

Neither the PaedF working party nor the EDQM make any recommendation to use the below listed drugs for experimental treatment of COVID-19. Available knowledge is limited. The prescriber remains responsible to make an individual assessment of risks and benefits for each patient.

Product	Strength	How to Formulate	Excipients†	Comments
<b>Chloroquine sulphate</b>				
Expert opinion for extemporaneous preparation: chloroquine sulfate is a highly soluble drug (BCS class I ( <a href="#">Verbeeck RK, Junginger HE, Midha KK et al. J Pharm Sci 2005;94(7):1389-95.</a> )). It is expected that manipulation of the formulation will have a minimal impact on bioavailability. Caution: when manipulating tablets, be aware of the moiety (e.g. 136 mg chloroquine sulfate equals 100 mg chloroquine base).				
Oral syrup				
Nivaquine®	5 mg/mL chloroquine (base) oral solution (Sanofi, FR), corresp. 6.81 mg/mL chloroquine sulfate		purified water citric acid monohydrate <b>caramel flavor (E150)</b> <b>coffee dry extract</b> <b>sucrose</b>	Protect from light
Tablets				
Nivaquine® (FR)	100 mg chloroquine (base) corresp. to 136 mg chloroquine sulfate		<b>gelatin</b> <b>sucrose</b> <b>wheat starch</b> magnesium stearate silica hydrated	
<b>Chloroquine phosphate</b>				
Expert opinion for extemporaneous preparation: chloroquine phosphate is a highly soluble drug (BCS class I ( <a href="#">Verbeeck RK, Junginger HE, Midha KK et al. J Pharm Sci 2005;94(7):1389-95.</a> )). It is expected that manipulation of the formulation will have minimal impact on bioavailability. The extemporaneously prepared oral liquids described in literature show that tablets can be processed in various aqueous bases. When the described commercialised bases are unavailable, it is expected that every aqueous base can be used. Removing the film-coating is usually not necessary before crushing the tablets, but it may ease the crushing and further processing. The tablets can be crushed to be used in capsules delivering the right dose. Using a mortar to crush the tablets might result in some loss of the API (Oralia.nl). Caution: when manipulating tablets, be aware of the moiety (e.g. 160 mg chloroquine phosphate equals 100 mg chloroquine base).				
Tablets				
A-Cq® 100 tablets (Ace Pharma, NL)	161 mg Chloroquine phosphate, eq. to 100 mg Chloroquine (base)	---	<b>Lactose</b> monohydrate <b>maize starch</b> pre-gelatinised maize starch crospovidone magnesium stearate colloidal anhydrous silica	

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Klorokinofosfat film-coated tablets 160 mg or 250 mg (RPH Pharma, SE)	160 mg / 250 mg Chloroquine phosphate, eq. to 100 mg / 155 mg Chloroquine (base)	'---	<b>Titanium dioxide</b> microcrystalline cellulose talc magnesium stearate colloidal silica <b>basic-butylated-methacrylate copolymer (Eudragit E)</b> macrogol vanilla	
Avloclor® tablets (Alliance Pharmaceuticals, UK)	250 mg Chloroquine phosphate, eq. to 155 mg Chloroquine (base)	'---	<b>Maize starch</b> magnesium stearate	
Delagil® tablets (Bausch Health, HU, IR)	250 mg Chloroquine phosphate, eq. to 155 mg Chloroquine (base)	'---	Potato starch colloidal silica magnesium stearate carbomer talc <b>polyvinyl butyral</b>	
Arechin® tablets (Adamed, PL)	250 mg Chloroquine phosphate, eq. to 155 mg Chloroquine (base)	'---	<b>Potato starch gelatin</b> magnesium stearate colloidal silica	Potentially not available due to batches saved for use in Poland
Aralen® film-coated tablets (Sanofi, US)	500 mg Chloroquine phosphate, eq. to 311 mg Chloroquine (base)	---	Carnauba wax colloidal silicon dioxide dibasic calcium phosphate hypromellose magnesium stearate microcrystalline cellulose polyethylene glycol <b>polysorbate 80</b> pregelatinized starch sodium starch glycolate stearic acid <b>titanium dioxide</b>	

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Product	Strength	How to Formulate	Excipients†	Comments
Oral suspension				
Extemporaneous preparation ( <a href="#">Ferreira AO, Polonini HC, Silva SL, et al. J Pharm Biomed Anal 2016;118:105-12.</a> )	15 mg/mL Chloroquine phosphate, eq. to 9.33 mg Chloroquine (base)	4.5 g Chloroquine phosphate powder (Fagron US) are weighed and triturated in a mortar; small amount of SyrSpend® SF PH4 liquid cherry (Fagron) is added and mixed to a uniform paste; SyrSpend® SF PH4 liquid cherry is added in geometric portions up to 300 mL and mixed well; fill into low-actinic prescription bottles	SyrSpend® SF PH4 liquid cherry 473 mL: Modified starch, <b>sucralose</b> , artificial cherry flavor, sodium benzoate (0.09 %), sodium citrate, citric acid, malic acid, <b>simethicone</b> , purified water	Storage: up to 3 months in amber glass bottle; stable in fridge (2-8 °C) and at room temperature (20-25 °C); no data on microbiological stability
Extemporaneous preparation ( <a href="#">USP-NF</a> )	15 mg/mL Chloroquine phosphate, eq. to 9.33 mg Chloroquine (base)	Comminute 3x 500 mg Aralen® tablets; add 15 mL vehicle and mix to a paste; add vehicle stepwise up to 100 mL, filled into tight, light-protected containers	Aralen® tablets + OraSweet* : OraPlus* 1:1	Storage: 60 d stability at controlled room temperature or in the fridge
Extemporaneous preparation ( <a href="#">USP-NF; Allen, Erickson. Am J Health Syst Pharm 1998; 55(18):1915-20.</a> )	15 mg/mL Chloroquine phosphate, eq. to 9.33 mg Chloroquine (base)	Comminute 3x 500 mg Aralen® tablets; add 15 mL vehicle and mix to a paste; add vehicle stepwise up to 100 mL, filled into amber plastic vials	Aralen® tablets + 1) OraSweet* : OraPlus* 1:1, 2) OraSweet SF* : OraPlus* 1:1, 3) Cherry syrup : Simple syrup NF 1:4	Protect from light; Shake well before use; 60 d stability at 20°C (also stable at 5°C); no data on microbiological stability
Extemporaneous preparation ( <a href="#">Nahata, Pai. Pediatric Drug Formulations, 7th ed.</a> )	16.67 mg/mL Chloroquine phosphate, eq. to 10 mg/mL Chloroquine (base)	Remove film-coating from 4x 500 mg Aralen® tablets by wet paper towel; comminute tablet cores, add small volume of sterile water and mix to a paste; add vehicle stepwise up to 120 mL	Aralen® tablets + sterile water q.s., cherry syrup NF	No stability data
Extemporaneous preparation ( <a href="#">Mirochnik M, et al. Pediatr Infect Dis 1994; 13(9): 827-8.</a> )	16.67 mg/mL Chloroquine phosphate, eq. to 10 mg/mL Chloroquine (base)	Remove film-coating from 2x 500 mg Aralen® tablets and comminute tablet cores; remove film-coating, add small volume of sterile water and mix to a paste; add vehicle stepwise up to 60 mL; filled into amber glass bottles	Aralen® tablets + Sterile water for irrigation NF, cherry syrup q.s.	Storage: up to 4 weeks in amber glass bottle; stable in fridge at 5°C, at room temperature and at 29°C (poor justification by data)

API=active pharmaceutical ingredient. BCS=biopharmaceutical classification system

†Excipients raising concern for children in bold

\*OraSweet: Purified water, sucrose, glycerol, **sorbitol**, citrus-berry flavor, citric acid, sodium phosphate, methylparaben, potassium sorbate  
OraSweet SF: Purified water, glycerol, **sorbitol**, sodium saccharin, xanthan gum, flavor, citric acid, sodium citrate, methylparaben (0.03%), **propylparaben (0.008%)**, potassium sorbate (0.1%).

OraPlus: Purified water, microcrystalline cellulose, carmellose, xanthan gum,  $\kappa$ -**carrageenan**, calcium sulfate, trisodium phosphate, citric acid, sodium phosphate, **dimethicone**, methylparaben, potassium sorbate.

Cherry Syrup NF: cherry juice, sucrose, **ethanol (2 %)**, purified water.

Syrup NF: sucrose (85%), purified water.

#### **Not marketed**

Resochin tablets by Bayer (DE, PT), contains 250 mg phosphate salt eq. to 155 mg chloroquine (base); **maize starch**, talc, magnesium stearate; hypromellose, macrogol 4000, **titanium dioxide**

Resochin junior tablets by Bayer (DE), contains 81 mg phosphate salt eq. to 50 mg chloroquine (base); **maize starch**, talc, magnesium stearate; hypromellose, macrogol 4000, **titanium dioxide**

Chloroquine phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/ 5 mL; sodium chloride, water for injection