Diagnosis and therapy of SARS-CoV-2 infection: recommendations of the Polish Association of Epidemiologists and Infectiologists as of November 12, 2021

Annex no. 1 to the Recommendations of April 26, 2021

To the editor Due to new research results and decisions of drug registration institutions as well as our own experience, it became necessary to amend the recommendations for the management of SARS-CoV-2 infection by the Polish Association of Epidemiologists and Infectiologists, published on April 26, 2021.[1] The introduced changes relate primarily to the basic treatment (TABLE 1) and are a consequence of the rapid accumulation of knowledge about the effectiveness of the considered therapeutic options. The results of subsequent studies justify the use of molnupiravir or kasirivimab / imdevimab in stage 1 and 2, and baricitinib in stage 3 of the disease.[2-5] On the other hand, the recommendation to use convalescent plasma was discontinued due to the negative results of the research.[6,7] Due to lack of scientific evidence on the effectiveness, the following drugs are still not recommended for use in COVID-19: lopinavir / ritonavir, chloroquine, hydrochloroquine, azithromycin, favipiravir, amantadine, oseltamivir, or ivermectin.

TABLE 1 Recommended pharmacological management in adults at different clinical stages of SARS-CoV-2 infection, including basic and supportive treatment[a] (continued on the next page)

Disease stage	Primary treatment	Supportive treatment
Stage 1: mildly symptomatic • SpO_2 ≥94% • No hospitalization is necessary	The commencement of antiviral therapy is recommended up to 5 days after the onset of symptoms, with particular emphasis on patients at risk of a severe course[b] and under direct medical supervision during the qualification and monitoring of treatment. These drugs should not be used in pregnant and lactating women. • Molnupiravir used orally twice daily 800 mg for 5 days[9] or • Kasirivimab / imdevimab used intravenously or subcutaneously as a single dose of 1200 mg (600/600 mg)[9]	• Inhaled budesonide at a dose of 2 × 800 µg daily[1] • Antipyretic drugs (paracetamol, ibuprofen, etc) • Rest • Oral hydration • Low-molecular-weight heparin in patients who are chronically bedridden only • Antitussive drugs for persistent cough • Systemic corticosteroids are contraindicated. • Antibiotics and anti-influenza medications are contraindicated, unless there is a coinfection with bacterial infection or concomitant influenza. • Oxygen saturation control using the Pulsocare remote alarm system (using pulse oximeters)
Stage 2: fully symptomatic • SpO_2 <94% • Usually week 1 after disease onset • Hospitalization is required	The initiation of antiviral therapy with each of the following drugs is recommended up to 5 days after the onset of symptoms. • Remdesivir intravenously administered once daily for 5 days, loading dose on day 1: 200 mg, then maintenance dose: 100 mg for 4 days. Contraindicated in patients with: eGFR <30 ml/min/1.73 m^2; ALT activity ≥5 times the upper limit of normal[10] or • Molnupiravir administered orally twice daily 800 mg for 5 days[8] or • Kasirivimab / imdevimab administered intravenously or subcutaneously in a single dose of 1200 mg (600/600 mg)[9]	• Low-molecular-weight heparin in prophylactic or therapeutic doses • Dexamethasone can be considered, but only in patients receiving antiviral drugs and oxygen therapy, orally or intravenously 4–8 mg/d; should not be used in the first week of the disease if antiviral drugs are not used. • Antibiotic therapy in the case of secondary bacterial infections • Symptomatic treatment • Oxygen therapy • Oral or intravenous hydration

TABLE 1 Recommended pharmacological management in adults at different clinical stages of SARS-CoV-2 infection, including basic and supportive treatment[a] (continued from the previous page)

Disease stage	Primary treatment	Supportive treatment
Stage 3: respiratory failure (cytokine storm) • SpO_2 <90% • Usually week 2 after disease onset • Hospitalization is required	• Tocilizumab (in people with IL-6 concentration >100 pg/ml) in a single intravenous infusion of 800 mg if BW >90 kg; 600 mg if BW 65–90 kg; 400 mg if BW 40–65 kg and 8 mg/kg if BW ≤40 kg. In case of no improvement, the second dose may be repeated after 8–24 hours. Contraindicated in patients with: absolute neutrophil count <2000/μl; active tuberculosis.[11] or • Baricitinib orally 4 mg a day until the end of hospitalization, but not longer than 14 days; recommended especially in patients requiring high-flow oxygen therapy. There is no evidence of benefit with tocilizumab. Contraindicated in patients with: eGFR <30 ml/min/1.73 m^2, dose reduced to 2 mg daily in patients with eGFR 30–60 ml/min/1.73 m^2 and >75 years of age; risk of thrombosis and embolism; active tuberculosis.[12] and/or • Dexamethasone phosphate administered intravenously in a daily dose of 6–8 mg[c] for 7–10 days	• Low-molecular-weight heparin in prophylactic or therapeutic doses • Antibiotic therapy in the case of secondary bacterial infections • Symptomatic treatment • Low-/high-flow oxygen therapy • Intravenous hydration
Stage 4: acute respiratory distress syndrome (ARDS) • Unsuccessful pharmacotherapy to date • Need for mechanical ventilation • ICU treatment is required	• Dexamethasone phosphate administered intravenously in a daily dose of 6–8 mg[c] for 7–10 days. If dexamethasone is not available, other corticosteroids may be given at equivalent doses, eg: hydrocortisone, 3 × 50 mg intravenously; methylprednisolone 4 × 10 mg intravenously; prednisone 1 × 40 mg orally and/or • Tocilizumab in combination with dexamethasone can be administered to patients who require mechanical lung ventilation. It should be administered as soon as possible, in the first 24 hours of ventilation. Contraindicated in patients with: absolute neutrophil count <2000/μl; active tuberculosis.[11]	• High-flow oxygen therapy • Noninvasive ventilation • Invasive ventilation • Extracorporeal veno-venous transmembrane oxygenation (VV ECMO) in selected patients • Low-molecular-weight heparin in prophylactic or therapeutic doses depending on the clinical situation • Empiric antibiotic therapy is strongly discouraged unless there is evidence of a bacterial infection.

a Detailed information on the posology and restrictions on use is provided in the Summary of Product Characteristics (SmPC) for the European Union/Poland. Pending European Union registration and availability of the Polish SmPC, it is appropriate for molnupiravir to use the SmPC issued by the Medicines and Healthcare products Regulatory Agency (United Kingdom), and for kasirivimab/imdevimab, by the Food and Drug Administration (United States).

b Age >60 years, obesity, diabetes mellitus, neoplastic disease, chronic heart failure, chronic respiratory failure, chronic kidney disease, immunodeficiency, immunosuppression

c According to the manufacturer's information, 6 or 8 mg/ml of dexamethasone phosphate in the available injection solutions corresponds to 4.95 or 6.6 mg/ml of dexamethasone

Abbreviations: ALT, alanine aminotransferase; BW, body weight; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; IL, interleukin, SpO_2, oxygen saturation

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