, gown, and eye protection such as a face shield or safety goggles) because ventilator circuits may become disrupted unexpectedly [4] **(BIII)**.
- The Panel recommends that endotracheal intubation in patients with COVID-19 be performed by health care providers with extensive airway management experience, if possible [4] **(AIII)**.
- The Panel recommends that intubation be performed using video laryngoscopy, if possible [4] **(CIIa)**.

Hemodynamics

- For adults with COVID-19 and shock, the Panel recommends using dynamic parameters, skin temperature, capillary refilling time, and/or lactate levels over static parameters to assess fluid responsiveness [4] **(BIIa)**.
- For the acute resuscitation of adults with COVID-19 and shock, the Panel **recommends using buffered/balanced crystalloids over unbalanced crystalloids** [4] **(BIIa)**.
- For the acute resuscitation of adults with COVID-19 and shock, the Panel **recommends against** the initial use of albumin for resuscitation [4] **(BIIa)**.

- The Panel **recommends against** using hydroxyethyl starches for intravascular volume replacement in patients with sepsis or septic shock [4] **(AIIa)**.
- The Panel **recommends norepinephrine as the first-choice vasopressor (AIIa)**. The Panel recommends adding either vasopressin (up to 0.03 units/min) [4] **(BIIa)** or epinephrine **(CIIb)** to norepinephrine to raise mean arterial pressure to target or adding vasopressin (up to 0.03 units/min) **(CIIa)** to decrease norepinephrine dosage [4].
- When norepinephrine is available, the Panel **recommends against using dopamine** for patients with COVID-19 and shock [4] **(AIIa)**.
- The Panel **recommends against using low-dose dopamine** for renal protection [4] **(BIIa)**.
- The Panel **recommends using dobutamine** in patients who show evidence of cardiac dysfunction and persistent hypoperfusion despite adequate fluid loading and the use of vasopressor agents [4] **(BIII)**.
- The Panel recommends that all patients who require vasopressors have an arterial catheter placed as soon as practical, if resources are available [4] **(BIII)**.
- For adults with COVID-19 and **refractory septic shock** who are not receiving corticosteroids to treat their COVID-19, the **Panel recommends using low-dose corticosteroid therapy ("shock-reversal") over no corticosteroid therapy** [4] **(BIIa)**.

Oxygenation And Ventilation

- For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, the Panel **recommends high-flow nasal cannula (HFNC) oxygen over noninvasive positive pressure ventilation (NIPPV)** [4] **(BIIa)**.
- In the absence of an indication for endotracheal intubation, the Panel recommends a closely monitored trial of NIPPV for adults with COVID-19 and acute hypoxemic respiratory failure and for whom HFNC is not available [4] **(BIIa)**.
- For patients with persistent hypoxemia despite increasing supplemental oxygen requirements in whom endotracheal intubation is not otherwise indicated, the Panel recommends considering a trial of awake prone positioning to improve oxygenation [4] **(CIIa)**.
- The Panel **recommends against** using **awake prone positioning as a rescue therapy** for refractory hypoxemia to avoid intubation in patients who otherwise meet the indications for intubation and mechanical ventilation [4] **(AIII)**.
- Do not delay endotracheal intubation and mechanical ventilation in patients with COVID-19 who are deteriorating despite optimised, less invasive respiratory therapies [3]. **(Consensus recommendation)**
- If intubation becomes necessary, the procedure should be performed by an experienced practitioner in a controlled setting due to the enhanced risk of severe acute respiratory syndrome coronavirus 2 exposure to health care practitioners during intubation [4] **(AIII)**.
- In adults with COVID-19 undergoing endotracheal intubation, consider using videolaryngoscopy over direct laryngoscopy if available and the operator is trained in its use [3]. **(Conditional recommendation)**

For Mechanically Ventilated Adults With COVID-19 And Acute Respiratory Distress Syndrome (ARDS) [4]:

- The Panel **recommends using low tidal volume (VT) ventilation (VT 4–8 mL/kg of predicted body weight**) over higher VT ventilation (VT >8 mL/kg) **(AIIa)**.
- The Panel **recommends targeting plateau pressures of <30 cm H_2O (AIIa)**.
- The Panel recommends using a conservative fluid strategy over a liberal fluid strategy **(BIIa)**.
- The Panel **recommends against** the **routine use of inhaled nitric oxide (AIIa)**.

For Mechanically Ventilated Adults With COVID-19 And Moderate-To-Severe ARDS:

- The Panel **recommends using a higher positive end-expiratory pressure (PEEP >10cm H_2O) strategy over a lower PEEP strategy [4] (BIIa)**.
- For mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimized ventilation, the Panel **recommends prone ventilation for 12 to 16 hours per day over no prone ventilation [4] (BIIa)**.
- The Panel **recommends using, as needed**, **intermittent boluses of neuromuscular blocking agents (NMBA) or continuous NMBA infusion to facilitate protective lung ventilation [4] (BIIa)**.
- In the event of persistent patient-ventilator dyssynchrony, or in cases where a patient requires ongoing deep sedation, prone ventilation, or persistently high plateau pressures, the Panel recommends using a continuous NMBA infusion for up to 48 hours as long as patient anxiety and pain can be adequately monitored and controlled [4] **(BIII)**.
- For mechanically ventilated adults with COVID-19 and moderate to severe ARDS, do not routinely use continuous infusions of neuromuscular blocking agents (NMBAs) [3]. **(Conditional recommendation against)**
- However, if protective lung ventilation cannot be achieved, consider using NMBAs for up to 48 hours. If indicated, consider cisatracurium as first-line agent, if cisatracurium is not available alternatives include atracurium or vecuronium by infusion[3].

For Mechanically Ventilated Adults With COVID-19, Severe ARDS And Hypoxemia Despite Optimized Ventilation And Other Rescue Strategies:

- The Panel **recommends using recruitment maneuvers** rather than not using recruitment maneuvers [4] **(CIIa)**.
- If recruitment maneuvers are used, the Panel **recommends against** using staircase (incremental PEEP) recruitment maneuvers [4] **(AIIa)**.
- Types of manoeuvres include: prolonged high continuous positive airway pressure; progressive incremental increases in positive end-expiratory pressure at a constant driving pressure (incremental PEEP, stepwise or staircase); and high driving pressures [3].
- The Panel recommends using an inhaled pulmonary vasodilator as a rescue therapy; if no rapid improvement in oxygenation is observed, the treatment should be tapered off [4] **(CIII)**.

Acute Kidney Injury And Renal Replacement Therapy

- For critically ill patients with COVID-19 who have acute kidney injury and who develop indications for renal replacement therapy, the Panel recommends continuous renal replacement therapy (CRRT), if available [4] **(BIII)**.

- If CRRT is not available or not possible due to limited resources, the Panel recommends prolonged intermittent renal replacement therapy rather than intermittent hemodialysis[4] **(BIII)**.

Pharmacologic Interventions

- In patients with COVID-19 and severe or critical illness, there are **insufficient data to recommend empiric broad-spectrum antimicrobial therapy in the absence of another indication [4].**
- If antimicrobials are initiated, the Panel recommends that their use should be reassessed daily in order to minimize the adverse consequences of unnecessary antimicrobial therapy[4] **(AIII)**.
- **Consider using increased prophylactic dosing of anticoagulants, preferably LMWH (e.g. enoxaparin 40 mg twice daily or dalteparin 5000 IU twice daily)** in **adults with severe or critical COVID-19 or other indications**, unless there is a contraindication, such as risk for major bleeding or platelet count < 30 x 10^9/L.
- Where eGFR (see below) is less than 30 mL/min/1.73m^2, **unfractionated heparin 60U/kg bolus+12units/kg/hr infusion-for ACS and 80U/Kg bolus +18units/kg/hr infusion-for VTE and AF or clearance-adjusted doses of LMWH may be used (e.g. enoxaparin 40 mg once daily or dalteparin 5000 IU once daily)** [3]. **(Consensus recommendation)**

Extracorporeal Membrane Oxygenation

- There are insufficient data to recommend either for or against the use of extracorporeal membrane oxygenation in patients with COVID-19 and refractory hypoxemia [4].
- Consider early referral to an ECMO centre for patients developing refractory respiratory failure in mechanically ventilated adults with COVID-19 (despite optimising ventilation, including proning and neuromuscular blockers) [3]. **(Conditional recommendation)**
- Due to the resource-intensive nature of ECMO and the need for experienced centres, healthcare workers and infrastructure, ECMO should only be considered in selected patients with COVID-19 and severe ARDS [3].

Antithrombotic Therapy In Patients With COVID-19

Summary Recommendations

Laboratory Testing

- **In nonhospitalized** 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**) [4] **(AIII)**.
- In hospitalized patients with COVID-19, hematologic and coagulation parameters are commonly measured, although there are currently insufficient data to recommend either for or against using this data to guide management decisions [4].
- All patients admitted to hospital with confirmed or suspected COVID-19 should at least have the following tests: Full blood count (FBC), Urea and electrolytes, LFTs, Coagulation screening (PT, APTT, Fibrinogen), D-dimer [5].

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 [4] **(AIII)**.

Venous Thromboembolism (VTE) Prophylaxis and Screening

- **For nonhospitalized 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 [4] **(AIII)**.
- Use **prophylactic doses of anticoagulants**, preferably low molecular weight heparin (LMWH) (e.g. **enoxaparin 40 mg once daily or dalteparin 5000 IU once daily)** in adults with moderate COVID-19 or other indications, unless there is a contraindication, such as risk for major bleeding [3].
- Where the estimated glomerular filtration rate (eGFR) is less than 30 mL/min/1.73m^2, **unfractionated heparin or clearance-adjusted doses of LMWH may be used (e.g. enoxaparin 20 mg once daily or dalteparin 2500 IU once daily)** [3]. (**Consensus recommendation**)
- **VTE prophylaxis can be guided by D-Dimer levels as shown in table I.** Monitor D-dimer on admission and again only if the clinical picture changes. Consider clinically assessing patient for a VTE if D-dimer is raised. **Current evidence suggests that it is safe to administer dalteparin prophylaxis once daily in patients with thrombocytopenia, provided the platelet count remains greater than 30.** So if platelets are between 30-50, reduce dose to once daily (from twice daily doses in table I below) [5].

Table I. VTE Prophylaxis Dalteparin Dose Adjustment For Patients With An eGFR >30ml/Min, According To Weight And D-Dimer Levels [5]

COVID-19 VTE Prophylaxis According To D-Dimer and PLT>50, eGFR≥ 30ml/min		
D-Dimer	**Weight**	**Dalteparin**
<1000	<50kg 50-99.9Kg 100-150Kg >150 Kg	2500 units once daily 5000 units once daily 5000 units twice daily 7500 units twice daily
>1000	<50kg 50-99.9Kg 100-150Kg >150 Kg	2500 units twice daily 5000 units twice daily 7500 units twice daily Discuss with Haematology on Call
>3000	Dosing as >1000 but actively consider thrombotic event	Dosing as >1000 but actively consider thrombotic event

Table II. VTE Prophylaxis Dalteparin Dose Adjustment For Patients With An eGFR <30ml/Min (Including Dialysis Patients), According To Weight [5]

COVID-19 VTE PROPHYLAXIS with eGFR<30ml/min and Platelet >50	
Body weight	**Dalteparin**
< 50 kg	2500 units **twice daily**
50-99.9 kg	2500 units **twice daily**
100-179.9 kg	5000 units **twice daily**
>180 kg	Haematology advice

- Hospitalized nonpregnant adults with COVID-19 should receive **prophylactic dose anticoagulation (AIII)**. Anticoagulant or antiplatelet therapy should not be used to prevent arterial thrombosis outside of the usual standard of care for patients without COVID-19 [4] **(AIII)**.
- Consider using increased prophylactic dosing of anticoagulants, preferably LMWH (e.g. enoxaparin 40 mg twice daily or dalteparin 5000 IU twice daily) in **adults with severe or critical COVID-19 or other indications**, unless there is a contraindication, such as risk for major bleeding or platelet count < 30 x 10^9/L [3].

- Where eGFR is less than 30 mL/min/1.73m^2, unfractionated heparin or clearance-adjusted doses of LMWH may be used (e.g. enoxaparin 40 mg once daily or dalteparin 5000 IU once daily) [3]. (**Consensus recommendation**)
- 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 trial [4].
- Hospitalized patients with COVID-19 should not routinely be discharged from the hospital while on VTE prophylaxis **(AIII)** [4].
- Continuing anticoagulation with a Food and Drug Administration-approved regimen for extended VTE prophylaxis after hospital discharge can be considered for patients who are at low risk for bleeding and high risk for VTE, as per the protocols for patients without COVID-19 [4] **(BI)**.
- **Clinicians should consider extended thromboprophylaxis for up to 4 weeks from the date of discharge with LMWH/DOAC** (i.e. apixaban 2.5mg twice daily or rivaroxaban 10mg daily) on the basis of individual risk/benefit assessment (e.g critical care stay, reduced mobility, previous VTE) and D-Dimer levels (i.e >1000) [5].
- 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 [4].
- 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 [4] **(AIII)**.
- 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 [4] **(AIII)**.
- 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 [4] **(AIII)**.

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 [4] **(AIII)**.
- For pregnant patients hospitalized for severe COVID-19, prophylactic dose anticoagulation is recommended unless contraindicated [4] **(BIII)**.
- For pregnant or postpartum women who are **self-isolating at home** with mild COVID-19 and where **additional risk factors for VTE are present**, consider using **prophylactic doses of anticoagulants**, preferably LMWH (e.g. enoxaparin 40 mg once daily or dalteparin 5000 IU once daily) unless there is a contraindication, such as risk for major bleeding or imminent birth [3].
- Prophylactic anticoagulants should be continued for at least 14 days or until COVID-19-related morbidity (including immobility, dehydration and/or shortness of breath) has resolved [3]. (**Consensus recommendation**)
- For pregnant or postpartum women who are **admitted to hospital** (for any indication) and who have COVID-19, use **prophylactic doses of anticoagulants**, preferably LMWH (e.g. enoxaparin 40 mg once daily or dalteparin 5000 IU once daily) unless there is a contraindication, such as risk for major bleeding or imminent birth [3]. **(Consensus recommendation).**

- Prophylactic anticoagulants should be continued for at least 14 days after discharge or until COVID-19-related morbidity (including immobility, dehydration and/or shortness of breath) has resolved [3]. (**Consensus recommendation**)
- Like for nonpregnant patients, VTE prophylaxis after hospital discharge **is not recommended** for pregnant patients **(AIII)** [4].
- Decisions to continue VTE prophylaxis in the pregnant or postpartum patient after discharge should be individualized, considering concomitant VTE risk factors [4].
- For pregnant women with severe or critical COVID-19, or where there are additional risk factors for VTE, consider using **increased prophylactic dosing of anticoagulants**, preferably LMWH (e.g. enoxaparin 40 mg twice daily or dalteparin 5000 IU twice daily) unless there is a contraindication, such as risk for major bleeding or platelet count < 30 x 109/L [3]. (Consensus recommendation) [3].
- Prophylactic anticoagulants should be continued for **at least four weeks** after discharge or until COVID-19-related morbidity (including immobility, dehydration and/or shortness of breath) has resolved [3]. (**Consensus recommendation**)
- Anticoagulation therapy use during labor and delivery requires specialized care and planning [4].
- 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 [4] **(AIII)**.
- For postpartum women who have had COVID-19 during pregnancy, consider using at least 14 days of prophylactic dosing of anticoagulants, preferably LMWH (e.g. enoxaparin 40 mg once daily or dalteparin 5000 IU once daily) unless there is a contraindication, such as risk for major bleeding [3].
- Increased duration of six weeks should be considered if severe or critical COVID-19 and/or additional risk factors for VTE are present [3]. (**Consensus recommendation**)
- 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 by breastfeeding individuals with or without COVID-19 who require VTE prophylaxis or treatment **(AIII)** [4].
- **In contrast, use of direct-acting oral anticoagulants during pregnancy** is **not routinely recommended** due to lack of safety data [4] **(AIII)**.

Coagulopathy Management In COVID-19 Patients [5]

- Abnormal coagulation results do not require correction in patients who are not bleeding unless an interventional procedure is planned.
- **In patients with major bleeding, stop any anticoagulation, give empirical Fresh frozen plasma (FFP) and red cells followed by blood products determined by repeat coagulation screens, using PT/INR >1.5 or APTT > 1.5 as an indication to give FFP 15-25mg/Kg.**
- **For fibrinogen <1g/l give cryoprecipitate or fibrinogen concentrate. If platelets <30x 109/L give a pool of platelets**.
- Disseminated intravascular coagulation (DIC) can occur in patients in intensive care with COVID-19 which may lead to multi-organ failure.
- It is uncertain whether COVID-19 has unique characteristics to cause DIC.
- It seems more plausible that DIC develops in patients with COVID-19 after they become hypoxic, and/or have secondary bacterial infection. To aid diagnosis of DIC, it is recommended to use the International Society on Thrombosis and Haemostasis (ISTH) DIC score **(Table III)**.

Table III. Society On Thrombosis And Haemostasis (ISTH) DIC Score [5]

Parameter	Score
Platelet Count	
>100 x 10^9/L	0
50-100 x 10^9/L	1
<50 x 10^9/L	2
D-dimer	
No increase	0
Moderate increase (1 – 10 times upper limit of normal)	2
Strong increase (> 10 times upper limit of normal)	3
Fibrinogen	
> 1.0 g/L	0
≤ 1.0 g/L	1
Prothrombin Time Prolongation	
< 3 s	0
3 – 6 s	1
> 6 s	2
Overt Disseminated Intravascular Coagulation	≥ **5**

- A score < 5 means DIC is unlikely and the score should be recalculated every 1-2 days as necessary. The best management of DIC is to identify and treat the underlying condition.

- Recovery from DIC is dependent on endogenous fibrinolysis breaking down the disseminated thrombi. This process will be inhibited by tranexamic acid which is an anti-fibrinolytic, hence **tranexamic acid should not be used in COVID-associated DIC [5]**.

- **Manage bleeding with blood product replacement as per managing major bleeding as above i.e. if PT/INR or APTT ratios are greater than 1.5 then give FFP 15-25mg/Kg.**

- **If fibrinogen is <1.5g/l then give a source of fibrinogen- either cryoprecipitate or fibrinogen concentrate. If platelet are < 30x 10^9/L then give platelets [5]**.

- If overt thromboembolism or organ failure due to clot (i.e. purpura fulminants) consider low dose anticoagulation with unfractionated heparin pump to switch off stimulus to coagulation activation. Be mindful that there has been no mortality benefit of therapeutic anticoagulation and so run APTT target < 1.5 or anti-Xa levels 0.6-1.0 in DIC [5].

Tocilizumab For The Treatment Of COVID-19

- Tocilizumab is a recombinant humanized anti-interleukin (IL)-6 receptor monoclonal antibody approved by the Food and Drug Administration (FDA) for the treatment of certain rheumatologic disorders and cytokine release syndrome induced by chimeric antigen receptor T cell (CAR-T cell) therapy [4].
- It is hypothesized that modulating the levels of proinflammatory IL-6 or its effects may reduce the duration and/or severity of COVID-19 illness [4].
- To date, no IL-6 inhibitor is FDA-approved or authorized for the treatment of COVID-19 [4].
- On February 3, 2021, the COVID-19 Treatment Guidelines Panel (the Panel) issued a statement on the use of tocilizumab that included recommendations based on a preliminary report of results from the Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) [6].
- Since the statement was issued, the Panel has reviewed published results of REMAP-CAP [6] and the preliminary results of the open-label, pragmatic Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial [7], released on February 11, 2021.
- Based on this review, the Panel has updated its recommendations on the use of tocilizumab in certain populations of patients with COVID-19.

Recommendations

- The Panel recommends the use of **tocilizumab** [a] (single intravenous dose of 8 mg/kg of actual body weight, up to 800 mg) **in combination with dexamethasone** (6 mg daily for up to 10 days) [b] in certain hospitalized patients who are exhibiting rapid respiratory decompensation due to COVID-19 [c].
- Tocilizumab should be administered as a **single intravenous infusion over 60 minutes**, with the potential for a second dose to be administered either 12 or 24 hours later if the patient's condition has not improved.
- Following protocol information in the RECOVERY trial [6], the suggested dose is dependent on body weight:
  - Patients > 90 kg: 800 mg tocilizumab
  - Patients 66–90 kg: 600 mg tocilizumab
  - Patients 41–65 kg: 400 mg tocilizumab
  - Patients ≤ 40 kg: 8 mg/kg tocilizumab
- In addition, the REMAP-CAP [6] and RECOVERY [7] trials have demonstrated a significant benefit when using corticosteroids in conjunction with tocilizumab in adults. Use of combined tocilizumab and corticosteroids should be considered in children and adolescents hospitalised with COVID-19 who require oxygen, however, the optimal sequencing of tocilizumab and corticosteroid use is unclear in all populations.
- As tocilizumab **inhibits the production of C-reactive protein (CRP)**, a reduction in CRP **should not be used as a marker of clinical improvement** [3].

- **Indication Of Tocilizumab [6,7]:**
  - Recently hospitalized patients [d] who have been admitted to the intensive care unit (ICU) within the prior 24 hours and who require invasive mechanical ventilation, noninvasive mechanical ventilation (NIV), or high-flow nasal canula (HFNC)oxygen (>0.4 FiO_2/30 L/min of oxygen flow) **(BIIa)**; *or*
  - Recently hospitalized patients [d] (not in the ICU) with rapidly increasing oxygen needs who require NIV or HFNC and have significantly increased markers of inflammation **(BIIa)**

    (**Note**: The RECOVERY trial [6] inclusion criterion for inflammation was C-reactive protein [CRP] ≥75 mg/L).
  - There is insufficient evidence to specify which of these patients [For hospitalized patients with hypoxemia who require conventional oxygen supplementation, the Panel recommends using one of the following options: **remdesivir (BIIa)**, **dexamethasone plus remdesivir (BIII)**, or **dexamethasone alone (BI)**] would benefit from the addition of tocilizumab. Some Panel members would also give tocilizumab to patients who are exhibiting rapidly increasing oxygen needs while on dexamethasone and have a CRP ≥75 mg/L but who do not yet require NIV or HFNC.

[a] Tocilizumab **should be avoided** in patients with any of the following:

- Significant immunosuppression, particularly in those with a history of recent use of other biologic immunomodulating drugs
- Alanine transaminase >5 times the upper limit of normal
- High risk for gastrointestinal perforation
- An uncontrolled, serious bacterial, fungal, or non-SARS-CoV-2 viral infection
- Absolute neutrophil count <500 cells/μL; or (6) platelet count <50,000 cells/μL.

[b] As an alternative to dexamethasone, corticosteroids at a dose equivalent to dexamethasone 6 mg are acceptable.

[c] Respiratory decompensation should be due to progressive COVID-19 and not due to alternative causes, such as volume overload or asthma exacerbation.

[d] For example, within 3 days. Median days of hospitalization until randomization were 1.2 days (IQR 0.8–2.8 days) in REMAP-CAP and 2 days (IQR 1–5 days) in the RECOVERY trial.

Additional Considerations

- Tocilizumab should be **given only in combination with dexamethasone** (or another corticosteroid at an equivalent dose) [4].
- Some clinicians may assess a patient's clinical response to dexamethasone first, before deciding whether tocilizumab is needed [4].
- Although some patients in the REMAP-CAP and RECOVERY trials [6,7] **received a second dose of tocilizumab at the discretion of treating physicians, there are insufficient data to determine which patients, if any, would benefit from an additional dose of the drug**.
- Cases of severe and disseminated strongyloidiasis have been reported with the use of tocilizumab and corticosteroids in patients with COVID-19 [8,9]. **Prophylactic treatment with ivermectin** should be considered for persons who are from areas where strongyloidiasis is endemic[10].
- **As tocilizumab inhibits the production of C-reactive protein (CRP), a reduction in CRP should not be used as a marker of clinical improvement [3]**.

Antiviral Drugs That Are Approved Or Under Evaluation For The Treatment Of COVID-19

Summary Recommendations

Remdesivir

- **Remdesivir is the only** Food and Drug Administration-approved drug for the treatment of COVID-19**.** As in the management of any disease, treatment decisions ultimately reside with the patient and their health care provider [4].
- **The recommended regimen** is daily intravenous infusion (**200 mg initial dose, 100 mg maintenance) [4].**
- **Optimal duration of remdesivir treatment is unclear, however current evidence does not suggest a clear benefit of 10 days over 5 days** [3].
- **The Australian Government provided specific criteria that needed to be met in order to access remdesivir for clinical treatment [3]:**
  - Age ≥ 18 years (or 12 to 17 years weighing ≥ 40 kg).
  - An oxygen saturation of SpO2 ≤ 92% on room air and requiring supplemental oxygen.
  - Alanine aminotransferase (ALT) < 5 x upper limit of normal (ULN) and/or ALT < 3 x ULN and bilirubin < 2 ULN.
  - Patients with evidence of multiorgan failure, renal failure or those receiving mechanical ventilation for > 48 hours at time of application or extracorporeal membrane oxygenation (ECMO) are unable to receive remdesivir.
- Due to antagonism observed in vitro, concomitant use of remdesivir with chloroquine or hydroxychloroquine is not recommended [3].

Favipiravir

- **Not recommended** [3].
- Do not use favipiravir for the treatment of COVID-19 outside of randomised trials with appropriate ethical approval [3].
- Favipiravir should still be considered for other evidence-based indications in people who have COVID-19 [3].

Chloroquine Or Hydroxychloroquine With Or Without Azithromycin

- The Panel **recommends against** the use of chloroquine or hydroxychloroquine with or without azithromycin for the treatment of COVID-19 in hospitalized patients [4] **(AI)**.
- In nonhospitalized 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 [4] **(AIIa)**.
- The Panel **recommends against** the use of high-dose chloroquine (600 mg twice daily for 10 days) for the treatment of COVID-19 [4] **(AI)**.

Lopinavir/Ritonavir And Other HIV Protease Inhibitors

- The Panel **recommends against** the use of lopinavir/ritonavir and other HIV protease inhibitors for the treatment of COVID-19 in hospitalized patients [4] **(AI)**.
- The Panel **recommends against** the use of lopinavir/ritonavir and other HIV protease inhibitors for the treatment of COVID-19 in nonhospitalized patients [4] **(AIII)**.

Ivermectin

- **There are insufficient data for the Panel to recommend either for or against the use of ivermectin 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 ivermectin in the treatment of COVID-19 [3,4].

Anti-SARS-CoV-2 Antibody Products

Summary Recommendations

- There are insufficient data for the COVID-19 Treatment Guidelines Panel (the Panel) to **recommend either for or against the use** of the following products for the treatment of COVID-19 [4]:

❖ COVID-19 Convalescent Plasma

- The Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for the use of convalescent plasma for hospitalized patients with COVID-19.

❖ Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Immunoglobulins

- The Panel **recommends the use of bamlanivimab 700 mg plus etesevimab 1,400 mg** for the treatment of outpatients with mild to moderate COVID-19 who are at high risk of clinical progression as defined by the EUA criteria [4] **(BIIa)**.
- **Treatment should be started as soon as possible after the patient has received a positive result on a SARS-CoV-2 antigen or nucleic acid amplification test and within 10 days of symptom onset [4].**
- The Panel **recommends against** the use of **bamlanivimab 700 mg plus etesevimab 1,400 mg for patients who are hospitalized because of COVID-19, except in a clinical trial.** However, the combination should be considered for persons with mild to moderate COVID-19 who are hospitalized for a reason other than COVID-19 but who otherwise meet the EUA criteria [4].
- Bamlanivimab plus etesevimab should not be withheld from a pregnant individual who has a condition that poses a high risk of progression to severe COVID-19 if the clinician thinks that the potential benefit of the combination outweighs the potential risk [4].

Supplements

Vitamin C

- **There are insufficient data** for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of vitamin C for the treatment of COVID-19 [4].

Vitamin D

- **There are insufficient data** for the Panel to recommend either for or against the use of vitamin D for the treatment of COVID-19 [4].

Zinc

- **There are insufficient data** for the Panel to recommend either for or against the use of zinc for the treatment of COVID-19.
- The Panel **recommends against** using zinc supplementation above the recommended dietary allowance for the prevention of COVID-19, except in a clinical trial [4] **(BIII)**.

Cell-Based Therapy Under Evaluation For The Treatment Of COVID-19

Mesenchymal Stem Cells

Recommendation

- The COVID-19 Treatment Guidelines Panel r**ecommends against** the use of **mesenchymal stem cells** for the treatment of COVID-19, except in a clinical trial[4] **(AIIb)**.

Immunomodulators Under Evaluation For The Treatment Of COVID-19

Summary Recommendations

Guidelines Panel's (the Panel's) recommendations on the use of the following [4]:

- Dexamethasone (or other corticosteroids) with or without remdesivir
- Baricitinib with remdesivir.

Other Immunomodulators

There are insufficient data for the Panel to **recommend either for or against the use of the** following immunomodulators for the treatment of COVID-19 [4]:

- Baricitinib in combination with corticosteroids. Because both agents are potent immunosuppressants, there is potential for an additive risk of infection.
- Baricitinib in combination with remdesivir for hospitalized COVID-19 patients when corticosteroids can be used
- Interleukin (IL)-1 inhibitors (e.g. anakinra)
- Interferon beta for the treatment of early (i.e. <7 days from symptom onset) mild to moderate COVID-19

The Panel r**ecommends against** the use of the following immunomodulators for the treatment of COVID-19, except in a clinical trial [4]:

- **Siltuximab**, an anti-IL-6 monoclonal antibody **(AIII)**
- **Baricitinib** without **remdesivir (AIII)**
- **Interferons (alfa or beta)** for the treatment of severely or critically ill patients with COVID-19 **(AIII)**
- **Kinase inhibitors:**
  - Bruton's tyrosine kinase inhibitors (e.g., **acalabrutinib**, **ibrutinib**, **zanubrutinib**) **(AIII)**
  - Janus kinase inhibitors other than baricitinib (e.g., **ruxolitinib**, **tofacitinib**) **(AIII)**
- **Non-SARS-CoV-2-specific intravenous immune globulin (IVIG) (AIII)**. This recommendation should not preclude the use of IVIG when it is otherwise indicated for the treatment of complications that arise during the course of COVID-19.

Therapies For Existing Indications In Patients With COVID-19

ACEIs/ARBs In Patients With COVID-19

- In patients with COVID-19 who are receiving ACEIs/ARBs, there is currently no evidence to deviate from usual care and these medications should be continued unless contraindicated [3].
- Stopping these medications abruptly can lead to acute heart failure or unstable blood pressure [3]. **(Recommended)**

ACEIs In Postpartum Women

- In postpartum women with COVID-19 who have hypertension requiring treatment with ACE inhibitors, there is currently no evidence to deviate from usual care. These medications should be initiated or continued unless otherwise contraindicated [3].
- ACE inhibitors are contraindicated in the antenatal period due to risk of fetal and neonatal harm [3]. **(Consensus recommendation)**
- Steroids For People With Asthma Or COPD With COVID-19

  Use inhaled or oral steroids for the management of people with co-existing asthma or chronic obstructive pulmonary disease (COPD) and COVID-19 as you would normally for viral exacerbation of asthma or COPD. Do not use a nebuliser[3]. **(Consensus recommendation)**

Oestrogen-Containing Therapies

- **Consider stopping** oral menopausal hormone therapy (MHT), also known as hormone replacement therapy (HRT), in women with **mild or moderate COVID-19** [3]. **(Consensus recommendation)**
- Before restarting oral MHT, review the indication for this. If MHT is continued, consider using a transdermal preparation [3]. **(Consensus recommendation)**
- Stop oral menopausal hormone therapy (MHT) in women with **severe or critical COVID-19** [3]. **(Consensus recommendation)**
- Before restarting oral MHT, review the indication for this and consider transitioning to a transdermal preparation [3]. **(Consensus recommendation)**
- In women who have COVID-19 and who are taking oestrogen-containing contraception, manage these medications as per usual care [3]. **(Consensus recommendation)**
- In women who stop or suspend contraception when they have COVID-19, restart contraception at the time of discharge or when acute symptoms have resolved [3]. **(Consensus recommendation)**

Asthma Patient With COVID-19 [11]

- Advise patients to continue taking their prescribed asthma medications, particularly inhaled corticosteroids.
- Make sure that all patients have a written asthma action plan.
- Avoid nebulizers where possible, to reduce the risk of spreading virus.
- Pressurized metered dose inhaler via a spacer is preferred except for life-threatening exacerbations.
- Add a mouthpiece or mask to the spacer if required.
- Avoid spirometry in patients with confirmed or suspected COVID-19, or if community transmission of COVID-19 is occurring in your region.

Disease-Modifying Treatments Under Review [4]

- Budesonide
- Clarithromycin
- CT-P59 monoclonal antibody
- Interferon β-1a plus lopinavir-ritonavir
- Itraconazole
- Levamisole
- Bevacizumab

References

1. World Health Organization : Critical preparedness, readiness and response actions for COVID-19: interim guidance. 2020.
2. National Guidelines on Clinical Management of COVID-19 in Bangladesh. Version 9. 2021.
3. Australian guidelines for the clinical care of people with COVID-19 - Australian National COVID-19 Clinical Evidence Taskforce. 2021:47.
4. National Institutes of Health (NIH). COVID-19 treatment guidelines. 2021. https://www.covid19 treatmentguidelines.nih.gov
5. Guidance on Thromboprophylaxis and management of coagulopathy for adult inpatients with COVID-19. National Health Service (NHS), UK. 2021.
6. 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. https://www.ncbi.nlm.nih.gov/pubmed/ 33631065.
7. RECOVERY Collaborative Group, Horby PW, Pessoa-Amorim G, et al. Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): preliminary results of a randomised, controlled, open-label, platform trial. medRxiv. 2021. https://www.medrxiv.org/content/10.1101/2021.02.11. 21249258v1.
8. Lier AJ, Tuan JL, Davis MW, et al. Case report: disseminated strongyloidiasis in a patient with COVID-19. Am J Trop Med Hyg. 2020. http://www.ajtmh.org/docserver/fulltext
9. Marchese V, Crosato V, Gulletta M, et al. Strongyloides infection manifested during immunosuppressive therapy for SARS-CoV-2 pneumonia. Infection. 2020. https://www.ncbi. nlm.nih.gov/pubmed/32910321.
10. Stauffer WM, Alpern JD, Walker PF. COVID-19 and dexamethasone: a potential strategy to avoid steroid-related strongyloides hyperinfection. JAMA. 2020. https://www.ncbi.nlm.nih.gov/pubmed/ 32761166.
11. Interim guidance about COVID-19 and Asthma. GINA Global Strategy for Asthma Management and Prevention. GINA. 2020.