

UPDATED 26 MARCH 2020

FIP HEALTH ADVISORY

COVID-19: CLINICAL INFORMATION AND TREATMENT GUIDELINES

INTERNATIONAL PHARMACEUTICAL FEDERATION



COVID-19: CLINICAL INFORMATION AND TREATMENT GUIDELINES

FIP will update this interim guidance as more information becomes available.

Table of Contents

	Purpose of this document	2			
SAR	ARS-CoV-2 Coronavirus: Basic facts				
	What is a coronavirus?	2			
	What is the SARS-CoV-2 coronavirus / COVID-19 pandemic?	3			
Cord	Coronavirus Disease 2019 (COVID-19) – Clinical information				
	Modes of transmission	4			
	Disease prevention	5			
	Diagnostic testing for COVID-19 in suspected human cases	5			
	Disease onset	5			
	Symptoms	6			
COVID-19: Treatment guidelines and research updates					
	Clinical treatment medicines	6			
	Convalescent plasma therapy	8			
	Advances in vaccines development for the treatment of COVID-19	8			
	Progress of clinical trials for the treatment of COVID-19	9			
Bibli	libliography				
ANN	ANNEX 1: List of key medicines for the treatment of COVID-19				
Vali	/alidity				
Ackı	cknowledgements				

Purpose of this document Since December 2019, an outbreak of a new human coronavirus has spread to many countries and caused thousands of cases and deaths. COVID-19 is the disease caused by the new virus SARS-CoV-2. Most people who are infected get mild respiratory symptoms that will disappear on their own, but some people develop more severe illness, like pneumonia. The virus is transmitted through contact with an infected person or via respiratory droplets when an infected person coughs or sneezes. There is a higher risk of infection if you have been in an area where the virus is spreading, or if you have been in close contact with a person infected with the new coronavirus. There is also a higher risk if you suffer from comorbidities already.

The purpose of this document is to provide relevant clinical information and treatment guidelines on the COVID-19 pandemic. – for pharmacists and the pharmacy workforce, both in a primary care context (i.e. community pharmacies and primary healthcare facilities) and in hospital settings, as well as for pharmacists working as clinical biologists in medical analysis laboratories, for example, as clinical biologists, and offer a set of references that may be consulted for more information.

Coronavirus infections can be prevented and an outbreak can be stopped through the active engagement of decision-makers, healthcare professionals, the media and the community. This was demonstrated in previous coronavirus outbreaks such as in 2003 with SARS-CoV (Severe Acute Respiratory Syndrome Coronavirus) or in 2012 with MERS-CoV (Middle East Respiratory Syndrome Coronavirus). This document aims to assist pharmacists and the pharmacy workforce in preventing the spread of the disease and contributing to its efficient management in the healthcare system.

SARS-CoV-2 Coronavirus: Basic facts

What is a coronavirus?

Coronaviruses (CoVs) are a large family of viruses that cause illness ranging from the common cold to more severe diseases such as <u>Middle East Respiratory Syndrome (MERS-CoV)</u> and <u>Severe Acute Respiratory Syndrome (SARS-CoV)</u>. <u>A novel coronavirus (nCoV)</u> is a new strain that has not been previously identified in humans.

Coronaviruses are zoonotic, meaning they are transmitted between animals and people. Detailed investigations found that SARS-CoV was transmitted from civet cats to humans and MERS-CoV from dromedary camels to humans. Several known coronaviruses are circulating in animals that have not yet infected humans.

Coronaviruses are large, enveloped, positive-stranded RNA viruses. They have the largest genome among all RNA viruses. The genome is packed inside a helical capsid formed by the nucleocapsid protein and further surrounded by an envelope. Associated with the viral envelope are at least three structural proteins: the membrane protein and the envelope protein are involved in virus assembly, whereas the spike protein mediates virus entry into host cells. Among the structural proteins, the spike forms large protrusions from the virus surface, giving coronaviruses the appearance of having crowns (hence their name; *corona* in Latin means crown). In addition to mediating virus entry, the spike is a critical determinant of viral host range and tissue tropism and a major inducer of host immune responses. (Li, 2016)

Coronaviruses usually affect mammals and birds, causing a variety of lethal diseases. In general, coronaviruses cause widespread respiratory, gastrointestinal and central nervous system diseases in humans and other animals, threatening human health and causing economic loss from mild upper to lower respiratory tract infections. (Li, 2016) Coronaviruses are capable of adapting to new environments through mutation and recombination with relative ease. (Li, 2016) As such, they can affect new hosts and tissues. For this reason, although rarely, certain coronaviruses that usually affect only certain animal species can generate new strains that can cross over to human hosts and then be transmitted between humans. Since humans had not been exposed to such viruses before and cannot be protected by either existing vaccines or natural immunity, these mutations can rapidly lead to disease outbreaks and, eventually, pandemics. This was the case with the previous outbreaks of SARS and MERS.

What is the SARS-CoV-2 coronavirus / COVID-19 pandemic?

The SARS-CoV-2 is a novel strain of coronavirus that was first detected in the city of Wuhan, in the province of Hubei, in the People's Republic of China – a city with a population of 11 million. The outbreak started as a pneumonia of unknown causal agent at the end of December 2019.

Phylogenetics analyses undertaken with available full genome sequences suggest that bats appear to be the reservoir of COVID-19 virus, but the intermediate host(s) has not yet been identified. (World Health Organization, 2020)

On 30 January 2020, the World Health Organization (WHO) declared the outbreak a Public Health Emergency of International Concern. The WHO recommended that the interim name of the disease causing the current outbreak should be 2019-nCoV acute respiratory disease. In the 2019-nCoV acronym, "2019" is the year the virus was first detected, "n" means "new", and "CoV" corresponds to the coronavirus family.

On 11 February 2020, the International Committee on Taxonomy of Viruses (ICTV) decided to name the virus as **severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)**, and the WHO finally decided to name the disease caused by this virus as **COVID-19** (for **Co**rona**vi**rus **d**isease identified in 20**19**).

Following large outbreaks of the disease in multiple countries, with thousands of deaths around the world, on 11 March 2020 the WHO declared the outbreak to be a pandemic.

For updated figures of the number of confirmed cases and deaths, as well as demographic and epidemiological data on the pandemic, you can consult the webpage <u>https://www.worldometers.info/coronavirus/</u> and/or the <u>webpage</u> developed by the <u>Center for Systems Science and Engineering at Johns Hopkins University.</u>

The virus seems to have mutated already after its original transmission from the animal host or reservoir to humans, leading to at least two different strains. Population genetic analyses of 103 SARS-CoV-2 genomes indicated that these viruses evolved into two major types (designated L and S). Although the L type (\sim 70%) is more prevalent than the S type (\sim 30%), the S type was found to be the ancestral version. (Xiaolu Tang, 2020)

While both types play a part in the current outbreak, the higher prevalence of the L-type suggests that it is more aggressive. However, it is important to keep in mind that viruses mutate all the time and that not all mutations are indicative of increased disease severity or transmission rates. In fact, differences between the two types of the novel coronavirus are so small that researchers are reluctant to even classify them as separate strains. Given that multiple groups around the world are working on a vaccine, knowing the exact number of strains (or types) of the virus is crucial because, in order to be effective, the eventual vaccine will have to target features present in all known strains (or types). Luckily, many of the identified genetic differences are unlikely to affect the production of proteins, meaning there should not be significant changes to how the virus operates or the symptoms it causes. (Technology.org, 2020)

Coronavirus Disease 2019 (COVID-19) – Clinical information

		c .				
Mode	יט אי	t ti	ran	sm	1221	on

The transmission of SARS-CoV-2 occurs by the following mechanisms:

- a. Most often, spread from person to person among close contacts (about 6 feet/1.8 metres).
- b. Person-to-person spread is thought to occur mainly via respiratory droplets produced when an infected person coughs or sneezes, similar to how influenza and other respiratory pathogens spread.
- c. These droplets can land in the mouths, noses or eyes of people who are nearby or possibly be inhaled into the lungs.
- d. It may be possible that a person can get COVID-19 by touching a surface or object that has the virus on it and then touching their own mouth, nose or possibly their eyes, but this is not thought to be the main way the virus spreads (Centers for Disease Control and Prevention, 2020). There is evidence that coronaviruses can remain infectious on inanimate surfaces for several hours or even days. (Kampf G, 2020). See also the section on "Cleaning and disinfection management".
- e. Typically, with most respiratory viruses, people are thought to be most contagious when they are most symptomatic (the sickest). With COVID-19, however, there have been reports of spread from an asymptomatic infected patient to a close contact. (Centers for Disease Control and Prevention, 2020) (Rothe, 2020). Recent studies suggest that asymptomatic (or pre-symptomatic) patients may indeed be driving the rapid expansion of the disease (Ruiyun Li, 2020).
- f. Also, patients may remain contagious up to two weeks after the remission of symptoms. According to Wölfel and collaborators, whereas symptoms mostly waned by the end of the first week, viral RNA remained detectable in throat swabs well into the second week. Stool and sputum samples remained RNA-positive over even longer periods, in spite of full resolution of symptoms. (Roman Wölfel, 2020)
- g. Minimal information is available regarding COVID-19 during pregnancy. Intrauterine or perinatal transmission has not been identified. In two reports including a total of 18 pregnant women with suspected or confirmed COVID-19 pneumonia, there was no laboratory evidence of transmission of the virus to the neonate. However, two neonatal cases of infection have been documented. In one case, the diagnosis was made at day 17 of life after close contact with the infant's mother and a maternity matron who were both infected with the virus. The other case was diagnosed 36 hours after birth; the source and time of transmission in that case were unclear. (McIntosh, 2020) Much of the advice in various countries, such as UK, about pregnant women moving to socially isolate is preventive rather than based on evidence of increased risk of harm.
- h. In limited studies on women with COVID-19 and another coronavirus infection, Severe Acute Respiratory Syndrome (SARS-CoV), the virus has not been detected in breast milk; however it is not known whether mothers with COVID-19 can transmit the virus via breast milk. Breast milk provides protection against many illnesses.
- i. There are rare exceptions when breastfeeding or feeding expressed breast milk is not recommended. The CDC has no specific guidance for breastfeeding during infection with similar viruses like SARS-CoV or Middle Eastern Respiratory Syndrome (MERS-CoV) also both coronaviruses. In a similar situation to COVID-19, the CDC recommends that a mother with flu continue breastfeeding or feeding expressed breast milk to her infant while taking precautions to avoid spreading the virus to her infant. Given low rates of transmission of respiratory viruses through breast milk, the World Health Organization presently states that mothers with COVID-19 can breastfeed. (Academy of Breastfeeding Medicine, 2020)

Disease prevention To help control further spread of the virus, people who are suspected or confirmed to have the disease should be isolated from other patients and treated by health workers using strict infection control precautions.

People who have had social contact with symptomatic individuals with confirmed COVID-19 should be followed up as a contact through the local healthcare teams.

The WHO's standard recommendations for the general public to reduce exposure to and transmission of this and other respiratory illnesses are as follows, which include hand and respiratory hygiene, and safe food practices:

- 1. Frequently clean hands by using alcohol-based hand rub or soap and water;
- 2. When coughing and sneezing cover the mouth and nose with a flexed elbow or tissue throw the tissue away immediately and wash hands;
- 3. Avoid close contact with anyone who has fever and cough;
- 4. If you have fever, cough and difficulty breathing seek medical care early and share previous travel history with your healthcare provider;
- 5. When visiting live markets in areas currently experiencing cases of novel coronavirus, avoid direct unprotected contact with live animals and surfaces in contact with animals;
- The consumption of raw or undercooked animal products should be avoided. Raw meat, milk or animal organs should be handled with care, to avoid crosscontamination with uncooked foods, as per good food safety practices. (World Health Organization, 2020)

Self-isolation by persons with symptoms and/or persons who may have been in contact with infected persons

Self-isolation means avoiding situations where you could infect other people. This means all situations where you may come in contact with others, such as social gatherings, workplaces, schools, child care/pre-school centres, universities, faith-based gatherings, aged care and health care facilities, prisons, sports gatherings, supermarkets, restaurants, shopping malls, and all public gatherings. (Ministry of Health of New Zealand, 2020)

Diagnostic testing for COVID-19 in suspected human cases	There are currently several tests available in the market or under development for diagnosing COVID-19 (SARS-COV-2 infection). They are mostly based on molecular diagnosis (complex polymerase chain reaction (PCR) or reverse transcription polymerase chain reaction (RT-PCR) techniques) targeting different parts of the viral genome.		
	Some serological assays are also in development, but currently they cannot compete in accuracy with molecular diagnosis, particularly in the early phase of infection. This is particularly true for patients who are immunocompromised, and in the elderly. This lack of equivalency is also true in terms of analytical performance.		
	For further details about diagnostic tests and the roles of pharmacists in this area, see the FIP guidance "COVID-19: Guidelines for pharmacists and the pharmacy workforce" at <u>www.fip.org/coronavirus</u> .		
Disease onset	The SARS-CoV-2 has an incubation period of 2 to 14 days before the onset of symptoms.		
	A study led by researchers at Johns Hopkins Bloomberg School of Public Health yielded an estimate of 5.1 days for the median disease incubation period. This median time from exposure to onset of symptoms suggests that the 14-day guarantine period		

recommended by the WHO and other organisations is reasonable.

The analysis suggests that about 97.5% of people who develop symptoms of SARS-CoV-2 infection will do so within 11.5 days of exposure. The researchers estimated that for every 10,000 individuals quarantined for 14 days, only about 101 would develop symptoms after being released from quarantine. (Lauer SA, 2020)

Symptoms

For confirmed COVID-19 cases, reported illnesses have ranged from people with little to no symptoms to people being severely ill and dying. Symptoms can include (on admission to hospital) (Nanshan Chen, 2020):

- Fever (>80% of the patients)
- Cough (>80%)
- Shortness of breath (31%)
- Muscle ache (11%)

The disease may also occur with mild symptoms only, including: low-grade fever, cough, malaise, rhinorrhoea, sore throat without any warning signs, such as shortness of breath or difficulty in breathing, increased respiratory secretions (i.e. sputum or haemoptysis), gastrointestinal symptoms such as nausea, vomiting, and/or diarrhoea and without changes in mental status (i.e. confusion, lethargy). (World Health Organization, 2020)

Preliminary data report 11% lethality among hospitalised patients. Complications occurred in 33% of the patients, and included: acute respiratory distress syndrome (ARDS) (17%), acute renal injury, acute respiratory injury, septic shock and ventilator-associated pneumonia. (Nanshan Chen, 2020)

Risk factors for severe illness are not yet clear, although older patients or patients with underlying medical comorbidities (diabetes, hypertension, cardiovascular disease, cancer) may be at higher risk. In the most severe cases, infection can cause pneumonia, severe acute respiratory syndrome, kidney failure and even death. (World Health Organization, 2020)

Disease in children appears to be relatively rare and mild with approximately 2.4% of the total reported cases reported among individuals aged under 19 years. A very small proportion of those aged under 19 years have developed severe (2.5%) or critical disease (0.2%).(World Health Organization, 2020)

COVID-19: Treatment guidelines and research updates

Clinical treatmentCurrently, there is no specific medicine or vaccine for COVID-19 and no medicines or
vaccines have been fully tested for safety and efficacy.

At present, antiviral therapy is mainly used, as well as symptomatic and supportive treatment based on the clinical condition of the patient. Supportive treatments include oxygen therapy, hydration, fever/pain control, and antibiotics in the presence of bacterial co-infection.

According to the diagnosis and treatment plan recommended by the Chinese health authorities, the antiviral drugs that can be tested for treatment mainly include α -Interferon (aerosol inhalation therapy), lopinavir/ritonavir, ribavirin, chloroquine phosphate, umifenovir and others. Authorities suggested further evaluation of the efficacy of the currently recommended trial drugs in clinical applications.

With regards to immunotherapy, for patients with extensive lung disease and severe disease, and laboratory testing of elevated IL-6 levels, tocilizumab can be tried. It is not

recommended to use three or more antiviral drugs at the same time. And relevant diagnosis and treatment guidelines emphasize the avoidance of blind or unreasonable application of antibacterial drugs or glucocorticoids. (National Health Commission of the People's Republic of China, 2020)

In the report of the first case of COVID-19 patients in the United States published in NEJM, the patient's symptoms improved significantly after receiving Remdesivir. (Michelle L. Holshue, 2020)

In a study by the Professor Li Lan-juan's team, the antiviral effects of the triple combination (umifenovir + recombinant interferon α -2b + lopinavir/ritonavir) and the dual combination (recombinant interferon α -2b + lopinavir/ritonavir) were compared. The results of the study showed that the triple combination including umifenovircan significantly shorten the negative nucleic acid time of respiratory virus and the average hospitalization time. (Wei Runan, 2020)

Also, Professor Li Lan-juan and XU Kai-jun's team evaluated the effect of low and medium doses of glucocorticoids on virus clearance. The results of the study showed that low and medium doses of glucocorticoids did not significantly shorten the median time to negative nucleic acid conversion of respiratory virus and median time to improve lung imaging. No significant benefit was observed when classification was limited to patients with COVID-19. (Ni Qin, 2020)

In summary, most of the currently published related studies focus on the COVID-19 epidemiological investigation or clinical characteristics analysis. There are still few studies to evaluate the effectiveness / safety of drugs, and the related studies are still in the clinical research stage. When using the above-mentioned possible drugs to treat COVID-19, it is necessary to carefully formulate the dosing regimen and closely monitor the safety and effectiveness of the medicine to avoid adverse drug reactions or drug interactions.

For mild cases in the community, patients are advised to stay home in isolation, except for patients who may be at higher risk of developing severe forms of the disease, including older adults (>65 years old in some countries, >70 in others), people with underlying conditions (such as cardiovascular diseases, diabetes, respiratory diseases such as COPD, or cancer) and patients with compromised immunity (congenital or acquired).

The management of symptoms may involve the use of antipyretics and/or antiinflammatory medicines for fever and mild pain. The safety of the use of ibuprofen in COVID-19 patients has been questioned by an opinion article published by The Lancet suggesting that patients being treated with medicines that increase the expression of angiotensin converting enzyme 2 (ACE2) may be at increased risk of infection and/or severe COVID-19 disease. (Lei Fang, 2020) ACE2 has been proven to mediate cell entry by SARS-CoV-2 in another paper (Markus Hoffmann, 2020). However, the evidence against the use of ibuprofen in COVID-19 patients is not robust enough to rule it out. In overall clinical practice, ibuprofen has well-established effectiveness in controlling the symptoms it is indicated for, both in mild and severe infectious disease. There is currently no conclusive evidence to establish a direct association between the use of non-steroidal antiinflammatory medications (including ibuprofen) and increased risk of infection or severity of disease. (European Medicines Agency, 2020) Nevertheless, other medicines such as paracetamol /acetaminophen may be considered for the management of fever in COVID-19 patients if appropriate.

Likewise, there is no evidence to support the assertion and that treatment with ACE inhibitors (ACEi) or angiotensin receptor blockers (ARB) could predispose individuals to adverse outcomes should they become infected with COVID-19. Various scientific and professional societies have stated that patients should continue treatment with ACEi and ARB unless specifically advised to stop by their medical team. (British Cardiovascular Society and British Society for Heart Failure, 2020)

Corticosteroids are not routinely recommended for viral pneumonia or acute respiratory distress syndrome (ARDS) and should be avoided because of the potential for prolonging viral replication as observed in MERS-CoV patients, unless indicated for other reasons (e.g., COPD exacerbation, refractory septic shock following Surviving Sepsis Campaign Guidelines). (Centers for Disease Control and Prevention, 2020) (Russell CD, 2020)

For patients with progressive deterioration of oxygenation indicators, rapid imaging progress, and excessive activation of the body's inflammatory response, consider using glucocorticoids for a short period of time (3-5 days). The recommended dose of methylprednisolone should not exceed 1 - 2mg / kg / day.

For a rationale for different treatment options, as well as guidance for the treatment of special populations (pregnant patients, newborns, children and young people) and nutritional support, see the guidance document (in English or Chinese) prepared by the Chinese Pharmaceutical Association, also available from the <u>dedicated FIP webpage</u>. (Chinese Pharmaceutical Association, 2020), a well as the table developed by the CPA in <u>Annex 1</u>.

Further country-level information from countries in Europe is available on the European Association of Hospital Pharmacists <u>website</u>. The American Society of Health-System Pharmacists had also produced a comprehensive "Assessment of Evidence for COVID-19-Related Treatments", which is available <u>here</u>.

Convalescent plasma therapy

For COVID-19 patients with rapid disease progression, severe and critical illness, convalescent plasma therapy (CPT) can be tried (National Health Commission of the People's Republic of China, 2020). CPT utilises a certain titre of virus-specific antibodies in the plasma of the convalescent individual to enable the patient receiving the infusion to obtain passive immunity and remove pathogens from the blood circulation. This method has been successfully used in the treatment of SARS and H1N1 influenza, and is an effective treatment (Chen L, 2020).

The use of CPT treatment can follow the following principles (National Health Commission of the People's Republic of China, 2020):

- 1. In principle, the course of disease does not exceed three weeks. Also, the patient should have a positive viral nucleic acid test or viraemia certified by clinical experts.
- Patients with severe disease with rapid disease progression, or critically ill early stage patients, or patients comprehensively evaluated by clinical experts as requiring plasma therapy. The infusion dose is determined according to the clinical situation and the weight of the patient, usually the infusion dose is 200-500 ml (4-5 ml/kg).

Before, during, and after the infusion, detailed records and clinical observation should be made to assess the adverse effects of plasma infusion. The main types of adverse transfusion reactions include transfusion-related circulation overload, transfusion-related acute lung injury, transfusion-related dyspnoea, allergic reactions, transfusion-associated hypotension reactions, non-haemolytic febrile reactions, acute haemolytic transfusion reactions, and delayed haemolytic transfusion reaction, infectious transfusion reaction, other/unknown, etc.

Advances in vaccines development for the treatment of COVID-19 Since the vaccine development process involves procedures such as virus strain isolation and selection, in vitro experiments, animal experiments, clinical trials, and administrative approvals, it takes a long time. At present, some recognition sites for SARS-CoV-2 have been found and can be used for vaccine development (Ahmed SF, 2020) (Ramaiah A, 2020). The Ministry of Science and Technology of the People's Republic of China has organised
national key units to carry out joint research, and arranged five technical routes in parallel,
including inactivated vaccines, recombinant genetically engineered vaccines, adenovirus
vector vaccines, nucleic acid vaccines (mRNA vaccine and DNA vaccine), and vaccines made
from attenuated influenza viral vaccine vectors.Some vaccines have entered the research stage for safety and effectiveness in
experimental animals. It is expected that by April 2020, according to the relevant national
laws and regulations, some vaccines will enter clinical research or emergency use. (Sun C,
2020)Progress of clinical trials
for the treatment ofAt present, clinical research projects on new coronavirus pneumonia drugs are ongoing. As
of 9 am on 8 March 2020, a total of 436 clinical trials were retrieved from the Chinese

for the treatment of COVID-19

At present, clinical research projects on new coronavirus pneumonia drugs are ongoing. As of 9 am on 8 March 2020, a total of 436 clinical trials were retrieved from the Chinese Clinical Trials Registry, and a total of 181 clinical trials involving drug treatment were screened out, of which 107 were randomised controlled trials, four were real-world studies, and 70 were non-randomised controlled trials.

Of the 181 studies, 176 were initiated by Chinese research institutions, mainly distributed in Hubei (43), Shanghai (25), Beijing (20), Zhejiang (20) and Guangdong (19). The remaining five studies were initiated by other countries.

The drugs involved in clinical trials mainly include traditional Chinese medicine (TCM) interventions (64 items), antiviral drugs (40 items), immunotherapy drugs (28 items, such as Interferon, Thymosin, Immunoglobulin, PD1 inhibitors, etc.), anti-malaria drugs (21 items, such as chloroquine, hydroxychloroquine, chloroquine phosphate), glucocorticoids (6 items), and other drugs (22 items, such as vitamin C, vitamin D, polymyocyte injection, zinc sulphate, acetylcysteine, etc.).

The most clinical trials of antiviral medicines are anti-HIV medicines (14 items, such as lopinavir/ritonavir, darunavir/cobistastat, azivudine), followed by anti-influenza viruses medicines (13, such as umifenovir, fapilavir), and five clinical trials of remdesivir, which are considered to have potential efficacy against COVID-19.

Bibliography

Academy of Breastfeeding Medicine. (2020, March 10). ABM Statement on Coronavirus 2019 (COVID-19). Retrieved from https://www.bfmed.org/abm-statement-coronavirus

Ahmed SF, Q. A. (2020). Preliminary Identification of Potential Vaccine Targets for the COVID-19 Coronavirus (SARS-CoV-2) Based on SARS-CoV Immunological Studies. *Viruses*. Retrieved from https://doi.org/10.3390/v12030254

British Cardiovascular Society and British Society for Heart Failure. (2020, March 16). *Treatment of patients with ACEi or ARB in relation to COVID-19.* Retrieved from https://www.britishcardiovascularsociety.org/news/ACEi-or-ARB-and-COVID-19#.Xm_GR8MqGdQ.whatsapp

Centers for Disease Control and Prevention. (2020, March 4). *How COVID-19 Spreads*. Retrieved February 1, 2020, from CDC - Coronavirus Disease 2019 (COVID-19): https://www.cdc.gov/coronavirus/2019ncov/prepare/transmission.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019ncov%2Fabout%2Ftransmission.html

Centers for Disease Control and Prevention. (2020, March 7). *Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19)*. Retrieved from https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html

Centers for Disease Control and Prevention. (2020, March 13). Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons for Coronavirus Disease 2019 (COVID-19). Retrieved from https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html

Chen L, X. J. (2020, February 27). Convalescent plasma as a potential therapy for COVID-19 [J]. *Lancet Infect Dis*. Retrieved from https://doi.org/10.1016/S1473-3099(20)30141-9

Chinese Pharmaceutical Association. (2020). Coronavirus SARS-CoV-2 Infection: Expert Consensus on Guidance and Prevention Strategies for Hospital Pharmacists and the Pharmacy Workforce (2nd Edition). Beijing: Chinese Pharmaceutical Association.

European Medicines Agency. (2020, March 18). EMA gives advice on the use of non-steroidal antiinflammatories for COVID-19 (press release). Retrieved from https://www.ema.europa.eu/en/news/ema-gives-advice-use-non-steroidal-anti-inflammatories-covid-19

Kampf G, T. D. (2020). Persistence of coronaviruses on inanimate surfaces and its inactivation with biocidal agents. *J Hosp Infect*. doi:https://doi.org/10.1016/j.jhin.2020.01.022

Lauer SA, G. K. (2020, March 10). The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Ann Intern Med*. Retrieved from https://annals.org/aim/fullarticle/2762808/incubation-period-coronavirus-disease-2019-covid-19-from-publicly-reported

Lei Fang, G. K. (2020, March 11). Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *The Lancet*. Retrieved March 15, 2020, from https://www.thelancet.com/action/showPdf?pii=S2213-2600%2820%2930116-8

Li, F. (2016, September 29). Structure, Function, and Evolution of Coronavirus Spike Proteins. *Annual Review of Virology*, *3*(1), 237-261. doi:10.1146/annurev-virology-110615-042301

Markus Hoffmann, H. K.-W. (2020, April 6). SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Retrieved from https://doi.org/10.1016/j.cell.2020.02.052

McIntosh, K. (2020, March 13). Coronavirus disease 2019 (COVID-19) - Special situation: Pregnant women. (M. S. Hirsch, Editor) Retrieved from UpToDate: https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19?search=covid%2019&source=search_result&selectedTitle=1~18&usage_type=default&display_rank=1#H2133052422

Michelle L. Holshue, M. C.-C. (2020, January 31). First Case of 2019 Novel Coronavirus in the United States. *New England Journal of Medicine*, NA. doi:DOI: 10.1056/NEJMoa2001191

Ministry of Health of New Zealand. (2020, March 14). Updated Advice for Health Professionals: Novel Coronavirus (COVID-19). Retrieved from https://www.health.govt.nz/system/files/documents/pages/updated-advice-for-health-professionals-14mar20-v3.pdf

Nanshan Chen, M. Z. (2020). Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet*, NA. Retrieved February 4, 2020, from https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30211-7/fulltext

National Health Commission of the People's Republic of China. (2020, March 03). *New coronavirus pneumonia(COVID-19) diagnosis and treatment plan (Interim guidance V7)[EB/OL]*. Retrieved from http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989.shtml

National Health Commission of the People's Republic of China. (2020, March 04). The clinic guideline of convalescent plasma therapy (trial version 2) [EB/OL]. Retrieved from http://www.nhc.gov.cn/yzygj/s7658/202003/61d608a7e8bf49fca418a6074c2bf5a2.shtml

Ni Qin, D. C. (2020, March 02). Retrospective study of low-to-moderate dose glucocorticoids on viral clearance in patients with novel coronavirus pneumonia[J/OL]. *Chinese Journal of Clinical Infectious Diseases*. Retrieved from http://rs.yiigle.com/yufabiao/1183306.htm

Ramaiah A, A. V. (2020). Insights into Cross-species Evolution of Novel Human Coronavirus 2019-nCoV and Defining Immune Determinants for Vaccine Development[D]. *bioRxiv*. doi:https://doi.org/10.1101/2020.01.29.925867

Roman Wölfel, V. M. (2020, March 8). Clinical presentation and virological assessment of hospitalized cases of coronavirus disease 2019 in a travel-associated transmission cluster. *medRxiv*. Retrieved from https://www.medrxiv.org/content/10.1101/2020.03.05.20030502v1.full.pdf

Rothe, C. (2020, January 30). *Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany*. Retrieved from New England Journal of Medicine - Correspondence: https://www.nejm.org/doi/full/10.1056/NEJMc2001468

Ruiyun Li, S. P. (2020, March 16). Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2). *Science*. doi:10.1126/science.abb3221

Russell CD, M. J. (2020, February 6). Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *The Lancet, 395*(10223), 473-475. Retrieved from https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30317-2/fulltext

Sun C, H. Q. (2020, March 8). Exploring preventive measures for COVID-19 based on the existing virus vaccines [J/OL]. . *Shandong Science*, 02, 1-18. Retrieved from http://kns.cnki.net/kcms/detail/37.1188.N.20200303.1027.002.html

Technology.org. (2020, March 9). *The Coronavirus has already Mutated into Two Different Types, Researchers Find*. Retrieved March 13, 2020, from https://www.technology.org/2020/03/09/the-coronavirus-has-already-mutated-into-two-different-types-researchers-find/

Wei Runan, Z. N. (2020, February 28). Early antiviral therapy of abidor combined with lopinavir/ritonavir and re-combinant interferonα-2b in patients with novel coronavirus pneumonia in Zhejiang: A multicenter and prospective study[J/OL]. *Chinese Journal of Clinical Infectious Diseases*. Retrieved from http://rs.yiigle.com/yufabiao/1182773.htm.

World Health Organization. (2020, March). *Coronavirus disease (COVID-19) advice for the public*. Retrieved from https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public

World Health Organization. (2020, January 20). *Home care for patients with suspected novel coronavirus (nCoV) infection presenting with mild symptoms and management of contacts.* Retrieved from https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-with-mild-symptoms-and-management-of-contacts

World Health Organization. (2020, March 9). *Q&A on coronaviruses*. Retrieved from https://www.who.int/news-room/q-a-detail/q-a-coronaviruses

World Health Organization. (2020). *Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)*. Retrieved from https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf

Xiaolu Tang, C. W. (2020, March 3). On the origin and continuing evolution of SARS-CoV-2. *National Science Review*. doi:https://doi.org/10.1093/nsr/nwaa036

ANNEX 1: List of key medicines for the treatment of COVID-19

This list was compiled by the Chinese Pharmaceutical Association, except for paracetamol, which was added by FIP. For the rationale and supporting references for each therapeutic option, consult the original document (in English), available on the FIP dedicated webpage. (Chinese Pharmaceutical Association, 2020) Note: This list is for reference only, medical institution can make adjustments according to their specific conditions.

Type of treatment	Drug name	Dosage form and specifications			
		Recombinant human interferon α -2a injection: 3			
		million IU, 5 million IU;			
	Recombinant Human Interferon	Recombinant human interferon α -2b injection;			
Antiviral treatment		Recombinant human interferon α -2b injection			
		(P.putida): 3 million IU, 5 million IU			
	Lopinavir/ritonavir	Capsule : lopinavir 200mg, ritonavir 50mg			
	Ribavirin	Injection: 1ml: 0.1g			
Antimicrobial agents	According to the existing drug list of the medical institution				
		Tablet, granules: 0.1g,0.2g ;			
	Ibuprofen	Capsule: 0.2g ;			
Antipyretic and analgesic		Slow release (tablet, capsule): 0.3g;			
treatment		Suspension: 60ml:1.2g, 100ml:2g			
	Paracetamol / acetaminophen	Up to 4 g per day			
	According to the existing drug list of your medical institution				
Corticosteroids (when strictly		Tablet: Amg			
necessary, as per medical	Mothularadaicalana	(Codium quesingte) starile recuder for injection			
assessment of individual patients,	weurypreamsolone	(Sodium succinate) sterile powder for injection :			
mostly in hospital settings)		40mg, 500mg			
Intestinal microecological	Association to the existing drug list of your p	adical institution			
preparations	According to the existing drug list of your h				
Other gastrointestinal treatment	According to the existing drug list of your medical institution				
Antitussive treatment	According to the existing drug list of your medical institution				
Sputum removal treatment	According to the existing drug list of your medical institution				
Anti-asthmatic treatment	According to the existing drug list of the medical institution				
		Soft capsule: 0.45g;			
		Dripping pill: 2.6g/bag			
	Huoxiangzhenggi	Concentrated pills: 8 pills drops are equivalent to			
	nuonungznengqi	3g herbal slices			
		Tincture : 10ml;			
		Oral Solution: 10ml			
	Jinhua Qinggan	Granules: 5g (equivalent to 17.3g herbal slices)			
	LianhuaOingwen	Capsule: 0.35g;			
Chinasa natant madiainaa		Granules: 6g/bag			
Chinese patent medicines	ShufengJiedu	Capsule: 0.52g			
		Concentrated pills: 8 pills equivalent to 6g herbal			
	Fangfangtongshang	slices;			
	rangrengtongsneng	Watered pill: 6g/bag			
		Granules: 3g/bag			
	Xiyanping	Injection : 2ml:50mg,5ml:125mg			
	Xuebijing	Injection : 10ml			
	Shenfu	Injection : 10ml			
	Shengmai	Injection: 10ml, 20ml			

Validity

This document was initially prepared based on commonly accepted evidence as of 5 February 2020. It was updated with regards to the nomenclature of the virus and the disease on 12 February 2020, and updated again on 26 March 2020 according to newly available evidence.

Disclaimer

This document is based on the available evidence and the recommendations of reputable organisations such as the World Health Organization, the United States and the European Centres for Disease Control and Prevention, and others, as cited at the time of publishing. The available knowledge about COVID-19 is rapidly changing and such recommendations may change accordingly. Although FIP will strive to keep these guidelines up to date, we recommend consulting the websites of these organisations and any newly available evidence for the most recent updates.

Acknowledgements

FIP acknowledges the international taskforce who produced this document:

Chair: Jane Dawson, FPS – FIP Military and Emergency Pharmacy Section, New Zealand

Marwan Akel, Lebanese International University, Lebanon

Julien Fonsart, FIP Clinical Biology Section President, France

Scarlett Pong, Pharmaceutical Society of Hong Kong

Eduardo Savio, Uruguayan Association of Chemistry and Pharmacy, Uruguay

Lars-Åke Söderlund, FIP Community Pharmacy Section President, Sweden

Gonçalo Sousa Pinto, FIP Lead for Practice Development and Transformation

Jacqueline Surugue, FIP Vice President, Hospital Pharmacist, France

Zhao Rongsheng, Peking University Third Hospital, Pharmacy Department; Deputy Chairman of the Hospital Pharmacy Committee of Chinese Pharmaceutical Association; Deputy chairman of Committee of Evidence Based Pharmacy of the Chinese Pharmaceutical Association, China



International Pharmaceutical Federation (FIP) Andries Bickerweg 5 2517 JP The Hague The Netherlands Tel.: +31-70-3021970 Fax: +31-70-3021999 Email: fip@fip.org

www.fip.org/coronavirus

Updated 26 March 2020