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Add the following:

▲Hydroxychloroquine Sulfate Compounded Oral Suspension

DEFINITION

Hydroxychloroquine Sulfate Compounded Oral Suspension contains NLT 93.0% and NMT 107.0% of the labeled amount of hydroxychloroquine sulfate ($C_{18}H_{26}ClN_3O \cdot H_2SO_4$).

Prepare Hydroxychloroquine Sulfate Compounded Oral Suspension 25 mg/mL as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩).

Hydroxychloroquine sulfate tablets,[a] or powder equivalent to	3000 mg of hydroxychloroquine sulfate
Vehicle: a 1:1 mixture of Ora-Plus[b] and Ora-Sweet SF,[b] a sufficient quantity to make	120 mL

[a] Hydroxychloroquine sulfate 200 mg tablets, Sandoz Inc., Princeton, NJ.

[b] Perrigo, Allegan, MI.

Place the *Hydroxychloroquine Sulfate tablets* or *powder* in a suitable container. If using tablets, add a small amount of *Vehicle* to cover the tablets and allow to soak for 15 min. Mix well with a sufficient amount of *Vehicle* to form a smooth paste. Add a sufficient amount of *Vehicle* to make the contents pourable. Transfer the contents stepwise and quantitatively to a calibrated container using the remainder of the *Vehicle*. Add a sufficient amount of *Vehicle* to bring to final volume. Shake to mix well.

Hydroxychloroquine sulfate powder	2500 mg
Acesulfame potassium	200 mg
Steviol glycoside 95%[a]	200 mg
Flavor, crème DeMenthe[a]	0.2 mL
PCCA suspendIt,[a] a sufficient quantity to make	100 mL

[a] PCCA, Houston, TX.

Place the *Hydroxychloroquine Sulfate powder*, *Acesulfame Potassium*, and *Steviol Glycoside 95%* in a suitable container and mix well. Add approximately 50 mL of *PCCA SuspendIt* and mix to form a smooth paste. Add a sufficient amount of *PCCA SuspendIt* to make the contents pourable. Transfer the contents stepwise and quantitatively to a calibrated container using the *PCCA SuspendIt*. Add the *Flavor*. Add sufficient *Vehicle* to bring to final volume and mix well.

ASSAY

• **Formulation in Ora-Plus and Ora-Sweet SF**

Solution A: Water and phosphoric acid (400:1); adjusted with 1 N sodium hydroxide to a pH of 3.0

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Acetonitrile (%)
0	90	10
2	90	10
5	80	20
5.1	90	10
10	90	10

Standard solution: 0.1 mg/mL of hydroxychloroquine sulfate prepared from USP Hydroxychloroquine Sulfate RS in water. Sonicate for 5 min.

Sample solution: Transfer 1.0 mL of the Oral Suspension into a 250-mL volumetric flask. Add approximately 200 mL of water and sonicate for 15 min. Add water to volume. Centrifuge an aliquot for 10 min, and transfer the supernatant to an HPLC vial.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 340 nm

Column: 4.6-mm × 15-cm; 5-µm packing L1

Temperatures

Autosampler: 4°

Column: 40°

Flow rate: 1.2 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

[Note—The retention time of hydroxychloroquine sulfate is about 4.5 min.]

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of hydroxychloroquine sulfate ($C_{18}H_{26}ClN_3O \cdot H_2SO_4$) in the portion of Oral Suspension taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of hydroxychloroquine sulfate from the *Sample solution*

r_S = peak response of hydroxychloroquine sulfate from the *Standard solution*

C_S = concentration of USP Hydroxychloroquine Sulfate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of hydroxychloroquine sulfate in the *Sample solution* (mg/mL)

Acceptance criteria: 93.0%–107.0%

- **Formulation in PCCA SuspendIt**

Solution A: 0.1% trifluoroacetic acid in water

Solution B: 0.1% trifluoroacetic acid in acetonitrile

Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0.0	97	3
1.5	45	55
1.6	97	3
3.0	97	3

Standard solution: 0.1 mg/mL of hydroxychloroquine sulfate from USP Hydroxychloroquine Sulfate RS in water

Sample solution: Transfer 1.0 mL of Oral Suspension into a 50-mL centrifuge tube. Add approximately 24 mL of water and vortex for 15 min. Sonicate for 2 min and vortex for 30 s. Centrifuge for 15 min at 6000 rpm. Transfer 1 mL of supernatant to a 10-mL volumetric flask and dilute with water to final volume. Transfer the solution to a micro-centrifuge tube and centrifuge for 10 min at 14,000 rpm. Transfer the solution to an HPLC vial.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 343 nm

Column: 2.1-mm × 5-cm; 1.7-µm packing L1

Temperatures

Autosampler: 25°

Column: 65°

Flow rate: 1 mL/min

Injection volume: 1 µL

System suitability

Sample: *Standard solution*

[NOTE—The retention time of hydroxychloroquine sulfate is about 1.2 min.]

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of hydroxychloroquine sulfate ($C_{18}H_{26}ClN_3O \cdot H_2SO_4$) in the portion of Oral Suspension taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of hydroxychloroquine sulfate from the *Sample solution*

r_S = peak response of hydroxychloroquine sulfate from the *Standard solution*

C_S = concentration of USP Hydroxychloroquine Sulfate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of hydroxychloroquine sulfate in the *Sample solution* (mg/mL)

Acceptance criteria: 93.0%–107.0%

SPECIFIC TESTS

- **APPEARANCE:** Off-white to faint beige suspension
- **pH** ⟨791⟩

Formulation in Ora-Plus and Ora-Sweet SF

Oral suspension from Hydroxychloroquine Sulfate powder: 3.6–4.6

Oral suspension from Hydroxychloroquine Sulfate tablets: 4.4–5.4

Formulation in PCCA SuspendIt: 4.7–5.7

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Package in tight, light-resistant, plastic containers. Store in a refrigerator or at controlled room temperature.

• **Beyond-Use Date**

Oral Suspension in Ora-Plus/Ora-Sweet SF: NMT 90 days after the date on which it was compounded when stored in a refrigerator or at controlled room temperature

Oral Suspension in PCCA SuspendIt: NMT 180 days after the date on which it was compounded when stored in a refrigerator or at controlled room temperature. This formulation meets the requirements in *Antimicrobial Effectiveness Testing* ⟨51⟩.

• **Labeling:** Label it to indicate that it is to be well shaken before use and to state the *Beyond-Use Date*.

• **USP Reference Standards** ⟨11⟩

USP Hydroxychloroquine Sulfate RS▲ (USP 1-Aug-2023)

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
HYDROXYCHLOROQUINE SULFATE COMPOUNDED ORAL SUSPENSION	Brian Serumaga Science Program Manager	CMP2020 Compounding 2020
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CMP2020 Compounding 2020

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