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# Algorithms for adult outpatient care of coronavirus disease 2019 (COVID-19) and its assumption

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The paper presents algorithms for adult outpatient care of coronavirus disease 2019 (COVID-19) and its assumption.

**Keywords:** algorithms, coronavirus infection, outpatient care, follow-up monitoring, COVID-19.

**Relationships and Activities:** none.

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The pandemic of a novel coronavirus disease, the germ of which was officially named severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) and the disease itself — Coronavirus disease 2019 (COVID-19) [1], changed the life of all mankind. It challenged medical workers to rapidly diagnose and manage COVID-19 patients in conditions, where data on the epidemiology, clinical features, prevention and treatment of a novel disease was extremely limited, and often completely absent.

In this emergency, the Russian healthcare system was able to mobilize in a timely manner and refocus on the fight against COVID-19. Interim guidelines have played and continue to play a huge role at present, aimed at combining and the fastest spread of best experience in the prevention, diagnosis and treatment of COVID-19. Already on January 29, 2020, the Ministry of Health of the Russian Federation released the first version of the interim guidelines on prevention, diagnosis and treatment of COVID-19 [2].

Currently, significant experience has been accumulated in combating COVID-19, a constantly updated comprehensive research, practical, methodological and legal base has been formed. Measures to prevent the COVID-19 spread are regulated by orders of the Russian Federation Government (dated January 30, 2020 № 140-r, dated January 31, 2020 № 154-r, dated February 03, 2020 № 194-r, dated February 18, 2020 № 338-r, dated February 27, 2020 № 447-r, dated February 27, 2020 № 446-r, dated February 27, 2020 № 448-r, dated March 16, 2020 № 635-r, dated March 6, 2020 № 550-r, dated March 12, 2020 № 597-r, dated March 14, 2020 № 622-r, dated March 16, 2020 № 730-r, dated March 27, 2020 № 763-r, dated August 1, 2020 № 1996-r, dated August 1, 2020 № 1997-r , dated September 2, 2020 № 2236-r, dated September 12, 2020 № 2338-r, dated September, 20 2020 № 2406-r, dated October 14, 2020 № 2649-r) and by decrees of the Chief State Sanitary Doctor of the Russian Federation (dated January 2, 2020 № 2, dated January 31, 2020 № 3,

dated March 2, 2020 № 5, dated March 13, 2020 № 6, dated March 18, 2020 № 7, dated March 30, 2020 № 9, dated April 3, 2020 № 10, dated April 13, 2020 № 11, dated May 5, 2020 № 15, dated July 7, 2020 № 18, dated July 13, 2020 № 20, dated July 15, 2020 № 21, dated July 27, 2020 № 22, dated September 18, 2020 № 27, dated October 16, 2020 № 31, dated November 13, 2020 № 34, dated November 13, 2020 № 35). Measures to prevent the COVID-19 spread in medical organizations are carried out in accordance with the order of the Ministry of Health of Russia dated March 19, 2020 № 198n. On May 7, 2021, the Russian Ministry of Health published the 12th version of the interim guidelines on prevention, diagnosis and treatment of COVID-19 [3].

Interim guidelines contain detailed information for all healthcare levels for patients with COVID-19 — outpatient, inpatient, rehabilitation and prevention. At the same time, this format of guidelines somewhat limits their immediate use in outpatient practice.

In this respect, on the initiative of the Omsk Oblast Ministry of Health and the Omsk State Medical University, with the active participation of National Medical Research Center, a working group and an expert committee were created, the purpose of which was to develop an algorithm for adult outpatient care of COVID-19 and its assumption, with regular updating based on the current interim guidelines on prevention, diagnosis and treatment of COVID-19 and the order of the Ministry of Health of Russia dated March 19, 2020 № 198n. One of the important tasks of working group was to format the algorithms in compact manner, convenient to visual perception (Appendix 1).

Core of the working group was made up of teaching staff of the clinical profile, chief external expert of various levels and health professionals, as well as the expert committee — the heads of outpatient and inpatient medical organizations, researchers, and workers of regional and practical healthcare system.

Currently, algorithms (version 5) have been prepared and updated, based on version 11 of the interim guidelines on prevention, diagnosis and treatment of COVID-19 and the order of the Russian Ministry of Health dated March 19, 2020 № 198n.

The first part of algorithm is devoted to COVID-19 diagnosis. The algorithm begins with a table for classifying COVID-19 by severity. Taking into account the empirically changing approach to x-ray imaging (primarily computed tomography, CT) for diagnostics, to optimize the work of primary care physicians, this part includes a block of CT criteria for involvement extent and indications for CT scanning. In addition, the attention of doctors is focused on the fact that imaging data do not replace the results of tests for SARS-CoV-2 ribonucleic acid (RNA). The absence of CT changes does not rule out the COVID-19 and pneumonia risk after the analysis. In the absence of symptoms and a mild acute respiratory infection (AVI), the use of radiography, CT and ultrasound is not recommended, unless the patient has risk factors. Additionally, it is indicated that MRI and ultrasound are not standard procedures and do not replace CT. It is not recommended to use x-ray methods in patients without ARI manifestations and positive test for SARS-CoV-2.

This part includes a diagnostic screening scheme for suspected, probable (clinically confirmed) and confirmed COVID-19 cases. The algorithm draws the doctors' attention to the fact that laboratory tests for SARS-CoV-2 RNA should be carried out for all persons with ARI manifestations. In case of a negative test by immunochromatography or other immunochemical methods, it is recommended to use nucleic acid amplification techniques. In a mandatory manner, such an examination must be performed in following cases: persons who arrived to Russia with ARI symptoms or when they appear during the medical observation; those who have been in contact with a COVID-19 patient, if there are symptoms that do not rule out COVID-19, as well as in the absence of clinical manifestations — on the 8-10th day of medical follow-up after the day of contact with a COVID-19 patient; those with community-acquired pneumonia; those aged >65 years who seek medical attention with respiratory symptoms.

The algorithm includes a table for the interpretation of laboratory test results, developed for the 10th version of guidelines, which, being simple and intuitive, is of great value for practical use.

The main clinical characteristics, types and manifestations of COVID-19 are highlighted in separate blocks of the algorithm for primary care practitioners. Given the disease peculiarities with an atypical mild performance without fever and cough in elderly and senile patients, which do not correspond to the severity of disease and prognosis, but at the same time often accompanied by delirium, the algorithm includes the Richmond Agitation-Sedation Scale (RASS).

The second part of algorithm provides action options for outpatient medical workers on managing patients with ARI, in particular — those contacted with a COVID-19 patient, as well as low- and high-risk patients with mild, moderate and severe ARI.

The approaches to management of patients at home are considered. The physicians' attention was drawn to necessarity to inform a patient about the need to call a doctor or an ambulance team in case of condition deterioration, as well as about possible ways to seek medical help. Persons living with a patient in the same room should be informed about the risks of COVID-19 and the need to temporarily reside elsewhere.

A patient and persons living with him must also be informed about responsibility for violation of sanitary and epidemiological rules, which entailed an infection spread. At the same time, a patient and those living with him should be provided with information

materials on caring COVID-19 patients, and general recommendations for protection against airborne diseases. If a decision is made on the further provision of outpatient care to a patient, informed consent on provision of outpatient healthcare and compliance with the isolation regime must be signed.

In the same section of the algorithm, the criteria for outpatient monitoring are given. Particular attention of doctors is focused on episodes of a repeated increase in body temperature after its normalization for ⩾1 day, on respiratory rate values and the indications for hospitalization of COVID-19 outpatients.

The third section is devoted to outpatient drug prevention, depending on the clinical situation and therapy regimens for COVID-19 outpatients with mild and moderate course. It is important to note that the algorithm reflects the fundamental changes in drug therapy that appeared in the 11th version of guidelines, the most important of which is the final exclusion of hydroxychloroquine from the recommended therapy.

This made it possible to significantly optimize and simplify a number of aspects of outpatient management of patients, since there was no need to predict and monitor the cardiotoxic effects of chloroquine. With hydroxychloroquine therapy, all patients were required to additionally perform electrocardiography (ECG) before starting treatment, as well as every 5 days with an assessment of QT interval. To control cardiotoxicity, it was necessary to perform an ECG on the 3rd day of therapy, 2-3 hours after taking the drug. All outpatients were required to closely monitor their symptoms, paying attention to risk factors (RFs) for arrhythmias (syncope, dehydration, new medications). When arrhythmia RFs were detected, an unscheduled ECG was required. With outpatient hydroxychloroquine therapy under quarantine conditions and limited resources, it was also necessary to assess the risk of drug-induced QT interval prolongation using the Tisdale Risk Score and identify additional RFs for QT prolongation using a modified checklist.

In the same section, the attention of doctors is drawn to three issues when organizing outpatient care for COVID-19 patients. These are the features of antibiotic, corticosteroid and symptomatic therapy.

The final section of the algorithm describes the outpatient monitoring of patients with COVID-19. In particular, it is indicated that patients discharged after prolonged mechanical ventilation and/or with significant functional/organic disorders requires remote counseling and then follow-up visit to office 4 and 8 weeks after discharge, respectively. In the absence of complaints and pathological changes in such patients, further outpatient monitoring should be carried out in accordance with the order of the Russian Ministry of Health dated March 29, 2019 № 173n. If lung CT reveals signs of pulmonary fibrosis, interstitial lung disease, vasculitis, a patient should be referred to pulmonologist. Patients without such abnormalities but with complaints or changes according to other studies require differential diagnosis with other diseases/conditions. Patients with prior mild or moderate pneumonia who was not managed in the intensive care unit (ICU), including those treated on an outpatient basis, should be followed up in accordance with the order of the Russian Ministry of Health dated March 29, 2019 № 173n, with the determination of blood oxygen saturation and a chest x-ray.

The doctors' attention is focused on the fact that during the outpatient monitoring of patients after COVID-19, it is necessary to assess psychosocial RFs, including anxiety and depression symptoms, with the treatment of the identified abnormalities, as well as with the involvement of a psychologist, psychiatrist, social workers.

Monitoring of practical application of preliminary algorithm versions, carried out by a committee of experts and a working group in the outpatient medical organizations of Omsk Oblast, showed good applicability and convenience in the outpatient service. This made it possible, starting from 3rd version, to use all subsequent updated revisions in the work of therapeutic service of the Russian Ministry of Health.

The authors hope that further application of the algorithm will be useful for outpatient health care professionals in Russia.

**Relationships and Activities:** none.

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# Appendix 1

## ALGORITHM FOR ADULT OUTPATIENT CARE OF CORONAVIRUS DISEASE 2019 (COVID-19) AND ITS ASSUMPTION
Version 5.0 (08.05.2021)

| COVID-19 SEVERITY | | | |
|---|---|---|---|
| **MILD** | **MODERATE** | **SEVERE** | **VERY SEVERE** |
| **t <38° C**, cough, weakness, sore throat *with no criteria for more severe course* | **t >38° C, RR >22/min**, exertional dyspnea, **CT score 1-2, $SpO_2$ <95%, Serum CRP >10 mg/L** | **RR >30/min, $SpO_2$ ⩽93%, $PaO_2/FiO_2$ ⩽300 mm Hg**, decreased level of consciousness, agitation, **SBP <90 mm Hg** or **DBP <60 mm Hg**, diuresis **<20 ml/h**, **CT score 1-2**, arterial lactate **>2 mmol/l**, qSOFA **>2** | **stable t >38° C, ARF** with the need for respiratory support, **septic shock**, multiple organ failure, **CT score 4 or ARDS** |

***Lung involvement: CT score 1 (minimum) <25%, CT score 2 (moderate) — 25-50%, CT score 3 (significant) — 50-75%, CT score 4 (subtotal) ⩾75%.***
Indications for CT: primary assessment of thoracic organs in patients with severe disease progressive; differential diagnosis of identified changes; triage and dynamic assessment in case of moderate, severe and very severe disease course.

***IMPORTANT!*** *X-ray data does not replace SARS-CoV-2 RNA test results. The absence of CT changes does not rule out the COVID-19 and pneumonia risk after the analysis.* ***In the absence of symptoms and a mild AVI, the use of radiography, CT and ultrasound is not recommended, unless the patient has risk factors****. Additionally, it is indicated that MRI and ultrasound are not standard procedures and do not replace CT. It is not recommended to use x-ray methods in patients without ARI manifestations and positive test for SARS-CoV-2.*

## Outpatient diagnostic screening

| | | |
|---|---|---|
| **Clinical manifestations of AVI:** t >37,5° C, + one or more of the following features: cough (dry/scanty sputum); dyspnea; chest congestion; $SpO_2$ ⩽95%; sore throat; nasal congestion or mild rhinorrhea; loss of smell and/or taste; conjunctivitis; weakness; muscle pain; headache; vomiting; diarrhea; skin rash in the absence of other known causes of it, regardless of the epidemiological history | 1. **ARI clinical performance (see) +** one or more of the following signs: return from a foreign trip 14 days before the onset; close contacts in the past 14 days with a person followed up for COVID-19, who subsequently fell ill or who had a laboratory confirmed COVID-19; having professional contacts with individuals with a suspected or confirmed COVID-19<br><br>2. **ARI clinical performance (see) +** presence of characteristic lung CT abnormalities, regardless of a single laboratory test for SARS-CoV-2 RNA and epidemiological history<br><br>3. **ARI clinical performance (see) +** presence of characteristic lung CT abnormalities, if it is impossible to conduct a laboratory test for SARS-CoV-2 RNA and epidemiological history<br><br>3. ARI clinical performance, + presence of characteristic lung x-ray abnormalities, if it is impossible to conduct a laboratory test for SARS-CoV-2 RNA | 1. A positive test for SARS-CoV-2 RNA using nucleic acid amplification or SARS-CoV-2 antigen by immunochromatography, regardless of clinical manifestations.<br><br>2. A positive result for IgA, IgM and/or IgG antibodies in patients with clinically confirmed COVID-19 |
| ↓ | ↓ | ↓ |
| **Suspicious COVID-19 case** | **Probable (clinically confirmed) case of COVID-19** | **Confirmed case of COVID-19** |
| ↓ | ↓ | ↓ |

**Laboratory test for SARS-CoV-2** RNA should be carried out for all persons with ARI signs. The main type of biomaterial for laboratory research is oropharyngeal and nasopharyngeal swabs. In case of a negative test for SARS-CoV-2 antigen by immunochromatography or other immunochemical methods, the determination of SARS-CoV-2 RNA using nucleic acid amplification is recommended. The detection of anti-SARS-CoV-2 IgA, IgM and IgG antibodies is also used.

**In a mandatory manner, such an examination must be performed in following cases**: persons who arrived to Russia with ARI symptoms or when they appear during the medical observation; those who have been in contact with a COVID-19 patient, if there are symptoms that do not rule out COVID-19, as well as in the absence of clinical manifestations — on the 8-10$^{th}$ day of medical follow-up after the day of contact with a COVID-19 patient; those with community-acquired pneumonia; those aged >65 years who seek medical attention with respiratory symptoms. For workers of medical organizations who have a professional risk of infection, before the appearance of IgG, a laboratory test for SARS-CoV-2 RNA should be carried out 1 time a week; if symptoms do not rule out COVID-19 — immediately.

## Interpretation of nucleic acid amplification and immunochemical results

| SARS-CoV-2 test results | | | | Interpretation*<br>* results of total antibody tests are interpreted in accordance with the type of antibodies included |
|---|---|---|---|---|
| RNA | Antigen | IgM/IgA | IgG | |
| – | – | – | – | No current and prior COVID-19 |
| + | + | – | – | Acute phase of infection. Seronegative phase. The result may precede the COVID-19 onset |
| + | + | + | – | Acute phase of infection. Onset of immune response |
| + | + | + | + | Acute phase of infection, pronounced immune response to COVID-19 |
| – | – | + | + | Late phase or convalescence, pronounced immune response |
| – | – | – | + | Prior COVID-19 or recovery period. Immunity to SARS-CoV-2 is developed |

## Clinical features of COVID-19

The incubation period ranges from 2 to 14 days (on average 5-7 days). COVID-19 is characterized by the clinical symptoms of ARI: increased body temperature (>90%); cough (dry or with little phlegm) in 80% of cases; shortness of breath (30%); fatigue (40%); chest congestion (>20%).
***Also, may be noted***: sore throat, runny nose, decreased smell and taste, conjunctivitis.

The most severe shortness of breath develops by day 6-8 from the onset. Also, among the first symptoms may be myalgia (11%), confusion (9%), headache (8%), hemoptysis (2-3%), diarrhea (3%), nausea, vomiting, palpitations.
These symptoms at the disease onset can be observed without increase in body temperature.

## Clinical types and manifestations of COVID-19

ARI (upper respiratory tract involvement only); Pneumonia without respiratory distress; ARDS (pneumonia with ARF);
Sepsis, septic shock; Disseminated intravascular coagulation, thrombosis and thromboembolism.
Hypoxemia ($SpO_2$ <88%) occurs in >30% of patients.

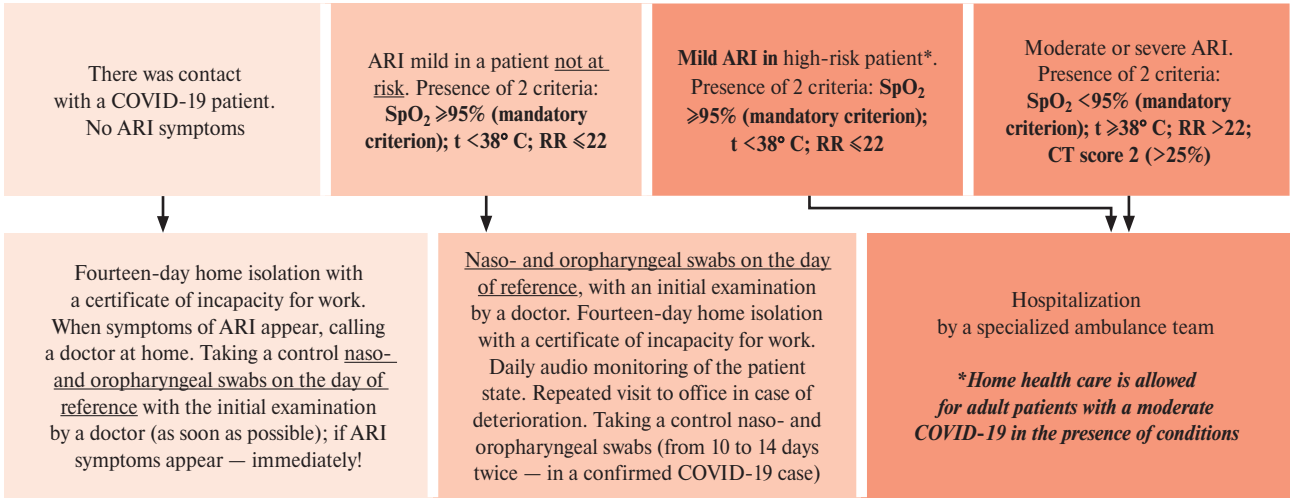
## Clinical manifestations in elderly and senile patients

In elderly patients, an atypical performance without fever and cough may be observed due to reduced reactivity.
COVID-19 symptoms may be mild and not consistent with the severity of disease and prognosis.
Atypical symptoms of COVID-19 in elderly and senile patients include delirium.

## Brief confusion assessment score (identification of delirium in elderly and senile patients)

| | |
|---|---|
| **STEP 1. Assessment of the severity and undulation of mental status** | |
| **Assessment:** Are there changes in mental status from baseline?<br>OR Have there been any undulant changes in mental status in the past 24 hours? | If the answers to both questions are "NO" → NO DELIRIUM ;<br>if 1 question "YES" → step 2 |
| **STEP 2. Impaired attention assessment** | |
| **Assessment:** "Squeeze my hand every time I say the letter A"<br>"Read the following sequence of letters:<br>L A M P A A L A D D I N A ERRORS: does not squeeze to the letter A and squeezes to other letters | 0-2 errors → NO DELIRIUM;<br>⩾2 errors → step 3 |
| **STEP 3. Assessment of level of consciousness changes** | |
| **The Richmond Agitation-Sedation Scale (RASS):**<br>+4 COMBATIVE: belligerent, aggressive, dangerous to others<br>(urgently inform the doctor about these phenomena);<br>+3 VERY AGITATION: pulls on or removes tube(s) or catheter(s) or has aggressive behavior (inform doctor);<br>+2 AGIATED: Frequent no purposeful movement or patient-ventilator desynchrony;<br>+1 RESTLESS: anxious or apprehensive but movements not aggressive or vigorous; 0 ALERT AND CALM ;<br>-1 DROWSY: not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice;<br>-2 LIGHT SEDATION: briefly (less than 10 seconds) awakens with eye contact to voice;<br>-3 MODERATE SEDATION: Any movement (but no eye contact) to voice | RASS* is not 0 → DELIRIUM;<br>RASS* = 0 → step 4 |
| **STEP 4. Assessment of impaired consciousness** | |
| **Assessment:** 1. Will the stone float on the water? 2. Does the fish live in the sea?<br>3. Does one kilogram weigh more than two? 4. is it possible to hammer a nail with a hammer?<br>Command: "Show this number of fingers" (show 2 fingers) "Now do the same with the other hand"<br>(do not show) OR "Add another finger" (if the patient cannot move both hands) | ⩾2 errors → DELIRIUM;<br>0-1 error → NO DELIRIUM |
| **CONSEQUENCE: DELIRIUM/NO DELIRIUM** | |

## Options for actions of medical workers in outpatients with ARI




**TREATMENT AT HOME:** Medical care for a patient with a positive test result for COVID-19 can be provided at home in the absence of clinical manifestations of a mild disease course (**t <38,0° C, RR ⩽22 per minute, $SpO_2$ ⩾93%**), *as well as in case of moderate course in adults in the presence of conditions (the possibility of self-isolation, no persons living with the patient >65 years old, etc.)*. A patient should be informed by a medical professional about the need to call a doctor or an ambulance team in case of deterioration (body t >38,5° C for 3 days or more, shortness of breath, $SpO_2$ <93%), as well as possible ways to seek medical help. Persons living with the patient in same room should be informed about the risks of COVID-19 and the need to temporarily reside elsewhere. A patient and persons living with him should be informed that a violation of sanitary and epidemiological rules, which entailed an infection spread, may lead to their prosecution. If a decision is made on the further provision of outpatient care, informed consent on provision of outpatient healthcare and compliance with the isolation regime must be signed.

OUTPATIENT MONITORING. **Body temperature monitoring** (daily at least 2 times a day in the morning and evening); particular attention should be focused on episodes of a repeated increase in body temperature after its normalization for ⩾1 day. **RR monitoring** is assessed daily; in case of an increase in RR, it is necessary to focus not only on its standard normal values, but also on the increase in comparison with the initial ones. When signs of respiratory failure develop or worsen, $SpO_2$ should be carefully monitored. In case of **RR ⩾22** per min during treatment at home, it is necessary to consider hospitalization of a patient.

**A patient with a positive test for COVID-19** should be hospitalized: with moderate, severe and very severe coarse (severity criteria are in the table "Severity of COVID-19"); in case of maintaining t ⩾38,0° C during the outpatient treatment for ⩾3 days; regardless of temperature, in the presence of **RR ⩾22** per min and/or **$SpO_2$ <93%**; with a mild disease course, if the patient's age is >65 years or there are symptoms of ARI in combination with HF, diabetes, respiratory diseases (asthma, COPD); in case of living with risk-group persons (*>65 years old; persons with chronic respiratory, cardiovascular, endocrine diseases, as well as systemic connective tissue diseases, chronic kidney disease, cancer, immunodeficiencies, motor neuron diseases, liver cirrhosis, chronic inflammatory bowel diseases*) and the impossibility of their resettlement, regardless of disease severity in a patient; with a mild disease course in children who have ARI symptoms in combination with following chronic diseases: heart failure, diabetes, asthma, congenital heart and lung diseases, those receiving immunosuppressive therapy, and others; living with risk-group persons.

**The following patients should be hospitalized, regardless of severity**: patients at risk (age >65 years in combination with following disorders: hypertension; HF; cancer; hypercoagulation; disseminated intravascular coagulation; ACS; diabetes; motor neuron disease; liver cirrhosis; long-term intake of GC and biological therapy for inflammatory bowel disease; rheumatoid arthritis; patients receiving hemodialysis or peritoneal dialysis; patients with immunodeficiencies, including those with HIV infection without antiretroviral therapy; receiving chemotherapy); patients living in a hostel, a crowded apartment, with persons >65 years old, with persons suffering from chronic respiratory, cardiovascular and endocrine diseases.

## Outpatient medication prophylaxis, depending on the clinical situation

| Healthy and at-risk individuals (>60 years of age or with concomitant chronic diseases) | Post-exposure prophylaxis in individuals with a single contact with a COVID-19 patient, including health workers |
|---|---|
| **REGIMEN 1:** IFN-α (intranasal) in accordance with product instruction (spray, drops, solution, lyophilisate, gel, ointment), OR | |
| **REGIMEN 2:** Umifenovir 200 mg 2 times a week for 3 weeks | **REGIMEN 2:** Umifenovir 200 mg 1 times a week for 10-14 days |
| If necessary, prophylaxis cycle is repeated; pregnant women are prescribed only recombinant IFN-α2b | |

## Outpatient therapy for mild COVID-19 patients

**REGIMEN 1 (PRIORITY):**

***1). Favipiravir:*** with a weight <75 kg — 1600 mg 2 times a day on the 1st day and then 600 mg 2 times a day from the 2nd to the 10th day; with a weight ⩾75 kg — 1800 mg 2 times a day on the 1st day and then 800 mg 2 times a day from the 2nd to the 10th days

***2). IFN-α (intranasal):*** in accordance with product instruction (spray, drops, solution, lyophilisate, gel, ointment)

***3). Paracetamol:*** 1-2 tab (0,5-1,0 g) 2-3 times a day, not >4 g a day (at body t >38° C)

**REGIMEN 2:**

***1). Umifenovir:*** 200 mg 4 times a day for 5-7 days

***2). IFN-α (intranasal):*** in accordance with product instruction (spray, drops, solution, lyophilisate, gel, ointment)

***3). Paracetamol:*** 1-2 tab (0,5-1,0 g) 2-3 times a day, not >4 g a day (at body t >38° C)

## Outpatient therapy for moderate COVID-19 patients

**REGIMEN 1:**

***1). Favipiravir:*** with a weight <75 kg — 1600 mg 2 times a day on the 1st day and then 600 mg 2 times a day from the 2nd to the 10th day; with a weight ⩾75 kg — 1800 mg 2 times a day on the 1st day and then 800 mg 2 times a day from the 2nd to the 10th days.

***2). IFN-α (intranasal):*** in accordance with product instruction (spray, drops, solution, lyophilisate, gel, ointment)

***3). Paracetamol:*** 1-2 tab (0,5-1,0 g) 2-3 times a day, not >4 g a day (at body t >38° C)

***4). Rivaroxaban[1]:*** 10 mg once a day or ***Apixaban[1]:*** 2,5 mg 2 twice a day or ***Dabigatran etexilate[1,2]***: 110 mg twice a day (with creatinine clearance 30-49 ml/min — 75 mg twice a day) — up to 30 days

[1] — in the presence of thrombosis risk factors (limited mobility, history of DVT/PE, active cancer, major surgery or trauma within past month; thrombophilia carriage — deficiencies of antithrombin, proteins C or S, antiphospholipid syndrome, factor V Leiden, prothrombin G20210A mutation), as well as with a combination of additional risk factors for DVT/PE; age >70 years;

[2] — efficacy of dabigatran etexilate in DVT/PE prevention has been studied only in major orthopedic interventions.

## Medication therapy for adult outpatients

**ANTIBIOTIC THERAPY** ***lasting 3-7 days is prescribed only with convincing data suggestive for CAP: leukocytosis >12x10$^9$/L (without prior GC therapy), left shift ⩾10%, purulent sputum, increased procalcitonin ⩾0,5 ng/ml).*** *Mild CAP without concomitant diseases in patients who did not receive antibiotics for ⩾2 days within prior 3 months and without other risk factors:* ***oral amoxicillin*** *(drug of choice) or* ***oral macrolides (alternative)****. Non-severe CAP in patients with concomitant diseases and/or taking antibiotics within last 3 months for ⩾2 days and/or with other risk factors:* ***oral amoxicillin/clavulanic acid (or other inhibitor-protected aminopenicillins)*** *(drugs of choice) or* ***oral respiratory quinolones (levofloxacin, moxifloxacin) or oral cefditoren (alternative).***

**CORTICOSTEROIDS** ***(methylprednisolone, dexamethasone) are indicated only in cytokine storm! It is not recommended to use GCs for the treatment of patients with mild to moderate COVID-19 severity, including on an outpatient basis.*** **Early predictors of cytokine storm:** increased serum CRP >46 mg/l, ferritin >250 ng/ml; lymphopenia (<10%) and/or increased ALT >60 U/L, and/or AST >87 U/L, and/or LDH >416 U/L, and/or D-dimer level (by 4 times or more compared to the reference value) or its rapid increase, and/or the troponin I >1,09 ng/ml. There are following laboratory signs of a cytokine storm: leukopenia, a decrease in the number of monocytes, eosinophils and basophils, T- and B-lymphocytes, an increase in the serum interleukin-6 (>40 pg/ml), an increase in fibrin degradation products level, hyperfibrinogenemia, normal or decreased prothrombin and activated partial thromboplastin time, normal antithrombin III level.

**SYMPTOMATIC THERAPY** includes: **relief of fever** (antipyretic drugs such as paracetamol); **complex therapy of rhinitis and/or rhinopharyngitis; complex therapy of bronchitis** (mucoactive, bronchodilator and other drugs). Antipyretics are prescribed at t >38,0-38,5° C. With poor tolerance of fever, headache, increased blood pressure and severe tachycardia (especially in the presence of ischemia or arrhythmias), antipyretic drugs are also used at lower body temperature. The safest drug is paracetamol. For the local treatment of rhinitis, pharyngitis, with nasal congestion and/or nasal discharge, agents based on saltwater should be considered (isotonic, and with congestion — hypertonic). If it is ineffective, nasal decongestants are indicated. In case of ineffectiveness or severe symptoms, various antiseptic solutions can be used.

## Outpatient monitoring in COVID-19 patients

**Patients discharged after long-term mechanical ventilation, and/or with significant functional/organic disorders:** ***4 weeks after discharge***: remote counseling (assessment of the general condition, detection of depression, symptoms of suspected thromboembolism, other syndromes and diseases); ***8 weeks after discharge:*** visit to office, with following investigations (according to indications): chest x-ray; spirography; oxygen saturation at rest and during exercise (6-minute walk test is possible with determination of oxygen saturation before and after the test); echocardiography (other tests if indicated). In the absence of complaints and pathological changes — outpatient monitoring in accordance with the order of the Russian Ministry of Health dated March 29, 2019 № 173n is indicated. If lung CT reveals signs of pulmonary fibrosis, interstitial lung disease, vasculitis, a patient should be referred to pulmonologist. Patients without such abnormalities but with complaints or changes according to other studies require differential diagnosis with other diseases/conditions.

**Patients with prior mild or moderate pneumonia who was not managed in the intensive care unit, including those treated on an outpatient basis**, should be followed up in accordance with the order of the Russian Ministry of Health dated March 29, 2019 № 173n, with the determination of blood oxygen saturation and a chest x-ray. If there is a suspected cancer was revealed during inpatient treatment, repeated chest x-ray 6 weeks after discharge is indicated (if necessary — lung CT and oncologist consultation).

**Patients with persistent lung X-ray or CT abnormalities after discharge from the hospital** require lung X-ray of CT 8 weeks after the last scan. *When pathological changes are detected*, the following investigation should be performed: spirography; blood oxygen saturation at rest and during exercise (including a 6-minute walk test); echocardiography. *If pulmonary embolism* is suspected, immediate CT pulmonary angiography. *If pulmonary fibrosis or interstitial lung disease* is suspected, high-resolution CT should be performed. If lung CT reveals signs of interstitial lung diseases, pulmonary vasculitis, pulmonary hypertension, a patient should be referred to pulmonologist and/or cardiologist. In the absence of such abnormalities, but the presence of complaints (or changes according to other investigations), a differential diagnosis with other diseases should be carried out.

During the outpatient monitoring, it is necessary to assess psychosocial RFs, including anxiety and depression symptoms, with the treatment of the identified abnormalities, as well as with the involvement of a psychologist, psychiatrist, social workers. **All patients should be informed that in case of progressing or developing new respiratory symptoms before the scheduled examination, they should immediately seek medical attention**.

**Note:** ALT — alanine aminotransferase, AST — aspartate aminotransferase, HIV — human immunodeficiency virus, CAP — community-acquired pneumonia, GCs — glucocorticoids, DBP — diastolic blood pressure, IFN-α — interferon-α, CT — computed tomography, LDH — lactate dehydrogenase, MRI — magnetic resonance imaging, ARF — acute respiratory failure, ACS — acute coronary syndrome, ARI — acute respiratory infection, ARDS — acute respiratory distress syndrome, RNA — ribonucleic acid, SBP — systolic blood pressure, CRP — C-reactive protein, DVT — deep vein thrombosis, PE — pulmonary embolism, COPD — chronic obstructive pulmonary disease, HF — heart failure, RR — respiratory rate, ECG — electrocardiography, COVID-19 coronavirus disease 2019, $FiO_2$ — fraction of inspired oxygen, Ig — immunoglobulin, $PaO_2$ — partial pressure of oxygen, qSOFA — quick Sequential Organ Failure Assessment, organ-system dysfunction, SARS- CoV-2 — Severe Acute Respiratory Syndrome CoronaVirus 2, $SpO_2$ — blood oxygen saturation level.