

In line with the <u>updated advice from WHO</u>, neither the PaedF working party nor the EDQM recommend the use of the below listed drugs outside their authorised indications for experimental treatment of COVID-19. The prescriber remains responsible to make an individual assessment of risks and benefits for each patient. The <u>European Medicines Agency</u> also advises to only use the below listed drugs for their authorised indications or within clinical trials or emergency use programmes in hospitalised patients.

		I	T	
Product	Strength	How to Formulate	Excipients†	Comments
Chloroquine sulphate				
Junginger HE, Midha KI minimal impact on bio Health 2001;6(7):496-5	K et al. J Pharm Sci 2 availability. Chloroqu 504).	ration: chloroquine sulfate is a homosis of the moiety (e.g. 136 mg care of the moiety (e.g. 1	ted that manipulation of the <u>F, Gyapong JO, Agyepong IA,</u>	e formulation will have a et at Trop Med Int
Nivaquine®	5 mg/mL chloroquine (base) oral solution (Sanofi, FR), corresp. 6.81 mg/mL chloroquine sulfate		purified water citric acid munohydrate caramel flavor (E150) coffee dry extract suc ose	Protect from light
Tablets		.00		
Nivaquine® (FR)	100 mg chloroquine (base) corresp. to 136 mg chloroquine sulfate	- Sticacy at	gelatin sucrose wheat starch magnesium stearate silica hydrated	
Chloroquine phosphat	e	( O		
Junginger HE, Midha KI minimal impact on biod Health 2001;6(7):496-5 The extemporaneously bases. When the descri	K et al. J Pharm (2012) availability (Albroqu 504). prepared oral liquic theo commercialised	ation: chloroquine phosphate is 005;94(7):1389-95)). It is expect uine has a bitter taste (Ansah EK) ds described in literature show the bases are unavailable, it is expected says before crushing the tab	ted that manipulation of the <i>Gyapong JO, Agyepong IA,</i> hat tablets can be processed ected that every aqueous ba	e formulation will have et al. Trop Med Int d in various aqueous ase can be used.

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 (<u>Oralia.nl</u>).

Caution: were manipulating tablets, be aware of the moiety (e.g. 160 mg chloroquine phosphate equals 100 mg chloroquine base).

Tablets		
A-Ca® 100 tablets	161 mg	 Lactose monohydrate
Ace Pharma, NL)	Chloroquine phosphate, eq. to 100 mg Chloroquine (base)	maize starch pre-gelatinised maize starch crospovidone magnesium stearate colloidal anhydrous silica

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Product	Strength	How to Formulate	Excipients†	Comments
Tablets (continued)				
Klorokinfosfat film-	160 mg / 250		Titanium dioxide	
coated tablets 160	mg Chloroquine		microcrystalline	
mg or 250 mg (RPH	phosphate, eq.		cellulose	
Pharma, SE)	to 100 mg / 155		talc	
Thairna, 32,	mg Chloroquine		magnesium stearate	
	(base)		colloidal silica	
	(base)			_( )
			basic-butylated-	
			methacrylate copolymer	
			(Eudragit E)	-O
			macrogol	
			vanilla	
Avloclor® tablets	250 mg		Maize starch	
(Alliance	Chloroquine		magnesium stearat	
Pharmaceuticals, UK)	phosphate, eq.			
	to 155 mg		•••	
	Chloroquine			
	(base)		L× 1	
Delagil® tablets	250 mg		Potato starch	
(Bausch Health, HU,	Chloroquine		coloidal silica	
IR)	phosphate, eq.		magnesium stearate	
1117	to 155 mg		Carbomer	
	Chloroquine	-0	talc	
	(base)		polyvinyl butyral	
Arechin® tablets		<del>\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \</del>	Potato starch	Detentially not
	250 mg			Potentially not
(Adamed, PL)	Chloroquine	(C)	gelatin	available due to
	phosphate, eq.	" COC.	magnesium stearate	batches saved for use
	to 155 mg	.00	colloidal silica	in Poland
	Chloroquine			
	(base)	<b>(2)</b>		
Aralen® film-coated	500 mg		Carnauba wax	
tablets (Sanofi, US)	Chloroquine		colloidal silicon dioxide	
	phosphate, eq.		dibasic calcium	
	to 311 mg		phosphate	
	Chlorodiile		hypromellose	
	(base)		magnesium stearate	
	XO		microcrystalline	
	$oldsymbol{O}$		cellulose	
			polyethylene glycol	
tablets (Sanofi, US)			polysorbate 80	
			pregelatinized starch	
			sodium starch glycolate	
· O ·			stearic acid	
			titanium dioxide	
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Product	Strength	How to Formulate	Excipients†	Comments
Oral suspension	_			
Oral suspension  Extemporaneous preparation (Ferreira AO, Polonini HC, Silva SL, et al. J Pharm Biomed Anal 2016;118:105-12)	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-	SyrSpend® SF PH4 liquid cherry 473 mL: Modified starch, sucralose, artificial cherry flavor, sodium benzoate (0.09%), sodium citrate, citric acid, malic acid, simethicone, 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 micropiological stability
Extemporaneous preparation ( <i>USP-NF</i> )  Extemporaneous preparation ( <i>USP-NF</i> ;	15 mg/mL Chloroquine phosphate, eq. to 9.33 mg Chloroquine (base) 15 mg/mL Chloroquine	actinic prescription bottles  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  Comminute 3x 500 mg  Aralen® tablets; add 15 mL	Aralen® tablets + OraSweet* OraPlus* 1:1  Aralen® tablets + 1) OraSweet* : OraPlus*	Storage: 60 d stability at controlled room temperature or in the fridge  Protect from light; Shake well before
Allen, Erickson. Am J Health Syst Pharm 1998; 55(18):1915- 20)	phosphate, eq. to 9.33 mg Chloroquine (base)	vehicle and mix to a paste; add vehicle stepwis up to 100 mL, filled into amber plastic vials	1:1, 2) OraSweet SF*: OraPlus* 1:1, 3) Cherry syrup: Simple syrup NF 1:4	use; 60 d stability at 20°C (also stable at 5°C); no data on microbiological stability
Extemporaneous preparation (Nahata, Pai. Pediatric Drug Formulations, 7th ed)	16.67 mg/mL Chloroquine phosphate, eq. to 10 mg/mL Chloroquine (base)	Remine film-coating from 4x 500 ng 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 (Mirochnik M, et al. Pediatr Infect Dis. 1994; 13(9): 8(7-8)	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)

Pl=aetive pharmaceutical ingredient. BCS=biopharmacetuical classification system

rexcipients 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.

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## 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

Resochin junior tablets by Bayer (DE), contains \$1 mg phosphate salt eq. to 50 mg chloroquine (base); maize starch, talc, magnesium sterate; hypromellose, macrogol 4000, titanium dioxide
Choloroquine phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almiro, S.A. (PT), contains 250 mg/5 mL; sodium phosphate injectable solution by Labesfal - Laboratórios Almi

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