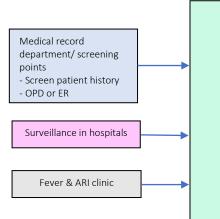
Guidelines on clinical practice, diagnosis, treatment, and prevention of healthcare-associated infection for COVID-19





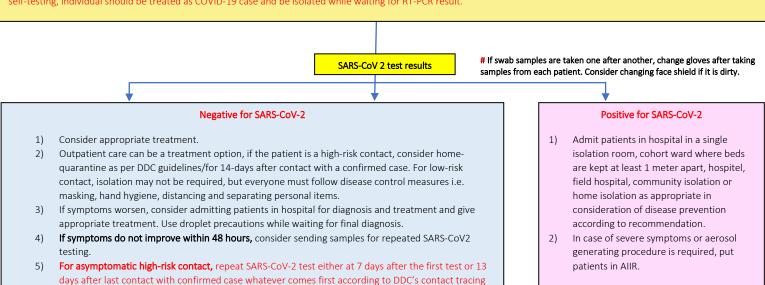
- 1. Patients with any of the following symptoms: History of fever or temp ≥ 37.5° C, cough, nasal mucus, sore throat, loss sense of smell, loss sense of taste rapid breathing, shortness of breath, or dyspnea, red eye, rash, diarrhea and have any of following risk history within 14-day prior to the onset of symptoms:
 - a) Travel history to/ from or reside in areas with ongoing local transmission of COVID-19 in the past month
 - b) Exposure to confirmed cases of COVID-19
 - c) Travel history to crowded places in the community or places of gathering where confirmed cases have been reported in the past month e.g. entertainment venues, flea markets, malls, hospitals, public transportation
 -) Work in quarantine facilities
- 2. Pneumonia patients suspected of having COVID-19 infection by their attending physicians
- 3. Healthcare workers in hospitals, clinics, health promotion hospitals, laboratories, drug stores or disease investigation teams or personnel in quarantine facilities with any of the respiratory symptoms: cough, nasal mucus, sore throat, loss sense of smell, loss sense of taste, rapid breathing, shortness of breath, or dyspnea, red eye, rash, diarrhea and/or with fever or temp ≥ 37.5° C, whose attending physician suspects a COVID-19 infection.
- Detecting a cluster of patients at least 5 individuals in the same place within the same week posing epidemiological linkage (e.g. In school setting = within the same classroom, etc.).
- 5. Symptomatic and asymptomatic high-risk contacts (as defined by DDC)



- 1) Patients must wear masks while waiting at arranged waiting area or wait to hear test results at home and follow the guidelines. If there are indications that patients should be hospitalized, separate them in a single or isolation room (AIIR is not required).
- 2) Healthcare workers wear appropriate PPE. Generally, use droplet and contact precautions (gown, gloves, mask and face shield). If aerosol generating procedure is involved e.g. taking nasopharyngeal swab is performed, healthcare workers must wear a protective suit according to airborne and contact precautions (waterproof gown, gloves, N-95 mask, face shield or goggles, and hair cover). #
- 3) Perform basic laboratory testing as deemed appropriate. (Designated receiving area is not required. Adhere to standard laboratory practices.)
- 4) Collect specimen for RT-PCR testing of SARS-CoV2

guidelines version 13 April 2021

- a) In case of patient without pneumonia symptoms, collect one nasopharyngeal or oropharyngeal swab in a UTM or VTM (at least 2 ml.).
- b) In case of patient with pneumonia symptoms without endotracheal intubation
 - o Collect sputum sample in one sterile container with UTM or VTM.
 - o In case of children < 5 years old or individuals whose sputum cannot be collected, collect one nasopharyngeal or suction samples in a UTM or VTM.
- c) In case of patient with pneumonia symptoms and endotracheal intubation, collect tracheal suction or cut the tip of the suction tube and put it in one UTM or VTM.
- 5) During outbreak, there may be a need for using of antigen test kit (ATK) for diagnosis and should be confirmed with RT-PCR according to NIH guidelines. If positive result by self-testing, individual should be treated as COVID-19 case and be isolated while waiting for RT-PCR result.



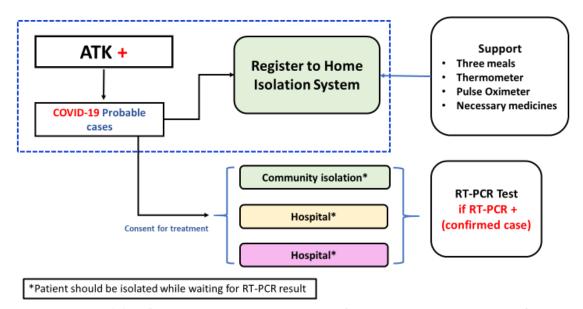
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Guideline for ATK screening and COVID-19 testing

(According to NIH guidelines version 20 July 2021)

- 1. Use Thai FDA validated and certified ATK
- 2. Collect specimen from nasopharynx, oropharynx, nasal swab and use buffer specified by test kit
- 3. May consider using for initial screening (fig 1)



Picture 1: Guideline for COVID-19 provision services (DMS, MOPH: August 2, 2021)

COVID-19 case definition (Division of Epidemiology, Department of Disease Control, MOPH 13 July 2021)

- Probable case: ATK positive for SARS-CoV-2 regardless of symptoms
- Confirmed case:
 - o PUI with positive for SARS-COV-2 by RT-PCR or sequencing from culture from at least one NIH certified Lab
 - o Asymptomatic or symptomatic s with positive for SARS-COV-2 by RT-PCR or sequencing from culture from at least one NIH certified Lab

During outbreak, ATK may be needed for diagnosis and should be confirmed with RT-PCR according to NIH guidelines. If positive result by self-testing, individual should be treated as COVID-19 case and be isolated while waiting for RT-PCR result.

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Treatments for COVID-19

For probable cases, positive ATK for SARS-CoV-2 and confirmed cases are classified into 4 categories by clinical symptom as follows:

1. Asymptomatic COVID-19 confirmed case

- Recommend home isolation or facility arranged by the State at least for 14 days from the day the patient tested positive. the length of isolation (in health facility plus home isolation) may be longer depending on physician's discretion.
- o Provide supportive care without prescribing antivirals since most patients can recover on their own and might suffer from side effects.
- o Consider prescribing Andrographis Paniculata (Far Ta Lai Jone) depending on physician's discretion
- o Not recommend prescribing Andrographis Paniculata (Far Ta Lai Jone) and favipiravir in combination due to possible drug adverse reaction

2. Symptomatic COVID-19 confirmed cases without pneumonia and no risk for severe diseases

- o Consider prescribing favipiravir as soon as possible
- o if infection was detected >7 days, case has no symptom or mild symptom, antiviral may not be needed because the patient will recover without complication.
- Recommend home isolation or facility arranged by the State if fulfil criteria for home isolation or community isolation, treatment should be provided and follow the isolation precaution of respiratory infection (all treatment modules) for at least 14 days from symptom onset, or until symptoms improve. Consider discharging patient if there is no fever or other symptoms for at least 24 48 hours.
- 3. Symptomatic COVID-19 confirmed case with risk factors for severe disease or having co-morbidity or mild pneumonia.

Risk factors include any of the following: Aged >60 years old, COPD and other chronic lung diseases, CKD, chronic CVD and congenital heart disease, cerebrovascular disease, diabetes, obesity (body weight >90 kg.), cirrhosis, immune deficiency conditions, and lymphocyte count <1,000 cells/cu. mm. or patient without risk factors but tend to have more severity of the disease

- o Recommend hospitalization at least 14 days or until symptoms improve (patient may hospitalize <14 days and follow by home isolation until complete 14 days)
- o Recommend prescribing Favipiravir as early as possible for 5 days or more, depending on clinical manifestation or consultation with experts.
- o May consider administering Corticosteroid together with Favipiravir If patient's symptoms or chest roentgenography got worsen; progression of infiltration or Sp02 at room air ≤96% or SpO2 room air reduces >3% from the first-time test is performed when exercise (exercise-induced hypoxia),
- 4. **Confirmed case with pneumonia and hypoxia** (resting O2 saturation ≤96%) or SpO2 at room air reduces ≥3% from the first time on exercise (exercise-induced hypoxia), or progression of pulmonary infiltrates on chest x-ray.
 - o Recommend prescribing Favipiravir for 5-10 days depending on clinical manifestation
 - o May consider Lopinavir/Ritonavir for 5-10 days (depending on physician's discretion)
 - o Recommend Corticosteroid as in Table 1

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Treating COVID-19 in child patients < 15 years old

For probable cases, positive ATK for SARS-CoV-2 and confirmed cases both symptomatic and asymptomatic cases should be provided the following specific treatment and duration of hospitalization similarly to adult patients.

- 1. Asymptomatic COVID-19 case
 - o Providing treatment according to physician's discretion
- 2. COVID-19 case with mild symptom without pneumonia and no risk factors
 - o Recommend giving supportive care and consider prescribing Favipiravir for 5 days.
- 3. COVID-19 case with mild symptom with pneumonia or risk factors but not fulfil criteria of COVID-19 with pneumonia (4)
 - o Risk factor/ comorbid disease such as ≤1 year of age and other factors same criteria as adults
 - Consider prescribing Favipiravir for 5-10 days, depending on clinical manifestation and physician's discretion
- 4. COVID-19 with pneumonia breathing taster than the age-related respiratory rate (60/min for <2 months of age, 50/min for 2-12 months of age, 40/min for 1-5 years of age, 30/min in >5 years of age)
 - o Recommend Favipiravir for 5-10 days (may consider adding Lopinavir/Ritonavir for 5-10 days)
 - Recommend Corticosteroid as in Table 1

Other recommendations

- 1. Retrospective analysis of 744 cases in Thailand showed that important factor in reducing the risk of disease's severity such as the use of high flow oxygenation, endotracheal intubation, adding in ICU or death is the treatment with favipiravir within 4 days of symptom onset. Moreover, studies showed favipiravir helps reduce the viral load, therefore the medicine should be prescribed before the symptom get worse and considered in patient with severe symptom especially patient with underlying condition the medicine should be prescribe as soon as possible.
- Exercise-induced hypoxemia conduct by having the patient do he air cycling (in supine position and cycling like riding the bicycle)
 for 3 minutes or walking at bedside for > 3 minutes then measure SpO2 before and after the activity. if SpO2 drops ≥3% interpreting as positive test.
- 3. Using Favipiravir in pregnant women may cause teratogenic effect. Therefore, if the patient is in the reproductive age, pregnancy test should be done before prescribing the medicine. Consider prescribing antiviral medicine with the same indication as other patients, Remdesivir only benefit in patient with pneumonia that requiring oxygen therapy following additional consideration:
 - Pregnant women with mild symptom and without pneumonia provide symptomatic treatment
 - **Pregnant women with pneumonia**, the use of **Remdesivir** may be considered because there is a data on the safety of using Remdesivir in pregnancy and no teratogenic effect
 - Pregnant women from second to third trimester if physician determines that the benefit of Favipiravir is greater than risk may consider Favipiravir in non-severe case with decisions make in conjunction with patient and relatives. Consider prescribing Remdesivir if having *pneumonia*.
 - There are only 2-5% of vertical transmission and majority of fetus do not have sever symptom and infected pregnant woman tend to have severe symptom therefore treatment is focus to the mother.
- 4. The WHO studies found that Remdesivir does not reduce mortality and does not recommend using Remdesivir beyond the studies. But study in the US study pointed out that this drug may be benefit therefore have recommended the use as mentioned above

 Remdesivir may be considered in the following condition
 - Hospitalized severe pneumonia case within 48 hours that on NFNC, NIV FiO2 at least 0.6 to maintain oxygen level at 94% or requiring ventilator
 - Pregnancy with pneumonia
 - Oral administration of drugs is prohibited or if there are drug absorption issues

Choose either favipiravir or Remdesivir, not recommend using both drugs together because they act on the same target.

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5. Consider using Andrographis Paniculata (Far Ta Lai Jone) for treatment of COVID-19

- Andrographis Paniculata (Far Ta Lai Jone) is anti SARS-CoV-2, anti-inflammatory and reduce symptoms such as fever, common cold, and sore throat.
- Consider using in patient with mild symptom, no risk factor for severe COVID-19 infection, no contraindication of using Far Ta Lai Jone, initial
 study showed that it may help reduce the chance of progressing to pneumonia. More study is on-going.
- No data on the use of Andrographis Paniculata (Far Ta Lai Jone) with other antiviral medicines. Using Andrographis Paniculata (Far Ta Lai Jone) to
 prevent COVID-19 infection is not recommended.
- 6. Chloroquine, Hydroxychloroquine and Azithromycin are not recommended for the treatment of COVID-19
- 7. Studies on the use of boosted Lopinavir/Ritonavir (LVP/r) conducted overseas which involved numerous subjects indicated no clear evidence that the drug reduces mortality rate, but can reduce time in the ICU; however, there is insufficient data on Darunavir/ritonavir, so these antiretrovirals are not recommended for the treatment of COVID-19 except in studies.
- 8. Corticosteroid is not recommended in cases with mild symptom (not require oxygen therapy) or without pneumonia.
- 9. Use of corticosteroid recommended in
 - Pneumonia with O2 saturation ≤93% or on O2 supplement ≥3 liter/minute or positive exercise-induced hypoxemia consider prescribing dexamethasone dose 6-20 mg/day adjusted by physician discretion according to patient's body weight and severity of disease for at least 7 days
 - Pneumonia requiring HFNC, NIV or mechanical ventilation to prescribe dexamethasone 20 mg/day at least 5 days then taper off when clinically improve If worsening of symptoms, adjusting to higher dose steroid and weigh the risk, benefit from superimposed infection
- 10. Use of others Anti-inflammatory agent and IL-6 receptor antagonist
 - Tocilizumab may be considered with consultation the experts
- 11. Antibiotics should be prescribed when there is indication of bacterial infection/complication. It should not be prescribed when patient is first admitted.
- 12. If patient is suspected to have pneumonia and bacterial infection, collect sputum for bacterial culture in order to select antibiotic that best matches the causative pathogen. Sputum exam can be done in a biosafety cabinet to prevent generating droplets or aerosol in the process. Laboratory staff must wear full PPE (coverall, N95 respirator, face shield, gloves, shoe cover) as per COVID-19 lab standards
- 13. There is no clear evidence of treatment with convalescent plasma or other combination regimens which has not been a standard of treatment. It may be used depending on physician's discretion.
- 14. Preliminary data of in vitro study showed that ivermectin has synergistic effect with favipiravir, but no clinical trial data are available. There are some published clinical trials of ivermectin, and some are on-going studies. therefore, no further recommendation for ivermectin at this time.
- 15. There is evidence of some studies in vitro and animas of other medicines such as Fluvoxamine that help reducing inflammatory of blood vessels.

 Fluvoxamine, according to US FDA guideline is for treatment of obsessive-compulsive disorder and depression. common side effects are insomnia and agitation. It is dose related ADR, patient cannot tolerate the side effect for high dose. Therefore, titrating of the dose for initial administration is needed.

 Special precaution for drug interaction when administer with other medicines including SSRI that may have GI bleeding tendency associated with serotonin receptor in platelets. Even though, RCT showed good result, but there was limit evidence on sample size and duration, there is not enough evidence to add it to CPG and recommend conducting pilot study for treatment with close monitoring.
- 16. There is report of using Cyproheptadine and Niclosamide in vitro study but not enough RCTs available yet.
- 17. The regimen in this CPG is based on available evidence to date. Currently there is insufficient randomized controlled trials to endorse any specific therapeutic; therefore, the attending physician must closely monitor the treatment outcome and must be ready to modify the regimen/ treatment accordingly. The clinical guideline practice will be revised when more evidence becomes available.

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Table 1 showing recommended drug dosages for adults and children

Drugs/dosage for adults	Dosage for children	Cautions/ common side effects
Favipiravir (200 mg/tab) Day 1: 1,800 mg (9 tablets) twice daily following days: 800 mg (4 tablets) twice daily If body weight >90 kg Day 1: 2,400 mg (12 tablets) twice daily Following days: 1,000 mg (5 tablets) twice daily	Day 1: 60 mg/kg/day twice daily following days: 20 mg/kg/day twice daily	 Possible teratogenic effects. Carefully administer the drug to pregnant women or women who may be pregnant, and advice must be given to engage the patient in decision making. Be cautious for increasing of uric acid level when use in conjunction with pyrazinamide. Be cautious for hypoglycemia when use in conjunction with repaglinide or pioglitazone. Tablet can be broken or crushed and feed via NG tube. No need to adjust the dosage for CRF patient. Adjusted dosage in patient with moderate to severe liver problem, Day 1: 4 tablets twice daily the following days: 2 tablets twice daily.
Lopinavir/ritonavir (LPV/r) (tablet 200/50 mg/tab, liquid 80/20 mg/ml) Take two tablets every 12 hrs. Remdesivir Day 1: 200 mg. IV Days 2-5: 100 mg IV once daily (US NIH recommends 5 days, but for severe case requiring ECMO, recommends 10 days) Corticosteroid for 7-10 days Dexamethasone: 6 mg once daily or Hydrocortisone: 160 mg per day or Prednisolone: 40 mg per day or Methylprednisolone: 32 mg single dose	2 wks-1 yr: 300/75 mg/m²/ dose twice daily 1-18 yrs. 230/57.5/m²/ dose twice daily Tablet dosage by weight 15-25 kg: 200/50 mg twice daily 25-35 kg: 300/75 mg twice daily > 35 kg: 400/100 mg twice daily Day 1: 5 mg/kg IV once daily Following days: 2.5 mg/kg IV once daily	 May cause diarrhea, nausea or vomiting. Liquid drug must be refrigerated and should be taken with food to increase absorption. Tablets may be taken without food. May cause QT prolongation arrhythmia. May cause liver or pancreas inflammation (low incidence). Constipation, hypokalemia, anemia, thrombocytopenia, increased total bilirubin, transaminitis, hyperglycemia Be cautious when use in patient with compromised kidney and liver function. Drug should be dripped longer than 30 minutes but not over 120 minutes. Dissolve drug powder with 20 mL of sterile water for injection then mix the drug in 0.9% NSS, drug can stay for 24 hours at 20-25°C and 48 hours at 2-8 °C. Be cautious of high blood sugar level, especially in diabetes patients. Daily corticosteroid dosage could be adjusted according to physician's discretion such as the use in overweight patient and always monitor for side effect for high dose corticosteroid.
Andrographis Paniculata (Far Ta Lai Jone) Administration - Capsule or tablet of Fa Ta Lai Jone containing either extract or crude drug that specify the andrographolide in mg per capsule or % of drug quantity -Calculated dosage of andrographolide is 180 mg/person/day in 3-4 times/day before meal for 5 consecutive days	There is not enough data to recommend using in pediatric to treat COVID-19, please consult expert level medical doctor	Contraindication Allergic to Andrographis Paniculata (Far Ta Lai Jone) Pregnant or may be pregnant woman, breast feeding because data suggested that it may have effect on uterine contraction and teratogenic effect Precaution Use in combination with antihypertensive drugs and anticoagulant such as warfarin, aspirin, and clopidogrel due to synergistic effect. No data on dose adjusting in patient with kidney or liver diseases Side effect abdominal pain, diarrhea, nausea, palpitation, anorexia, dizzy (more likely with high dosage or long tern use) May cause urticaria or anaphylaxis (rare) other side effects when use with other drugs

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Recommendation for COVID-19 patient referrals

- If a patient is in a condition beyond the healthcare facility's capacity, refer to a hospital with higher capacity.
- The original healthcare facility should coordinate referrals/transfers at an early stage.

By using the following criteria:

- SpO2 room air ≤96%
- Rapid progressive pneumonia within 48 hrs. of treatment

Table 2 Level of hospitals admitting patients

COVID -19 patients	Hospital
Asymptomatic confirmed case or probable case	Home isolation or facility arranged by the State
Confirmed case with mild symptoms Normal chest x-ray No risk factors/comorbid disease	Home isolation or facility arranged by the State or hospital
Confirmed case with mild symptoms Normal chest x-ray <u>but have</u> risk factors/comorbid disease	Hospital or facility arranged by the State
4) Confirmed case with pneumonia SpO2 room air <96%	Hospital

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Discharging patients from a hospital

When the patient's conditions improve, they are allowed to be home quarantine. but have to maintain the principles of preventing infection according to the new standards.

- 1) Asymptomatic confirmed cases will be in home isolation or designated facility for at least 14 days from the day the patient tested positive (For provinces that have problems with bed management, patient will be in hospital for 10 days follow by 4 days of home quarantine to complete 14 days from the day infection was detected).
- 2) Mild cases will be in home isolation or in designated facility for at least 14 days from symptom onset. When completed, if symptoms persist, continue to be in hospital or a place designated by the state until there is no manifestation for at least 24-48 hours. (For provinces that have problems with bed management, patient will be in hospital for 10 days follow by 4 days of home quarantine to complete 14 days from the day infection was detected).
- 3) For the patients being discharged earl and going to be home quarantined to complete 14 days (from the day the patient tested positive (for asymptomatic case) or symptom onset date). The patient must strictly follow the home quarantine guideline located on the last page of this document
- 4) For severe cases or severe immunocompromised host including patients who are currently under chemotherapy for cancer treatment, bone marrow or organ transplantation within 1 year, untreated HIV case with CD4 count < 200 cell/ml3, patient with combined primary immunodeficiency disorder, patient receives prednisolone >20 mg/day for more than 14 days, and those with other causes of low immunity should be treated in the health facility and discharged when symptoms are improved they must be home quarantined to complete at least 21 days from the symptom onset date.
- 5) Criteria to discharge patients:
 - a) Patients whose symptoms improved and whose film chest x-ray does not show declined conditions
 - b) Body temperature not exceeding 37.8c for the past 24-48 hrs.
 - c) Respiratory rate of no more than 20 times/min.
 - d) SpO2 room air >96% at rest.
- 6) No need to repeat testing with RT-PCR, antigen or antibody detection in in patients who are already confirmed cases as well as when they're discharged except for a research's purpose and the researcher must clearly explain to the patient.
- 7) After discharging when completed the quarantine period, they should follow new normal practices; wearing mask, hand washing, social distancing, avoid crowded area or poor ventilated area.
 - a) Patient may rest at home or return work as usual since the disease transmitted period has passed.
 - b) Returning to work mainly depends on the health condition of the patient. No need to repeat the testing before returning to work, but strictly follow new normal practice.
 - c) If any symptoms occur, consider identifying the cause(s) and provide treatment accordingly.
 - d) Patient who recovered from COVID-19 less than 3 months has low risk of getting infection again. Therefore, repeating SARS-CoV-2 testing with RT-PCR, antigen or antibody testing has less benefit unless having strong contact history may consider case by case.

Remark: In case patient requested medical certificate, attending physician can specify as.... patient got better, recovered from COVID-19.... considering from patient symptoms

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Guidelines for COVID-19 patients

Most COVID-19 patients develop only mild symptoms and maybe hospitalized for a short period of time before being discharged to convalesce in a home care setting. Those in mild condition will gradually get better until they are fully recovered; however, at the end of the first week, some patients may exhibit worse symptoms. For patients with mild or improved conditions, the virus that causes Covid-19 can still be detected in their mucus and saliva specimen for up to 50 days, yet studies found that virus could not detected from culture of respiratory secretion of patients who have symptoms for 8 days, yet still be detected by RT-PCR. There are various strains of COVID-19, some strains may live longer. Therefore, the detectable RNA could be fragments of inactive viral RNA remaining from viral shedding. In addition, detecting any viral DNA/virus particles will depend on the quality of the specimen collected.

The CPG also indicates a swab sample is not required before discharging a patient from a healthcare facility since it will not affect treatment plan. In addition, testing positive by PCR technique does not translate to potential infectivity. The clinician will make a decision based on the patient's clinical symptoms based on the above criteria. According to current evidence, there is no further risks to transmit the virus. The convalescing patient can continue a normal life by following general infection prevention and control precautions, until it is assured that the transmission is under control.

Recommendation for patient after being discharged to complete 14 days quarantine at home (from date of onset or date of positive test result if asymptomatic)

- 1. Refrain from leaving home to the community in all cases except travel to the hospital by appointment and manage by hospital
- 2. **A person should separate bedroom from others.** If there is no separate bedroom, a person must be placed downwind 3-5 meters away from others in a well-ventilated room. If this could not be arranged, a person must be in community isolation until complete isolation period.
- 3. If possible, a person should separate toilet from others. If not, all touched surfaces must be cleaned with cleaning solution or disinfectant solution such as alcohol after every use.
- 4. Personal hygiene: Wear a surgical mask or cloth mask if living with others.
- 5. Wash hands regularly with soap and water, especially after urinating or excreting, or use alcohol-based sanitizer.
- 6. No dining with others.
- 7. Keep distance at least 2 meters from others and wearing mask at all time
- 8. Drink plenty of water and eat nutritious food.
- 9. If any symptoms are reintroduced or the same symptoms worsen, for example, high fever, frequent cough, fatigue, chest pain, panting, difficulty breathing, loss of appetite, immediately contact a healthcare facility. If the patient wishes to go to the hospital/healthcare facility, do not use public transport. Use a personal vehicle or request to be picked up by an ambulance.
- 10. After completion of quarantine period, persons can continue social activity and work according to new normal practice such as wearing mask when in contact with others, hand washing and social distancing.

If there are any inquiries, the patients may call the hospital where they were treated, or the hotline 1422 or 1668.