

Table S1. Serbian National guidelines for COVID-19 Treatment, Version 11. (Translated from Serbian to English and the original Serbian Version).

Protocol for the treatment of COVID-19 patients		
Version 11		
Form of the disease	Institution	Treatment
FORM 1		
1. Positive nasopharyngeal swab (PCR for SARS-CoV-2, Ag test)	At-home treatment and home isolation with monitoring and follow-up by Covid clinic staff	Vitamin therapy: alphacalcidol tablets (Alpha D3), 1x2 mcg, vitamin C 1x 1g (if there are no kidney issues)
2. Asymptomatic		<u><i>*Do not routinely prescribe antibiotics due to the risk of serious adverse effects and the rising resistance to antimicrobial drugs</i></u>
3. Very mild clinical presentation		Antiviral therapy (to be introduced no later than the 5 th day of symptom onset): favipiravir tablets, 1,600 mg every 12 h on the first day, then 600 mg every 12 h for another 4 days (the drug is applied in patients with symptoms)
4. Patients without comorbidities and with the mild form of the infection (hospitalized patients with sO ₂ >94% and without signs of pneumonia on X-ray)		
FORM 2		
1. Positive nasopharyngeal swab (PCR for SARS-CoV-2, Ag test)	1. Covid centers: general wards	Anticoagulant therapy: low-molecular-weight heparin
2. Mild clinical presentation	2. General hospitals: isolation units	Antiviral therapy (to be introduced no later than the 5 th day of symptom onset): favipiravir tablets, 1,600 mg every 12 h on the first day, then 600 mg every 12 h for another 4 days
3. Patients without comorbidities and with the mild form of the infection (hospitalized patients with sO ₂ >94% and with signs of pneumonia on X-ray, but without signs of hypoxia at admission)	Increased monitoring measures Checking patient temperature, sO ₂ and respiration rate several times a day	Corticosteroid therapy
FORM 3		
1. Positive nasopharyngeal swab (PCR for SARS-CoV-2, Ag test)	1. Covid centers: semi-intensive care units	Vitamin therapy: alphacalcidol tablets (Alpha D3), 1x2 mcg, vitamin C 1x1 g
2. Moderate clinical presentation	2. General hospitals: isolation units with constant monitoring (≤1h) of intensive care specialist, anesthesiologist, infectologist or internal medicine specialist	Convalescent plasma: (within 2 weeks of symptom onset and after consultation with an infectologist and transfusiologist, according to the score)
3. Severe hypoxia with necessary oxygen therapy (sO ₂ <90%), fever, multiple opacities on chest X-ray (or characteristic changes in the lungs visible on CT)	3. In case of further deterioration transportation to Covid intensive care	<u><i>Application of antibiotics only in likely or proven bacterial infection</i></u>
4. Cytokine storm (deterioration of general health status with ↑CRP,		Anticoagulant therapy: low-molecular-weight heparin
		Vitamin therapy: alphacalcidol tablets (Alpha D3), 1x2 mcg, vitamin C 1x1 g
		Oxygen therapy: nasal catheter or mask O ₂ (10 – 15 l/minute)
		Antiviral therapy (if less than 5 days have elapsed since symptom onset): favipiravir (as above) or remdesivir ampules 200 mg intravenously on the first day, then 100 mg IV/day for another 4 days

↑fibrinogen, ↑D-dimer, ↑IL-6) (at least one parameter elevated)

(**Corticosteroid therapy** and/or **tocilizumab** 8 mg/kg IV per dose. Two doses are administered (max 800 mg per dose)

Antibiotic therapy: in keeping with the guidelines for rational application of antibiotics

Convalescent plasma: (within 2 weeks of symptom onset and after consultation with an infectologist and transfusiologist, according to the score)

FORMS 4 and 5

1. Positive nasopharyngeal swab
2. Very severe/severe clinical presentation
3. Onset or development of ARDS
4. Cytokine storm (deterioration of general health status with ↑CRP, ↑fibrinogen, ↑D-dimer, ↑IL-6)

Covid centers: intensive care units

All available measures/combinations of measures need to be applied

Maintaining ↑ O₂ flow as long as possible, MV in case of further deterioration

Corticosteroid therapy: methylprednisolone 1-2 mg/kg, 3-5 days, then gradual reducing of the dose (dose should be adjusted to body mass in order to reduce the risk of bleeding and other adverse effects)

Tocilizumab: 8 mg/kg IV per dose. Two doses (max 800 mg per dose)

Immunoglobulins: 10 – 20 g per day Ig over a period of 3 – 5 days

PROTOKOL ZA LEČENJE PACIJENATA SA KOVID-19 VERZIJA 11		
FORMA BOLESTI	USTANOVA	TERAPIJA
OBLIK 1 1. Pozitivan nazofaringealni bris (PCR na SARS-KoV-2, Ag test) 2. Asimptomatska 3. Vrlo blaga klinička slika 4. Bolesnici bez komorbiditeta i sa blagim oblikom infekcije (hospitalizovani pacijenti sa $SO_2 > 94\%$ i bez Rtg znakova pneumonije)	Kućno lečenje i izolacija uz kontrole i nadzor Kovid ambulanti	Vitaminska th: alfa-kalcidol tbl. (Alpha D ₃) 1x2 mcg, vitamin C 1x1g (ukoliko nema bubrežnih smetnji) * Ne davati antibiotike rutinski! Zbog rizika ozbiljnih neželjenih dejstava i rastuće rezistencije na antimikrobne lekove. Antivirusna th. (započeti najkasnije do 5. dana od početka tegoba): Favipiravir tbl. 1600 mg na 12 h, prvi dan, zatim 600 mg na 12h još 4 dana (lek se primenjuje kod obolelih koji imaju simptome) Simptomatska th. Antikoagulantna th: Niskomolekulni heparin Antivirusna th. (započeti najkasnije do 5. dana od početka tegoba): Favipiravir tbl. 1600 mg na 12 h, prvi dan, zatim 600 mg na 12h još 4 dana Kortikosteroidna th. Vitaminska th: alfa-kalcidol tbl. (Alpha D ₃) 1x2 mcg, vitamin C 1x1g Plazma rekonvalescenata (unutar 2 nedelje od početka tegoba i nakon konsultacije sa infektologom i transfuziologom, prema skor) <i>Primena antibiotika samo kod verovatne ili dokazane bakterijske infekcije!</i>
OBLIK 2 1. Pozitivan nazofaringealni bris (PCR na SARS-KoV-2, Ag test) 2. Blaga klinička slika 3. Bolesnici bez komorbiditeta i sa blagim oblikom infekcije (hospitalizovani pacijenti sa $SO_2 > 94\%$ i sa Rtg znacima pneumonije sa ili bez znakova hipoksije pri prijemu)	1. Kovid centri: odelj. opšteg tipa 2. Opšte bolnice: odelj. izolacije Mere pojačanog nadzora Više puta dnevno praćenje temperature, SO_2 i fr. disanja	Antikoagulantna th: Niskomolekulni heparin Vitaminska th: alfa-kalcidol tbl. (Alpha D ₃) 1x2 mcg, vitamin C 1x1g Oksigenoterapija: nazalni kateter ili maska (O_2 10-15 L/min) Antivirusna th. (ako je prošlo manje od 5. dana od početka tegoba) Favipiravir (kao gore) ili Remdesivir amp. 200 mg i.v. prvi dan, zatim 100 mg i.v./dan još 4 dana Kortikosteroidna th. i/ili tocilizumab 8 mg/kg i.v. po dozi. Daju se 2 doze (max. 800 mg/dozi) Antibiotska th: prema vodiču za racionalnu primenu antibiotika, Plazma rekonvalescenata (unutar 2 nedelje od početka tegoba i nakon konsultacije sa infektologom i transfuziologom, prema skor)
OBLIK 3 1. Pozitivan nazofaringealni bris (PCR na SARS-KoV-2, Ag test) 2. Umereno teška klinička slika 3. Teška hipoksija sa potrebom za oksigenu Th ($SO_2 < 90\%$), febrilnost, multiple opacifikacije na Rtg-u pluća (ili specifične promene na plućima videne na CT-u) 4. Citokinska oluja (pogoršanje opšteg stanja uz \uparrow CRP, \uparrow fibrinogen, \uparrow D-dimer, \uparrow IL-6) (bar jednog parametra)	1. Kovid centri: odelj. poluintenzivne nege 2. Opšte bolnice: odelj. izolacije sa <u>stalnim</u> nadzorom ($\leq 1h$) intenziviste, anesteziologa, infektologa ili interniste 3. U slučaju daljeg pogoršanja: transport u Kovid intenzivne nege	Antikoagulantna th: Niskomolekulni heparin Vitaminska th: alfa-kalcidol tbl. (Alpha D ₃) 1x2 mcg, vitamin C 1x1g Oksigenoterapija: nazalni kateter ili maska (O_2 10-15 L/min) Antivirusna th. (ako je prošlo manje od 5. dana od početka tegoba) Favipiravir (kao gore) ili Remdesivir amp. 200 mg i.v. prvi dan, zatim 100 mg i.v./dan još 4 dana Kortikosteroidna th. i/ili tocilizumab 8 mg/kg i.v. po dozi. Daju se 2 doze (max. 800 mg/dozi) Antibiotska th: prema vodiču za racionalnu primenu antibiotika, Plazma rekonvalescenata (unutar 2 nedelje od početka tegoba i nakon konsultacije sa infektologom i transfuziologom, prema skor)
OBLIK 4 i 5 1. Pozitivan nazofaringealni bris 2. Veoma teška/teška klinička slika 3. Početak ili razvoj ARDS-a 4. Citokinska oluja (pogoršanje opšteg stanja uz \uparrow CRP, \uparrow fibrinogen, \uparrow D-dimer, \uparrow IL-6)	Kovid centri: intenzivna nega	Primeniti <u>sve dostupne mere/kombinacije intenzivnog lečenja</u> 1. Što duže održavanje na \uparrow protoku O_2 , MV u slučaju pogoršanja 2. Kortikosteroidna th: Metilprednizolon 1-2 mg/kg, 3-5 dana, a zatim postupno redukovanje doze (dozu prilagoditi telesnoj masi da bi se smanjio rizik krvarenja i drugih neželjenih efekata) 3. Tocilizumab: 8 mg/kg i.v. po dozi - 2 doze (max. 800 mg/dozi) 4. Imunoglobulini: 10-20 g/dan lg tokom 3-5 dana