

Chinese Pharmaceutical Association
Hospital Pharmacy Professional Committee
Expert Consensus on Rational Drug Use in Clinical Practice for
COVID-19
2020.03

On March 12, 2020, the World Health Organization (WHO) announced that the new Coronavirus Disease 2019 (COVID-19) has caused a pandemic. As of March 31, the COVID-19 pandemic has infected nearly 700,000 patients in 203 countries and regions globally, caused more than 30,000 dead. In some countries, the mortality rate reached more than 10%. At the same time, with the resolution and hard work of the Chinese government and people, China's situation has been improving and has basically passed the peak period. Against the current grim global context, close international cooperation is conducive to the rapid and effective control of this pandemic. China's experience is worthy of reference by the international community.

During the epidemic, pharmacists in Chinese hospitals have been adhering to the principle of aligning medication with clinical needs, actively participating in clinical treatment under the premise of ensuring medicine supply, enhancing medication education and guidance for patients, and achieving effective improvement in medication efficacy and clinical results. In order to provide good reference for pharmacists worldwide and better services in the prevention and control of the pandemic, experts from the Hospital Pharmacy Professional Committee of the Chinese Pharmaceutical Association compiled the *Expert Consensus on Rational Drug Use in Clinical Practice for COVID-19*.

Combining with real-world experiences in various provinces in China, the consensus was formed based on: 1) the *Diagnosis and Treatment Plan for COVID-19 (the 7th Tentative Version)* issued by the National Health Commission of the People's Republic of China; 2) other diagnosis and treatment plans, and 3) other expert consensus. The full text is divided into 10 parts, categorizing and explaining COVID-19's clinical treatment. Therapeutic efficacy, selection principles, uses and doses, adverse reactions and precautions of medicines are included.

According to the *China-WHO Joint Inspection Report*, China's prevention and control model can be copied. Possessing China's experiences, it is unnecessary for other countries to start from scratch. Clinical methods and strategies may be the easiest to replicate and the most feasible to implement for countries around the world. Serving as powerful support and complement for clinical methods, pharmacy methods and strategies are also crucial in the battle against COVID-19. By providing this consensus, pharmacists in Chinese hospitals sincerely share our clinical experiences with the world, in the fluid, electrolyte, nutrition, and pharmacologic management of patients infected with COVID-19. We hope that with global cooperation, we mankind can win the war against COVID-19!

Contents

1. Anti-SARS-CoV-2 Medications 1

- 1.1 Chloroquine Phosphate 1
- 1.2 Hydroxychloroquine Sulfate 2
- 1.3 Favipiravir 3
- 1.4 Interferon 3
- 1.5 Ribavirin 4
- 1.6 Lopinavir/Ritonavir 4
- 1.7 Abidol 5

2. Anti-Secondary-Infection Medications 6

- 2.1 Secondary Bacterial Infection 6
- 2.2 Secondary Fungal Infection 7
- 2.3 Precautions for Anti-Secondary-Infection Medications 7

3. Anti-Hypoxic Medications 9

4. Anti-Septic-Shock Medications 10

5. Medications for Nutrient Balance Maintenance 11

- 5.1 Mild and Moderate Cases 11
- 5.2 Severe and Critical Cases 12

6. Medications for Micro-ecological Balance Maintenance 13

7. Medications for Cytokine Storm Prevention and Treatment 14

- 7.1 Corticosteroids 14
- 7.2 Heparin 14
- 7.3 High-dose Vitamin C 14
- 7.4 High-dose Broad-spectrum Protease Inhibitor (Ulinastatin) 15
- 7.5 IL-6 Antagonist Tocilizumab 15
- 7.6 Oral Administration of Diammonium Glycyrrhizate + Vitamin C 15

8. Medications for Immunoregulation 15

- 8.1 Thymosin α 1 (Thymalfasin) 15
- 8.2 Human Immunoglobulin 16

9. Medications in Patients with Underlying Diseases 16

- 9.1 Prevention and Treatment for Venous Thromboembolism 16

9.2 Rational Use of Antihypertensive Medications 16

9.3 Medication Adjustment for Patients with Hepatic Insufficiency 17

9.4 Medication Adjustment for Patients with Renal Insufficiency 18

9.5 Medication Adjustment for Patients with CRRT 19

10. Anti-Pyretic Medications 21

10.1 Acetaminophen 21

10.2 Ibuprofen 21

References 22

Appendix A (Traditional Chinese Medicine Treatment) 26

1. Anti-SARS-CoV-2 Medications

- Inhibiting viral replication is a key link to control the progression of COVID-19, caused by SARS-CoV-2, a brand new virus. At present, there is no confirmed medical evidence to prove the effectiveness of anti-SARS-CoV-2 drugs. Only a few antiviral drugs have obtained preliminary clinical recommendation by the China National Diagnosis and Treatment Plan for COVID-19 (the 7th Tentative Version) ^[1] and other expert consensus: chloroquine phosphate, hydroxychloroquine sulfate, favipiravir, interferon, ribavirin, lopinavir/ritonavir (Kaletra®), arbidol.
- In principle, a patient diagnosed with SARS-CoV-2 infection should be treated with antiviral drugs as soon as possible. One of the antiviral treatments can be selected from chloroquine phosphate, hydroxychloroquine sulfate, favipiravir, arbidol, and lopinavir/ritonavir. Interferon or ribavirin is used with other antiviral drugs. However, the combination of three or more antiviral drugs will not benefit patients, but increase the adverse drug reactions.
- Neuraminidase inhibitors (such as oseltamivir) and ganciclovir are not recommended ^[2, 3].
- Almost all antiviral drugs have adverse reactions ^[4], and adverse drug reactions need to be closely observed. The administration should be withdrawn immediately once intolerable side effects occur.
- The treatment course of chloroquine phosphate should be no more than 7 days. The treatment course of other regimens are usually around 10 days. Antiviral drugs should be stopped if nucleic acid test results from sputum specimens remain negative for more than 3 times.

1.1 Chloroquine Phosphate

- Usage and dosage^[1, 5]
 - For adults between 18 and 65 years old, weighing 50 kg or more, 500 mg of chloroquine phosphate (equivalent to 300 mg of chloroquine) should be administered twice a day for 7 days.
 - For those who weigh less than 50 kg, 500 mg twice a day should be given on the first and second day, and 500 mg once a day on the 3rd to the 7th day.
- Adverse reactions
 - Orally administered chloroquine phosphate has a plasma half-life of 2.5 to 10 days and a longer half-life in tissue elimination. Adverse reactions must be closely monitored.

- Common adverse reactions include dizziness, headache, nausea, vomiting, diarrhea and various kinds of rashes, etc.
- Serious adverse reactions such as retinal lesions, arrhythmia, severe extrapyramidal system diseases, psychiatric symptoms, must be dealt with in time^[6-9]. And drug interactions should be watched out for, especially in combination with macrolides, fluoroquinolones or other drugs that can cause a prolonged QT interval.
- Responses to adverse reactions^[10]
 - Administer intravenous infusions that promote excretion, such as vitamin C, mannitol and furosemide.
 - Administer ammonium chloride orally for acidifying urine to accelerate chloroquine phosphate excretion.
 - Epinephrine ($0.25 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, titrating by $0.25\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) could be used to improve the low systolic arterial pressure caused by chloroquine poisoning.
 - Diazepam ($2 \text{ mg}\cdot\text{kg}^{-1}$ IV over 30 minutes, then $2 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{day}^{-1}$) is recommended to reduce cardiotoxicity caused by chloroquine poisoning.
- Warnings/Precautions
 - Blood routine test, levels of electrolytes, and levels of myocardial enzymes should also be rechecked every other day.
 - Electrocardiograms should be reviewed ^[5]. Reducing the dose or stopping the drug if the patients have a prolonged QT interval or a slowed heart rate.
 - This medication is ocular/ototoxic, so the patients' vision and hearing should be checked before and during treatment.
 - For patients with heart diseases and the pregnant, the use of chloroquine phosphate is contraindicated. Patients with retinal or mental illness should be treated with caution.

1.2 Hydroxychloroquine Sulfate

- The mechanism of hydroxychloroquine sulfate is similar to that of chloroquine phosphate ^[11], but there are relatively few adverse reactions. Studies have found that hydroxychloroquine sulfate is better than chloroquine in inhibiting SARS-CoV-2 in *vitro* ^[12].
- Up to now, the optimal dosage and duration of hydroxychloroquine for treatment of COVID-19 are still unknown. The alternative regimens of hydroxychloroquine sulfate from CDC include 400 mg BID on day one, then daily for 5 days; 400 mg BID on day one, then 200 mg BID for 4 days; 600 mg BID on day one, then 400 mg daily on days 2~5 ^[13].

1.3 Favipiravir

Favipiravir is a broad-spectrum RNA polymerase inhibitor, which was approved for marketing in Japan in March 2014. After oral absorption, favipiravir is converted into a bioactive nucleoside triphosphate compound that shares a similar structure with purine and competes with purine to inhibit RNA polymerase by viruses, thereby inhibiting virus replication. The nucleoside triphosphate compound of favipiravir can also be inserted into the virus RNA chain to induce fatal mutations of the virus. Due to its anti-viral mechanism, favipiravir has a potential effect against a range of RNA viruses ^[14].

- Usage and dosage

To be taken for 5 days, 1600 mg twice on Day 1, and 600 mg twice daily on Day 2-5^[15].

- Adverse reactions

Hyperuricemia, diarrhea, neutropenia, abnormal liver function, teratogenic effects.

- Warnings/Precautions

- Favipiravir raises uric acid level, and thus patients with gout and hyperuricemia should use it with caution.
- Favipiravir cannot be used in women already pregnant or suspected of being pregnant. Lactating women taking favipiravir should discontinue breastfeeding ^[15].

1.4 Interferon

- Usage and dosage

Interferon should be nebulized and inhaled. Aerosol inhalation of α -interferon: 5 million units or an equivalent dose for adults, diluted with 2 ml of sterile water for injection, twice a day. The conversion equation for the dose of recombinant human interferon α 1b is $50 \mu\text{g} = 5 \text{ million U}$.

Interferon κ is also recommended as the first choice ^[16].

- Adverse reactions

Well tolerated, nebulized inhalation treatment has few adverse reactions. Low-grade fever occurs occasionally.

- Warnings/Precautions

Patients with a history of allergy should be closely monitored for anaphylaxis when using α -interferon for the first time. Avoid contact with eyes during atomization.

- Drug interactions

Interferon may denature when heated, so ultrasonic nebulization is not recommended. Please note that it cannot be atomized concurrently with chymotrypsin, acetylcysteine, and ipratropium bromide.

1.5 Ribavirin [3, 16-18]

- Usage and dosage

Combine with α -interferon or lopinavir/ritonavir, 500 mg IV infusion each time, 2 to 3 times a day. The solution should be diluted with NS or 5% GS to 1 mg· ml⁻¹ or 5 mg· ml⁻¹ solution and administer it by slowly IV infusion.

- Adverse reactions

Hemolytic anemia, heart damage and dyspnea and chest pain in patients with respiratory diseases (chronic obstructive pulmonary disease or asthma).

- Warnings/Precautions

- It is not recommended for the seniors. With a strong teratogenic effect, it is contraindicated in pregnant women. For both men and women in preparation for pregnancy, it should be avoided within 6 months after the treatment stopped. Breastfeeding women should stop breastfeeding during treatment.
- It is not recommended for patients with renal insufficiency when the creatinine clearance rate is lower than 50 ml·min⁻¹. Dose adjustment is needed when using in these patients. Use with caution in liver insufficiency patients with Child-Pugh B/C.
- Pay attention to bone marrow suppression during treatment, and discontinue the medication in time when red blood cells, white blood cells, hemoglobin and platelets decreased and treat the patient symptomatically.

1.6 Lopinavir/Rritonavir [3, 16-18]

- Usage and dosage

- Tablets: 200 mg/50 mg per tablet, 2 tablets each time for adults, twice a day. Take the whole tablet orally, do not chew it, break it apart or crush it.
- Oral solution (80 mg/20 mg per ml): 5 ml each time, twice daily. Oral solutions should be taken with food to increase bioavailability. It should be noted that the oral liquid adjuvant contains 42.4% (v/v) ethanol and 15.3% (w/v) propylene glycol.

- Adverse reactions

- Common adverse reactions include diarrhea, nausea and vomiting, migraine, liver damage, pancreatitis and rash, among others.

- Blood triglyceride and cholesterol concentrations can be significantly increased, leading to lipid metabolism disorders.
- Cautions should be taken when increasing the PR interval, second- or to third-degree atrioventricular block, having an abnormal conduction system, or receiving drugs that can cause a prolonged PR interval.
- Warnings/Precautions
 - It is unnecessary to adjust doses for patients with mild to moderate liver dysfunction, renal dysfunction, or those who are on continuous renal replacement therapy (CRRT). The use is contraindicated in patients with severe liver dysfunction.
 - It is best for pregnant women to use it after the 28th week of pregnancy. It can be taken by breastfeeding women.
- Drug interactions

Lopinavir/ritonavir is a CYP3A inhibitor, which can increase the blood concentration of drugs that are mainly metabolized by CYP3A. Combined use of these drugs requires special caution. Lopinavir/ritonavir can reduce the blood concentration of voriconazole, and should not be used in combination.

1.7 Abidol

- Usage and dosage

Orally administered: 0.2 g each time for adults, 3 times a day, the course of treatment should be no more than 10 days.
- Adverse reactions

Nausea, diarrhea, dizziness, and elevated serum aminotransferases, which can cause bradycardia.
- Warnings/Precautions

It should be used with caution in pregnant and breastfeeding women, patients with severe renal dysfunction, and those with a sinus node disease or dysfunction.
- Drug interactions

Abidol is mainly metabolized by CYP3A4, and there may be drug interactions with UGT1A9's substrates, enzyme inhibitors, and inducers. Combined uses should be noted.
- Dietary considerations

It is recommended to take it after meals to reduce gastrointestinal adverse reactions and should be avoided with aluminum preparations.

2. Anti-Secondary-Infection Medications

2.1 Secondary Bacterial Infection

- According to reports ^[19], about 10% of patients with COVID-19 have developed secondary bacterial infections, while 31% of critically ill patients admitted to the intensive care unit have developed secondary bacterial infections. Effective prevention and control of secondary infections for COVID-19 patients is one of the key measures for successful treatment. But aimless or inappropriate use of antimicrobials should be avoided, especially the combined use of broad-spectrum ones ^[1].
- Qualified samples should be collected as early as possible for microbiological monitoring. Blood culture should be performed in time for patients with high fever. For patients with suspected sepsis who are inserted with vascular catheters, both peripheral blood culture and catheter blood culture should be tested.
- Antimicrobials for empirical treatment should be selected according to local epidemiology and adjusted in time according to etiology results.
- Table 1 presents the principles and indications of prophylactic or empirical use of antimicrobials in various types of patients. The patient's symptoms, blood count, level of C-reactive protein, level of procalcitonin, imageology and other indicators should be closely monitored ^[2].

Table 1 Antimicrobials for secondary bacterial infection in patients with COVID-19

Patient type	Basic principle	Indication of application	Choice of medicines
Mild	Antimicrobials are not recommended to prevent bacterial infection	No	No
Moderate	In principle, antimicrobials are not recommended to prevent bacterial infection	For patients with any one of the following risk factors ^[20] 1) Persistent high fever; 2) Advanced age (over 60 years of age); 3) Severe underlying diseases; 4) Pulmonary images showing significant lesion progression greater than 50% within 24 to 48 hours of onset; 5) Immunosuppression.	1) Antimicrobials could be administered intravenously or orally for community-acquired pneumonia ^[21] . Use β -lactams \pm macrolides or use respiratory fluoroquinolones alone; 2) It is not recommended to empirically use glycopeptides, carbapenems and other special class antibacterial drugs. Laboratory evidence of bacterial infection should be obtained, and consult an infectious diseases specialist before

Severe and critically ill	Routine prophylactic use of antimicrobials is not recommended, especially combined use with broad-spectrum ones	<p>Antimicrobials may be considered in the patients who may develop into severe cases</p> <p>1) Antimicrobials can be used in patients with excess bronchial secretions, chronic airway diseases with a history of pathogen colonization in the lower respiratory tract, taking glucocorticoids ($\geq 20 \text{ mg} \times 7 \text{ d}$ prednisone equivalent)</p> <p>2) Prophylactic use may be considered in patients with open airways such as invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO)^[16]</p>	<p>using such antimicrobials when necessary</p> <p>1) Based on patients' high-risk factors, options include quinolones, the third generation cephalosporins, β-lactamase inhibitor compounds, carbapenems and glycopeptides, etc;</p> <p>2) For patients with septic shock, empirical antimicrobials can be used in combination before obtaining an etiological diagnosis, while covering the most common pathogenic bacteria, including enterobacteriaceae^[22], staphylococcus and enterococcus^[16]</p>
---------------------------	---	--	---

2.2 Secondary Fungal Infection

- High-risk factors: an advanced age, comorbidity of chronic diseases, impaired immune function, receiving high-dose glucocorticoids during treatment ($>1.0 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ prednisone equivalent), and invasive treatment measures such as traumatic intubation and venous catheters^[23].
- Fungal surveillance in respiratory secretion samples should be performed in these patients. Procedures include smears and cultures. For suspected cases, 1, 3- β -D-glucan (G test) and galactomannan (GM test) should be tested timely in either blood samples or bronchoalveolar lavage fluid samples.
- When an invasive candidiasis disease is suspected, fluconazole or echinocandin can be selected for anti-fungal therapy. In case of invasive pulmonary aspergillosis, voriconazole, posaconazole or echinocandin can be used. We recommend against a combination of two anti-fungal drugs.

2.3 Precautions for Anti-Secondary-Infection Medications

- Therapeutic drug monitoring (TDM) can be conducted for some anti-infective drugs when necessary. Table 2 presents for the blood concentration monitoring and dosage adjustment of common anti-infective drugs.
- TDM for patients with COVID-19 must be performed in a biosafety level 2 or higher laboratory.

Table 2 Blood concentration monitoring and dosage adjustment of common anti-infective drugs in patients with COVID-19

Drug category	Drug names	Time points of blood collection	The range of concentrations	Principles of dosage adjustment
	Vancomycin	30 min before the drug administration	10~20 mg·L ⁻¹ (AUC / MIC is set for 400~600 in severe MRSA infection(assuming MIC of vancomycin is 1 mg·L ⁻¹)[24])	The trough concentration correlates with the failure rate of anti-infective therapy and renal toxicity. When the concentration is overly high, reduction of drug frequency or single dose is required
Glycopeptides	Linezolid	30 min before the drug administration	2~7 µg·ml ⁻¹	The trough concentration correlates with myelosuppression adverse reactions. The blood routine test needs to be closely monitored
	Teicoplanin	30 min before the drug administration	10~20 mg·L ⁻¹ (≥ 20 mg·L ⁻¹ in case of severe infection)	Tough concentration is related to treatment effect, and is an important index for adjusting load dose
Carbapenems	Meropenem	10 min before the drug administration	1~16 µg·ml ⁻¹	Interpretation and adjust the plasma drug concentration based on MIC of the pathogen testing
	Imipenem	10 min before the drug administration	1~8 µg·ml ⁻¹	
Polypeptides	Colistin	Load dose: 10 min before the next administration after one load dose; Non load dose: 10 min before the next administration after 5~6 doses	Colistin B: AUC _{0-24h} 50~100 mg·h·L ⁻¹ , Steady state concentration 2~4 mg/L; Colistin E: AUC _{0-24h} 50 mg·h·L ⁻¹ , Steady state concentration 2 mg·L ⁻¹	The concentration correlates with the antibacterial effect and nephrotoxicity closely

Triazole antifungal drugs	Voriconazol	30 min before the drug administration	$1\sim 5.5 \mu\text{g}\cdot\text{ml}^{-1}$	The trough concentration correlates with the therapeutic efficacy and adverse reactions such as impaired liver function
	Pozonazole	30 min before the drug administration	Preventive treatment : $>0.5 \text{ mg}\cdot\text{L}^{-1}$ Rescue treatment : >1.0 $\text{mg}\cdot\text{L}^{-1}$	The trough concentration correlates with clinical effect, and it needs 7 days to reach steady state after adjusting dose

3. Anti-Hypoxic Medications

- Expectorants such as ambroxol and bromhexine can be used to dilute or dissolve the mucus and improve the state of hypoxia ^[25].
- Avoid combining ambroxol hydrochloride injection with antitussive dextromethorphan which targets at the central nervous system to prevent airway blockage with diluted sputum ^[26].
- Aerosolized bronchodilator medicines have limited efficacy and may increase the risk of SARS-CoV-2 aerosol transmission, so they should be used with caution ^[27-28].
- Patients receiving oxygen therapy are not recommended with analgesic and sedatives that affect breathing. Oral anxiolytics and hypnotic drugs can relieve tension and anxiety ^[29].
- Since SARS-CoV-2 can inhibit the function of the sinoatrial node and cause sinus bradycardia, sedative medicines that have an inhibitory effect on the heart should be used with caution.
- When using ECMO, it is recommended to use low-dose muscle relaxants. Opioids and dexmedetomidine should be used with caution ^[16].
- Drugs that may need to increase the initial dose during ECMO treatment include midazolam, dexmedetomidine, propofol, fentanyl, morphine, remifentanyl, and voriconazole ^[30-36]. The maintenance dose is recommended to be adjusted according to clinical efficacies. If possible, adjust the dose according to blood concentration monitoring results.
- Drugs that do not need dose adjustment during ECMO treatment include vancomycin, aminoglycosides, fluoroquinolones, β -lactams, fluconazole and oseltamivir ^[30, 37-42].

- Insufficient or controversial data on drug dose adjustment during ECMO treatment include lopinavir/ritonavir, ribavirin, caspofungin, and linezolid [37-39, 42-47]. We suggest administer these drugs according to the conventional recommended dosage, and adjust the dosage based on clinical effects and reference to blood concentration monitoring results when conditions allow.

4. Anti-Septic-Shock Medications

- Its prevalence in COVID-19 patients stands at approximately 1% [48].
- In its initial treatment, the reasonable use of the following medicines (Table 3) should be noted [49].

Table 3 Drug selection and precautions of septic shock

Medicines	Application conditions	Drug selection	Precautions
Antimicrobials	In case of bacterial or fungal infections, initiate IV antimicrobials as soon as possible	1) Before obtaining a pathogen identification, empirically use broad-spectrum antimicrobials that may cover all pathogens 2) After the pathogen identification and drug sensitivity test, adopt a step-wise approach to narrow down the spectrum of antimicrobials	1) Adjust the dose based on analysis of the patient's pathophysiological status and assessment of organ dysfunction 2) For most severely infected patients, 7 to 10 days of treatment is considered sufficient [50]
Fluid resuscitation	Start early and emphasize at least 30 ml·kg ⁻¹ of intravenous fluid be given within the first 3 hours	1) Recommended to mainly use balanced-crystalloids 2) Appropriately increase colloid fluid 3) Recommend albumin for patients with hypoalbuminemia 4) Hydroxyethyl starch is not recommended for higher mortality and increasing the risk of CRRT	1) Follow hemodynamic therapy principles guided by tissue perfusion, and closely monitor the patients' circulation 2) At hemodynamically unstable status, maintain the minimum blood volume required for tissue perfusion. The unnecessary fluid input can cause a volume overload and aggravate the lung injury [2]

Vasoactive medications	<p>(1) Use vasopressors when blood pressure still cannot meet the standard after adequate fluid resuscitation</p> <p>(2) After adequate fluid resuscitation and use of vasopressors, patients with: 1) signs of persistent hypoperfusion; 2) increased cardiac filling pressure; 3) low cardiac output indicating cardiac insufficiency; or 4) bed-side ultrasound results indicating a decreased diastolic and systolic capacity, can use positive inotropic drugs</p>	<p>1) Noradrenaline is preferred, or vasopressin in addition to noradrenaline (maximum dose 0.03 U·min⁻¹) or epinephrine</p> <p>2) Only when the risk of arrhythmia and cardiac output are low can dopamine be considered as an alternative</p> <p>3) Isoprenaline can be used for patients with sinus bradycardia</p> <p>4) Dobutamine or levosimendan can be used as positive inotropic drugs</p>	<p>1) Norepinephrine, epinephrine and terlipressin are recommended to inject through central vein. Leakage of the solution can cause local tissue necrosis. A long-term or high-dose use may lead to ischemia of extremities. A high dose dopamine may induce arrhythmia and tachycardia</p> <p>2) Recommend cardioprotective drugs for severe and critically ill patients. Avoided sedative drugs that have an inhibitory effect on the heart</p> <p>3) For patients with a sinus rhythm, a heart rate <50 beats·min⁻¹ and hemodynamic instability, it is recommended to inject intravenously low doses of isoproterenol or dopamine to maintain the heart rate at about 80 beats·min⁻¹ [16]</p> <p>4) Pay attention to levosimendan injection related blood pressure reduction and reflexively heart rate increase</p>
------------------------	---	--	---

5. Medications for Nutrient Balance Maintenance

Nutritional risk screening and nutritional assessment are recommended for all inpatients with COVID-19 (NRS2002 scale is recommended for assessment). Malnutrition risk assessment should be initiated as early as possible for all critically ill patients admitted to the ICU (NUTRIC is recommended for assessment) [51-52]. Nutritional support should follow the "five-step" principle [53].

5.1 Mild and Moderate Cases

- The total caloric and protein in-take in these patients should be targeted at 20~30 kcal·kg⁻¹·d⁻¹ and 1.0~1.5 g·kg⁻¹·d⁻¹, respectively [52].
- For patients with normal gastrointestinal function who can meet the target energy and protein requirements by oral feeding, the balanced diet can be recommended.

- If patients are unable to eat, it is recommended to provide enteral nutrition within 48 hours.

5.2 Severe and Critical Cases [2, 20, 52, 54-57]

- Enteral nutrition should be initiated as early as possible for these patients after 24~48 hours of hemodynamic stability, even during prone position ventilation or ECMO. However, in the acute phase of severe systemic infection or septic shock, the adoption of parenteral nutrition alone or the use of supplementary parenteral nutrition in combination with enteral nutrition is not recommended.
- It is recommended that the gastric nutrition with nasogastric tube should be preferred. Nasointestinal tube and other post-pyloric feeding pathways can be adopted for patients who are not suitable for gastric nutrition.
- For enteral nutrition, the intact protein-based preparations with complete protein as nitrogen source should be preferred. Different enteral nutrition preparations should be selected specifically for the patients with digestive diseases (such as gastrointestinal dysfunction and intestinal motility disorder) and the patients with underlying diseases (such as diabetes and fat digestion disorder). The patients can use the enteral nutrition preparations rich in ω -3 fatty acids.
- It is recommended to use a simplified weight-based formula ($20\sim30 \text{ kcal}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$) to determine the target feeding amount, starting with a low dose. In the case of feeding intolerance, trophic feeding (infusion rate: $10\sim20 \text{ kcal}\cdot\text{h}^{-1}$ or $10\sim30 \text{ ml}\cdot\text{h}^{-1}$) can be considered. The protein supply should be strengthened and the protein requirement should be targeted at $1.5\sim2.0 \text{ g}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$.
- Adverse reaction needs to be closely monitored for the patients receiving EN support, especially diarrhea. The analysis should address the causes of diarrhea and the corresponding measures should be adopted.
- For the patients with oral feeding disorders or enteral nutrition contraindications, parenteral nutrition should be initiated within 3~7 days. Parenteral nutrition formulations should be developed individually.
- For parenteral nutrition, the ratio of non-protein energy supply should be (50~60) / (40~50) for sugar/lipid, and (100~150) / 1 for non-protein calorie/nitrogen. Fat emulsions rich in EPA and DHA can be added to the parenteral nutrition preparations. Attention should be paid to the supplementation of vitamin B₁₂. Intravenous nutrition preparations rich in fat emulsion should be used with caution when patients receiving ECMO and continuous blood purification therapy are given parenteral nutrition.
- The patients receiving parenteral nutrition support should be routinely monitored for blood glucose, blood lipids, blood routines, coagulation indicators, liver and kidney function etc.; The patients admitted to the ICU should be monitored for electrolytes daily when receiving parenteral nutrition preparations.

- Over-feeding should be avoided. For the enteral nutrition and parenteral nutrition in severe patients, the target feeding volume should be achieved gradually within 3~7 days.

6. Medications for Micro-ecological Balance Maintenance

Intestinal micro-ecological regulators can be used according to the medical necessity of patients with COVID-19 to maintain intestinal micro-ecological balance and prevent secondary bacterial infection.

Micro-ecological regulators are a kind of physiological living bacteria (microorganism) products that are manufactured under the guidance of micro-ecology theory, and can adjust the intestinal micro-ecological imbalance, maintaining the micro-ecological balance, improving the health level of the host (human, animal and plant) or enhancing the health status. They also include metabolites of these bacteria and substance products that promote the growth and reproduction of these physiological flora. Micro-ecological regulators are divided into probiotics, prebiotics, and synbiotics, among which probiotics are commonly used clinical preparations ^[58-60].

- Common probiotic products include: VSL#3 (Bifidobacterium breve, B. longum, B. infantis, Lactobacillus acidophilus, L. plantarum, L. paracasei, L. bulgaricus, Streptococcus thermophilus), Align (B. infantis), Culturelle (L. rhamnosus GG), DanActive (L. casei), Mutaflor (E. coli Nissle 1917), Florastor (S. boulardii), Bacid (Lactobacillus), Lactinex (Lactobacillus).
- The number of live bacteria reach the intestinal tract can be affected by medication time, probiotics are recommended to be taken half an hour after a meal. S. boulardii is basically unaffected by food, but if a quick effect is expected, being taken with food should be avoided.
- As living microorganisms, probiotics should be avoided in combination with antibiotics so as to avoid affecting the efficacy. If patients need to take antibiotics at the same time, it is recommended to take them at different time, preferably at an interval of more than 2 to 3 hours. Saccharomyces boulardii, Clostridium butyricum and Bacillus preparations are insensitive to antibiotics and can be taken together with antibiotics.
- The Bacillus licheniformis, Clostridium butyricum, Bacillus coagulans and Bacillus subtilis preparations can be stored at room temperature, while other intestinal micro-

ecological preparations need to be stored in a refrigerator (2~8°C), avoiding light and sealing.

- Probiotics are a class of drugs with high safety, with the rare adverse reaction of bacteremia. For the elderly with low immune function, attention should be paid when they take this drug.

7. Medications for Cytokine Storm Prevention and Treatment

7.1 Corticosteroids

- Systematic application of corticosteroids in mild and moderate cases are not recommended, nor routine use in severe and critical cases with COVID-19^[1-3].
- In the following cases^[1-3,16], systemic corticosteroids should be considered:
 - Progressive deterioration of oxygenation index and acute respiratory distress syndrome ($\text{PaO}_2/\text{FiO}_2 < 200 \text{ mmHg}$);
 - Symptoms (including fever, cough or other related infection symptoms) developed within 10 d and imaging manifestations progress rapidly;
 - Excessive activation of inflammatory response.
- Intravenous infusion of methylprednisolone $1\sim 2 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ for 3 to 5 days. The immunosuppressive effects of high doses of glucocorticoids will delay the clearance of SARS-CoV-2.

7.2 Heparin

We recommend low molecular weight heparin (LMWH) 1~2 syringe injection per day to protect endothelial cells until the D-dimer level returned to normal. Once the fibrin degradation product (FDP) $\geq 10 \mu\text{g}\cdot\text{ml}^{-1}$ and (or) D-dimer $\geq 5 \mu\text{g}\cdot\text{ml}^{-1}$, switch to unfractionated heparin.

7.3 High-dose Vitamin C

We recommend Vitamin C administered intravenously at $100\sim 200 \text{ mg}\cdot\text{kg}^{-1}$ per day until the oxygenation index significantly improve.

7.4 High-dose Broad-spectrum Protease Inhibitor (Ulinastatin)

It can reduce the level of inflammatory markers IL-6 and increase the level of anti-inflammatory cytokine IL-10^[61]. We recommend the infusion of Ulinastatin of 0.6~1 million units per day until pulmonary imaging improve.

7.5 IL-6 Antagonist Tocilizumab

- Tocilizumab is a humanized immunoglobulin that functions in the immune response and blocks IL-6 receptor binding to IL-6, which is in ongoing trials (registration number: ChiCTR2000029765).
- We recommend patients with extensive lesions in two lungs and severe patients with elevated IL-6 level try to administer Tocilizumab intravenously.
- We suggest the first dose of 4~8 mg·kg⁻¹, and it can be 400 mg. Tocilizumab requires to be dissolved in 100 ml normal saline and continuous infusion for more than 1 hour. An additional dose (same as the first dose) should be given within 12 hours for poor response of the first dose, with a maximum administration of 2 times in total and a single maximum dose of 800 mg. The allergic reaction requires special caution. We recommend against tocilizumab for patients with active infections such as tuberculosis.

7.6 Oral Administration of Diammonium Glycyrrhizate + Vitamin C ^[62]

- We recommend oral administration of diammonium glycyrrhizate to patients with acute fever, 150 mg three times a day. Use in patients with hypertension with caution.
- We recommend oral administration of vitamin C to patients in the acute phase and rehabilitation period, 0.5 g daily.

8. Medications for Immunoregulation

8.1 Thymosin α 1 (Thymalfasin) ^[2, 16, 63]

We recommend it to severe patients with low lymphocyte and cellular immune function. It should be subcutaneous injected twice a week. Patients with overactive inflammatory response should not use it.

8.2 Human Immunoglobulin

We recommend against the routine treatment of human immunoglobulin [1-3, 16]. Children with severe and critically ill condition cases can be administered intravenously by $10 \text{ g}\cdot\text{d}^{-1}$, for 3 to 5 days [1, 16].

9. Medications in Patients with Underlying Diseases

9.1 Prevention and Treatment for Venous Thromboembolism

9.1.1 Mild and moderate cases

- We encourage patients to take active activities and drink more water.
- We recommend low-molecular-weight heparin for the prevention of venous thromboembolism for patients with high or moderately high risk according to Padua or Caprini assessment [16, 64].

9.1.2 Severe and Critical cases

- We recommend intermittent pneumatic compression pump (IPC) for prevention if patients are at high risk of bleeding.
- We recommend low-molecular-weight heparin for prevention if patients are at low risk of bleeding.
- We recommend unfractionated heparin for patients with severe renal failure (creatinine clearance $<30 \text{ ml}\cdot\text{min}^{-1}$).
- We recommend anticoagulants such as argatroban, bivalirudin and rivaroxaban for patients with thrombocytopenia or heparin-induced thrombocytopenia during heparin administration.

9.2 Rational Use of Antihypertensive Medications

- It has been reported that about 46.4% of COVID-19 patients suffer from hypertension [65]. Dry cough is a common adverse reaction of angiotensin -converting enzyme inhibitor (ACEI) and should be distinguished from the clinical symptoms of COVID-19 [65-66].
- For patients with hypertension on a long-term treatment with ACEI or angiotensin II receptor antagonist (ARB), we recommend maintaining the original regimen as long as

their current blood pressure remains stable. Regular blood pressure monitoring is essential for treatment [67-68].

- When selecting antihypertensive medications of ACEI, ARB and diuretics, we suggest to monitor the condition changes relating to COVID-19 and the antihypertensive effect.

9.3 Medication Adjustment for Patients with Hepatic Insufficiency

Previous studies reported that 28.9% of the patients have abnormal liver functions, with a mortality rate of 61.5% at 28 days [69]. SARS-CoV-2 may hurt bile duct cells. Infection and the use of antiviral drugs can also cause serious damage to liver cells. Therefore, liver function should be monitored, and accordingly adjusting the dosage of drugs.

- For the patients with acute liver injury, we recommend the drugs mainly excreted by the kidney, such as penicillin G, cefazolin, ceftazidime, vancomycin, daptomycin and levofloxacin, etc.
- For patients with chronic liver function injury, we recommend patients to adjust the dosage of drug mainly excreted by liver according to the Child-Pugh classification guidance [70]. See Table 4 for details.
- For patients suffering from drug-induced liver injury, we recommend anti-inflammatory and hepato-protective drugs such as glycyrrhizin. We recommend against more than two hepato-protective drugs or use for prophylaxis.

Table 4 Drug dosage adjustment for hepatic insufficiency

Drugs	Child-Pugh A	Child-Pugh B	Child-Pugh C
Lopinavir/ritonavir	No need to adjust		Prohibited
Ribavirin	No need to adjust	Use with caution	
α -interferon	No need to adjust		Prohibited in decompensated cirrhosis
Arbidol	Lack of data. Use with caution		
Prezista/cobicistat	No need to adjust	Use with caution	Prohibited
Tigecycline	No need to adjust	No need to adjust	Initial dosage of 100 mg, 25 mg/12 h thereafter
Linezolid	No need to adjust	No need to adjust	Lack of data
Metronidazole	No need to adjust	No need to adjust	Dosage decreased by 50%

Voriconazole	Loading dose unchanged, maintenance dose halved	Not recommended	Not recommended
Caspofungin	No need to adjust	Loading dose unchanged, maintenance dose 35 mg·d ⁻¹	Lack of data
Micafungin	No need to adjust	No need to adjust	150 mg·d ⁻¹

9.4 Medication Adjustment for Patients with Renal Insufficiency

The incidence of acute kidney injury (AKI) in patients with severe and critically ill COVID-19 is 28.9% [69,71], mainly manifested as tubular injury. Patients with severe infection and multiple concomitant medications should monitor their renal function and accordingly adjust the dose. It is also necessary to adjust the medication of COVID-19 patients with chronic renal insufficiency.

- We recommend against neither routine use of loop diuretics for the prevention and treatment of AKI in the absence of fluid volume overload, nor use of low-dose dopamine for prevention and treatment of AKI.
- We recommend against drugs with higher nephrotoxicity for patients with AKI (such as amphotericin B, aminoglycosides, first-generation cephalosporin and sulfonamides, etc.). Dosage of drugs mainly excreted by the kidney should be adjusted according to the creatinine clearance.
- Antibiotics dose adjustment for sepsis AKI [70]
 - Initial dose

At the early stage of severe sepsis, hydrophilic antibiotics, such as β -lactams, glycopeptides, daptomycin, and aminoglycosides require administration of a loading dose is needed, as Vd and drug clearance rate may increase. The variations in Vd of liposoluble antibiotics, such as macrolides, fluoroquinolones, rifampicin, and linezolid, possess little effect on the drug concentration, which can be regulated according to renal function.
 - Maintenance dose

It should be adjusted according to renal function. We recommend therapeutic drug concentration monitoring for dose adjustment.

- Dose adjustment for chronic renal insufficiency^[70]
 - To maintain dosing intervals and reduce single dose
Suitable for the drugs with short half-life and time-dependent antibiotics such as β -lactams.
 - To prolong dosing intervals and maintain single dose
Suitable for the drugs with long half-life and concentration-dependent antibiotics such as aminoglycosides.
 - To reduce single dose and prolong dosing interval
Suitable for concentration-time-dependent drugs such as quinolones.
 - For patients with end-stage renal disease and receiving regular renal replacement therapy, we recommend to adjust the dosing regimen according to CrCl and various hemodialysis parameters.

9.5 Medication Adjustment for Patients with CRRT

CRRT is an important treatment for severe COVID-19 patients with high inflammatory response or AKI. During the application of CRRT treatment, it can affect the clearance of the drug, and the dose needs to be adjusted ^[63].

9.5.1 Anticoagulant Therapy of CRRT for COVID-19 ^[72]

- For patients without active bleeding and with normal or hyperactive coagulation function, we recommend heparin or low-molecular-weight heparin.
- For patients with combined active bleeding or high risk of bleeding: we suggest not to use anticoagulants if the patient's pre-treatment international normalization ratio (INR) \geq 1.5.
- For patients with combined active bleeding or high risk of bleeding: we recommend the standard citrate anticoagulation regimen for patients with pre-treatment INR $<$ 1.5 (without citrate contraindications). Argatroban can be used in the event of citrate contraindications.
- For patients with disseminated intravascular coagulation (DIC): after the supplement of

blood coagulation factors and heparin-based anticoagulation therapy, if INR ≥ 1.5 , anticoagulants are not required; if INR < 1.5 , heparin dosage can appropriately be administered.

9.5.2 Dosage Adjustment of Anti-infective Drugs in CRRT for COVID-19^[73-74]

Recommendation on the dosage adjustment of antimicrobials in CRRT are shown in Table 5.

- Drugs that generally do not require dosage adjustment: ribavirin, lopinavir / ritonavir, moxifloxacin, azithromycin, tigecycline, polymyxin B, voriconazole, posaconazole, caspofungin, micafungin and amphotericin B, etc.
- Drugs that require dosage adjustment: piperacillin / tazobactam, meropenem, imipenem/cilastatin, aztreonam, amikacin, levofloxacin, ciprofloxacin, vancomycin, daptomycin, SMZ/TMP and fluconazole, etc.

Table 5 Antimicrobial drugs dosage recommendation in CRRT

Drugs	Loading dose	CVVH	CVVHD	CVVHDF
Piperacillin/tazobactam	None	2.25~3.375 g q6~8h	2.25~3.375 g q6h	2.25~3.375 g q6h
Imipenem/Cilastatin	1.0 g	0.5 g q8h	0.5 g q6~8h	0.5 g q6h
Meropenem	1.0 g	0.5 g q12h	0.5 g q6~8h	0.5 g q6h
Aztreonam	2 g	1~2 g q12h	1 g q8h or 2 g q12h	1 g q8h or 2 g q12h
Amikacin	10 mg·kg ⁻¹	7.5 mg·kg ⁻¹ q24~48h	Same as CVVH	Same as CVVH
Levofloxacin	500~750 mg	250 mg q24h	250~500 mg q24h	250~750 mg q24h
Ciprofloxacin	None	200~400 mg q12~24h	400 mg q12~24h	400 mg q12h
Vancomycin	15~25 mg·kg ⁻¹	10~15 mg·kg ⁻¹ ·d ⁻¹	Same as CVVH	Same as CVVH
Daptomycin	None	4~6 mg·kg ⁻¹ q48h	Same as CVVH	Same as CVVH
SMZ/TMP	None	2.5~7.5 mg·kg ⁻¹ (TMP) q12h	Same as CVVH	Same as CVVH
Fluconazole	400~800 mg	200~400 mg q24h	400~800 mg q24h	800 mg q24h

Note: CRRT: continuous renal replacement therapies; CVVH: continuous veno-venous hemofiltration; CVVHD: continuous veno-venous hemodialysis; CVVHDF: continuous veno-venous hemodiafiltration; SMZ/TMP: sulfamethoxazole/trimethoprim.

10. Anti-Pyretic Medications

In patients with axillary temperature exceeding 38.5°C may consider the use of antipyretics to relieve fever, which ensures that patients eat and sleep well to have the physical strength to fight against the virus. Acetaminophen and ibuprofen are recommended by WHO.

10.1 Acetaminophen

Acetaminophen can be orally used in patients older than 3 months.

- Adolescents (≥ 12 years old) and adults dosing: 0.5 g every 4 to 6 hours as needed, maximum daily dose for adult is 2 g.
- Infants and children (age from 3 months to 12 years old) dosing: weight-directed dosing: 10 to 15 mg·kg⁻¹ per dose, do not exceed 4 doses in 24 h, maximum daily dose is 90 mg·kg⁻¹.
- It is highly safe to use at the recommended dose, but it will cause liver damage when exceeding the maximum dose. Commonly use cold medicines often contain ingredient “acetaminophen”, avoid overdose of medicines containing the same active ingredients.
- For patients who are allergic to acetaminophen or patients with favism, it is recommended to avoid the use of acetaminophen and choose other antipyretic drugs.

10.2 Ibuprofen

Ibuprofen is an alternative antipyretic drug orally used for patients older than 6 months.

- Adolescents (≥ 12 years old) and adults dosing: 0.2 g every 4 to 6 hours as needed, do not exceed 4 doses in 24 h.
- Infants and children (age from 6 months to 12 years old) dosing: weight-directed dosing: 5 to 10 mg·kg⁻¹ per dose every 6 hours. For rectal administration: 20 mg·kg⁻¹ per dose every 6 hours.
- Ibuprofen is an anti-inflammatory drug that can increase the level of angiotensin-converting enzyme 2(ACE2), but there is no evidence to support claims that ibuprofen may worsen COVID-19 symptoms^[75].

References

1. General Office of the National Health Commission. Notice on issuing a diagnosis and treatment plan for COVID-19 (7th Tentative Version) (NHC No.[2020]145)[EB/OL]. (In Chinese). <http://www.nhc.gov.cn/zyygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989.shtml>.
2. Critical Care Medicine Specialized Committee of Chinese Research Hospital Association. Expert consensus on the diagnosis and treatment of severe and critical COVID-19 cases [J/OL]. *Chinese Critical Care Medicine*, 2020, 32. (In Chinese). DOI: 10.3760/cma.j.cn121430-20200218-00001.
3. Military Frontline Expert Group. Diagnosis and treatment plan of COVID-19 from military medical teams supporting Hubei Province (1st Tentative Version) [J/OL]. *Chinese Journal of Tuberculosis and Respiratory Diseases*, 2020, 43. (In Chinese). DOI: 10.3760/cma.j.cn112147-20200224-00172.
4. Cai HD. Safe use of antiviral medicines for COVID-19 [J]. *Journal of Adverse Drug Reactions*, 2020, 22(2): 95-102. (In Chinese).
5. Multi-center Chloroquine Phosphate Treatment Collaboration Group of Guangdong Provincial Department of Science and Technology and Guangdong Provincial Health Commission. Expert consensus on treating COVID-19 with chloroquine phosphate [J/OL]. *Chinese Journal of Tuberculosis and Respiratory Diseases*, 2020, 43(00): E019-E019. (In Chinese). DOI: 10.3760/cma.j.issn.1001-0939.2020.0019.
6. Zhang B, Zuo W, Hu Y, *et al.* Research progress on serious adverse reactions related to chloroquine [J/OL]. *Journal of Adverse Drug Reactions*, 2020, 22. (In Chinese). DOI: 10.3760/cma.j.cn114015-20200222-00148.
7. Ducharme J, Farinotti R. Clinical pharmacokinetics and metabolism of chloroquine. Foc-us on recent advancements[J]. *Clin Pharmacokinet*, 1996, 31(4): 257-274.
8. Semb SO, Jacobsen D. Chloroquine poisoning[J]. *Tidsskr Nor Laegeforen*, 1996, 116(4): 478-80.
9. Liu QY and Yan SY. Research status and of pharmaceutical care of chloroquine used for COVID-19 treatment[J/OL]. *Journal of Adverse Drug Reactions*, 2020, 22. (In Chinese). DOI: 10.3760/cma.j.cn114015-20200224-00158.
10. Riou B, Barriot P, Rimailho A and Baud FJ. Treatment of severe chloroquine poisoning[J]. *N Engl J Med*, 1988, 318(1): 1-6.
11. Hydroxychloroquine[EB/OL]. U.S. National Library of Medicine. <https://pubchem.ncbi.nlm.nih.gov/compound/Hydroxychloroquine>.
12. Yao XT, Ye F, Zhang M, *et al.* In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)[J/OL]. *Clinical Infectious Diseases*, ciaa237. <https://doi.org/10.1093/cid/ciaa237>.
13. Centers for Disease Control and Prevention [EB/OL]. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html>
14. Furuta Y, Komeno T, Nakamura T. Favipiravir (T-705), a Broad Spectrum Inhibitor of Viral RNA Polymerase[J]. *Proc Jpn Acad Ser B Phys Biol Sci*. 2017;93(7):449-463. doi: 10.2183/pjab.93.027.
15. Favipiravir Instruction [EB/OL]. <http://www.mhlw.go.jp/file/05-Shingikai10901000-Kenkoukyoku-Soumuka/img-X28195440.pdf>.
16. Shanghai COVID-19 Clinical Treatment Expert Group. 2019 Expert consensus on the comprehensive treatment of COVID-19 in Shanghai[J/OL]. *Chinese Journal of Infectious Diseases*, 2020, 38. <http://rs.yiigle.com/yufabiao/1183266.htm>. (In Chinese). DOI: 10.3760/cma.j.issn.1000-6680.2020.0016.
17. Du B, Qiu HB, Zhan X, *et al.* Thoughts on medicine therapy of COVID-19[J]. *Chinese Journal of Tuberculosis and Respiratory Diseases*, 2020, 43(03): 173-176. (In Chinese). DOI: 10.3760/cma.j.issn.1001-0939.2020.03.005.
18. Liu YN. Thoughts on medicines to treat COVID-19[J]. *Chinese Journal of Tuberculosis and Respiratory Diseases*, 2020, 43(03): 161-162. (In Chinese). DOI: 10.3760/cma.j.issn.1001-0939.2020.03.001.
19. General Office of the National Health Commission. Diagnosis and treatment plan for severe and critical cases of COVID-19 (2nd Tentative Version) (NHC No. [2020]127)[EB/OL]. (In Chinese).
20. Wuhan Tongji Hospital COVID-19 Collaboration Group. Consensus on treatment and management of severe COVID-19 cases[EB/OL]. <http://guide.medlive.cn/guideline/19946>. (In Chinese).

21. Respiratory Branch of Chinese Medical Association. Diagnosis and treatment guide of community acquired pneumonia for Chinese adults (2016 Edition) [J]. *Chinese Journal of Tuberculosis and Respiratory Diseases*, 2016, 39(4): 253-279. (In Chinese).
22. Hu M, Li XY, Qiu HB, *et al.* Thoughts and suggestions on prevention and treatment of secondary bacterial infection in patients with COVID-19[J/OL]. *Chinese Journal of Critical Care Medicine*, 2020, 06. <http://rs.yiigle.com/yufabiao/1183367.htm>. (In Chinese). DOI: 10.3877/cma.j.issn.2096-1537.2020.0030.
23. Liu W and Li RY. Thoughts on secondary fungal infections of COVID-19 J]. *Microbes and Infections*, 2020, 15(1): 58-61. (In Chinese).
24. Therapeutic monitoring of vancomycin for serious methicillin-resistant *Staphylococcus aureus* infections: A revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. *Am J Health-Syst Pharm*.2020.
25. Wang Dongmei, Sun Shu, Hu Songxue, The therapeutic efficacy of high-dose ambroxol and the nursing effects in the treatment of severe pneumonia[J]. *Pak J Pharm Sci*, 2019, 32: 1409-1413.
26. Wu Huiwei, Ye Xiaofen, Jin Meilin, Cai Yingyun. Prescription analysis of expectorants and antitussive[J]. *Shanghai Med J*, 2011,32(09):421-424. (In Chinese).
27. Van Doremalen Neeltje, Bushmaker Trenton, Morris Dylan H, *et al.* Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1[J]. *N. Engl. J. Med.*,2020. DOI:10.1056/NEJMc2004973.
28. Yu Y X, Sun L, Yao K, *et al.* Consideration and prevention for the aerosol transmission of 2019 novel coronavirus[J]. *Zhonghua Yan Ke Za Zhi*, 2020, 56: E008. (In Chinese).
29. CSCCM, CMDACCM, CAPCCM. Expert consensus on the management of critically ill with coronavirus disease 2019[J/OL] . *Chin J Crit Care Med(Electronic Edition)*, 2020,06. (In Chinese). <http://rs.yiigle.com/yufabiao/1183272.htm>.
30. Cheng V, Abdul-Aziz MH, Roberts JA, *et al.* Optimising drug dosing in patients receiving extracorporeal membrane oxygenation[J]. *J Thorac Dis*. 2018. 10(Suppl 5): S629-S641.
31. Nigoghossian CD, Dzierba AL, Etheridge J, *et al.* Effect of Extracorporeal Membrane Oxygenation Use on Sedative Requirements in Patients with Severe Acute Respiratory Distress Syndrome [J]. *Pharmacotherapy*. 2016. 36(6): 607-616.
32. Wagner D, Pasko D, Phillips K, *et al.* In vitro clearance of dexmedetomidine in extra-corporeal membrane oxygenation[J]. *Perfusion*. 2013. 28(1): 40-46.
33. Lemaitre F, Hasni N, Leprince P, *et al.* Propofol, midazolam, vancomycin and cyclosporine therapeutic drug monitoring in extracorporeal membrane oxygenation circuits primed with whole human blood[J]. *Crit Care*. 2015. 19: 40.
34. Shekar K, Roberts JA, McDonald CI, *et al.* Sequestration of drugs in the circuit may lead to therapeutic failure during extracorporeal membrane oxygenation[J]. *Crit Care*. 2012. 16(5): R194.
35. Heith CS, Hansen LA, Bakken RM, *et al.* Effects of an Ex Vivo Pediatric Extracorporeal Membrane Oxygenation Circuit on the Sequestration of Mycophenolate Mofetil, Tacrolimus, Hydromorphone, and Fentanyl[J]. *J Pediatr Pharmacol Ther*. 2019. 24(4): 290-295.
36. Yang S, Noh H, Hahn J, *et al.* Population pharmacokinetics of remifentanyl in critically ill patients receiving extracorporeal membrane oxygenation[J]. *Sci Rep*. 2017. 7(1): 16276.
37. Ha MA, Sieg AC. Evaluation of Altered Drug Pharmacokinetics in Critically Ill Adults Receiving Extracorporeal Membrane Oxygenation[J]. *Pharmacotherapy*. 2017. 37(2): 221-235.
38. Di Nardo M, Wildschut ED. Drugs pharmacokinetics during veno-venous extracorporeal membrane oxygenation in pediatrics[J]. *J Thorac Dis*. 2018 ,(Suppl 5):S642-S652.
39. Ruiz S, Papy E, Da SD, *et al.* Potential voriconazole and caspofungin sequestration during extracorporeal membrane oxygenation[J]. *Intensive Care Med*. 2009. 35(1): 183-184.
40. Spriet I, Annaert P, Meersseman P, *et al.* Pharmacokinetics of caspofungin and voriconazole in critically ill patients during extracorporeal membrane oxygenation[J]. *J Antimicrob Chemother*. 2009. 63(4): 767-770.
41. Himebauch AS, Kilbaugh TJ, Zuppa AF. Pharmacotherapy during pediatric extracorporeal membrane oxygenation: a review[J]. *Expert Opin Drug Metab Toxicol*. 2016. 12(10): 1133-1142.
42. Shekar K, Roberts JA, Welch S, *et al.* ASAP ECMO: Antibiotic, Sedative and Analgesic Pharmacokinetics during Extracorporeal Membrane Oxygenation: a multi-centre study to optimise drug therapy during ECMO[J]. *BMC Anesthesiol*. 2012. 12: 29.

43. Ghazi SMA, Ogungbenro K, Kosmidis C, *et al.* The effect of veno-venous ECMO on the pharmacokinetics of Ritonavir, Darunavir, Tenofovir and Lamivudine[J]. *J Crit Care*. 2017. 40: 113-118.
44. Argel CL, Aboud M, Forster A, *et al.* Intravenous Ribavirin for Parainfluenza and Re-spiratory Syncytial Virus in an Infant Receiving Extracorporeal Membrane Oxygenation and Continuous Renal Replacement Therapy[J]. *J Pediatr Pharmacol Ther*. 2018. 23(4): 337-342.
45. De Rosa FG, Corcione S, Baietto L, *et al.* Pharmacokinetics of linezolid during extra-corporeal membrane oxygenation[J]. *Int J Antimicrob Agents*. 2013. 41(6): 590-591.
46. Watt KM, Cohen-Wolkowicz M, Williams DC, *et al.* Antifungal Extraction by the Ext-racorporeal Membrane Oxygenation Circuit[J]. *J Extra Corpor Technol*. 2017,49(3):150-159.
47. Autmizguine J1, Hornik CP, Benjamin DK Jr, *et al.* Pharmacokinetics and Safety of Micafungin in Infants Supported With Extracorporeal Membrane Oxygenation[J]. *Pediatr Infect Dis J*. 2016, 35(11):1204-1210.
48. Guan WJ, Ni ZY, Hu Y, *et al.* Clinical characteristics of 2019 novel coronavirus infection in China[J]. *N Engl J Med*. 2020 Feb 28. DOI: 10.1056/NEJMoa2002032.
49. Rhodes A, Evans LE, Alhazzani W, *et al.* Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016[J]. *Intensive Care Med*. 2017,43(3):304-377.
50. Emergency Physician Branch of Chinese Medical Association, Shock and Sepsis Specialized Committee of Chinese Research Hospital Association. Guidelines for emergency treatment of sepsis/septic shock in China (2018)[J]. *Chinese Emergency Medicine*, 2018, 38(9). (In Chinese). DOI:10.3969/j.issn.1002-1949.2018.09.001.
51. CSPEN, Chinese Society for Parenteral and Enteral Nutrition. Expert advice of CSPEN on medical nutrition therapy for patients with COVID-19. ZXYF No.3 [2020][EB/OL]. (In Chinese). https://www.cma.org.cn/art/2020/1/30/art_2928_32261.html.
52. Liu J, Chen EZ, Wang HL, *et al.* Expert advice on nutrition support therapy for severe patients with COVID-19[J/OL]. *Chinese Journal of Critical Care & Intensive Care Medicine (Electronic Edition)*, 2020, 06. <http://rs.yiigle.com/yufabiao/1182256.htm>. (In Chinese). DOI: 10.3877/cma.j.issn.1672-6448.2020.0013.
53. Shi HP. Cancer nutrition therapy [J]. *Chinese Journal of Clinical Oncology*. 2014; 41 (18):1141-1145. (In Chinese).
54. McClave SA, Taylor BE, Martindale RG, *et al.* Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)[J]. *JPEN J Parenter Enteral Nutr*. 2016;40(2):159–211.
55. CSPEN, Chinese Society for Parenteral and Enteral Nutrition. Expert advice on parenteral and enteral nutrition therapy for severe patients with COVID-19[J]. *Journal of Surgery Concepts & Practice*. 2020, 25(1):35-39. (In Chinese). DOI: 10.16139/j.1007-9610.2020.01.008.
56. Yang CX, Li SJ, Diao CD, *et al.* Standardized pathways of nutritional therapy pharmaceutical services for severe and critically ill patients with COVID-19[J/OL]. *Herald of Medicine*. <http://kns.cnki.net/kcms/detail/42.1293.R.20200309.2130.006.html>. (In Chinese).
57. Xu JQ, Zeng F, Wu Y, *et al.* Advice on nutritional support and monitoring of severe patients with COVID-19[J/OL]. *Chinese Journal of Hospital Pharmacy*. (In Chinese). <http://kns.cnki.net/kcms/detail/42.1204.r.20200218.0954.002.html>.
58. Society of Microecology, China Preventive Medicine Association. Chinese expert consensus on clinical application of microecological agent in digestive tract (2016 version) [J]. *Chinese Journal of Microecology*, 2016, 28(06):621-631. (In Chinese).
59. Chinese Geriatric Society, Chinese Medical Association. Chinese expert consensus on clinical application of Intestinal microecological preparations in the elderly (2019) [J]. *Chinese Journal of Geriatrics*, 2019, 38(4):355-361. (In Chinese).
60. Du S, Liu XX, Yang Y, *et al.* Discussion on the application of intestinal microecological modulator in novel coronavirus pneumonia [J/OL]. *Adverse Drug Reactions Journal*, 2020, 22. <http://rs.yiigle.com/yufabiao/1182715.htm>. (In Chinese). DOI: 10.3760/cma.j.issn.1008-5734.2020.0006.
61. Karnad DR, Bhadade R, Verma PK, *et al.* Intravenous administration of ulinastatin (human urinary trypsin inhibitor) in severe sepsis: a multicenter randomized controlled study[J]. *Intensive Care Med*. 2014 Jun;40(6):830-8. DOI: 10.1007/s00134-014-3278-8.

62. Zhongnan Hospital of Wuhan University. A randomized, open-label, parallel controlled clinical research for evaluation the efficacy and safety of diammonium glycyrrhizinate enteric-coated capsules combined with Vitamin C tablets in treating COVID-19 on the basis of standard clinical antiviral treatment (ChiCTR2000029768)[EB/OL]. <http://www.chictr.org.cn/showproj.aspx?proj=49131>. (In Chinese).
63. Kang K, Zhao MY, Wang CS, *et al*. Thoughts on diagnosis and treatment of severe COVID-19 patients [J/OL]. *Chinese Journal of Critical Care and Intensive Care Medicine*, 2020, 06. <http://rs.yiigle.com/yufabiao/1183257.htm>. (In Chinese). DOI: 10.3877/cma.j.issn.2096-1537.2020.0025.
64. Chinese Medical Association, Society of Respiriology, Pulmonary Embolism and Pulmonary Vascular Disease Group, *et al*. Suggestions on prevention and treatment of COVID-19 associated venous thromboembolism (Trial) [J]. *Chinese Medical Journal*, 2020,100 (00): E007-E007. (In Chinese). DOI: 10.3760/cma.j.issn.0376-2491.2020.0007.
65. Wang D, Hu B, Hu C, *et al*. Clinical Characteristics of Patients With 2019 Novel Co-ronavirus (2019-nCoV)-Infected Pneumonia in Wuhan, China[J/OL]. *JAMA*, 2020 Feb 7. DOI: 10.1001/jama.2020.1585.
66. Huang C, Wang Y, Li X, *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China[J]. *The Lancet*, 2020,395 (10223): 497-506.
67. Dong SJ, Zhai SD, Li ZJ. Controversy over ACEI in COVID-19: too early to conclude [J/OL]. *Clinical Medication Journal*. 2020, 18 (2): <https://mp.weixin.qq.com/s/sIHjvWJnW8ioVPHJ6LbZQ>. (In Chinese).
68. Zheng P, Li J, Zhang JX, *et al*. No COVID-19 patients are advised to stop taking angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers [J/OL]. *Adverse Drug Reactions Journal*, 2020, 22. <http://rs.yiigle.com/yufabiao/1182716.htm>. (In Chinese). DOI: 10.3760/cma.j.issn.1008-5734.2020.0005.
69. Yang, X, Yu Y, Xu J, *et al*. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study [J/OL]. *Lancet*. Published Online February 21, 2020. [https://doi.org/10.1016/S2213-2600\(20\)30079-5](https://doi.org/10.1016/S2213-2600(20)30079-5).
70. Infectious Diseases Society of China. Expert consensus on clinical application of antibiotic pharmacokinetic/pharmacodynamic theory [J]. *Chinese Journal of Tuberculosis and Respiratory Diseases*. 2018. 41(6): 409-446. (In Chinese).
71. Chinese Medical Association, Expert Group of Nephrology Society. Expert consensus on diagnosis and treatment of COVID-19 combined with acute kidney injury [EB/OL]. <https://www.cn-healthcare.com/articlewm/20200226/wap-content-1090750.html>. (In Chinese).
72. National Nephrology Professional Medical Quality Management and Control Center, Blood Purification Treatment and Engineering Technology Society of China International Exchange and Promotive Association for Medical and Health Care, Blood Purification and Therapeutics Committee of the Whole Army. Expert advice on the application of CRRT in the treatment of COVID-19[EB/OL]. [http://www.cnrd.net/Static/file/Expert advice on the application of CRRT in the treatment of COVID-19 %2020200206.pdf](http://www.cnrd.net/Static/file/Expert%20advice%20on%20the%20application%20of%20CRRT%20in%20the%20treatment%20of%20COVID-19%2020200206.pdf). (In Chinese).
73. Choi G, Gomersall CD, Tian Q, *et al*. Principles of antibacterial dosing in continuous renal replacement therapy[J]. *Blood Purif*, 2010, 30(3): 195.
74. Heintz BH, Matzke GR, Dager WE. Antimicrobial dosing concepts and recommendations for critically ill adult patients receiving continuous renal replacement therapy or intermittent hemodialysis [J]. *Pharmacotherapy*, 2009, 29(5): 562.
75. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection?[J]. *Lancet Respir Med*. 2020 Mar 11. pii: S2213-2600(20)30116-8.

Appendix A (Traditional Chinese Medicine Treatment)

There are currently no effective drugs for the treatment of COVID-19. Traditional Chinese Medicine (TCM) and western medicine can complement each other to give full play to their respective advantages and emphases. TCM can serve a full range of functions through the entire course of treatment. At the press conference on "The Important Role of Traditional Chinese Medicine in the Prevention and Treatment of COVID-19" held by the State Council Information Office of China on March 23, 2020, it was reported that among the confirmed cases of COVID-19 in China, 74,187 or 91.5% had used TCM. Among those in Hubei Province, 61,449 or 90.6% had used TCM. Clinical observation shows that the overall efficacy rate of TCM treatments has been over 90%. TCM can effectively alleviate symptoms, reduce disease progression from mild and moderate to severe, improve the cure rate, reduce the mortality rate, and promote the recovery process.

In TCM, COVID-19 is considered a "pestilence" disease caused by the "epidemic pestilential qi." Thus, treatment based on syndrome differentiation should take into account the local climate, the patient's illness condition and constitution. In this paper, people who may require TCM treatment are divided into three groups, namely, the medical observation period, the clinical treatment period, and the recovery period. TCM treatment plans are recommended for each group.

For the medical observation group, if there is fatigue with gastrointestinal discomfort, the recommended Chinese patent medicine is Huoxiang Zhengqi capsules (pills, liquid, or oral liquid); for those who have fatigue with fever, Jinhua Qinggan granules, Lianhua Qingwen capsules (granules), or Shufeng Jiedu capsules (granules) are recommended.

Patients in the clinical treatment period can be divided into four types: mild, moderate, severe, and critical. Treatment based on syndrome differentiation needs to take into account the actual condition of each patient. According to their clinical

symptoms, patients are mainly diagnosed with the following TCM syndromes (patterns): Mild cases--Cold-damp constraint in the lung or Damp-heat accumulation in the lung; Moderate cases--Damp-toxin constraint in the lung or Cold-damp obstructing the lung; Severe cases--Epidemic toxin blocking the lung or Blazing of both qi and ying; Critical cases-- Internal blockage and external desertion. The mild and moderate cases, according to their syndrome classification, should take the corresponding decoctions orally. Severe cases, according to their syndrome classification, should take the corresponding decoctions by oral administration or nasal feeding (Table 1), and if necessary, in combination with Chinese patent medicine injection (Table 2). In critically ill patients, Chinese patent medicine injection and TCM decoctions are generally used together. Commonly used Chinese patent medicine injections include: Xiyanping injection, Xuebijing injection, Reduning injection, Tanreqing injection, Xingnaojing injection, Shenfu injection, Shengmai injection, or Shenmai injection. The use of TCM injections should follow the medication instruction manual, starting from small doses and adjusted gradually based on syndrome differentiation. See Table 1 for the different Chinese patent medicine injections and their corresponding clinical symptoms as well as usage and dosage instructions.

People in the recovery phase may have the Lung-spleen qi deficiency and Deficiency of both qi and yin patterns. They only need to take the corresponding decoctions orally.

Note: For TCM formulas corresponding to the syndromes discussed above, please refer to the "Diagnosis and Treatment Protocol for COVID-19 (Trial Version 7)".

Table 1 TCM Formula Name, Syndrome, Composition, Usage and Dosage

Formula Name	Scope of Application (Syndrome)	Formula Composition	Instructions for Use
Qingfei Paidu Tang (Clear the Lung and Eliminate Toxins Decoction)	Mild, moderate, severe, critical	Ma Huang (Ephedrae Herba) 9 g, Zhi Gan Cao (Glycyrrhizae Radix) 6 g, Xing Ren (Armeniacae Semen) 9 g, Sheng Shi Gao (Gypsum fibrosum) (decocted first) 15~30 g, Gui Zhi (Cinnamomi Ramulus) 9 g, Ze Xie (Alismatis Rhizoma) 9 g, Zhu Ling (Polyporus) 9 g, Bai Zhu (Atractylodis macrocephalae Rhizoma) 9 g, Fu Ling (Poria) 15 g, Chai Hu (Bupleuri Radix) 16 g, Huang Qin (Scutellariae Radix) 6 g, Jiang Ban Xia (Pinellinae Rhizoma Praeparatum) 9 g, Sheng Jiang (Zingiberis Rhizoma recens) 9 g, Zi Wan (Asteris Radix) 9 g, Kuan Dong Hua (Farfarae Flos) 9 g, She Gan (Belamcandae Rhizoma) 9 g, Xi Xin (Asari Radix et Rhizoma) 6 g, Shan Yao (Dioscoreae Rhizoma) 12 g, Zhi Shi (Aurantii Fructus immaturus) 6 g, Chen Pi (Citri reticulatae Pericarpium) 6 g, Huo Xiang (Pogostemonis Herba) 9 g	Traditional Chinese medicine herbal pieces in decoction; Take 1 dose daily, drink warm decoction twice (40 minutes after meals in morning and evening), three doses per treatment course
	Mild (Cold-damp constraint in the lung pattern)	Sheng Ma Huang (Ephedrae Herba) 6 g, Sheng Shi Gao (Gypsum fibrosum) 15 g, Xing Ren (Armeniacae Semen) 9 g, Qiang Huo (Notopterygii Rhizoma seu Radix) 15 g, Ting Li Zi (Lepidii/Descurainiae Semen) 15 g, Guan Zhong (Cyrtomii Rhizoma) 9 g, Di Long (Pheretima) 15 g, Xu Chang Qing (Cynanchi paniculati Radix) 15 g, Huo Xiang (Pogostemonis Herba) 15 g, Pei Lan (Eupatorii Herba) 9 g, Cang Zhu (Atractylodis Rhizoma) 15 g, Yun Ling (Poria) 45 g, Sheng Bai Zhu (Atractylodis macrocephalae Rhizoma) 30 g, Jiao San Xian (Jiao Shan Zha (Crataegi Fructus), Jiao Shen Qu (Massa medicata fermentata), and Jiao Mai Ya (Hordei Fructus germinatus)) 9 g each, Hou Po (Magnoliae officinalis Cortex) 15 g, Jiao Bing Lang (Arecae Semen) 9 g, Wei Cao Guo (Tsaoko Fructus) 9 g, Sheng Jiang (Zingiberis Rhizoma recens) 15 g	Take 1 dose daily, 600 ml decoction, take 3 times daily before each meal
	Mild (Damp-heat	Bing Lang (Arecae Semen) 10 g, Cao Guo (Tsaoko Fructus) 10 g, Hou	Take 1 dose daily, 400 ml

accumulation in the lung pattern)	Po (Magnoliae officinalis Cortex) 10 g, Zhi Mu (Anemarrhenae Rhizoma) 10 g, Huang Qin (Scutellariae Radix) 10 g, Chai Hu (Bupleuri Radix) 10 g, Chi Shao (Paeoniae Radix rubra) 10 g, Lian Qiao (Forsythiae Fructus) 15 g, Qing Hao (Artemisiae annuae Herba) (added later) 10 g, Cang Zhu (Atractylodis Rhizoma) 10 g, Da Qing Ye (Isatidis Folium) 10 g, Sheng Gan Cao (Glycyrrhizae Radix) 5 g	decoction, take twice daily in morning and evening
Moderate (Damp-toxin constraint in the lung pattern)	Sheng Ma Huang (Ephedrae Herba) 6g, Ku Xing Ren (Armeniacae Semen) 15 g, Sheng Shi Gao (Gypsum fibrosum) 30 g, Sheng Yi Yi Ren (Coicis Semen) 30 g, Mao Cang Zhu (Atractylodis Rhizoma) 10g, Guang Huo Xiang (Pogostemonis Herba) 15 g, Qing Hao Cao (Artemisiae annuae Herba) 12 g, Hu Zhang (Polygoni cuspidati Rhizoma) 20 g, Ma Bian Cao (Verbenae Herba) 30 g, Gan Lu Gen (Phragmitis Rhizoma) 30 g, Ting Li Zi (Lepidii/Descurainiae Semen) 15 g, Hua Ju Hong (Citri grandis Exocarpium rubrum) 15 g, Sheng Gan Cao (Glycyrrhizae Radix) 10 g	Take 1 dose daily, 400 ml decoction, take twice daily in morning and evening
Mild (Cold-damp obstructing the lung pattern)	Cang Zhu (Atractylodis Rhizoma) 15 g, Chen Pi (Citri reticulatae Pericarpium) 10 g, Hou Po (Magnoliae officinalis Cortex) 10 g, Huo Xiang (Pogostemonis Herba) 10 g, Cao Guo (Tsaoko Fructus) 6 g, ShengMa Huang (Ephedrae Herba) 6 g, Qiang Huo (Notopterygii Rhizoma seu Radix) 10 g, Sheng Jiang (Zingiberis Rhizoma recens) 10 g, Bing Lang (Arecae Semen) 10 g	Take 1 dose daily, 400 ml decoction, take twice daily in morning and evening
Severe (Epidemic toxin blocking the lung pattern)	(Huashi Baidu Decoction) Sheng Ma Huang (Ephedrae Herba) 6 g, Xing Ren (Armeniacae Semen) 9 g, Sheng Shi Gao (Gypsum fibrosum) 15 g, Gan Cao (Glycyrrhizae Radix) 3 g, Huo Xiang (Pogostemonis Herba) (added later) 10 g, Hou Po (Magnoliae officinalis Cortex) 10 g, Cang Zhu (Atractylodis Rhizoma) 15 g, Cao Guo (Tsaoko Fructus) 10 g, Fa Ban Xia (Pinellinae Rhizoma Praeparatum) 9 g, Fu Ling (Poria) 15 g, Sheng Da Huang (Rhei Radix et Rhizoma) (add later) 5 g, Sheng Huang Qi (Astragali Radix) 10 g, Ting Li Zi (Lepidii/Descurainiae Semen) 10 g, Chi Shao (Paeoniae Radix rubra) 10 g	Take 1~2 doses daily, 100 ml~200 ml decoction each time, take 2~4 times daily by oral administration or nasal feeding

	Severe (Blazing of both qi and ying pattern)	Sheng Shi Gao (Gypsum fibrosum) (decocted first) 30~60 g, Zhi Mu (Anemarrhenae Rhizoma) 30 g, Sheng Di (Rehmanniae Radix) 30~60 g, Shui Niu Jiao (Bubali Cornu) (decocted first) 30 g, Chi Shao (Paeoniae Radix rubra) 30 g, Xuan Shen (Scrophulariae Radix) 30 g, Lian Qiao (Forsythiae Fructus) 15 g, Dan Pi (Moutan Cortex) 15 g, Huang Lian (Coptidis Rhizoma) 6 g, Zhu Ye (Phyllostachys nigrae Folium) 12 g, Ting Li Zi (Lepidii/Descurainiae Semen) 15 g, Sheng Gan Cao (Glycyrrhizae Radix) 6 g	1 dose daily, Shi Gao and Shui Niu Jiao should be decocted first, 100 ml~200 ml decoction each time, take 2~4 times daily by oral administration or nasal feeding
	Critical (Internal blockage and external desertion pattern)	Ren Shen (Ginseng Radix) 15 g, Hei Shun Pian (Aconiti Radix lateralis praeparata) (decocted first) 10 g, Shan Zhu Yu (Corni Fructus) 15 g	Take Su He Xiang pill or Angong Niu Huang pill with the decoction

Table 2 Chinese Patent Medicine Injection Application, Usage and Dosage

Clinical Symptoms	Chinese Patent Medicine Injection	Usage and Dosage
	Xiyanping injection	100 ml (bid)
Viral infection with mild bacterial infection	Reduning injection	20 ml (bid)
	Tanreqing injection	40 ml (bid)
High fever with disturbance of consciousness	Xingnaojing injection	20 ml (bid)
Systemic inflammatory response syndrome (SIRS) and/or multiple organ failure (MOF)	Xuebijing injection	100 ml (bid)
Immunosuppression	Shenmai injection	20~60 ml (bid)
	Shengmai injection	20~60 ml (bid)
Shock	Shenfu injection	20~100 ml (bid)

《Expert consensus on clinical rational drug use of new coronavirus pneumonia》 Writing Group

Group leader: Yu Zhang, Xiao Chen, Bikui Zhang, Rongsheng Zhao, Liyan Miu, Xinan Wu.

Review expert list:

Helen Zhang--United Family Healthcare

Xiao Chen--The First Affiliated Hospital of Sun Yat-Sen University

Weihong Chen--Shanxi Bethune Hospital

Jianhong Chen--PLA Army Characteristic Medical Center (Daping Hospital)

Shicai Chen--Beijing Luhe Hospital, Capital Medical University

Yimin Cui--Peking University First Hospital

Deshi Dong--The First Affiliated Hospital of Dalian Medical University

Guang Du--Tongji Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology

Yalin Dong—First Affiliated Hospital of Xi'an Jiao Tong University

Xin Feng—Beijing Obstetrics and Gynecology Hospital, Capital Medical University

Cheng Guo-- The Sixth People's Hospital Affiliated to Shanghai Jiao Tong University

Xin Hu—Beijing Hospital

Jianxin Hu—Jiangxi Provincial People's Hospital

Fangxuan Han—Hainan General Hospital

Zhenguang Huang--The First Affiliated Hospital of Guangxi Medical University

Ruigang Hou-- The Second Hospital of Shanxi Medical University

Pinfang Huang-- The First Affiliated Hospital of Fujian Medical University

Lechuan Jia-- General Hospital of Ningxia Medical University

Hairu Lu-- Qinghai Provincial People's Hospital

Gaofeng Liu--The Second Affiliated Hospital of Harbin Medical University

Zhengxiang Li-- Tianjin Medical University General Hospital

Guohui Li-- Cancer Hospital, Chinese Academy of Medical Sciences

Xiaoyang Lu-- The First Affiliated Hospital, Medical College of Zhejiang University

Xianghong Liu-- Qilu Hospital of Shandong University

Pengmei Li—China-Japan Friendship Hospital

Zhiping Li-- Children's Hospital of Fudan University

Liyang Miu-- The First Affiliated Hospital of Soochow University

Manling Ma-- The First Affiliated Hospital of Harbin Medical University

Ruilian Ma—The Affiliated Hospital of Inner Mongolia Medical University

Feng Qiu-- The First Affiliated Hospital of Chongqing Medical University

Zhongguo Sui—The Affiliated Hospital of Qingdao University

Aizong Shen-- The First Affiliated Hospital of University of Science and Technology of China (Anhui Provincial Hospital)

Ouzhu Suolang-- The Second People's Hospital of Tibet Autonomous Region

Yanqing Song-- The First Bethune Hospital of Jilin University

Rongsheng Tong-- Sichuan Provincial People's Hospital

Xinan Wu-- The First Hospital of Lanzhou University

Jiawei Wang-- Beijing Tongren Hospital

Dongfang Wu—Zhongnan Hospital of Wuhan University

Jianhua Wang-- The First Affiliated Hospital of Xinjiang Medical University

Aidong Wen-- Xijing Hospital Affiliated to Air Force Military Medical University

Dujuan Xu-- The First Affiliated Hospital of Anhui Medical University

Ting Xu-- West China Hospital of Sichuan University

Guili Xu-- Kunming General Hospital of Chengdu Military Area Command

Juan Xie-- Guizhou Provincial People's Hospital

Peiyuan Xia-- The First Affiliated Hospital of Army Medical University (Southwest Hospital)

Min Yang-- Guangdong Provincial People's Hospital

Xiaofeng Yan-- The Second Affiliated Hospital of Zhejiang University School of Medicine

Yi Yao-- Jiangsu Province Hospital of Chinese Medicine

Dongfeng Yin-- General Hospital of Xinjiang Military Region

Qian Yu—China-Japan Friendship Hospital of Jilin University

Yu Zhang-- Union Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology

Zhu Zhu—Peking Union Medical College Hospital

Rongsheng Zhao—Peking University Third Hospital

Zhigang Zhao-- Beijing Tiantan Hospital, Capital Medical University

Bikui Zhang—The Second Xiangya Hospital of Central South University

Yanhua Zhang-- Beijing Cancer Hospital

Xiaojian Zhang-- The First Affiliated Hospital of Zhengzhou University

Xiacong Zuo—The Third Xiangya Hospital of Central South University

Huijuan Zhang-- Tianjin People's Hospital

Lingli Zhang-- West China Second Hospital, Sichuan University

Zhiqing Zhang-- The Second Hospital of Hebei Medical University

Limei Zhao-- Shengjing Hospital of China Medical University

Jian Zhang-- Xinhua Hospital Affiliated to Shanghai Jiaotong University School of
Medicine

Suodi Zhai-- Peking University Third Hospital

Bi Ze-- Tibet Autonomous Region People's Hospital

Lan Zhang-- Xuanwu Hospital of Capital Medical University

Bo Zhang-- Peking Union Medical College Hospital

Yusheng Zhou-- The Second Hospital, University of South China

《Expert consensus on clinical rational drug use of new coronavirus pneumonia》

Author list:

Xiao Chen--The First Affiliated Hospital of Sun Yat-Sen University

Jie Chen-- The First Affiliated Hospital of Sun Yat-Sen University

Cheng Guo-- The Sixth People's Hospital Affiliated to Shanghai Jiao Tong University

Xin Hu—Beijing Hospital

Pinfang Huang-- The First Affiliated Hospital of Fujian Medical University

Xiaoyang Lu-- The First Affiliated Hospital, Medical College of Zhejiang University

Guohui Li-- Cancer Hospital, Chinese Academy of Medical Sciences

Gaofeng Liu--The Second Affiliated Hospital of Harbin Medical University

Yongning Lv-- Union Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology

Liyan Miu-- The First Affiliated Hospital of Soochow University

Chen Shi-- Union Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology

Xinan Wu-- The First Hospital of Lanzhou University

Yu Zhang-- Union Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology

Rongsheng Zhao—Peking University Third Hospital

Bikui Zhang—The Second Xiangya Hospital of Central South University

Yanhua Zhang-- Beijing Cancer Hospital

Bo Zhang-- Peking Union Medical College Hospital

Xiacong Zuo—The Third Xiangya Hospital of Central South University

Acknowledgement: Thank the following clinical pharmacists for their contributions to the preparation of this consensus

Sanlan Wu, Ke Li, Fang Zeng, Jun Chen, Tingting Wu, Jiaqiang Xu, Qi Hu, Yifei Huang, Weijing Gong, Jinglin Wang, Ying Zhou, Liyun Ma, Ziming Zheng, Yan Gong, Jia Li, Meijuan Luo, Yanzhe Xia, Qiuyi He, Pan Chen, Jiawei Zeng, Liyan Zhao, Haiyan Wu, Chenfeng Xu, Tao Zhou.