Table 2 : Supportive care & antiviral treatment of hospitalized patients with suspected or confirmed COVID-19

Clinical category	Supportive Care	Additional antiviral therapy	Precautions
Suspicion of COVID-19 ➢ **Mild-to-moderate symptoms (no dyspnea)** ➢ **No risk group[3]** ***ex. Hospitalization for social-related reasons***	Symptomatic treatment	No	Use paracetamol in first-line (usual dosage), and NSAIDs with caution (if really required)
Suspicion of COVID-19 ➢ **Mild-to-moderate symptoms (no dyspnea)** ➢ **Risk group[3]** **Or** **Suspicion of COVID-19 AND alarming symptoms (dyspnea)**	*Case by case discussion, if possible with an Infectious Disease Specialist, to initiate an empirical antiviral therapy, based on the potential delay to obtain results (antiviral therapy is expected to be more efficient if started early in the course of the disease), or on other considerations (high risk of secondary complications).* *If decision to treat empirically (in hospitals), follow the treatment options as described for "CONFIRMED CASES".*		
Confirmed COVID-19 ➢ **Mild-to moderate disease (no O2 requirement/no evidence of pneumonia)** ➢ **Risk group[3]**	Symptomatic treatment	Consider start **hydroxychloroquine** (Plaquenil®) IF NO CONTRA-INDICATION • 400 mg at suspicion/diagnosis; • 400 mg 12 h later • Followed by 200 mg BID up to Day 5 *NB:*	**Contra-indications hydroxychloroquine** ➢ **Known allergy to the drug** **Precautions hydroxychloroquine:** ➢ **QTc > 500 msec** ➢ **drug interaction; check at** http://www.covid19-druginteractions.org **(Liverpool)** Interaction potential of hydroxychloroquine is likely the same as chloroquine

[3] Risk groups: age > 65 years AND/OR underlying end organ dysfunction (lung, heart, liver,…), diabetes, coronaropathy, chronic obstructive pulmonary disease, arterial hypertension

		stop hydroxychloroquine if follow-up at home *If no hydroxychloroquine available, consider chloroquine base 600 mg (10mg/kg) at diagnosis and 300mg (5 mg/kg) 12 h later, followed by 300 mg (5 mg/kg) BID up to Day 5 or chloroquine phosphate 1000mg at diagnosis and 500mg 12h later, followed by 300mg BID up to day 5.*	➢ **Myasthenia gravis** ➢ **Porphyria** ➢ **Retinal pathology** ➢ **Epilepsy** **NB: pregnancy is not a contra-indication as such** (large safety experience with chloroquine); see risk/benefit balance Perform ECG daily if initial QTc 450-500 msec, and biochemistry according to underlying disease *NB: Sanofi has requested that adverse events related to hydroxychloroquine are reported to* Pharmacovigilance.Belgium@sanofi.com
Confirmed COVID-19 Severe disease **≥ 1 of the following:** ➢ **Respiratory rate ≥30/min (adults); ≥40/min (children < 5)** ➢ **Blood oxygen saturation ≤93%** ➢ **PaO2/FiO2 ratio <300** ➢ **Lung infiltrates >50% of the lung field within 24-48 hours**	Optimal supportive care in hospital WARD (or ICU) Provide 02 Consider carefully antibiotics or antifungals according to local epidemiology	Start **hydroxychloroquine** (Plaquenil®) IF NO CONTRA-INDICATION • 400 mg at diagnosis; • 400 mg 12 h later • Followed by 200 mg BID up to Day 5 *NB: If no hydroxychloroquine available, consider chloroquine base 600 mg (10mg/kg) at diagnosis and 300mg (5 mg/kg) 12 h later, followed by 300 mg (5 mg/kg) BID up to Day 5 OR chloroquine phosphate 1000mg at diagnosis and 500mg 12h later, followed by 500mg BID up to day 5* Consider **lopinavir/ritonavir 400/100 mg** (= 2 tablets of 200/50 mg) BID for 14 days) *as second choice ONLY if hydroxychloroquine/chloroquine contra-indicated and provided it can be administered within 10 days after symptoms onset (check also drug interaction!); or in children < 10 kg (after IDS advice)*	**Contra-indications hydroxychloroquine:** ➢ **Known allergy to the drug** **Precautions hydroxychloroquine:** ➢ **QTc > 500 msec** ➢ **drug interaction (check at** http://www.covid19-druginteractions.org **(Liverpool)** Interaction potential of hydroxychloroquine is likely the same as chloroquine ➢ **Myasthenia gravis** ➢ **Porphyria** ➢ **Retinal pathology** ➢ **Epilepsy** **NB: pregnancy is not a contra-indication as such** (large safety experience with chloroquine); see risk/benefit balance **NB: use with caution if renal impairment, taking into account the paucity of PK data**; keep the same loading dose (D1) but decrease the D2-D5 dose to 50% if GFR between 10 and 30 ml/min, and to 25% if GFR < 10 ml/min or dialysis (very weak evidence) Perform basic biochemistry daily and ECG daily if initial QTc > 450 msec (+ other indicated investigations)

			Avoid quinolones if possible, or monitor closely the QT if these antibiotics are needed *NB: we stress again that there is no sufficient evidence about activity of azithromycin and therefore no reason to associate this antibiotic to the hydroxychloroquine treatment at this moment*
Confirmed COVID-19 **Critical disease** **≥ 1 of the following:** ➢ **Acute Respiratory Distress Syndrome** ➢ **Sepsis** ➢ **Altered consciousness** ➢ **Multi-organ failure**	Optimal supportive care in ICU Mechanical ventilation Specific prevention & treatment of ARDS Track secondary bacterial and opportunistic (*Aspergillus*) infections Prevention of sub-sequent lung fibrosis NB: ongoing studies with dexa-methasone, tocilizumab,… in this most critical group	**Remdesivir** (compassionate use) • 200 mg loading dose (IV, within 30 min) • 100 mg OD for 2 to 10 days If remdesivir unavailable: Consider (**hydroxy)chloroquine,** crushed in nasogastric tube, at the same dosage and monitoring as above; replace with remdesivir if it becomes available However, since the clinical efficacy of (hydroxy)chloroquine is not demonstrated, caution is required in severe cases with kidney/ liver/cardiac failure, and abstention in such situations may be preferred (see above) *NB: tocilizumab and other interleukins (6 or 1) blockers: Some preliminary Chinese and Italian data and very limited clinical experience in Belgium suggest a favorable effect in the most critical patients suffering from persistent and overwhelmed inflammation resembling cytokine release syndrome (CRS). At this moment however, this class of drugs should only be used in*	**At this moment very restricted availability of remdesivir (long delay for supply) and very strict criteria released by Gilead** **As on 24th of March, this drug is restricted in compassionate use for pregnant women and children only** **Request on** https://rdvcu.gilead.com/ **Inclusion criteria** **ICU + confirmation SARS-Cov-2 by PCR + mechanical ventilation** **Exclusion criteria** - **Evidence of MOF** - **Need of inotropic agents** - **Creatinine clearance < 30 ml/min, dialysis, or hemofiltration** - **Transaminases > 5X ULN** **Of note, remdesivir is one of the treatment arm in the DisCoVeRy trial** Still limited information on drug interaction is available. Risk-benefit assessment should be made individually. Close monitoring of remdesivir toxicity or diminished efficacy of concomitant drug is recommended. Check also for interaction with remdesivir at http://www.covid19-druginteractions.org (Liverpool).

	clinical trials or within international cohort studies if possible. The drug could be considered on an individual basis in patient with persistent inflammation (i.e. elevated IL-6, CRP, D Dimers, ferritin,..) without evidence of bacterial superinfection/sepsis and ARDS requiring mechanical ventilation.

Annex 2: Therapies for confirmed COVID-19 in some European countries

Disease category	Italy (Lombardia protocol)	France	Netherlands	Switzerland
➢ **Mild-to-moderate disease** ➢ **No risk group**	No antiviral treatment	No antiviral treatment	No antiviral treatment	No antiviral treatment
➢ **Mild-to-moderate disease** ➢ **Risk group**	lopinavir/ritonavir + chloroquine or hydroxychloroquine for 5-7 days	Consider lopinavir/ritona-vir; duration depending on monitoring of viral excretion	Consider chloroquine for 5 days	? (not mentioned)
➢ **Severe disease**	remdesivir + chloroquine or hydroxychloroquine for 5-20 days (if no remdesivir: maintain lopinavir/ritonavir with chloroquine)	remdesivir; duration depending on monitoring of viral excretion (No second choice)	chloroquine D1 (600-300 mg; D2-D5 300 mg BID) lopinavir/ritona vir as second option (for 10-14 days)	Lopinavir/ritonavir (atazanavir/ritonavir as second choice)
➢ **Critical disease**	remdesivir + chloroquine or hydroxychloroquine for 5-20 days (if no remdesivir: maintain lopinavir/ritonavir with chloroquine)	remdesivir; duration depending on monitoring of viral excretion Lopinavir/ritona vir as second choice (case by case)	remdesivir (for 10 days) + chloroquine (for 5 days)	remdesivir as first choice (for 10 days) lopinavir/ritonavir (+ hydroxychloroquine if < 65 years/no comorbidity) as second choice (if remdesivir unavailable). Tocilizumab (in case of MOF and inotropic support)