Inpatient clinical practice guidelines in COVID19 pneumonia
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HOSPITAL ADMISSION CRITERIA AT THE ER

Moderate to severe pneumonia according to	CURB65 > 2 or PORT risk class > II
	SatO2 < 93%, RR > 20 or PaO2 < 65 mm Hg
	Diffuse bilateral crackles
	Bilateral infiltrates at Chest X Ray
Mild pneumonia with additional risk factors	Age > 50 and any of the following: ischemic heart disease, hypertension, cancer, obesity, severe asthma, chronic pulmonary disease, chronic hepatic injury, immunosuppresion
	CURB65≥1 with lymphopenia < 800 cls/uL, ferritin > 500 ug/L, any of LDH, CK, D-dimer and Troponin-I above upper normal limit
Respiratory distress	PaO2/FiO2 < 150 — Consider direct admission to ICU
Sepsis	
Septic shock	

INPATIENT THERAPEUTIC GUIDANCE

Respiratory severity level on admission	requirements for oxygen administration					
Oxygen supply with nasal cannula or Venturi mask	Yellow 1	≥ FiO2 35%	Antimicrobial therapy (AT) + antiviral drugs (AV) + hydroxychloroquine + cyclosporin A + LMWH + acetylcysteine + cholecalciferol 50000 UI/week	Cyclosporin A	Methylprednisolone (MP), 250 mg/day (for 3 days) followed by 40 - 80 mg/day (4th and 5th days)	
	Yellow 2	40% ≥ FiO2 ≤ 60%				Consider tocilizumab 400 mg (single infusion) on 2nd day
	Yellow 3	FiO2 ≥ 60%			MP 250 mg/day on 1st day, followed by 40 - 80 mg/day for 4 - 5 days (consider new 250 mg pulses instead of tocilizumab)	Tocilizumab (400 mg, single dose) on 2nd day
Intermediate respiratory care unit	Orange 1	High flow nasal cannula with FiO2 < 50% or < 30 lpm				
	Orange 2	High flow nasal cannula with FiO2 > 50% or > 30 lpm			MP 250 mg/day (1 to 3 days) following tocilizumab administration	Tocilizumab (400 mg, single dose) on 1st day (consider anakinra 100 mg/ day s.c. as rescue therapy)
	Orange 3	Noninvasive ventilation (NIV) with CPAP or Helmet				
Intensive care unit	Red 1	invasive ventilation with PaO2/FiO2 ≥ 200			MP at sepsis schedule equivalent dose (consider pulses of 250 mg/ day as rescue therapy)	Tocilizumab (400 mg, single dose) on 1st day (consider anakinra 100 mg/ day s.c. as rescue therapy)
	Red 2	invasive ventilation with PaO2/FiO2 < 200				
	Red 3	invasive ventilation with PaO2/FiO2 < 200 plus qSOFA 2/3 and/or multi organ failure				

NOTES

Effectiveness of treatments	there is not enough scientific evidence showing efficacy of any of the therapeutic measures included in general guidelines for the management of COVID-19 pneumonia
	While RCT are launched, adhesion to an internal clinical protocol facilitates extraction of real-world based data of safety and effectiveness of drugs
ANTIBIOTICS	
First choice	Cotrimoxazole 800/160 or Doxycycline 100 mg/12h for five days
Comment	Macrolide use was claimed to be effective on decreasing viral load but data lack consistency. Additional antimicrobials may be used according to patient profile to manage concomitant infections.
ANTIVIRAL DRUGS	
First choice	Lopinavir/ritonavir 200/50, 2 comp/12 h. Darunavir 800 mg/24 h + ritonavir 100 mg/24 h. Remdesivir 200 mg iv followed by 100 mg i.v. day is restricted to severe / critically ill patients depending on availability.
Comment	Problems of shortage, not proven effects. Limited to first week of symptoms. Remdesivir requires written informed consent
CORTICOSTEROIDS	
Dose schedule	250 mg methylprednisolone daily pulses (1-3 days) as induction therapy to prevent rapid progression to respiratory distress, as rescue therapy after tocilizumab failure or in case of limitation of therapeutic efforts
	Short course of methylprednisolone at the sepsis recommended schedule
Comment	Use of corticosteroids remains controversial according to current literature although it could improve survival in critically ill patients. The rationale for their use as induction at first days of admission is to try to impair recruitment of inflammatory cells and hyper-production of inflammatory mediators, which can aggravate the condition.
IMMUNOMODULATORS	
ANTIMALARIALS	
First choice	Hydroxycloroquine 400 mg/12h 1st day, followed by 200 mg/12h. Cloroquine 500 mg/12h as an alternative
Comment	Included in National Guidelines. No clear effect in available literature. Could low infectiveness. Risk of prolonged QT interval in combination (e.g. Azythromycin). Limited to first 5 days of admission
CYCLOSPORIN A	
Dose schedule	Starting at 100 mg/day (< 60 kg weight), 150 mg/day (60 to 80 kg/da) and 200 mg/day (> 80 kg weight). Consider scaling dose after 48h to 150 mg/day, 200 mg/day and 300 mg/day, respectively. Individualized scaling thereafter.
Comment	Written informed consent required. Data showing its ability to interfere with viral activity. Antiapoptotic and cytoprotective effect in cell stress responses. Cost-effective. Rapid action. Easy to monitor side-effects. Avoid its use in stages 4-5 of chronic renal disease. Do not start if uncontrolled hypertension. Dose reduction in case of a 30% increase in serum creatinine. To be maintained during the whole process (2 to 3 weeks) if a clinical benefit is observed
TOCILIZUMAB	
Administration criteria	Written informed consent required. Effective in short trials. A role in macrophage activation syndrome and also in acute respiratory failure associated to immunotherapy /CAR-T. Problems of shortage. Use in progression after cyclosporin, severe interstitial pneumonia (A3), rapid progression requiring ventilatory support (N or R), extrapulmonary organ failure, mostly in case of a severe systemic inflammatory status (as a reference, a threshold of 40 pg/ml for serum IL6 levels and of 400 ng/ml for D dimer are suggested). A second dose can be considered if partial response in individualised cases.
Precautions	Avoid its use in case of increased procalcitonin levels or bacterial infections, hepatic failure, neutropenia (< 500 cls/uL), thrombocytopenia (< 50000 cls /uL), pregnancy, past history of diverticulitis, those patients with limitation of therapeutic efforts
ANAKINRA	
Administration criteria	Written informed consent required. Failure to tocilizumab, instead of tocilizumab in fragile patients or in whom for other reasons may not be candidates to tocilizumab, non-desirable requirement of corticosteroids. 3 to 7 day courses.
Precautions	Avoid its use in case of neutropenia (< 1500 cls/uL). Watch for local skin reactions.
THROMBOPROPHYLAXIS	

First choice LMWH	Therapeutic dose	Intermediate dose	Prophylactic dose
Enoxaparin	1,5 mg/kg/24 h - 1 mg/kg/12 h	1 mg/kg/24 h	20 mg/24 h - 40 mg/24 h
Bemiparin	115 IU/kg/24 h	80 IU/kg/24 h	2500 IU/24 h - 3500 IU/24 h
Tinzaparin	175 IU/kg/24 h	100 IU/kg/24 h	3500 IU/24 h - 4500 IU/24 h

Administration criteria	To any patient with pneumonia and thrombosis risk factors discharged at the ER (at standard prophylactic schedule) and to all hospital admitted patients. Dose adjustment to intermediate dosage in case of D-dimer > 3000. Individually consider intermediate or therapeutic dosage in D-dimer < 3000 if risk of bleeding is negligible. Maintain a prophylactic schedule for 7 to 10 days after discharge. Antiplatelet agents can be co-administered. For further indications including dose adjustments, use of tinzaparin and fondaparinux, or pneumatic compression, clinicians are referred to the Hospital's thrombosis commission standard protocol and to on-call haematologist.
	To avoid in case of thrombocytopenia (< 30000 cls/uL)

First version launched on	15th March, 2020	
Approval from the 4 Public Quironsalud Hospitals Pharmacy committee on	26th March, 2020	
Principal revisions performed	26th March, 2020	Inclusion of MP pulses also in severity stages A1 and A2. Restriction of 2nd dose of tocilizumab
	30th March, 2020	Increasing in thromboprophylaxis measures
	3rd April, 2020	Inclusion of anakinra
	9th April, 2020	Addition of acetylcystein and cholecalciferol
	13th April, 2020	Inclusion of ruxolitinib, tocilizumab weight-based dose adjustment, information about ongoing CT