Saudi MoH Protocol for Patients Suspected of/Confirmed with COVID-19

Supportive care and antiviral treatment of suspected or confirmed COVID-19 infection

(Version 2.1) July 31st, 2020

Disclaimer: This is a living guidance that is subject to change as more evidence accumulates. It will be updated regularly and whenever needed. The guidance should be used to assist healthcare practitioners select the best available pharmacotherapy for COVID-19 infection according the best available and current evidence and is not intended to replace clinical judgement but rather to complement it. The evidence is inconclusive regarding the efficacy of most medications for covid-19. It is important to explain this to patient and family and obtain informed consent for use of these medications for unapproved indications.

COVID-19 Testing*	Category	Supportive Care	Pharmacotherapy	Precautions
Suspicious Cases (follow case definition published in Saudi CDC guidelines)	**Mild to Moderate:** Symptoms with no shortness of breath	– Treat symptoms – If no hospital admission required, need to follow instructions and recommendations published by Saudi CDC https://covid19.cdc.gov.sa/professionals-health-workers/	– Not required – Do not stop ACEI/ARBs in patients with hypertension, post-MI, or heart failure	– Paracetamol (acetaminophen) is the prefered agent for pain/fever see below table *"Medication Related Information"* – Labs and work-up: CBC, Urea/Electrolytes, Creatinine, CRP, LFTs, Chest X-ray, COVID-19 PCR tests
	Mild to Moderate: Symptoms with no shortness of breath in high risk patients[$] **Mild to Moderate**: Symptoms with shortness of breath in high risk patients[$]	– Treat symptoms – If hospital admission is not required, follow instructions and recommendations published by Saudi CDC https://covid19.cdc.gov.sa/professionals-health-workers/ – Consult Infectious Disease Specialist	– Case shall be discussed with infectious disease specialist, to initiate empirical antiviral therapy, while awaiting PCR result. – Do not stop ACEI/ARBs in patients with hypertension, post-MI, heart failure *If decision is to treat empirically, follow the treatment option under confirmed by PCR*	
PCR Confirmed Cases	**Asymptomatic**	– Follow instructions and recommendations published by Saudi CDC https://covid19.cdc.gov.sa/professionals-health-workers/	– Not required	

Saudi MoH Protocol for Patients Suspected of/Confirmed with COVID-19

Supportive care and antiviral treatment of suspected or confirmed COVID-19 infection

(Version 2.1) July 31st, 2020

COVID-19 Testing*	Category	Supportive Care	Pharmacotherapy	Precautions
PCR Confirmed Cases	**Mild to Moderate:** Symptoms (no O_2 requirements/no evidence of pneumonia but with other symptoms of covid-19 e.g. fever)	– Treat symptoms – Follow instructions and recommendations published by Saudi CDC https://covid19.cdc.gov.sa/professionals-health-workers/	Consider starting any of the following according to clinical evaluation and treating consultant's discretion): – Triple combination therapy (for adults): Lopinavir /Ritonavir, Ribavirin and interferon beta-1b for 14-days. Start within 7 days from symptoms appearance. • Lopinavir /Ritonavir ○ Adult Dosing: 400/100 mg (2 tablets of 200/50 mg) every 12 hrs. • Ribavirin ○ Adult Dosing: 400mg every 12hrs • Interferon beta-1b ○ Adult Dosing: 8 MIU on alternative days for 3 doses. **OR** – Consider Favipiravir ○ Adult Dosing: 1800 mg/dose twice a day on the first day; followed by 800 mg/dose twice a day for 7-10 days ○ Pediatric Dosing: - 10-15 kg: Loading Dose: One tablet PO BID for One day (maximum 400 mg/day). Maintenance from Day 2: Half tablet (100 mg) PO BID (maximum 200 mg/day) - 16-21 kg: Loading Dose: Two tablets PO BID One day (maximum 800 mg/day). Maintenance fromDay2: One Tablet PO BID (maximum 400 mg/day) - 22-35 kg: Loading Dose: Three Tablets PO BID for One day (maximum 1200 mg/day). Maintenance from Day2: One tablet PO TID (maximum 600 mg/day) - 36-45 kg: Loading Dose: Four tablets PO BID for One day (maximum 1600mg/day). Maintenance from Day2: Two tablets PO BID (maximum 800 mg/day) - 46-55 kg: Loading Dose: Five tablets PO BID for One day (maximum 2000 mg/day). Maintenance from Day2: Two Tablets qAM, Three Tablets qPM (maximum 1000 mg/day) - For >55 kg: Can use adult dosing if age ≥16 years, if age <16years use dosing of 46-55 kg range **OR** – Consider starting hydroxychloroquine, if no contraindications: ○ Adult Dosing: 400 mg every 12 hours for 1 day, followed by 200 mg BID for 5 – 7 days ○ Pediatric Dosing: 6.5 mg/kg/dose every 12 hours for day 1 (maximum day 1 dose: 400 mg/dose); followed by 3.25 mg/kg/dose every 12 hours for 5 – 7 days (maximum dose: 200 mg/dose)	**Lopinavir/ritonavir** see below table *"Medication Related Information"* – Current evidence doesn't support using Lopinavir/Ritonavir as monotherapy – Avoid co-administration with drugs that are highly dependent on CYP3A for clearance or with potent CYP3A inducers (check MOH formulary) – Patients with renal and/or hepatic impairment – Perform baseline ECG, if QT interval is more than 480 msec, do not use lopinavir/ritonavir. – Patients with prolonged QTc less than 480 msec, first-degree heart block or bundle branch block, or bradycardia upon ECG examination, and those who developed increased alanine transaminase of three times the upper limit of normal, reduce lopinavir/ritonavir dose to once per day. **Ribavirin** see below table *"Medication Related Information"* – Anemia associated with ribavirin may worsen underlying cardiac disease and lead to fatal and nonfatal myocardial infarctions. **Interferon beta-1b** see below table *"Medication Related Information"* – If patient presents more than 7 days since symptoms appearance, don't administer interferon beta-1b. **Favipiravir (non-formulary and non-SFDA registered)** see below table *"Medication Related Information"* – Contraindicated in pregnancy **Hydroxychloroquine & Chloroquine** see below table *"Medication Related Information"*

Saudi MoH Protocol for Patients Suspected of/Confirmed with COVID-19

Supportive care and antiviral treatment of suspected or confirmed COVID-19 infection

(Version 2.1) July 31st, 2020

COVID-19 Testing*	Category	Supportive Care	Pharmacotherapy	Precautions
PCR Confirmed Cases			– If hydroxychloroquine is not available, consider chloroquine ○ Adult Dosing: Chloroquine base 600 mg at diagnosis (equivalent to chloroquine phosphate 1000 mg), followed by 300 mg (equivalent to chloroquine phosphate 500 mg) 12 hours later BID for 5 – 7 days ○ Pediatric Dosing: Chloroquine base loading 10 mg/kg orally (maximum 600 mg) followed by 5 mg/kg orally once daily (maximum: 300 mg) 6 hours after the loading dose for 5 – 7 days	
	Severe: Symptoms ≥ 1 of the following: – Respiratory rate ≥30/min (adults); ≥40/min (children < 5 years) – Blood oxygen saturation ≤93% – PaO2/FiO2 ratio <300 – Lung infiltrates >50% of the lung field within 24-48 hours	– Treat symptoms – Follow instructions and recommendations published by Saudi CDC https://covid19.cdc.gov.sa/professionals-health-workers/ – ICU admission, decision by ICU treating team – Antibiotics and antifungals according to local antibiogram and institutional pneumonia management guidelines/ pathways.	**Consider starting any of the following according to clinical evaluation and treating consultant's discretion):** – Triple combination therapy (for adults): Lopinavir /Ritonavir, Ribavirin and interferon beta-1b for 14-days. Start within 7 days from symptoms appearance. • Lopinavir /Ritonavir ○ Adult Dosing: 400/100 mg (2 tablets of 200/50 mg) every 12 hrs. • Ribavirin ○ Adult Dosing: 400mg every 12hrs • Interferon beta-1b ○ Adult Dosing: 8 MIU on alternative days for 3 doses **OR** – Consider Favipiravir ○ Adult Dosing: 1800 mg/dose twice a day on the first day; followed by 800 mg/dose twice a day for 7-10 days. ○ Pediatric Dosing: - 10-15 kg: Loading Dose: One tablet PO BID for One day (maximum 400 mg/day). Maintenance from Day 2: Half tablet (100 mg) PO BID (maximum 200 mg/day) - 16-21 kg: Loading Dose: Two tablets PO BID One day (maximum 800 mg/day). Maintenance fromDay2: One Tablet PO BID (maximum 400 mg/day) - 22-35 kg: Loading Dose: Three Tablets PO BID for One day (maximum 1200 mg/day). Maintenance from Day2: One tablet PO TID (maximum 600 mg/day) - 36-45 kg: Loading Dose: Four tablets PO BID for One day (maximum 1600mg/day). Maintenance from Day2: Two tablets PO BID (maximum 800 mg/day) - 46-55 kg: Loading Dose: Five tablets PO BID for One day (maximum 2000 mg/day). Maintenance from Day2: Two Tablets qAM, Three Tablets qPM (maximum 1000 mg/day)	**Lopinavir/ritonavir** *(see precautions above)* **Ribavirin** *(see precautions above)* **Interferon beta-1b** *(see precautions above)* **Favipiravir (non-formulary and non-SFDA registered)** see below table *"Medication Related Information"* – Contraindicated in pregnancy **Dexamethasone** see below table *"Medication Related Information"* – Cardiovascular disease: Use with caution in patients with heart failure and/or hypertension; use has been associated with fluid retention, electrolyte disturbances, and hypertension. Use with caution following acute myocardial infarction; corticosteroids have been associated with myocardial rupture. – Diabetes: Use corticosteroids with caution in patients with diabetes mellitus; may alter glucose production/regulation leading to hyperglycemia. – Gastrointestinal disease: Use with caution in patients with GI diseases (diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, ulcerative colitis, abscess or other pyogenic infection) due to perforation risk. – Myasthenia gravis: Use with caution in patients with myasthenia gravis; exacerbation of symptoms has occurred especially during initial treatment with corticosteroids.

COVID-19 Testing*	Category	Supportive Care	Pharmacotherapy	Precautions
PCR Confirmed Cases			- For >55 kg: Can use adult dosing if age ≥16 years, if age <16years use dosing of 46-55 kg range **Corticosteroids use:** • For all patients who require supplemental oxygen inlcuding (but not limited to) those requiring non-invasive and invasive ventilation. • To be used up to 10 days, until discharged, or if patient becomes asymptomatic. • Dexamethasone: ○ Adult Dosing: 6 mg once daily oral (liquid or tablet) or intravenous preparation. Patients on chronic steroids, follow the usual recommendation of doubling steroids dose or start stress dose steroids based on clinical case basis on patients' condition **OR** • Prednisolone ○ Adult Dosing: In pregnant or breastfeeding women, prednisolone 40 mg PO twice daily should be used instead of dexamethasone. ○ Pediatric Dosing: Prednisolone (Oral/NG): 1 mg/kg once daily (max: 40 mg) **OR** • Hydrocortisone ○ Adult Dosing: In pregnant or breastfeeding women that cannot take oral, IV hydrocortisone 80 mg twice daily should be used instead of dexamethasone. ○ Preterm infants with a corrected gestation age of <40 weeks: 0.5 mg/kg every 12 hours **OR** Methylprednisolone sodium succinate (IV): 0.8 mg/kg once daily (max: 32 mg)	– Seizure disorders: Use corticosteroids with caution in patients with a history of seizure disorder; seizures have been reported with adrenal crisis. Labs and workup: Hemoglobin, occult blood loss, blood pressure, serum potassium, glucose, weight and height in children; HPA axis suppression
	Critical: – Symptoms ≥ 1 of the following: ○ ARDS ○ Sepsis ○ Altered consciousness ○ Multi-organ failure – Patient with cytokine release syndrome consider starting Tocilizumab – Criteria for patients at high-risk for developing cytokine storm (1 or more of the following):	– Treat symptoms – Follow instructions and recommendations published by Saudi CDC https://covid19.cdc.gov.sa/professionals-health-workers/ – ICU admission and management by ICU treating team – Antibiotics and antifungals according to local antibiogram and institutional pneumonia	**Consider starting any of the following according to clinical evaluation and treating consultant's discretion):** – Consider Remdesivir (once available) ○ Adult Dosing: 200 mg loading dose (IV, within 30 min), followed by 100 mg once daily for 5 to 10 days ○ Pediatric dosing - <40 kg: 5 mg/kg IV load, then 2.5 mg/kg q24h for 5 to 10 days - ≥40 kg: 200 mg IV load, then 100 mg IV q24h for 5 to 10 days **OR** – Consider Favipiravir ○ Adult Dosing: 1800 mg/dose twice a day on the first day; followed by 800 mg/dose twice a day for –14 days	**Use of triple therapy has not been evaluated in critically ill patients.** **Remdesivir (non-formulary and non-SFDA registered)** see below table *"Medication Related Information"* – Exclusion criteria evidence of multiorgan failure, need of inotropes, Creatinine clearance < 30 ml/min, dialysis/hemofiltration, transaminases > 5X ULN, or concomitant use of lopinavir/ritonavir **Favipiravir (non-formulary and non-SFDA registered)** see below table *"Medication Related Information"* – Contraindicated in pregnancy

COVID-19 Testing*	Category	Supportive Care	Pharmacotherapy	Precautions
PCR Confirmed Cases	○ Serum IL-6 ≥3x upper normal limit ○ Ferritin >300 ug/L (or surrogate) with doubling within 24 hours ○ Ferritin >600 ug/L at presentation and LDH >250 ○ Elevated D-dimer (>1 mcg/mL)	management guidelines/ pathways.	○ Pediatric Dosing: - 10-15 kg: Loading Dose: One tablet PO BID for One day (maximum 400 mg/day). Maintenance from Day 2: Half tablet (100 mg) PO BID (maximum 200 mg/day) - 16-21 kg: Loading Dose: Two tablets PO BID One day (maximum 800 mg/day). Maintenance from Day2: One Tablet PO BID (maximum 400 mg/day) - 22-35 kg: Loading Dose: Three Tablets PO BID for One day (maximum 1200 mg/day). Maintenance from Day2: One tablet PO TID (maximum 600 mg/day) - 36-45 kg: Loading Dose: Four tablets PO BID for One day (maximum 1600mg/day). Maintenance from Day2: Two tablets PO BID (maximum 800 mg/day) - 46-55 kg: Loading Dose: Five tablets PO BID for One day (maximum 2000 mg/day). Maintenance from Day2: Two Tablets qAM, Three Tablets qPM (maximum 1000 mg/day) - For >55 kg: Can use adult dosing if age ≥16 years, if age <16years use dosing of 46-55 kg range. **Corticosteroids use:** • For all patients who require supplemental oxygen inlcuding (but not limited to) those requiring non-invasive and invasive ventilation. • To be used up to 10 days, until discharged, or if patient becomes asymptomatic. • Dexamethasone: ○ Adult Dosing: 6 mg once daily oral (liquid or tablet) or intravenous preparation. Patients on chronic steroids, follow the usual recommendation of doubling steroids dose or start stress dose steroids based on clinical case basis on patients' condition **OR** • Prednisolone ○ Adult Dosing: In pregnant or breastfeeding women, prednisolone 40 mg PO twice daily should be used instead of dexamethasone. ○ Pediatric Dosing: Prednisolone (Oral/NG): 1 mg/kg once daily (max: 40 mg) **OR** • Hydrocortisone ○ Adult Dosing: In pregnant or breastfeeding women that cannot take oral, IV hydrocortisone 80 mg twice daily should be used instead of dexamethasone. ○ Preterm infants with a corrected gestation age of <40 weeks: 0.5 mg/kg every 12 hours	**Tocilizumab** see below table *"Medication Related Information"* – Should perform IL6 and other inflammatory markers testing prior to start (CRP, Ferritin, D-dimer) – Watch for infusion reaction **Dexamethasone**: *(see precautions above)*

Supportive care and antiviral treatment of suspected or confirmed COVID-19 infection

(Version 2.1) July 31st, 2020

COVID-19 Testing*	Category	Supportive Care	Pharmacotherapy	Precautions
PCR Confirmed Cases			**OR** – Methylprednisolone sodium succinate (IV): 0.8 mg/kg once daily (max: 32 mg) **If cytokine release syndrome is suspected or confirmed, consider tocilizumab** ○ Adult Dosing: Single dose 4 – 8 mg/kg (usual dose 400 mg; maximum 800 mg) by IV infusion; repeated within 12 hours for maximum of 2 doses ○ Pediatric Dosing (<18 years): - <30 kg: 12 mg/kg repeated within 12 hours for maximum of 2 doses - ≥30 kg: 8 mg/kg (max: 800 mg/dose) repeated within 12 hours for maximum of 2 dose	

NOTES:

(Lopinavir/ritonavir, ribavirin, interferon beta 1b and tocilizumab are registered medications in Saudi Arabia and available in MoH formulary for other indications but have not shown proven efficacy in many randomized clinical trials as of yet and their use in this setting is considered off-label. Remdesivir and favipiravir are not currently registered medications by SFDA.

Pregnancy and Lactation: Management of infection with SARS-COV2 in pregnancy is mainly based on supportive care. Consideration of antiviral therapy should be based on patient condition, safety profile and preference of the patient and treating team. Refer to the MoH COVID-19 guidance in pregnancy

Convalescent Plasma transfusion is available as part of a clinical trial for the following critically ill patients: ≥ 18 years old, confirmed COVID-19 PCR, requiring ICU care or severe or immediately life-threatening care (see severe and critical symptoms above). To enroll your patient, please visit https://plasmaforcovid.com/

Thromboprophylaxis:

Recommendations

- All admitted patients should be evaluated upon admission, and daily thereafter for both thrombotic and bleeding risk.
- Laboratory evaluation and monitoring: Baseline CBC, fibrinogen, PT, aPTT, D-dimer on admission, and serially.
- Baseline or surveillance imaging are not recommended in the absence of clinical symptoms of VTE
- Patients on chronic VTE prophylaxis should continue as planned before.
- Warfarin, DOAC and antiplatelet medications are not recommended to be used as prophylaxis
- For patients whom anticoagulant therapy is contraindicated, mechanical thromboprophylaxis, preferably with intermittent pneumatic compression devices, should be utilized, although there is limited evidence of efficacy in hospitalized medically ill patients
- Thromboprophylaxis should continue until the time of discharge or the patient becomes asymptomatic.

When to consult hematologist:

- Heparin induced thrombocytopenia (HIT)
- Platelets below 50 x 10^9/L
- Unexplained bleeding
- Inherited bleeding disorder (Hemophilia, thrombasthenia)
- Inherited red blood disorder (sickle cell disease)
- Previously on anticoagulation therapy
- Radiological evidence of thrombosis

Adults:

Thromboprophylaxis with low molecular weight heparin (LMWH) should be considered in ALL patients (including non-critically ill) who require hospital admission for COVID-19 infection, in the absence of any contraindications (active bleeding and platelet count less than 25 x 10^9/L; monitoring is advised in severe renal impairment; abnormal PT or APTT is not a contraindication)

COVID-19 Testing*	Category	Supportive Care	Pharmacotherapy	Precautions

D-Dimer (mcg/mL)	Weight (Kg)	LMWH
< 1	< 100	Enoxaparin 40 mg daily
	100-150	Enoxaparin 40 mg twice daily
	>150	Enoxaparin 60 mg twice daily
> 1	< 100	Enoxaparin 40 mg twice daily
	100-150	Enoxaparin 80 mg twice daily
	>150	Enoxaparin 120 mg twice daily

All doses may need adjustment based on renal function. In the absence of bleeding, coagulopathy is not a contraindication to anticoagulation with heparin/LMWH unless platelets fall below 30 for prophylaxis or below 50 for therapeutic heparin/LMWH.

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

Pediatrics:

Recommended anticoagulant prophylaxis:

Patient category	Age ≤ 2 months	Age >2 months & weight ≤ 60 kg	Age > 2 months & weight > 60 kg	Other VTE risk factors
Severely ill with severe respiratory symptoms	Enoxaparin: 0.75 mg/kg/dose q12 h	Enoxaparin 0.5 mg/kg SC every 12 hours (max 60 mg/day)	Enoxaparin 40 mg SC every 24 hours	– Altered Mobility – Active cancer (receiving chemotherapy/radiation in previous 6 months) – Burns: > 50% total body surface area – Severe dehydration – Severe systemic infection – Inflammatory disorders – Known acquired or inherited thrombophilia – Obesity (BMI ≥ 95 percentile) – Protein losing disorders – Sickle Cell Disease – Previous history of clots (DVT/PE) – Family history of VTE in 1st degree relative < 40 years old
Severely ill with clinical deterioration, or high risk of VTE (rising DIC score or D-dimer)	Enoxaparin: 1.5 mg/kg/dose q12 h	Enoxaparin 1 mg/kg SC every 12 hours (max 60 mg/day)	Enoxaparin 40 mg SC every 12 hours	
Mild symptomatic plus 1- in PICU AND CVC + ONE risk VTE factor 2- in PICU OR CVC + TWO risk VTE factor 3- THREE risk VTE factor	Enoxaparin: 0.75 mg/kg/dose q12 h	Enoxaparin 0.5 mg/kg SC every 12 hours (max 60 mg/day)	Enoxaparin 40 mg SC every 24 hours	

Patients with radiological evidence of VTE or arterial thrombosis (PE, stroke, others) should be treated as per institutional VTE guideline. (Consult hematologist)

Enoxaparin monitoring

Routine anti-Xa levels are not recommended.

- If an anti-Xa level is deemed necessary, it should be drawn 4-6 hours after enoxaparin administration with an anti-Xa goal of 0.2- 0.4 units/mL for prophylaxis and 0.5-1 Units/ml for therapeutic dose.
- Consider re-checking anti-Xa if the patient experiences active bleeding or has evidence of renal dysfunction while on enoxaparin therapy

Contraindications to Anticoagulation (Bleeding Risk Factors)

Intracranial hemorrhage, Brain ischemia/acute stroke, Ongoing and uncontrolled bleeding /hematoma, Congenital bleeding disorder

Uncorrected coagulopathy: INR >1.5, APTT >44 seconds, fibrinogen <100 g/dL, or platelet <50,000/microliter

Consider Avoiding Anticoagulation

Intracranial mass, Recent lumbar puncture / Epidural (<24 hours ago), The patient is likely to require an invasive procedure within 24 hours of starting enoxaparin, Neurosurgical procedure, Pelvic fracture within past 48 hours, Recent aspirin or antiplatelet use (<5-7 days ago), Uncontrolled hypertension

Enoxaparin dose Adjustments:

- Renal impairment (CrCl 30 to 80 mL/min): No adjustment necessary
- Renal impairment (CrCl less than 30 mL/min): reduce usual recommended dose by 50%.

COVID-19 Testing*	Category	Supportive Care	Pharmacotherapy	Precautions

Multisystem Inflammatory Syndrome in Children (MIS-C)

Criteria for Management:

- Patient aged < 21 years presenting with fever (>38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours), laboratory evidence of inflammation (Including, but not limited to, one or more of the following: an elevated CRP, ESR, fibrinogen, procalcitonin, D-dimer, ferritin, LDH, or IL-6; elevated neutrophils; reduced lymphocytes; and low albumin), and evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological)
- No alternative plausible diagnoses
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms

Management:

There are no established therapies for COVID-19-associated CSS or MIS-C. These medications are to be used only with guidance from Rheumatology, Cardiology and Infectious Diseases. Patients who are being evaluated for immunomodulatory therapy should also be considered for antiviral therapy if they are not already receiving it.

- Supportive Care: Children with moderate to severe signs and symptoms should be admitted to the hospital. Admission to a pediatric intensive care unit is appropriate for children with hemodynamic instability (shock, arrhythmia), significant respiratory compromise, or other potentially life-threatening complications
- Thromboprophylaxis (see above section)
- Antiviral therapy (see above based of patient category)
- Immunomodulator Dosing and Monitoring

Immunomodulator	Dosing	Safety monitoring
IVIG see below table *"Medication Related Information"* MIS-C with or without features of Kawasaki disease or signs of myocardial dysfunction OR Severe or critical COVID-19 with evidence of CSS	- 1-2 g/kg/dose IV - 2 g/kg/dose IV over 8-12 hrs. if Kawasaki disease stigmata	- Assess cardiac function and fluid status prior to giving to avoid fluid overload - Baseline renal function tests, urine output, IgG level, CBC - Monitor clinically for signs of hemolysis after first dose - Potential adverse reactions: anaphylaxis, - Infusion reaction, hemolysis, transaminitis, aseptic meningitis - Pulmonary adverse reactions; blood pressure (prior to, during, and following infusion); clinical response. - For patients at high risk of hemolysis (dose ≥2 g/kg, given as a single dose or divided over several days, and non-O blood type): Hemoglobin or hematocrit prior to and 36 to 96 hours post-infusion and again at 7 to 10 days post-infusion
Glucocorticoids MIS-C with features of shock or coronary artery dilation/aneurysm OR Severe or critical COVID-19 with evidence of CSS	- 1-2 mg/kg/day divided BID (prednisone, prednisolone, methylprednisolone) - 5 mg/m2 daily (dexamethasone)	*(see precautions above)*
Tocilizumab Severe or critical COVID-19 with evidence of CSS Elevated CRP and/or IL-6	*(see dosing above)*	*(see precautions above)*

Saudi MoH Protocol for Patients Suspected of/Confirmed with COVID-19

Supportive care and antiviral treatment of suspected or confirmed COVID-19 infection

(Version 2.1) July 31st, 2020

COVID-19 Testing*	Category	Supportive Care	Pharmacotherapy	Precautions
Abbreviations: ARDS: Acute respiratory distress syndrome, COVID-19: Coronavirus Disease 2019, CBC: Complete Blood Count, CRP: C-Reactive Protein, IL6: Interleukin 6, LFT: Liver Function Test, PCR: Polymerase Chain Reaction, ECG: Electrocardiogram, G6PD: Glucose-6-Phosphate Dehydrogenase, ACEI: Angiotensin-converting enzyme inhibitors, ARBs: Angiotensin II receptor blockers, MI: Myocardial infarction, MIS-C: Multisystem Inflammatory Syndrome in Children, CSS: Cytokine Storm Syndrome				
Footnotes: *Testing for SARS-COV2 virus shall be performed in accordance with published case definition by Saudi CDC guidelines. $High risk patients have one or more: 1. Elderly (age > 65 years), 2. With underlying end organ dysfunction, 3. Diabetes, 4. History of cardiovascular disease, 5. History of pulmonary disease, 6. Immunocompromised, and/or 7. Pregnancy				

Medication Related Information

Medication	Contraindication	Major Drug Interactions	Required dose adjustment	Pregnancy
Paracetamol (acetaminophen)	– Hypersensitivity to acetaminophen or any component of the formulation – Severe hepatic impairment or active liver disease	– Acetaminophen may increase the levels/effects of: Busulfan; Dasatinib; Imatinib; Local Anesthetics; Mipomersen; Phenylephrine (Systemic); Prilocaine; Sodium Nitrite; SORAfenib; Vitamin K Antagonists – The levels/effects of Acetaminophen may be increased by: Alcohol (Ethyl); Dapsone (Topical); Dasatinib; Flucloxacillin; Isoniazid; MetyraPONE; Nitric Oxide; Probenecid; SORAfenib	– Requires dose adjustment with patient with hepatic impairment *See MoH online formulary*	– Oral paracetamol is considered safe in normal therapeutic doses for short-term use as a minor analgesic/antipyretic in pregnancy. Consider Administering IV paracetamol to a pregnant woman only if clearly needed. Carefully assess maternal benefit and fetal risk before administering IV paracetamol during labor and delivery.
Lopinavir/ritonavir	– Hypersensitivity to lopinavir, ritonavir, or any component of the formulation; – Coadministration with drugs that are highly dependent on CYP3A for clearance or with potent CYP3A inducers – Patients with renal and/or hepatic impairment	– Avoid concomitant use of Lopinavir and Ritonavir with any of the following: Acalabrutinib; Ado-Trastuzumab Emtansine; Alfuzosin; Amiodarone; Antihepaciviral Combination Products; Aprepitant; Astemizole; Asunaprevir; Avanafil; Axitinib; Barnidipine; Blonanserin; Bosutinib; Bromocriptine; Budesonide (Systemic); Cisapride; Clarithromycin; Clobetasone; Cobicistat; Cobimetinib; Conivaptan; Dabrafenib; Dapoxetine; Darunavir; Disulfiram; Domperidone; Dronedarone; Elagolix; Eletriptan; Eplerenone; Ergot Derivatives; Everolimus; Flecainide; Flibanserin; Fluticasone (Nasal); Fosamprenavir; Fosaprepitant; Fusidic Acid (Systemic); Glecaprevir and Pibrentasvir; Grazoprevir; Halofantrine; Ibrutinib; Irinotecan Products; Isavuconazonium Sulfate; Ivabradine; Lapatinib; Lefamulin; Lercanidipine; Lomitapide; Lovastatin; Lurasidone; Macitentan; Meptazinol; MetroNIDAZOLE (Systemic); Midazolam; Naloxegol; Neratinib; NiMODipine; Nisoldipine; Palbociclib; PAZOPanib; Pimozide; Propafenone; QuiNIDine; QuiNINE; Radotinib; Ranolazine; Red Yeast Rice; Regorafenib; Revefenacin; RifAMPin; Rivaroxaban; Rupatadine; Salmeterol; Silodosin; Simeprevir; Simvastatin; Sonidegib; St John's Wort; Suvorexant; Tamsulosin; Terfenadine; Ticagrelor; Tipranavir; Tolvaptan; Topotecan; Trabectedin; Triazolam; Udenafil; Ulipristal; VinCRIStine (Liposomal); Vinflunine; Vorapaxar; Voriconazole; Voxilaprevir – Lopinavir and Ritonavir may increase the levels/effects of: Abemaciclib; Acalabrutinib; Ado-Trastuzumab Emtansine; Afatinib; Alfuzosin; Alitretinoin (Systemic); Almotriptan; Alosetron; Alpelisib; ALPRAZolam; Amiodarone; AmLODIPine; Antihepaciviral Combination Products; Apixaban; Aprepitant; ARIPiprazole; ARIPiprazole Lauroxil; Astemizole; Asunaprevir; AtorvaSTATin; Avanafil; Axitinib; Barnidipine; Bedaquiline; Benperidol; Benzhydrocodone; Betamethasone (Ophthalmic); Betrixaban; Bictegravir; Bilastine; Blonanserin; Bortezomib; Bosentan; Bosutinib; Brentuximab Vedotin; Brexpiprazole; Brigatinib; Brinzolamide; Bromocriptine; Budesonide (Nasal); Budesonide (Oral Inhalation); Budesonide (Systemic); Budesonide (Topical); Buprenorphine; BusPIRone; Cabazitaxel; Cabozantinib; Calcifediol; Calcium Channel Blockers (Nondihydropyridine); Cannabidiol; Cannabis; Cariprazine; Celiprolol; Ceritinib; Cilostazol; Cinacalcet; Cisapride; Cladribine; Clarithromycin; Clobetasone; Clorazepate; CloZAPine; Cobimetinib; Codeine; Colchicine; Conivaptan; Copanlisib; Corticosteroids (Orally Inhaled); Corticosteroids (Systemic); Crizotinib; Cyclophosphamide; CycloSPORINE (Systemic); CYP3A4 Substrates (High risk with Inhibitors); Dabigatran Etexilate; Dabrafenib; Daclatasvir; Dapoxetine; Darolutamide; Dasatinib; Deflazacort; Delamanid; Dexamethasone (Ophthalmic); Digoxin; Disulfiram; DOCEtaxel; Dofetilide; Domperidone; DOXOrubicin (Conventional); Dronabinol; Dronedarone; Drospirenone; Dutasteride; Duvelisib; Edoxaban; Elagolix; Eletriptan; Eliglustat; Eluxadoline; Elvitegravir; Encorafenib; Enfuvirtide; Entrectinib; Eplerenone; Erdafitinib; Ergot Derivatives; Erlotinib; Estazolam; Estrogen Derivatives; Eszopiclone; Etizolam; Everolimus; Evogliptin; Fedratinib; FentaNYL; Fesoterodine; Flecainide; Flibanserin; Fluticasone (Nasal); Fluticasone (Oral Inhalation); Fosaprepitant; Fostamatinib; Fusidic Acid (Systemic); Galantamine; Gefitinib; Gilteritinib; Glasdegib; Glecaprevir and Pibrentasvir; Grazoprevir; GuanFACINE; Halofantrine; HYDROcodone; Ibrutinib; Idelalisib; Iloperidone; Imatinib; Imidafenacin; Irinotecan Products; Isavuconazonium Sulfate; Itraconazole; Ivabradine; Ivacaftor; Ivosidenib; Ixabepilone; Ketoconazole (Systemic); Lacosamide; Lapatinib; Larotrectinib; Lefamulin; Lercanidipine; Levobupivacaine; Levomilnacipran; LinaGLIPtin; Lomitapide; Lorlatinib; Lovastatin; Lumefantrine; Lurasidone; Macitentan; Manidipine; Maraviroc; Meperidine; Meptazinol; Methadone; MethylPREDNISolone;	– No dose adjustment required with patient with hepatic impairment; however, lopinavir is metabolized by the liver – Requires to be avoided with patient on dialysis *See MoH online formulary*	– Fetal risk cannot be ruled out – Avoid the oral solution of this combination product during pregnancy due to the presence of ethanol as an excipient in the solution.

Medication Related Information

Medication	Contraindication	Major Drug Interactions	Required dose adjustment	Pregnancy
		MetroNIDAZOLE (Systemic); Midazolam; Midostaurin; MiFEPRIStone; Mirodenafil; Mirtazapine; Naldemedine; Nalfurafine; Naloxegol; Nefazodone; Nelfinavir; Neratinib; Nilotinib; NiMODipine; Nintedanib; Nisoldipine; Olaparib; Ospemifene; Oxybutynin; OxyCODONE; Palbociclib; Panobinostat; Parecoxib; Paricalcitol; PAZOPanib; Pexidartinib; P-glycoprotein/ABCB1 Substrates; Pimavanserin; Pimecrolimus; Pimozide; Piperaquine; Polatuzumab Vedotin; PONATinib; Pranlukast; Praziquantel; PrednisoLONE (Systemic); PredniSONE; Progestins (Contraceptive); Propafenone; Protease Inhibitors; Prucalopride; QT-prolonging Agents (Highest Risk); QUEtiapine; QuiNIDine; QuiNINE; Radotinib; Ramelteon; Ranolazine; Reboxetine; Red Yeast Rice; Regorafenib; Repaglinide; Retapamulin; Revefenacin; Ribociclib; Rifabutin; RifAXIMin; Rilpivirine; Riociguat; Rivaroxaban; RomiDEPsin; Rosuvastatin; Rupatadine; Ruxolitinib; Salmeterol; SAXagliptin; Sibutramine; Sildenafil; Silodosin; Simeprevir; Simvastatin; Sirolimus; Solifenacin; Sonidegib; SORAfenib; SUFentanil; SUNItinib; Suvorexant; Tacrolimus (Systemic); Tacrolimus (Topical); Tadalafil; Talazoparib; Tamsulosin; Tasimelteon; Tegaserod; Telithromycin; Temsirolimus; Tenofovir Disoproxil Fumarate; Terfenadine; Tetrahydrocannabinol; Tetrahydrocannabinol and Cannabidiol; Tezacaftor; Thiotepa; Ticagrelor; Tofacitinib; Tolterodine; Tolvaptan; Topotecan; Toremifene; Trabectedin; TraMADol; TraZODone; Triamcinolone (Systemic); Triazolam; Tricyclic Antidepressants; Udenafil; Ulipristal; Upadacitinib; Valbenazine; Vardenafil; Velpatasvir; Vemurafenib; Venetoclax; Vilazodone; VinBLAStine; VinCRIStine; VinCRIStine (Liposomal); Vindesine; Vinflunine; Vinorelbine; Vorapaxar; Voxilaprevir; Zolpidem; Zopiclone; Zuclopenthixol – The levels/effects of Lopinavir and Ritonavir may be increased by: ARIPiprazole; Cat's Claw; Clarithromycin; Cobicistat; Delavirdine; Enfuvirtide; Fusidic Acid (Systemic); Ketoconazole (Systemic); MetroNIDAZOLE (Topical); P-glycoprotein/ABCB1 Inhibitors; Posaconazole; QuiNINE; Rifabutin; RifAMPin; Simeprevir; Vilanterol		
Hydroxychloroquine	– Known hypersensitivity to hydroxychloroquine, 4-aminoquinoline derivatives, or any component of the formulation. – Preexisting retinopathy	– Avoid concomitant use: Artemether; Lumefantrine; Mefloquine – Hydroxychloroquine may increase the levels/effects of: Antipsychotic Agents (Phenothiazines); Beta-Blockers; Cardiac Glycosides; Dapsone (Systemic); Dapsone (Topical); Haloperidol; Hypoglycemia-Associated Agents; Lumefantrine; Mefloquine; QT-prolonging Agents (Highest Risk) – The levels/effects of Hydroxychloroquine may be increased by: Androgens; Antidiabetic Agents; Artemether; Dapsone (Systemic); Herbs (Hypoglycemic Properties); Maitake; Mefloquine; Monoamine Oxidase Inhibitors; Pegvisomant; Prothionamide; Quinolones; Salicylates; Selective Serotonin Reuptake Inhibitors; Tamoxifen	– No dose adjustment required with patient with hepatic nor renal impairment	– Fetal risk cannot be ruled out. Fetal ocular toxicity has been reported. – Hydroxychloroquine use should be avoided during pregnancy, unless absolutely indicated and only after assessing maternal benefit and fetal risk.
Chloroquine	– Hypersensitivity to chloroquine, 4-aminoquinoline compounds, or any component of the formulation – The presence of retinal or visual field changes of any etiology	– Avoid concomitant use of Chloroquine with any of the following: Agalsidase Alfa; Agalsidase Beta; Artemether; Conivaptan; Fusidic Acid (Systemic); Idelalisib; Lumefantrine; Mefloquine; Pimozide; QT-prolonging Strong CYP3A4 Inhibitors (Moderate Risk) – Chloroquine may increase the levels/effects of: Antipsychotic Agents (Phenothiazines); Beta-Blockers; Cardiac Glycosides; Dapsone (Systemic); Dapsone (Topical); Domperidone; Haloperidol; Hypoglycemia-Associated Agents; Local Anesthetics; Lumefantrine; Mefloquine; Ondansetron; Pentamidine (Systemic); Perhexiline; Prilocaine; Primaquine; QT-prolonging Antipsychotics (Moderate Risk); QT-prolonging Class IC Antiarrhythmics (Moderate Risk); QT-prolonging Quinolone Antibiotics (Moderate Risk); Sodium Nitrite – The levels/effects of Chloroquine may be increased by: Abiraterone Acetate; Androgens; Antidiabetic Agents; Aprepitant; Artemether; Asunaprevir; Cimetidine; CloBAZam; Clofazimine; Conivaptan; CYP2D6 Inhibitors (Moderate); CYP2D6 Inhibitors (Strong); CYP3A4 Inhibitors (Moderate); CYP3A4 Inhibitors (Strong); Dacomitinib; Dapsone (Systemic); Duvelisib; Erdafitinib; Fosaprepitant; Fosnetupitant; Fusidic Acid (Systemic); Herbs (Hypoglycemic Properties); Idelalisib; Imatinib; Larotrectinib; Maitake; Mefloquine; MiFEPRIStone; Monoamine Oxidase Inhibitors; Netupitant; Nitric Oxide; Palbociclib; Panobinostat; Peginterferon Alfa-2b; Pegvisomant; Perhexiline; Pimozide; Prothionamide; QT-prolonging Agents (Highest Risk); QT-prolonging Antidepressants (Moderate Risk); QT-prolonging Kinase Inhibitors (Moderate Risk); QT-prolonging Miscellaneous Agents (Moderate Risk); QT-prolonging Moderate CYP3A4 Inhibitors (Moderate Risk); QT-prolonging Strong CYP3A4 Inhibitors (Moderate Risk); Quinolones; Salicylates; Selective Serotonin Reuptake Inhibitors; Simeprevir; Stiripentol; Tamoxifen	– Requires dose adjustment with patient with renal impairment – *See MoH online formulary*	– Fetal risk cannot be ruled out. Fetal ocular toxicity has been reported – Administer chloroquine during pregnancy only if the potential maternal benefit outweighs the potential fetal risk

Medication Related Information

Medication	Contraindication	Major Drug Interactions	Required dose adjustment	Pregnancy
Remdesivir	– Safety and efficacy not established	– Avoid Concomitant Use: There are no known interactions where it is recommended to avoid concomitant use. – Increased Effect/Toxicity: There are no known significant interactions involving an increase in effect. – Decreased Effect: There are no known significant interactions involving a decrease in effect.	– No dose adjustment studied	– Not studied
Favipiravir	– Hematopoietic tissues such as decreased RBC production, and increases in liver function parameters – Testis toxicity was also noted – Teratogenic	– Acyclovir, Adefovir dipivoxil, Afatinib, Allopurinol, Almotriptan, Alprostadil, Ambrisentan, Aminohippuric acid, Aminophenazone, Amiodarone, Amitriptyline, Amodiaquine, Anastrozole, Antipyrine, Apalutamide, Apixaban, Atorvastatin, Avatrombopag, Avibactam, Azelastine, Baricitinib, Belinostat, Benzyl alcohol, Benzylpenicillin, Betrixaban, Bisoprolol, Bosutinib, Brentuximab vedotin, Brigatinib, Bumetanide, Buprenorphine, Cabazitaxel, Canagliflozin, Captopril, Cefaclor, Cefazolin, Cefdinir, Cefotiam, Ceftibuten, Ceftizoxime, Celecoxib, Cephalexin, Ceritinib, Cerivastatin, Chloroquine, Cholic Acid, Cidofovir, Cimetidine, Cisapride, Citrulline, Clobazam, Clomifene, Cobimetinib, Colchicine, Conjugated estrogens, Copanlisib, Crizotinib, Cyclophosphamide, Cyclosporine, Dabigatran etexilate, Zafirlukast, Zalcitabine, Zidovudine, Zopiclone	– No dose adjustment studied	– Contraindicated
Tocilizumab	– Known hypersensitivity to tocilizumab or any component of the formulation – Active infections	– Avoid Concomitant Use: Anti-TNF Agents; BCG (Intravesical); Belimumab; Biologic Disease-Modifying Antirheumatic Drugs (DMARDs); Cladribine; Natalizumab; Pimecrolimus; Tacrolimus (Topical); Vaccines (Live) – Increased Effect/Toxicity: Anti-TNF Agents; Biologic Disease-Modifying Antirheumatic Drugs (DMARDs); Fingolimod; Leflunomide; Natalizumab; Siponimod; Vaccines (Live) – The levels/effects of Tocilizumab may be increased by: Belimumab; Cladribine; Denosumab; Ocrelizumab; Pimecrolimus; Roflumilast; Tacrolimus (Topical); Trastuzumab – Tocilizumab may decrease the levels/effects of: BCG (Intravesical); Coccidioides immitis Skin Test; CYP3A4 Substrates (High risk with Inducers); Nivolumab; Pidotimod; Sipuleucel-T; Smallpox and Monkeypox Vaccine (Live); Tertomotide; Vaccines (Inactivated); Vaccines (Live) – The levels/effects of Tocilizumab may be decreased by: Echinacea	– Requires dose adjustment with patient with hepatotoxicity *See MoH online formulary*	– Fetal risk cannot be ruled out
Ribavirin	– Autoimmune hepatitis – Coadministration with didanosine; symptomatic hyperlactatemia/lactic acidosis, peripheral neuropathy, pancreatitis, and fatal hepatic failure. – Hemoglobinopathy (e.g., thalassemia major and sickle-cell anemia) – Hypersensitivity, including serious skin reactions – Pregnant women or men with pregnant wives – Renal impairment (CrCl less than 50 mL/min)	– Avoid combination: Cladribine and Didanosine – Consider therapy modification: Influenza Virus Vaccine, AzaTHIOprine, Zidovudine – Monitor therapy: Interferons (Alfa) and Vitamin K Antagonists (eg, warfarin)	– Requires dose adjustment *See MoH online formulary*	– Significant teratogenic
Interferon beta-1b	– History of hypersensitivity to natural or recombinant interferon beta, albumin (human), or any component of the formulation. – Documentation of allergenic cross-reactivity for interferons is limited. However, because of similarities in chemical structure	– Avoid combination with Cladribine – Monitor therapy with Zidovudine	– No dose adjustment is required	– Rating Fetal risk cannot be ruled out. – Available evidence is inconclusive or is inadequate for determining fetal risk when used in pregnant women or women of childbearing potential. Weigh the potential

Medication Related Information

Medication	Contraindication	Major Drug Interactions	Required dose adjustment	Pregnancy
	and/or pharmacologic actions, the possibility of cross-sensitivity cannot be ruled out with certainty. – Pregnancy, decompensated liver disease; current severe depression and/or suicidal ideation			benefits of drug treatment against potential risks before prescribing this drug during pregnancy.
Dexamethasone	– Concomitant use of more than a single dose of dexamethasone with rilpivirine – Hypersensitivity to dexamethasone or any component of the product – Systemic fungal infection	– Avoid concomitant use of DexAMETHasone (Systemic) with any of the following: Aldesleukin; BCG (Intravesical); Cladribine; Conivaptan; Desmopressin; Fusidic Acid (Systemic); Idelalisib; Indium 111 Capromab Pendetide; Lapatinib; Lasmiditan; Macimorelin; Mifamurtide; MiFEPRIStone; Natalizumab; Pimecrolimus; Rilpivirine; Simeprevir; Tacrolimus (Topical); Upadacitinib	– Use cautiously in the elderly at the lowest possible dose *See MoH online formulary*	– Pregnant or breastfeeding women, use prednisolone (Oral) or intravenous hydrocortisone instead of dexamethasone.
IVIG	– Hypersensitivity to IVIG or any component of the formula – Documentation of allergic cross-reactivity	– MMR, varicella vaccines	– Use with caution in patients with Renal impairment due to risk of immune globulin-induced renal dysfunction; the rate of infusion and concentration of solution should be minimized. Discontinue if renal function deteriorates during treatment.	
Enoxaparin	– Active major bleeding – History of immune-mediated heparin-induced thrombocytopenia within the past 100 days or in presence of circulating antibodies – Hypersensitivity to benzyl alcohol (present in multi-dose formulation) – – Hypersensitivity to enoxaparin.	Avoid combination : – Vorapaxar: May enhance the adverse/toxic effect of Anticoagulants. More specifically, this combination is expected to increase the risk of bleeding. – Urokinase: May enhance the anticoagulant effect of Anticoagulants. – Rivaroxaban: Anticoagulants may enhance the anticoagulant effect of Rivaroxaban – Omacetaxine: Anticoagulants may enhance the adverse/toxic effect of Omacetaxine – MiFEPRIStone: May enhance the adverse/toxic effect of Anticoagulants. Specifically, the risk of bleeding may be increased – Hemin: May enhance the anticoagulant effect of Anticoagulants. – Edoxaban: May enhance the anticoagulant effect of Anticoagulants. – Dabigatran Etexilate: May enhance the anticoagulant effect of Anticoagulants. – Apixaban: May enhance the anticoagulant effect of Anticoagulants.	– Renal impairment (CrCl 30 to 80 mL/min): No adjustment necessary – Renal impairment (CrCl less than 30 mL/min): reduce usual recommended dose by 50%.	Low molecular weight heparin (LMWH) does not cross the placenta; increased risks of fetal bleeding or teratogenic effects have not been reported (Bates 2012).

Drug Administration in patients with Swallowing Difficulties		
Drug	**Formulation**	**Remarks**
Lopinavir/ritonavir	Tablets	– Manufacturer does not recommend crushing of tablets. – Exposure of lopinavir was reduced by 45% when the tablet was crushed and administered with food. – Administration through NG tube, doubling lopinavir/ritonavir to 800/200 mg twice daily when crushed could be considered (depending on drug availability) with monitoring of ECG.
	Oral solution	– Administer syrup without dilution otherwise there is a risk of precipitation. – Rinse the administration feeding tube with milk (not water). – As the oral solution contains ethanol and propylene glycol, feeding tubes that are compatible with ethanol and propylene glycol, such as silicone and polyvinyl chloride (PVC) feeding tubes, can be used. – As the oral solution contains alcohol, disulfiram-like reactions may occur with disulfiram or other drugs that produce this reaction (e.g. metronidazole). – Co-administration is contraindicated with disulfiram or metronidazole due to the potential risk of toxicity from propylene glycol.
Favipiravir	Tablets	– Tablets can be crushed and mixed with liquid.
Chloroquine	Tablets Syrup	– It is preferable to avoid crushing tablets, however, chloroquine tablets may be crushed and mixed with jam, honey, pasteurized yoghurt, or similar foods. – Contains propylene glycol, but no recommendations are given in the product label as to compatibility with feeding tubes.
Hydroxychloroquine	Tablets	– Manufacturer does not recommend crushing of tablets, However, some sources suggest that tablets can be crushed and dispersed in water.

References:

1. Ministry of Health. Coronavirus Diseases 19 (COVID-19) guidelines. March 2020, version 1.2
2. Jin, Y.H., et al., A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Mil Med Res, 2020. 7(1): p. 4.
3. Li, J.Y., et al. The epidemic of 2019-novel-coronavirus (2019-nCoV) pneumonia and insights for emerging infectious diseases in the future. Microbes Infect, 2020.
4. Liying Dong, Shasha Hu, JianjunGao. Discovering drugs to treat coronavirus disease 2019 (COVID-19). Drug Discov & Ther 2020;14(1):58-60
5. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet Published Online First: 11 March 2020. doi:10.1016/S0140-6736(20)30566-3
6. Interim clinical guidance for patients suspected of/ confirmed with COVID-19 in Belgium. 19 March 2020, version 4.
7. B. Cao, Y. Wang, D. Wen, et al. Wang. A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19. The new england journal of medicine, March 18,2020
8. American Society of Health-System Pharmacists. Assessment of Evidence for COVID-19-Related Treatments. 03-21-2020.
9. NHS Thromboprophylaxis and anticoagulation in COVID-19 infection. Imperial College Healthcare V 0.1 08.04.2020 Covid Treatment Group
10. J. Grein, N. Ohmagari, D. Shin, G. Diaz, et al. Compassionate Use of Remdesivir for Patients with Severe Covid-19. The new england journal of medicine. April 10, 2020
11. University of Liverpool COVID-19 resources, www.covid19-druginteractions.org updated 3 April 2020
12. Thachil, Jecko, et al. "ISTH interim guidance on recognition and management of coagulopathy in COVID-19." Journal of Thrombosis and Haemostasis 18.5 (2020): 1023-1026.
13. Tang, Ning, et al. "Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia." Journal of Thrombosis and Haemostasis (2020).
14. Qiu, Haiyan, et al. "Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study." The Lancet Infectious Diseases (2020).
15. Bauman, Mary E., et al. "Evaluation of enoxaparin dosing requirements in infants and children." Thrombosis and haemostasis 101.01 (2009): 86-92.
16. Lee, Young R., et al. "Stratifying therapeutic enoxaparin dose in morbidly obese patients by BMI class: a retrospective cohort study." Clinical Drug Investigation 40.1 (2020): 33-40.
17. Li, Wei, et al. "Chest computed tomography in children with COVID-19 respiratory infection." Pediatric radiology (2020): 1-4.
18. Schloemer, Nathan J., et al. "Higher doses of low-molecular-weight heparin (enoxaparin) are needed to achieve target anti-Xa concentrations in critically ill children." Pediatric Critical Care Medicine 15.7 (2014): e294-e299.
19. Uptodate last access May 20, 2020
20. Micromedex last access May 20, 2020
21. Triple combination of interferon beta-1b, lopinavir–ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomised, phase 2 trial, Published online May 8, 2020 https://doi.org/10.1016/S0140-6736(20)31042-4
22. Geoffrey D. Barnes, et al. Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum. Journal of Thrombosis and Thrombolysis. 21 May 2020
23. World Health Organization Clinical management of COVID-19: interim guidance. 18 May 2020.
24. A Trial of Favipiravir and Hydroxychloroquine combination in Adults Hospitalized with moderate and severe Covid-19 CLINICAL TRIAL PROTOCOL, King Abdullah International Medical research Center, Protocol V1 date April 5th 2020.
25. Randomised Evaluation of COVid-19 thERapY (RECOVERY) Trial on dexamethasone, 16 June 2020
26. A.B. Cavalcanti, et al. " Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19" The New England Journal of Medicine July 23, 2020.
27. Llitjos JF, Leclerc M, Chochois C, et al. High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients. J Thromb Haemost. 2020.
28. Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. J Thromb Haemost. 2020;18(5):1094-1099.
29. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. Acta Paediatr. 2020
30. Loi M, Branchford B, Kim J, Self C, Nuss R. COVID-19 anticoagulation recommendations in children .Pediatr Blood Cancer. 2020;
31. American Society of Hematology. https://www.hematology.org/covid-19/covid-19-and-coagulopathy. http://www.hematology.orgcovid-covid-and-coagulopathy. .
32. Thachil J, Tang N, Gando S, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. J Thromb Haemost. 2020; 18(5): 1023- 1026
33. Panel on COVID-19 Treatment. COVID-19 Treatment Guidelines.
34. Available at https://www.covid19treatmentguidelines.nih.gov/overview/
35. Kache, S., Chisti, M.J., Gumbo, F. et al. COVID-19 PICU guidelines: for high- and limited-resource settings. Pediatr Res (2020)
36. World Health Organization. Pocket Book for Hospital Care of Children: Guidelines for the Management of Common Illness with Limited Resources (World Health Organization, Geneva, 2013)