

Hydroxychloroquine (All Populations Monograph)

Indications/Dosage

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Labeled

- malaria
- malaria prophylaxis

- rheumatoid arthritis
- systemic lupus erythematosus (SLE)

Off-Label, Recommended

- coronavirus disease 2019 (COVID-19) †
- lupus nephritis †
- polymorphous light eruption †
- † Off-label indication

severe acute respiratory syndrome coronavirus
2 (SARS-CoV-2) infection †

Per the manufacturer, this drug has been shown to be active against most strains of the following microorganisms either in vitro and/or in clinical infections:

Plasmodium falciparum, Plasmodium malariae, Plasmodium ovale, Plasmodium vivax.

NOTE: The safety and effectiveness in treating clinical infections due to organisms with in vitro data only have not been established in adequate and well-controlled clinical trials.

This drug may also have activity against the following microorganisms:

severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

NOTE: Some organisms may not have been adequately studied during clinical trials; therefore, exclusion from this list does not necessarily negate the drug's activity against the organism.

For the treatment of malaria due to susceptible strains of *P. falciparum*, *P. knowlesi†*, *P. malariae*, *P. ovale*, and *P. vivax*

Oral dosage

Adults

13 mg (10 mg base)/kg/dose [Max: 800 mg (620 mg base)/dose] PO, then 6.5 mg (5 mg base)/kg/dose [Max: 400 mg (310 mg base)/dose] PO at 6, 24, and 48 hours after the initial dose.[41806] [64059] For P. vivax or P. ovale, give in combination with primaquine phosphate or tafenoquine. Guidelines recommend hydroxychloroquine for uncomplicated malaria in patients with chloroquine-sensitive P. falciparum or P. vivax or in all patients with P. malariae, P. knowlesi, or P. ovale.[64059]

• Infants, Children, and Adolescents

13 mg (10 mg base)/kg/dose [Max: 800 mg (620 mg base)/dose] PO, then 6.5 mg (5 mg base)/kg/dose [Max: 400 mg (310 mg base)/dose] PO at 6, 24, and 48 hours after the initial dose.[41806] [63245] [64059] For P. vivax or P. ovale, give in combination with primaguine phosphate or tafenoguine (16 years and older). Guidelines recommend hydroxychloroquine for uncomplicated malaria in patients with chloroquine-sensitive P. falciparum or P. vivax or in all patients with P. malariae, P. knowlesi, or P. ovale. [64059]

For malaria prophylaxis in areas where chloroquine-resistance has not been reported

Oral dosage

Adults

6.5 mg (5 mg base)/kg/dose [Max: 400 mg (310 mg base)/dose] PO weekly on the same day of each week, starting 1 to 2 weeks before entering the endemic area and continuing for 4 weeks after leaving the area.[41806] [63990] Guidelines suggest hydroxychloroguine as an alternative to chloroguine.[63990]

• Infants, Children, and Adolescents

6.5 mg (5 mg base)/kg/dose [Max: 400 mg (310 mg base)/dose] PO weekly on the same day of each week, starting 1 to 2 weeks before entering the endemic area and continuing for 4 weeks after leaving the area.[41806] [63245] [63990] Guidelines suggest hydroxychloroquine as an alternative to chloroquine. [63990]

For the treatment of systemic lupus erythematosus (SLE)

Oral dosage

Adults

200 mg (155 mg base) to 400 mg (310 mg base) PO per day, administered as a single dose or in 2 divided doses.[41806] Antimalarials and/or glucocorticoids are of benefit and may be used for the treatment of SLE without major organ manifestations; however, judicious use of hydroxychloroquine is recommended.[34349]

Children† and Adolescents†

5 mg/kg/day PO (Max: 400 mg/day, 310 mg base/day) has been used.[34355]

For the treatment of rheumatoid arthritis

Oral dosage

Adults

400 mg (310 mg base) to 600 mg (465 mg base) PO daily, administered as a single daily dose or in 2 divided doses. Do not exceed 600 mg/day (465 mg base/day) or 6.5 mg/kg/day (5 mg base/kg/day), whichever is lower. Side effects may require a temporary initial dose reduction. After a clinical response is obtained, reduce the dose by 50%; continue 200 mg (155 mg base) to 400 mg (310 mg base) PO daily, administered as a single daily dose or in 2 divided doses. Corticosteroids and salicylates may be used in conjunction, and dosages may generally be decreased gradually or eliminated after hydroxychloroguine maintenance is achieved.[41806] A clinical study compared hydroxychloroquine 400 mg PO once daily vs. placebo in 101 patients over a period of 24 weeks. Significant improvements in joint score, pain, and grip strength but not erythrocyte sedimentation rate (ESR) were seen in the active drug group.[23560] In another study, patients were given 200 mg PO once daily, and if no side effects were noted after 2 weeks, the dose was increased to 7 mg/kg/day (Max: 400 mg/day) PO. After 36 weeks, synovitis, pain, and mobility were significantly improved relative to placebo. [24388] In another study, 200 mg PO twice daily for 2 years led to an ACR50 in 10 of 30 patients who were DMARD-naive with a mean disease duration of 5.8 months +/- 3.8 months.[34328] Clinical practice guidelines recommend DMARD monotherapy such as hydroxychloroquine for patients with a disease duration less than 6 months and low disease activity regardless of poor prognostic feature presence or moderate disease activity without poor prognostic features and is an option for high disease activity without poor prognostic features. For established disease, hydroxychloroquine monotherapy is only recommended for patients with low disease activity without poor prognostic features. The treatment goal is low disease activity or remission. [56233]

for use in combination with methotrexate† for rheumatoid arthritis

Oral dosage

Adults

200 mg PO twice daily plus methotrexate 7.5 to 17.5 mg PO once weekly for 2 years led to an ACR20 in 60% of 58 patients with active disease and a disease duration of at least 6 months. Thirty-three of the 58 patients had an inadequate response to previous methotrexate monotherapy, and 25 patients were methotrexate naive.[34327] Clinical practice guidelines recommend use of combination DMARDs such as hydroxychloroquine plus methotrexate for patients with a disease duration less than 6 months and moderate disease activity and poor prognostic features and is an option for high disease activity and poor prognostic features. The use of hydroxychloroquine plus methotrexate is also an option for patients with high disease activity without poor prognostic features. For established disease, DMARD combination therapy is an option for patients with low disease activity and poor prognostic features or with moderate or high disease activity regardless of poor prognostic feature presence. If moderate or high disease activity exists after 3 months of combination DMARDs, an option is to add or switch DMARDs and reassess in another 3 months. For patients with low disease activity without poor prognostic features who have moderate or high disease activity after 3 months of DMARD monotherapy, the addition of methotrexate is an option.[56233]

for use in combination with methotrexate and sulfasalazine† for rheumatoid arthritis

Oral dosage

Adults

200 mg PO twice daily plus sulfasalazine 500 to 1000 mg PO twice daily and methotrexate 7.5 to 17.5 mg PO once weekly for 2 years led to an ACR20 in 78% of 58 patients with active disease and a disease duration of at least 6 months. About half of the patients had an inadequate response to previous methotrexate monotherapy, and about half of the patients were methotrexate naive.[34327] For patients with a disease duration less than 6 months, clinical practice guidelines recommend use of combination DMARDs such as sulfasalazine, methotrexate, and hydroxychloroquine for those with moderate disease activity and poor prognostic features and is an option for those with high disease activity and poor prognostic features. For established disease, DMARD combination therapy is an option for patients with low disease activity and poor prognostic features or with moderate or high disease activity regardless of poor prognostic feature presence. If moderate or high disease activity exists after 3 months of combination DMARDs, an option is to add or switch DMARDs and reassess in another 3 months.[56233]

for use in combination with sulfasalazine† for rheumatoid arthritis

Oral dosage

Adults

200 mg PO twice daily plus sulfasalazine 500 mg PO twice daily led to at least a 50% improvement in composite symptoms of arthritis at 9 months that was maintained over 2 years in 14 of 35 patients. All patients had RA for at least 6 months and had poor responses to treatment with gold, hydroxychloroguine, penicillamine, sulfasalazine, or methotrexate.[24592] For patients with a disease duration less than 6 months, clinical practice guidelines recommend use of combination DMARDs such as sulfasalazine plus hydroxychloroquine for those with moderate disease activity and poor prognostic features and is an option for those with high disease activity and poor prognostic features. For established disease, DMARD combination therapy is an option for patients with low disease activity and poor prognostic features or with moderate or high disease activity regardless of poor prognostic feature presence. If moderate or high disease activity exists after 3 months of combination DMARDs, an option is to add or switch DMARDs and reassess in another 3 months.[56233]

For the suppression of polymorphous light eruption?

Oral dosage

Adults

200 mg (155 mg base) to 400 mg (310 mg base) PO per day in single or divided doses.[61732]

For the treatment of lupus nephritis†

Oral dosage

Adults

200 mg (155 mg base) to 400 mg (310 mg base) PO per day for all patients (except pregnant patients) with no evidence of disease activity.[52522] An average dose of 200 mg/day PO led to a longer time to renal damage (HR 0.12, 95% CI, 0.02 to 0.97, p = 0.0464), which was defined as at least 1 of the following that lasted for at least 6 months: estimated or measured glomerular filtration rate less than 50%, 24-hour proteinuria of 3.5 g or more, and end-stage renal disease regardless of dialysis or transplantation. Of note, among hydroxychloroquine recipients, the highest average daily dose was 384 mg among those who did not develop renal damage as compared with 331 mg for those who did.[52526]

INVESTIGATIONAL USE: For the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection†, the virus that causes coronavirus disease

2019 (COVID-19)†

Oral dosage

Adults weighing 50 kg or more

Available data are limited, and efficacy has not been established. 800 mg PO on day 1 then 400 mg PO daily for 4 to 7 days in patients in which enrollment in clinical trials is not feasible is suggested by the FDA in the Emergency Use Authorization (EUA) statement. [65171] [65173] Other dosing regimens, alone and in combination, are being evaluated, including 400 mg PO twice daily on day 1 then 200 mg PO twice daily for 4 days; 200 mg PO twice daily for 5 to 20 days; and 200 mg PO three times daily for 10 days. In vitro data suggests that hydroxychloroquine may be more potent than chloroquine for SARS-CoV-2. The mechanism of action is likely similar to that of chloroquine. Limited data suggest that chloroquine may inhibit the exacerbation of pneumonia, improve lung imaging findings, promote virusnegative conversion, and shorten the disease course. [65119] [65121] [65123] [65124] [65125] [65147] [65148]

Adults weighing less than 50 kg

Available data are limited, and efficacy has not been established. Dosing regimens, alone and in combination, are being evaluated, including 400 mg PO twice daily on day 1 then 200 mg PO twice daily for 4 days; 200 mg PO twice daily for 5 to 20 days; and 200 mg PO three times daily for 10 days. In vitro data suggests that hydroxychloroquine may be more potent than chloroquine for SARS-CoV-2. The mechanism of action is likely similar to that of chloroquine. Limited data suggest that chloroquine may inhibit the exacerbation of pneumonia, improve lung imaging findings, promote virus-negative conversion, and shorten the disease course.[65119] [65121] [65123] [65124] [65125] [65147] [65148]

Adolescents weighing 50 kg or more

Available data are limited, and efficacy has not been established. 800 mg PO on day 1 then 400 mg PO daily for 4 to 7 days in patients in which enrollment in clinical trials is not feasible is suggested by the FDA in the Emergency Use Authorization (EUA) statement.[65171] [65173] Based on extrapolation from pediatric dosing for other indications and comparative doses to adult dosing regimens suggested for COVID-19, doses of 6.5 mg (5 mg base)/kg/dose PO every 12 hours [Max: 400 mg/dose (310 mg base/dose)] for 2 doses, then 3.25 mg (2.5 mg base)/kg/dose every 12 hours [Max: 200 mg/dose (155 mg base/dose)] are being used in limited pediatric dosing protocols.[41806] [63245] [65159] A 5- to 20-day course is being used in adult patients.[65121] [65123] [65148]

Adolescents weighing less than 50 kg

Efficacy and optimal dosing in pediatric patients are not established; however, based on extrapolation from pediatric dosing for other indications and comparative doses to adult dosing regimens suggested for COVID-19, doses of 6.5 mg (5 mg base)/kg/dose PO every 12 hours [Max: 400 mg/dose (310 mg base/dose)] for 2 doses, then 3.25 mg (2.5 mg base)/kg/dose every 12 hours [Max: 200 mg/dose (155 mg base/dose)] are being used in limited pediatric dosing protocols.[41806] [63245] [65159] A 5- to 20-day course is being used in adult patients.[65121] [65123] [65148]

Infants and Children

Efficacy and optimal dosing in pediatric patients are not established; however, based on extrapolation from pediatric dosing for other indications and comparative doses to adult dosing regimens suggested for COVID-19, doses of 6.5 mg (5 mg base)/kg/dose PO every 12 hours [Max: 400 mg/dose (310 mg base/dose)] for 2 doses, then 3.25 mg (2.5 mg base)/kg/dose every 12 hours [Max: 200 mg/dose (155 mg base/dose)] are being used in limited pediatric dosing protocols.[41806] [63245] [65159] A 5- to 20-day course is being used in adult patients.[65121] [65123] [65148]

Maximum Dosage Limits

Adults

800 mg/dose (620 mg base/dose) PO for malaria up to a total of 2 g (1.55 g base) PO in 48 hours; 400 mg/week (310 mg base/week) PO for malaria prophylaxis; 600 mg/day (465 mg base/day) PO for other indications.

• Geriatric

800 mg/dose (620 mg base/dose) PO for malaria up to a total of 2 g (1.55 g base) PO in 48 hours; 400 mg/week (310 mg base/week) PO for malaria prophylaxis; 600 mg/day (465 mg base/day) PO for other indications.

Adolescents

13 mg/kg/dose (10 mg base/kg/dose) [Max: 800 mg (620 mg base)] PO for malaria up to a total of 32.5 mg/kg (25 mg base/kg) [Max: 2 g (1.55 g base)] PO in 48 hours; 6.5 mg/kg/week (5 mg base/kg/week) [Max: 400 mg/week (310 mg base/week)] PO for malaria prophylaxis.

• Children

13 mg/kg/dose (10 mg base/kg/dose) [Max: 800 mg (620 mg base)] PO for malaria up to a total of 32.5 mg/kg (25 mg base/kg) [Max: 2 g (1.55 g base)] PO in 48 hours; 6.5 mg/kg/week (5 mg base/kg/week) [Max: 400 mg/week (310 mg base/week)] PO for malaria prophylaxis.

Infants

13 mg/kg/dose (10 mg base/kg/dose) PO for malaria up to a total of 32.5 mg/kg (25 mg base/kg) PO in 48 hours; 6.5 mg/kg/week (5 mg base/kg/week) PO for malaria prophylaxis.

Neonates

Safety and efficacy have not been established.

Patients with Hepatic Impairment Dosing

A dosage reduction may be necessary in patients with hepatic disease or those taking concomitant medications known to affect the liver. However, no specific dosage adjustment guidelines are available for patients with hepatic impairment.[41806]

Patients with Renal Impairment Dosing

A dosage adjustment is not required in patients with renal impairment. However, a dosage reduction may be necessary in patients with renal disease or those taking concomitant medications known to affect the kidney. No specific dosage adjustment guidelines are available for patients with renal impairment.[41806]

† Off-label indication

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How Supplied

Hydroxychloroquine Sulfate Oral tablet

Hydroxychloroquine Sulfate 200mg Tablet (65162-0610) (Akyma Pharmaceuticals, a subsidiary of Amneal Pharmaceuticals) (off market)

Hydroxychloroquine Sulfate 200mg Tablet (68084-0269) (American Health Packaging)



Hydroxychloroquine Sulfate 200mg Tablet (69238-1544) (Amneal Pharmaceuticals LLC)

Hydroxychloroquine Sulfate 200mg Tablet (42291-0320) (AvKARE, Inc.) (off market)



Hydroxychloroquine Sulfate 200mg Tablet (42291-0318) (AvKARE, Inc.) (off market)



Hydroxychloroquine Sulfate 200mg Tablet (10544-0578) (Blenheim Pharmacal, Inc.) (off market)



Hydroxychloroquine Sulfate 200mg Tablet (43598-0721) (Dr. Reddy's Laboratories, Inc.)

Hydroxychloroguine Sulfate 200mg Tablet (00143-2128) (Hikma Pharmaceuticals USA Inc.) (off market)

Hydroxychloroquine Sulfate 200mg Tablet (00904-5107) (Major Pharmaceuticals Inc, a Harvard Drug Group Company) (off market)

Hydroxychloroquine Sulfate 200mg Tablet (00904-6508) (Major Pharmaceuticals Inc, a Harvard Drug Group Company)



Hydroxychloroquine Sulfate 200mg Tablet (00904-6884) (Major Pharmaceuticals Inc, a Harvard Drug Group Company)



Hydroxychloroquine Sulfate 200mg Tablet (52555-0642) (Martec Pharmaceuticals Inc) (off market)

Hydroxychloroquine Sulfate 200mg Tablet (63739-0777) (McKesson Packaging)



3/31/2020 Clinical Pharmacology powered by ClinicalKey Hydroxychloroquine Sulfate Oral tablet Hydroxychloroquine Sulfate 200mg Tablet (42292-0011) (Mylan Institutional LLC) Hydroxychloroquine Sulfate 200mg Tablet (00378-0373) (Mylan Pharmaceuticals Inc.) Hydroxychloroquine Sulfate 200mg Tablet (16714-0474) (Northstar Rx LLC) Hydroxychloroquine Sulfate 200mg Tablet (16714-0753) (Northstar Rx LLC) Hydroxychloroquine Sulfate 200mg Tablet (16714-0110) (Northstar Rx LLC) Hydroxychloroquine Sulfate 200mg Tablet (72789-0026) (PD-Rx Pharmaceuticals, Inc.) PLAQUENIL Hydroxychloroquine Sulfate 200mg Tablet (66993-0057) (Prasco Laboratories) Hydroxychloroquine Sulfate 200mg Tablet (17236-0610) (R&S Northeast, LLC, formerly Dixon-Shane Drug Company) (off market) Hydroxychloroquine Sulfate 200mg Tablet (42385-0927) (Rising Pharmaceuticals Inc) Hydroxychloroquine Sulfate 200mg Tablet (00781-1407) (Sandoz Inc. a Novartis Company) (off market) Hydroxychloroquine Sulfate 200mg Tablet (00781-5994) (Sandoz Inc. a Novartis Company)

Hydroxychloroquine Sulfate 200mg Tablet (62269-0250) (Sandoz, Inc. a Novartis Company) (off market)

Hydroxychloroquine Sulfate 200mg Tablet (00955-0790) (Sanofi U.S. LLC) (off market)

Hydroxychloroguine Sulfate 200mg Tablet (00677-1590) (Sun Pharmaceutical Industries, Inc.) (off market)

Hydroxychloroquine Sulfate Oral tablet Hydroxychloroquine Sulfate 200mg Tablet (63304-0296) (Sun Pharmaceutical Industries, Inc.) Hydroxychloroquine Sulfate 200mg Tablet (57664-0761) (Sun Pharmaceutical Industries, Inc.) Hydroxychloroquine Sulfate 200mg Tablet (00093-9774) (Teva Pharmaceuticals USA) (off market) Hydroxychloroquine Sulfate 200mg Tablet (52544-0698) (Teva/Actavis US) (off market) Hydroxychloroquine Sulfate 200mg Tablet (00591-0698) (Teva/Actavis US) (off market) Hydroxychloroquine Sulfate 200mg Tablet (00591-3041) (Teva/Actavis US) Hydroxychloroquine Sulfate 200mg Tablet (00955-0790) (Winthrop U.S., a business of Sanofi-Aventis) (off market) Hydroxychloroquine Sulfate 200mg Tablet (68382-0096) (Zydus Pharmaceuticals (USA) Inc.) Hydroxychloroquine Sulfate 200mg Tablet (Almus) (00378-0373) (Mylan Pharmaceuticals Inc.) PLAGUENIL Plaquenil 200mg Tablet (42291-0335) (AvKARE, Inc.) (off market)

Clinical Pharmacology powered by ClinicalKey		
Hydroxychloroquine Sulfate Oral tablet		
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Plaquenil 200mg Tablet (59212-0562) (Concordia F	harmaceuticals Inc.)	PLACUENIL 0 2005 GS
Plaquenil 200mg Tablet (00024-1562) (COVIS Pharmarket)	maceuticals Inc) (off	PLAQUENIL © 2005 GS
Plaquenil 200mg Tablet (24987-0562) (COVIS Pharmarket)	maceuticals Inc) (off	PLACUENIL © 2005 GS
Plaquenil 200mg Tablet (00024-1562) (Sanofi U.S.	LLC) (off market)	PLACUENIL © 2005 GS
Quineprox 200mg Tablet (52761-0377) (Genderm Corp) (off market)		

Description/Classification

Description

Hydroxychloroquine is an oral disease-modifying antirheumatic drug (DMARD) used to treat rheumatoid arthritis and systemic lupus erythematosus. It also is used to prevent and treat malaria. Irreversible retinal damage has been observed with use, and postmarketing cases of life-threatening and fatal cardiomyopathy, including ventricular arrhythmias and torsade de pointes, have been reported.[41806] Hydroxychloroquine was FDA-approved in 1955.

Updates for coronavirus disease 2019 (COVID-19):

Available data are limited. The FDA has issued an Emergency Use Authorization (EUA) for the use of hydroxychloroquine to treat COVID-19 patients for whom clinical trial participation is not feasible. [65171] [65173] Preliminary data suggest hydroxychloroquine may have clinical benefit in the treatment of COVID-19 due to SARS-CoV-2. In an open-label, non-randomized clinical trial (n = 26), the proportion of patients that had negative PCR results significantly differed between treated patients and controls. On day 6, 70% of hydroxychloroquine-treated patients were virologically cured compared to 12.5% in the control group. [65147] Additional data regarding clinical efficacy for COVID-19 are being evaluated. [65123][65148]

Classifications

- General Anti-infectives Systemic
 - o Antiparasitic Agents, Insecticides, and Repellants
 - Antiprotozoals
 - Antimalarials
- Musculo-Skeletal System
 - o Antiinflammatory Agents and Antirheumatic Agents
 - Antiinflammatory and Antirheumatic Agents
 - Other Antiinflammatory and Antirheumatic Agents

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Administration Information

General Administration Information

For storage information, see the specific product information within the How Supplied section.

Route-Specific Administration

Oral Administration

• Administer with meals or a glass of milk to minimize gastric indigestion or irritation.[41806]

Oral Solid Formulations

• Crushing or dividing hydroxychloroquine tablets is not recommended per the FDA-approved product labeling.[41806]

Extemporaneous Compounding-Oral

Extemporaneous 25 mg/mL oral suspension (using tablets)

- Remove the coating of hydroxychloroquine tablets, if necessary, with a towel moistened with alcohol.
- Crush fifteen 200 mg hydroxychloroquine tablets into a fine powder in a mortar.
- Add approximately 15 mL of the vehicle (e.g., Oral Mix or Oral Mix SF) to the mortar and levigate to form a fine paste.
- Add the vehicle in geometric portions almost to volume and mix thoroughly after each addition.
- Transfer the contents of the mortar to a graduated cylinder.
- Rinse the mortar and pestle using a small amount of vehicle and transfer to the graduated cylinder.
- Add enough vehicle to bring the final volume to 120 mL and transfer to an amber bottle.
- Storage: The suspension is stable for 112 days under refrigeration (4 degrees C) or at room temperature (25 degrees C).[65138] [65145]

Compounding Drug Information

From Trissel's 2™ Clinical Pharmaceutics Database

Hydroxychloroquine sulfate

1. Identity/Properties

Hydroxychloroquine sulfate is a white to almost white, odorless crystalline powder having a bitter taste. Hydroxychloroquine sulfate 100 mg is approximately equivalent to 77 mg of the base. Solubility: Hydroxychloroquine sulfate has a solubility of about 200 mg/mL in water but is

practically insoluble in ethanol. pH: A 1% hydroxychloroquine sulfate solution in water has a pH between 3.5 and 5.5. Tablet Dispersion: Martin et al. reported that commercial oral 200-mg tablets of hydroxychloroquine sulfate (Plaquenil) did not completely disperse in five minutes in 20 mL of water at 20degree C with swirling, even when halved.

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Martin TP, Hayes P, Collins DM. Tablet dispersion as an alternative to formulation of oral liquid dosage forms. Austral J Hosp Pharm. 1993; 23:378-86

McEvoy GK (ed). AHFS Drug Information (current edition). Bethesda, MD: American Society of Health-System Pharmacists.

2. General Stability Info

Hydroxychloroquine sulfate tablets should be packaged in tight, light-resistant containers and stored at controlled room temperature.

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3. Oral Liquid

Pesko reported on an extemporaneous suspension of hydroxychloroguine. Fifteen hydroxychloroquine sulfate 200-mg tablets were rubbed with a towel moistened with alcohol to remove the coating. The tablets were ground to a fine powder and levigated to a paste with 15 mL of Ora-Plus suspending agent. An additional 45 mL of the suspending agent was added and the mixture was brought to 120 mL with water for irrigation, yielding a suspension containing hydroxychloroquine sulfate 25 mg/mL. The author noted that sugar and artificial flavorings should not be added to the product. A 30-day expiration period was recommended, although stability testing was not performed.

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Adverse Reactions

- abdominal pain
- acute generalized exanthematous pustulosis (AGEP)
- agranulocytosis
- alopecia
- anemia
- angioedema
- anorexia
- aplastic anemia
- ataxia
- AV block
- blurred vision
- bronchospasm
- bullous rash
- bundle-branch block
- cardiomyopathy
- corneal deposits
- corneal edema
- corneal opacification
- diarrhea
- dizziness
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
- dyskinesia
- dystonic reaction
- · emotional lability
- erythema multiforme
- exfoliative dermatitis
- fatigue
- hair discoloration
- headache
- hearing loss
- heart failure
- hemolysis
- hepatic failure
- hypoglycemia

- irritability
- leukopenia
- macular degeneration
- myopathy
- nausea
- nightmares
- nystagmus
- photophobia
- photosensitivity
- porphyria
- pruritus
- psoriasis
- psychosis
- pulmonary hypertension
- QT prolongation
- rash
- retinal pigment changes
- retinopathy
- scotomata
- seizures
- skin discoloration
- Stevens-Johnson syndrome
- suicidal ideation
- thrombocytopenia
- tinnitus
- torsade de pointes
- toxic epidermal necrolysis
- tremor
- urticaria
- ventricular fibrillation
- ventricular tachycardia
- vertigo
- visual impairment
- vomiting
- weakness
- weight loss

Hydroxychloroquine can cause ocular toxicity including irreversible retinopathy with retinal pigment changes (bull's eye appearance), visual field defects (paracentral scotomata) and visual impairment (visual acuity), maculopathies (macular degeneration), decreased dark adaptation, color vision abnormalities, and corneal changes (corneal edema and corneal opacification) including corneal deposits of the drug with or without accompanying symptoms (halo around lights, photophobia, blurred vision). A baseline ocular exam should be performed within the first year of hydroxychloroquine treatment. This baseline exam should include best corrected distance visual acuity (BCVA), an automated threshold visual field (VF) of the central 10 degrees (with retesting if an abnormality is noted), and spectral domain ocular coherence tomography (SD-OCT). Annual exams are recommended for patients with significant risk factors for retinal damage. For patients without significant risk factors, annual exams may be deferred until 5 years of treatment. In Asian patients, retinal toxicity may first be noticed outside the macula; therefore, visual field testing should be performed in the central 24 degrees instead of the central 10 degrees. Discontinue hydroxychloroguine if ocular toxicity is suspected and monitor the patient closely for ocular disease (i.e., retinal changes) and visual disturbance which may progress even after discontinuation of therapy.[41806]

Allergic and dermatologic reactions have been reported with the use of hydroxychloroquine. These include urticaria, angioedema, bronchospasm, rash (unspecified), pruritus, pigmentations disorders in the skin (skin discoloration) and mucous membranes, hair color changes (hair discoloration), alopecia, drug reaction with eosinophilia and systemic symptoms (DRESS), photosensitivity, and exfoliative dermatitis. Dermatitis bullous eruptions (bullous rash), including erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis (TEN) have also been reported.[41806]

Hydroxychloroquine may precipitate a severe attack of psoriasis that may be associated with pyrexia and hyperleukocytosis. Hydroxychloroquine may also exacerbate or precipitate porphyria, which has been reported with hydroxychloroquine or other 4-aminoquinoline use.[41806]

Hydroxychloroquine has been associated with acute generalized exanthematous pustulosis (AGEP).[41806] The nonfollicular, pustular, erythematous rash starts suddenly and is associated with fever above 38 degrees C. Drugs are the main cause of AGEP. A period of 2 to 3 weeks after an inciting drug exposure appears necessary for a first episode of AGEP. Unintentional reexposure may cause a second episode within 2 days.[27736]

Sensorimotor disorder or skeletal muscle myopathy or neuromyopathy (neuropathy) leading to progressive weakness and atrophy of proximal muscle groups, depression of tendon reflexes, and abnormal nerve conduction has been reported. Muscle and nerve biopsies have been associated with curvilinear bodies and muscle fiber atrophy with vacuolar changes. Assess muscle strength and deep tendon reflexes periodically in patients on long-term therapy.[41806]

Hematological adverse reactions of hydroxychloroquine or other 4-aminoquinolines include bone marrow failure, anemia, aplastic anemia, agranulocytosis, leukopenia, and thrombocytopenia. Hemolysis was reported in individuals with glucose-6-phosphate dehydrogenase (G-6-PD) deficiency. Monitor blood cell counts periodically if patients are given prolonged hydroxychloroquine therapy. If any severe blood disorder, such as aplastic anemia, agranulocytosis, leukopenia, or thrombocytopenia which is not attributable to the disease under treatment occurs, consider discontinuing hydroxychloroquine.[41806]

Deafness (hearing loss), nerve deafness, and tinnitus have been reported with hydroxychloroquine or other 4aminoquinolines.[41806]

Cardiomyopathy, which may result in heart failure and in some cases a fatal outcome, has been noted in postmarketing reports of hydroxychloroquine or other 4-aminoquinolines. Patients may present with AV block, pulmonary hypertension, sick sinus syndrome, or with cardiac complications. ECG finding may include AV, right, or left bundle-branch block. Additionally, hydroxychloroquine causes QT prolongation. Ventricular arrhythmias (i.e., ventricular fibrillation and ventricular tachycardia) and torsade de pointes have been reported in patients taking hydroxychloroquine. Monitor ECG during hydroxychloroquine therapy. Chronic toxicity should be considered when conduction disorders (bundle-branch block, AV block) or biventricular hypertrophy are diagnosed. If cardiotoxicity is suspected, prompt discontinuation of hydroxychloroquine may prevent lifethreatening cardiac complications.[41806]

Adverse gastrointestinal (GI) effects reported with hydroxychloroquine or other 4-aminoquinolines include nausea, vomiting, abdominal pain, diarrhea, and decreased appetite (anorexia). These effects are associated with oral administration and can be minimized by taking hydroxychloroquine with food. Abnormal liver function tests and acute hepatic failure have also been reported.[41806]

Suicidal ideation/behavior has been rarely reported in patients treated with hydroxychloroquine. Other CNS or psychiatric adverse reactions reported with hydroxychloroquine or other 4-aminoquinolines include headache, dizziness, affect/emotional lability, irritability, psychosis, nervousness, nightmares, vertigo, nystagmus, ataxia, seizures, and extrapyramidal disorders such as dystonic reaction, dyskinesia, and tremor.[41806]

Weight loss and fatigue have been reported with the use of hydroxychloroquine or other 4-aminoquinolines. [41806]

Hydroxychloroquine has been shown to cause severe hypoglycemia including loss of consciousness that could be life threatening in patients treated with or without antidiabetic medications. Monitor blood glucose and adjust treatment as necessary in patients presenting with clinical symptoms of hypoglycemia during hydroxychloroquine treatment.[41806]

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Contraindications/Precautions

Absolute contraindications are italicized.

- accidental exposure
- alcoholism
- Asian patients
- bradycardia
- breast-feeding
- cardiac arrhythmias
- cardiac disease
- children
- coronary artery disease
- diabetes mellitus
- females
- G6PD deficiency
- geriatric
- GI disease
- heart failure
- hepatic disease

- hypertension
- hypocalcemia
- hypoglycemia
- hypokalemia
- hypomagnesemia
- infants
- long QT syndrome
- malnutrition
- myocardial infarction
- myopathy
- neonates
- neurological disease
- ocular disease
- porphyria
- pregnancy
- psoriasis

- QT prolongation
- · renal disease

- thyroid disease
- visual disturbance

Hydroxychloroquine is contraindicated in patients with known hypersensitivity to 4-aminoquinoline compounds. [41806]

Severe and irreversible retinal damage has been reported with the use of hydroxychloroquine. Risk factors for retinal damage include daily doses more than 6.5 mg/kg (5 mg/kg base) of actual body weight, durations of use greater than 5 years, subnormal glomerular filtration, use of concomitant drugs such as tamoxifen, and concurrent macular disease. A baseline ocular exam should be performed within the first year of hydroxychloroquine treatment. This baseline exam should include best corrected distance visual acuity (BCVA), an automated threshold visual field (VF) of the central 10 degrees (with retesting if an abnormality is noted), and spectral domain ocular coherence tomography (SD-OCT). Annual exams are recommended for patients with significant risk factors for retinal damage. For patients without significant risk factors, annual exams may be deferred until 5 years of treatment. In Asian patients, retinal toxicity may first be noticed outside the macula; therefore, visual field testing should be performed in the central 24 degrees instead of the central 10 degrees. Discontinue hydroxychloroquine if ocular toxicity is suspected and monitor the patient closely for ocular disease (i.e., retinal changes) and visual disturbance which may progress even after discontinuation of therapy.[41806]

Hydroxychloroquine should be used with extreme caution in patients with psoriasis or porphyria because it has been shown to precipitate severe attacks. Use hydroxychloroquine in patients with these conditions only if the potential benefit to the patient outweighs the possible risk.[41806]

Hydroxychloroquine should be used with caution in patients with hepatic disease, a history of alcoholism, or in conjunction with known hepatotoxic drugs. A dosage reduction may be necessary in patients with hepatic disease and in those taking medicines known to affect the liver.[41806]

Hydroxychloroquine can cause gastric irritation and should be used with caution in patients with GI disease. It can be taken with meals or milk to minimize gastric irritation.[41806]

Administer hydroxychloroquine with caution in patients with glucose-6-phosphate dehydrogenase deficiency (G6PD deficiency) due to the risk of hemolysis.[41806]

Hydroxychloroquine should be used with caution in patients with neurological disease and myopathy. Skeletal muscle myopathy or neuropathy leading to progressive weakness and atrophy of proximal muscle groups, depressed tendon reflexes, and abnormal nerve conduction have been reported. Assess muscle strength and deep tendon reflexes periodically in patients on long-term therapy with hydroxychloroquine.[41806]

The safety and efficacy of the chronic use of hydroxychloroguine for systemic lupus erythematosus and juvenile idiopathic arthritis in children and infants have not been established. Children are especially sensitive to the 4aminoquinoline compounds. Fatalities have been reported after accidental exposure of chloroquine; some cases involved relatively small doses (e.g., 0.75 g or 1 g in a 3-year-old child). Strongly warn patients to keep hydroxychloroquine out of the reach of pediatric patients, including neonates, infants, children, and adolescents. [41806]

Cases of human pregnancy resulting in live birth to women exposed to hydroxychloroquine have been reported in the literature; no increase in the rate of birth defects has been demonstrated. Embryonic deaths and malformations of anophthalmia and microphthalmia in the offspring have been reported when pregnant rats received large doses of chloroquine. [41806] Guidelines recommend hydroxychloroquine as an alternative to chloroquine as a treatment option for acute malaria and for prophylaxis in pregnant women during all trimesters. [63990] [64059] Hydroxychloroquine may also be appropriate for pregnancies complicated by lupus.[34349] [34358]

Use caution when administering hydroxychloroquine to breast-feeding women. Hydroxychloroquine is excreted in the breast milk, and it is known that infants are extremely sensitive to the toxic effects of 4-aminoquinolines. [41806] Breast milk concentrations ranged from 10.6 to 1392 mcg/L in small studies of women; breast-fed infants would likely receive 0.2 mg/kg or less of hydroxychloroquine.[48476] [48477] [48478] [48479] In infants monitored for up to at least 1 year of age, careful follow-up found no adverse effects on growth, vision, or hearing.[48474] [48475] Previous American Academy of Pediatrics (AAP) recommendations considered hydroxychloroguine as usually compatible with breast-feeding. [27500]

Use hydroxychloroquine with caution in patients with hypoglycemia or diabetes mellitus. Hydroxychloroquine can cause severe, life-threatening hypoglycemia in patients treated with or without antidiabetic medications. Warn patients about the risk of hypoglycemia and the associated clinical signs and symptoms. Monitor blood glucose and adjust treatment as necessary in patients presenting with clinical symptoms of hypoglycemia during hydroxychloroquine treatment.[41806]

Hydroxychloroquine prolongs the QT interval. Obtain a pre-treatment QTc using a standard 12-lead ECG, telemetry, or mobile ECG device. Obtain baseline electrolytes, including calcium, magnesium, and potassium. Determine if the patient is currently on any QT-prolonging medications that can be discontinued. Document high-risk cardiovascular and comorbid conditions. If the baseline QTc is 500 msec or more and/or the patient has an inherent tendency to develop an exaggerated QTc response (i.e., change of 60 msec or more), correct contributing electrolyte abnormalities, review and discontinue other unnecessary QTc prolonging medications, and proceed with close QTc surveillance. Obtain an initial on-therapy QTc approximately 2 to 4 hours after the first dose and then again at 48 and 96 hours after treatment initiation. If the baseline OTc is 460 to 499 msec (prepubertal), 470 to 499 msec (postpubertal males), or 480 to 499 msec (postpubertal females), correct contributing electrolyte abnormalities, review and discontinue other unnecessary OTc prolonging medications, and obtain an initial on-therapy QTc 48 and 96 hours after treatment initiation. If the baseline QTc is less than 460 msec (prepubertal), less than 470 msec (postpubertal males), or less than 480 msec (postpubertal females), correct electrolyte abnormalities and obtain an initial on-therapy QTc 48 and 96 hours after treatment initiation. [65170] Use hydroxychloroguine with caution in patients with cardiac disease or other conditions that may increase the risk of QT prolongation including cardiac arrhythmias, congenital long QT syndrome, heart failure, bradycardia, myocardial infarction, hypertension, coronary artery disease, hypomagnesemia, hypokalemia, hypocalcemia, or in patients receiving medications known to prolong the QT interval or cause electrolyte imbalances. Females, geriatric patients, patients with diabetes, thyroid disease, malnutrition, liver impairment, or those who drink alcohol to excess may also be at increased risk for QT prolongation.[28432] [28457] [41806] [56592] [56959] [56961] [56963] Consider chronic toxicity when conduction disorders (bundle-branch block, AV block) or biventricular hypertrophy are diagnosed. If cardiotoxicity is suspected, prompt discontinuation of hydroxychloroquine may prevent life-threatening cardiac complications.[41806]

Because renal clearance of hydroxychloroquine does not correlate with creatinine clearance, dosage adjustments are not required in patients with renal impairment. However, a dosage reduction may be necessary in patients with renal disease or in patients with concomitant medications known to affect the kidney. No specific dosage adjustment guidelines are available for patients with renal impairment.[41806]

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Mechanism of Action

Hydroxychloroquine is a weak base and may exert its antimalarial effect by concentrating in the acid vesicles of the plasmodia and by inhibiting the polymerization of heme. It can also inhibit certain enzymes by its interaction with DNA. Organisms with reduced susceptibilities to chloroquine also show reduced susceptibilities to hydroxychloroquine.[41806]

Although the mechanisms underlying the antiinflammatory and immunomodulatory effects of hydroxychloroquine are unknown, several possible mechanisms of action have been proposed. It is unclear if these mechanisms work similarly for rheumatic and autoimmune diseases. Potential mechanisms include reduced cytokine production, inhibition of immune effector cells, inhibition of platelet function, protection of the cell surface from external disturbances, competitive binding to nucleic acid ligands or toll-like receptors (TLRs), interference with lysosomal function, reduction of leakage of lysosomal enzymes, and interference with endosomal NADPH oxidase (NOX).[41806]_[61727] [61728] [61729]

There are several potential mechanisms by which hydroxychloroquine may be active against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). These include inhibition of viral enzymes or processes such as viral DNA and RNA polymerase, viral protein glycosylation, virus assembly, new virus particle transport, and virus release. Other mechanisms may also involve ACE2 cellular receptor inhibition, acidification at the surface of the cell membrane inhibiting fusion of the virus, and immunomodulation of cytokine release. [61729] [61732] [65120] [65121] [65139] [65140] [65141] [65142] [65143]

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Pharmacokinetics

Hydroxychloroquine is administered orally. It is widely distributed into body tissues, with high concentrations in the bone marrow, liver, kidneys, lungs, adrenal gland, and pituitary gland. Hydroxychloroquine has a high affinity for melanin and thus is concentrated in the choroid and ciliary body of the eye, which may account for the retinal toxicity. Cellular concentrations have been shown to be higher in mononuclear cells than in polymorphonuclear leukocytes.[41806] [61731] [61732]

Hydroxychloroquine is partially metabolized in the liver to 3 metabolites. These include the major metabolite, desethylhydroxychloroquine (DHCQ), as well as desethylchloroquine (DCQ) and bidesethylhydroxychloroquine (BDCQ). Elimination appears to take place in a biphasic manner. Renal clearance of unchanged drug ranges from 16% to 30% and does not correlate with creatinine clearance. The absorption half-life is approximately 3 to 4 hours and the terminal half-life is about 40 to 50 days. Urine concentrations are still detectable several months after single doses. The long-half life is attributed to extensive tissue uptake rather than decreased excretion. [41806] [61731]

Affected cytochrome P450 isoenzymes and drug transporters: none

Route-Specific Pharmacokinetics

• Oral Route

Bioavailability is approximately 74%. Hydroxychloroquine displays linear kinetics. Peak plasma concentrations are achieved in 3 to 4 hours. In rheumatoid arthritis patients, there is a large variability in absorption (30% to 100%) with mean concentrations significantly higher in patients with less disease activity.[41806]

Special Populations

• Renal Impairment

Renal clearance does not correlate with creatinine clearance.[41806]

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Pregnancy/Breast-feeding

Pregnancy

Cases of human pregnancy resulting in live birth to women exposed to hydroxychloroquine have been reported in the literature; no increase in the rate of birth defects has been demonstrated. Embryonic deaths and malformations of anophthalmia and microphthalmia in the offspring have been reported when pregnant rats received large doses of chloroquine. [41806] Guidelines recommend hydroxychloroquine as an alternative to chloroquine as a treatment option for acute malaria and for prophylaxis in pregnant women during all trimesters. [63990] [64059] Hydroxychloroquine may also be appropriate for pregnancies complicated by lupus.[34349] [34358]

Breast-Feeding

Use caution when administering hydroxychloroquine to breast-feeding women. Hydroxychloroquine is excreted in the breast milk, and it is known that infants are extremely sensitive to the toxic effects of 4-aminoquinolines. [41806] Breast milk concentrations ranged from 10.6 to 1392 mcg/L in small studies of women; breast-fed infants would likely receive 0.2 mg/kg or less of hydroxychloroquine.[48476] [48477] [48478] [48479] In infants monitored for up to at least 1 year of age, careful follow-up found no adverse effects on growth, vision, or hearing.[48474] [48475] Previous American Academy of Pediatrics (AAP) recommendations considered hydroxychloroquine as usually compatible with breast-feeding.[27500]

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Interactions

Level 1 (Severe)

- Cisapride
- Dronedarone

- Pimozide
- Thioridazine

Level 2 (Major)

Aclidinium; Formoterol

Albuterol

- Albuterol; Ipratropium
- Alfuzosin
- Amiodarone
- Amitriptyline
- Amitriptyline; Chlordiazepoxide
- Amoxicillin; Clarithromycin; Lansoprazole
- Amoxicillin; Clarithromycin; Omeprazole
- Anagrelide
- Antacids
- Apomorphine
- Arformoterol
- Aripiprazole
- Arsenic Trioxide
- Artemether; Lumefantrine
- Asenapine
- Aspirin, ASA; Citric Acid; Sodium Bicarbonate
- Atomoxetine
- Azithromycin
- Bedaquiline
- Bismuth Subcitrate Potassium; Metronidazole; Tetracycline
- Bismuth Subsalicylate; Metronidazole; Tetracycline
- Budesonide; Formoterol
- Buprenorphine
- Buprenorphine; Naloxone
- Calcium Carbonate
- Calcium Carbonate; Magnesium Hydroxide
- Calcium Carbonate; Risedronate
- Calcium Carbonate; Simethicone
- Ceritinib
- Chloroquine
- Chlorpromazine
- Ciprofloxacin
- Citalopram
- Clarithromycin
- Clofazimine
- Clomipramine
- Clozapine
- Codeine; Phenylephrine; Promethazine
- Codeine; Promethazine
- Crizotinib
- Dasatinib
- Degarelix
- Desflurane
- Desipramine
- Deutetrabenazine
- Dextromethorphan; Promethazine
- Dextromethorphan; Quinidine
- Disopyramide
- Dofetilide
- Dolasetron
- Dolutegravir; Rilpivirine

- Donepezil
- Donepezil; Memantine
- Doxepin
- Droperidol
- Efavirenz
- Efavirenz; Emtricitabine; Tenofovir
- Efavirenz; Lamivudine; Tenofovir Disoproxil Fumarate
- Eliglustat
- Emtricitabine; Rilpivirine; Tenofovir alafenamide
- Emtricitabine; Rilpivirine; Tenofovir disoproxil fumarate
- Encorafenib
- Enflurane
- Entrectinib
- Eribulin
- Erythromycin
- Erythromycin; Sulfisoxazole
- Escitalopram
- Ezogabine
- Fingolimod
- Flecainide
- Fluconazole
- Fluoxetine
- Fluoxetine; Olanzapine
- Fluphenazine
- Fluticasone; Salmeterol
- Fluticasone; Umeclidinium; Vilanterol
- Fluticasone; Vilanterol
- Fluvoxamine
- **Formoterol**
- Formoterol; Mometasone
- Foscarnet
- Gemifloxacin
- Gemtuzumab Ozogamicin
- Gilteritinib
- Glasdegib
- Glycopyrrolate; Formoterol
- Goserelin
- Granisetron
- Halogenated Anesthetics
- Haloperidol
- Halothane
- Histrelin
- Hydroxyzine
- Ibutilide
- Iloperidone
- Imipramine
- Indacaterol
- Indacaterol; Glycopyrrolate
- Inotuzumab Ozogamicin
- Isoflurane
- Itraconazole

- Ivosidenib
- Ketoconazole
- Lanthanum Carbonate
- Lapatinib
- Lefamulin
- Lenvatinib
- Leuprolide
- Leuprolide; Norethindrone
- Levalbuterol
- Levofloxacin
- Lithium
- Lofexidine
- · Long-acting beta-agonists
- Loperamide
- Loperamide; Simethicone
- Lopinavir; Ritonavir
- Macimorelin
- Maprotiline
- Mefloquine
- Meperidine; Promethazine
- Metaproterenol
- Methadone
- Metronidazole
- Midostaurin
- Mifepristone
- Mirtazapine
- Moxifloxacin
- Nilotinib
- Norfloxacin
- Nortriptyline
- Octreotide
- Ofloxacin
- Olanzapine
- Olodaterol
- Omeprazole; Sodium Bicarbonate
- Ondansetron
- Osimertinib
- Oxaliplatin
- Paliperidone
- Panobinostat
- Pasireotide
- Pazopanib
- Penicillamine
- Pentamidine
- Perphenazine
- Perphenazine; Amitriptyline
- Phenylephrine; Promethazine
- Pimavanserin
- Pirbuterol
- **Pitolisant**
- Posaconazole

- Primaquine
- Procainamide
- Prochlorperazine
- Promethazine
- Propafenone
- Protriptyline
- Quetiapine
- Quinidine
- Quinine
- Rabies Vaccine
- Ranolazine
- Ribociclib
- Ribociclib; Letrozole
- Rilpivirine
- Risperidone
- Romidepsin
- Salmeterol
- Saquinavir
- Sertraline
- Sevoflurane
- Short-acting beta-agonists
- Siponimod
- Sodium Bicarbonate
- Solifenacin
- Sorafenib
- Sotalol
- Sunitinib
- **Tacrolimus**
- Tamoxifen
- Telavancin
- Telithromycin
- **Terbutaline**
- Tetrabenazine
- Tiotropium; Olodaterol
- Tolterodine
- Toremifene
- Trazodone
- Tricyclic antidepressants
- Trifluoperazine
- Trimipramine
- Triptorelin
- Umeclidinium; Vilanterol
- Vandetanib
- Vardenafil
- Vemurafenib
- Venlafaxine
- Vigabatrin
- Voriconazole
- Vorinostat Ziprasidone

Level 3 (Moderate)

- Acarbose
- Acetazolamide
- Acetohexamide
- Albiglutide
- Alogliptin
- Alogliptin; Metformin
- Alogliptin; Pioglitazone
- Alpha-glucosidase Inhibitors
- Amobarbital
- Ampicillin
- Atropine; Hyoscyamine; Phenobarbital; Scopolamine
- Belladonna Alkaloids; Ergotamine; Phenobarbital
- Brivaracetam
- Canagliflozin
- Canagliflozin; Metformin
- Carbamazepine
- Chlorpropamide
- Cimetidine
- Clobazam
- Clonazepam
- Clorazepate
- Cyclosporine
- Dapagliflozin
- Dapagliflozin; Metformin
- Dapagliflozin; Saxagliptin
- Diazepam
- Digoxin
- Dipeptidyl Peptidase-4 Inhibitors
- Dulaglutide
- Empagliflozin
- Empagliflozin; Linagliptin
- Empagliflozin; Linagliptin; Metformin
- Empagliflozin; Metformin
- Ertugliflozin
- Ertugliflozin; Metformin
- Ertugliflozin; Sitagliptin
- Eslicarbazepine
- Ethosuximide
- Ethotoin
- Exenatide
- Felbamate
- Fosphenytoin
- Gabapentin
- Glimepiride
- Glimepiride; Pioglitazone
- Glimepiride; Rosiglitazone
- Glipizide
- Glipizide; Metformin
- Glyburide
- Glyburide; Metformin
- Incretin Mimetics
- Insulin Aspart

- Insulin Aspart; Insulin Aspart Protamine
- Insulin Degludec
- Insulin Degludec; Liraglutide
- Insulin Detemir
- Insulin Glargine
- Insulin Glargine; Lixisenatide
- Insulin Glulisine
- Insulin Lispro
- Insulin Lispro; Insulin Lispro Protamine
- Insulin, Inhaled
- **Insulins**
- Isophane Insulin (NPH)
- Lacosamide
- Lamotrigine
- Lente Insulin
- Levetiracetam
- Linagliptin
- Linagliptin; Metformin
- Liraglutide
- Lixisenatide
- Lorazepam
- Meglitinides
- Mephobarbital
- Metformin
- Metformin; Pioglitazone
- Metformin; Repaglinide
- Metformin; Rosiglitazone
- Metformin; Saxagliptin
- Metformin; Sitagliptin
- Methotrexate
- Methsuximide
- Miglitol
- Nateglinide
- Pentobarbital
- Perampanel
- Phenobarbital
- Phentermine; Topiramate
- Phenytoin
- Pioglitazone
- Pramlintide
- Pregabalin
- Primidone
- Regular Insulin
- Regular Insulin; Isophane Insulin (NPH)
- Repaglinide
- Rituximab
- Rituximab; Hyaluronidase
- Rosiglitazone
- Rufinamide
- Saxagliptin
- Semaglutide
- SGLT2 Inhibitors Simvastatin; Sitagliptin
- Sitagliptin

- Sulfonylureas
- Telbivudine
- Thiazolidinediones
- Tiagabine
- Tolazamide

- Tolbutamide
- Topiramate
- Ultralente Insulin
- Valproic Acid, Divalproex Sodium
- Zonisamide

Level 4 (Minor)

• Praziquantel

Acarbose: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the alpha-glucosidase inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Acetazolamide: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine and antiepileptic drugs, such as acetazolamide. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Acetohexamide: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including sulfonylureas, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Aclidinium; Formoterol: (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Betaagonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the OT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

Albiglutide: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the incretin mimetics, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Albuterol: (Major) Avoid coadministration of short-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [33925] [41806] [49951] [51793] [59321] [65157] [65170]

Albuterol; Ipratropium: (Major) Avoid coadministration of short-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Betaagonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at

higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [33925] [41806] [49951] [51793] [59321] [65157] [65170]

Alfuzosin: (Major) Avoid coadministration of alfuzosin and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Alfuzosin may prolong the QT interval in a dosedependent manner. [28261] [41806] [65157] [65170]

Alogliptin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Alogliptin; Metformin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Alogliptin; Pioglitazone: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the thiazolidinediones, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Alpha-glucosidase Inhibitors: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the alpha-glucosidase inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Amiodarone: (Major) Avoid coadministration of amiodarone and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, perform a baseline ECG to assess initial QT interval and determine frequency of subsequent ECG monitoring; also, evaluate baseline electrolytes and correct any abnormalities. Hydroxychloroquine prolongs the QT interval. Amiodarone, a class III antiarrhythmic agent, is associated with a well-established risk of QT prolongation and torsade de pointes (TdP). Although the frequency of TdP is less with amiodarone than with other Class III agents, amiodarone is still associated with a risk of TdP. Due to the extremely long half-life of amiodarone, a drug interaction is possible for days to weeks after discontinuation of amiodarone. [28224] [28432] [28457] [41806] [65157] [65170]

Amitriptyline: (Major) Avoid coadministration of tricyclic antidepressants and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). [28225] [28415] [28416] [41806] [65157] [65170]

Amitriptyline; Chlordiazepoxide: (Major) Avoid coadministration of tricyclic antidepressants and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any nonessential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). [28225] [28415] [28416] [41806] [65157] [65170]

Amobarbital: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine and antiepileptic drugs, such as amobarbital. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Amoxicillin; Clarithromycin; Lansoprazole: (Major) Avoid coadministration of clarithromycin and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any nonessential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Clarithromycin is associated with an established risk for QT prolongation and torsade de pointes (TdP). [28225] [28238] [41806] [65157] [65170]

Amoxicillin; Clarithromycin; Omeprazole: (Major) Avoid coadministration of clarithromycin and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any nonessential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Clarithromycin is associated with an established risk for QT prolongation and torsade de pointes (TdP). [28225] [28238] [41806] [65157] [65170]

Ampicillin: (Moderate) Administer oral ampicillin 2 hours before or 2 hours after hydroxychloroquine. Ampicillin bioavailability may be decreased with coadministration of hydroxychloroquine as a significant reduction in ampicillin bioavailability was observed with the structurally similar chloroquine in a study of healthy volunteers. The reduction of ampicillin bioavailability could be attributed to slower gastric emptying and enhancement of gut motility produced by chloroquine. [29758] [41806] [61761]

Anagrelide: (Major) Avoid coadministration of anagrelide and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Torsade de pointes (TdP) and ventricular tachycardia have been reported with anagrelide. In addition, dose-related increases in mean QTc and heart rate were observed in healthy subjects. [30163] [41806] [65157] [65170]

Antacids: (Major) Hydroxychloroquine absorption may be reduced by antacids as has been observed with the structurally similar chloroquine. Administer hydroxychloroquine and antacids at least 4 hours apart. Of note, a study demonstrated no significant difference in hydroxychloroquine serum concentration in patients taking concomitant antacids (n = 14) compared to those not taking antacids (n = 495). [30284] [30285] [41806] [61758]

Apomorphine: (Major) Avoid coadministration of apomorphine and hydroxychloroguine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Limited data indicate that QT prolongation is possible with apomorphine administration; the change in QTc interval is not significant in most patients receiving dosages within the manufacturer's guidelines. [28661] [41806] [65157] [65170]

Arformoterol: (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Beta-agonists may be

associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

Aripiprazole: (Major) Avoid coadministration of aripiprazole and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. QT prolongation has occurred during therapeutic use of aripiprazole and following overdose. [41806] [42845] [53394] [60196] [63328] [65157] [65170]

Arsenic Trioxide: (Major) Avoid coadministration of arsenic trioxide and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Torsade de pointes (TdP), QT interval prolongation, and complete atrioventricular block have been reported with arsenic trioxide use. [41806] [59438] [65157] [65170]

Artemether; Lumefantrine: (Major) Avoid coadministration of artemether; lumefantrine and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Artemether; lumefantrine is associated with prolongation of the QT interval. [34501] [41806] [65157] [65170] (Major) Avoid coadministration of artemether; lumefantrine and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Artemether; lumefantrine is associated with prolongation of the QT interval. [35401] [41806] [65157] [65170]

Asenapine: (Major) Avoid coadministration of asenapine and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Asenapine has also been associated with QT prolongation. [36343] [41806] [65157] [65170]

Aspirin, ASA; Citric Acid; Sodium Bicarbonate: (Major) Hydroxychloroquine absorption may be reduced by antacids as has been observed with the structurally similar chloroquine. Administer hydroxychloroquine and antacids at least 4 hours apart. Of note, a study demonstrated no significant difference in hydroxychloroquine serum concentration in patients taking concomitant antacids (n = 14) compared to those not taking antacids (n = 14) 495). [30284] [30285] [41806] [61758]

Atomoxetine: (Major) Avoid coadministration of atomoxetine and hydroxychloroguine due to the risk of increased OT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial OT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. QT prolongation has occurred during therapeutic use of atomoxetine and following overdose. [28405] [41806] [65157] [65170]

Atropine; Hyoscyamine; Phenobarbital; Scopolamine: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine and antiepileptic drugs, such as phenobarbital. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Azithromycin: (Major) Avoid coadministration of hydroxychloroquine and azithromycin due the risk of additive QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and

determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. QT prolongation and torsade de pointe (TdP) have been spontaneously reported during azithromycin postmarketing surveillance. [28855] [41806] [43974] [65157] [65170]

Bedaquiline: (Major) Avoid coadministration of bedaquline and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine and bedaquiline prolong the QT interval. Discontinue bedaquiline if evidence of serious ventricular arrhythmia or OTcF interval greater than 500 msec. [41806] [52746] [65157] [65170]

Belladonna Alkaloids; Ergotamine; Phenobarbital: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine and antiepileptic drugs, such as phenobarbital. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Bismuth Subcitrate Potassium; Metronidazole; Tetracycline: (Major) Avoid coadministration of metronidazole and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any nonessential OT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the OT interval. Potential QT prolongation has been reported in limited case reports with metronidazole. [41806] [57377] [57378] [65157] [65170]

Bismuth Subsalicylate; Metronidazole; Tetracycline: (Major) Avoid coadministration of metronidazole and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any nonessential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Potential QT prolongation has been reported in limited case reports with metronidazole. [41806] [57377] [57378] [65157] [65170]

Brivaracetam: (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as brivaracetam. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Budesonide; Formoterol: (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Betaagonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

Buprenorphine: (Major) Avoid coadministration of buprenorphine and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Buprenorphine has been associated with QT prolongation and has a possible risk of TdP. [41235] [41806] [59321] [60270] [65157] [65170]

Buprenorphine; Naloxone: (Major) Avoid coadministration of buprenorphine and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Buprenorphine has been associated with QT prolongation and has a possible risk of TdP. [41235] [41806] [59321] [60270] [65157] [65170]

Calcium Carbonate: (Major) Hydroxychloroquine absorption may be reduced by antacids as has been observed with the structurally similar chloroquine. Administer hydroxychloroquine and antacids at least 4 hours apart. Of note, a study demonstrated no significant difference in hydroxychloroquine serum concentration in patients taking concomitant antacids (n = 14) compared to those not taking antacids (n = 495). [30284] [30285] [41806] [61758]

Calcium Carbonate; Magnesium Hydroxide: (Major) Hydroxychloroquine absorption may be reduced by antacids as has been observed with the structurally similar chloroquine. Administer hydroxychloroquine and antacids at least 4 hours apart. Of note, a study demonstrated no significant difference in hydroxychloroquine serum concentration in patients taking concomitant antacids (n = 14) compared to those not taking antacids (n = 14) 495). [30284] [30285] [41806] [61758]

Calcium Carbonate; Risedronate: (Major) Hydroxychloroquine absorption may be reduced by antacids as has been observed with the structurally similar chloroquine. Administer hydroxychloroquine and antacids at least 4 hours apart. Of note, a study demonstrated no significant difference in hydroxychloroquine serum concentration in patients taking concomitant antacids (n = 14) compared to those not taking antacids (n = 495). [30284] [30285] [41806] [61758]

<u>Calcium Carbonate</u>; <u>Simethicone</u>: (Major) Hydroxychloroquine absorption may be reduced by antacids as has been observed with the structurally similar chloroquine. Administer hydroxychloroquine and antacids at least 4 hours apart. Of note, a study demonstrated no significant difference in hydroxychloroquine serum concentration in patients taking concomitant antacids (n = 14) compared to those not taking antacids (n = 495). [30284] [30285] [41806] [61758]

Canagliflozin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the SGLT2 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Canagliflozin; Metformin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the SGLT2 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Carbamazepine:</u> (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as carbamazepine. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Ceritinib: (Major) Avoid coadministration of ceritinib and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. An interruption of ceritinib therapy, dose reduction, or discontinuation of therapy may be necessary if QT prolongation occurs. Ceritinib causes concentration-dependent QT prolongation. Hydroxychloroquine also prolongs the QT interval. [41806] [57094] [65157] [65170]

<u>Chloroquine:</u> (Major) Avoid coadministration of chloroquine with hydroxychloroquine due to the increased risk of QT prolongation and similar toxicities. These drugs are both analogs of quinine. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Chloroquine is associated with an increased risk of QT prolongation and torsade de pointes (TdP); the risk of QT prolongation is increased with higher chloroquine doses. There is evidence that the use of halofantrine after mefloquine causes a significant

lengthening of the QTc interval. Mefloquine alone has not been reported to cause QT prolongation. [29758] [51806] [59321] [65157] [65170]

<u>Chlorpromazine:</u> (Major) Avoid coadministration of chlorpromazine and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Chlorpromazine is associated with an established risk of QT prolongation and torsade de pointes (TdP). [28415] [41806] [43065] [65157] [65170]

Chlorpropamide: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including sulfonylureas, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Cimetidine: (Moderate) Avoid concomitant use of hydroxychloroquine and cimetidine as cimetidine may inhibit the metabolism of hydroxychloroquine as observed with the structurally similar chloroquine. However, the mechanism of inhibition of chloroquine metabolism appears to be via CYP inhibition, and hydroxychloroquine is not a known CYP substrate; cimetidine inhibition of hydroxychloroquine metabolism has not been demonstrated. [29396] [41806] [61759] [61760]

Ciprofloxacin: (Major) Avoid coadministration of ciprofloxacin and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Rare cases of QT prolongation and torsade de pointes (TdP) have been reported with ciprofloxacin during postmarketing surveillance. [28432] [28457] [29833] [33144] [33145] [33146] [41806] [43411] [48869] [48871] [65157] [65170]

<u>Cisapride:</u> (Severe) Coadministration of cisapride and hydroxychloroquine is contraindicated due to the risk of increased QT prolongation. Hydroxychloroquine prolongs the QT interval. QT prolongation and ventricular arrhythmias, including torsade de pointes (TdP) and death, have been reported with cisapride. [28978] [41806] [47221]

Citalopram: (Major) Avoid coadministration of citalopram and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Citalogram causes dose-dependent QT interval prolongation. [28269] [41806] [65157] [65170]

<u>Clarithromycin:</u> (Major) Avoid coadministration of clarithromycin and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Clarithromycin is associated with an established risk for QT prolongation and torsade de pointes (TdP). [28225] [28238] [41806] [65157] [65170]

Clobazam: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine and antiepileptic drugs, such as clobazam. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

<u>Clofazimine:</u> (Major) Avoid coadministration of clofazimine and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. QT prolongation and torsade de pointes (TdP) have been reported in patients receiving clofazimine in combination with QT prolonging medications. [41806] [63936] [65157] [65170]

Clomipramine: (Major) Avoid coadministration of tricyclic antidepressants and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). [28225] [28415] [28416] [41806] [65157] [65170]

<u>Clonazepam:</u> (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as clonazepam. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Clorazepate: (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as clorazepate. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Clozapine: (Major) Avoid coadministration of clozapine and hydroxychloroguine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Treatment with clozapine has been associated with QT prolongation, torsade de pointes (TdP), cardiac arrest, and sudden death. [28262] [41806] [65157] [65170]

Codeine; Phenylephrine; Promethazine: (Major) Avoid coadministration of promethazine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any nonessential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Promethazine, a phenothiazine, is associated with a possible risk for QT prolongation. [28225] [41806] [55578] [65157] [65170]

Codeine; Promethazine: (Major) Avoid coadministration of promethazine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Promethazine, a phenothiazine, is associated with a possible risk for QT prolongation. [28225] [41806] [55578] [65157] [65170]

Crizotinib: (Major) Avoid coadministration of crizotinib and hydroxychloroguine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. An interruption of therapy, dose reduction, or discontinuation of therapy may be necessary for crizotinib if QT prolongation occurs. Crizotinib can cause concentration-dependent QT prolongation. Hydroxychloroquine also prolongs the QT interval. [41806] [45458] [65157] [65170]

Cyclosporine: (Moderate) Use caution with the coadministration of hydroxychloroquine and cyclosporine as increased serum concentrations of cyclosporine have been noted. Monitoring cyclosporine concentrations after starting or stopping hydroxychloroquine therapy may be necessary. Monitor patients for cyclosporine-related adverse events such as nephrotoxicity or hepatic toxicity. [41806]

<u>Dapagliflozin:</u> (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the SGLT2 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Dapagliflozin</u>; <u>Metformin</u>: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the SGLT2 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Dapagliflozin</u>; <u>Saxagliptin</u>: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the SGLT2 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroguine and an antidiabetic agent. [41806]

Dasatinib: (Major) Avoid coadministration of dasatinib and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. In vitro studies have shown that dasatinib has the potential to prolong the QT interval. [32387] [41806] [65157] [65170]

<u>Degarelix</u>: (Major) Avoid coadministration of degarelix and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Androgen deprivation therapy (i.e., degarelix) may prolong the QT/QTc interval. [41806] [46869] [65157] [65170]

Desflurane: (Major) Avoid coadministration of halogenated anesthetics and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Both hydroxychloroquine and halogenated anesthetics can prolong the QT interval. [28457] [28458] [28754] [28755] [28756] [41806] [65157] [65170]

<u>Desipramine:</u> (Major) Avoid coadministration of tricyclic antidepressants and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). [28225] [28415] [28416] [41806] [65157] [65170]

Deutetrabenazine: (Major) Avoid coadministration of deutetrabenazine and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. For patients taking a deutetrabenazine dosage more than 24 mg/day, assess the QTc interval before and after increasing the deutetrabenazine dosage or other medications that prolong the QTc interval. Hydroxychloroquine prolongs the QT interval. Clinically relevant QTc prolongation may occur with deutetrabenazine. [41806] [61845] [65157] [65170]

<u>Dextromethorphan; Promethazine:</u> (Major) Avoid coadministration of promethazine and hydroxychloroguine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Promethazine, a phenothiazine, is associated with a possible risk for QT prolongation. [28225] [41806] [55578] [65157] [65170]

Dextromethorphan; Quinidine: (Major) Avoid coadministration of quinidine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Quinidine administration is associated with QT prolongation and torsade de pointes (TdP). [41806] [42280] [47357] [65157] [65170]

<u>Diazepam:</u> (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as diazepam. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Digoxin: (Moderate) Monitor serum digoxin concentrations in patients receiving digoxin and hydroxychloroquine as coadministration may result in increased serum digoxin concentrations. [41806]

Dipeptidyl Peptidase-4 Inhibitors: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Disopyramide: (Major) Avoid coadministration of disopyramide and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Disopyramide administration is also associated with QT prolongation and torsade de pointes (TdP). [28228] [41806] [65157] [65170]

<u>Dofetilide:</u> (Major) Avoid coadministration of dofetilide and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Dofetilide, a Class III antiarrhythmic agent, is associated with a well-established risk of QT prolongation and torsade de pointes (TdP). Hydroxychloroquine also prolongs the QT interval. [28221] [28432] [28457] [41806] [65157] [65170]

Dolasetron: (Major) Avoid coadministration of dolasetron and hydroxychloroquine due to the risk of increased OT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial OT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Dolasetron has been associated with a dose-dependent prolongation in the QT, PR, and QRS intervals on an electrocardiogram. [41806] [42844] [65157] [65170]

<u>Dolutegravir</u>; <u>Rilpivirine</u>: (Major) Avoid coadministration of rilpivirine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Supratherapeutic doses of rilpivirine (75 to 300 mg/day) have caused QT prolongation. [41806] [44376] [65157] [65170]

<u>Donepezil:</u> (Major) Avoid coadministration of donepezil and hydroxychloroguine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Case reports indicate that QT prolongation and torsade de pointes (TdP) can occur during donepezil therapy. [41806] [59321] [59322] [65157] [65170]

Donepezil; Memantine: (Major) Avoid coadministration of donepezil and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Case reports indicate that QT

prolongation and torsade de pointes (TdP) can occur during donepezil therapy. [41806] [59321] [59322] [65157] [65170]

<u>Doxepin:</u> (Major) Avoid coadministration of tricyclic antidepressants and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). [28225] [28415] [28416] [41806] [65157] [65170]

Dronedarone: (Severe) Coadministration of dronedarone and hydroxychloroquine is contraindicated due to the risk of increased QT prolongation. Hydroxychloroquine prolongs the QT interval. Dronedarone administration is associated with a dose-related increase in the QTc interval. The increase in QTc is approximately 10 milliseconds at doses of 400 mg twice daily (the FDA-approved dose) and up to 25 milliseconds at doses of 1600 mg twice daily. Although there are no studies examining the effects of dronedarone in patients receiving other QT prolonging drugs, coadministration of such drugs may result in additive QT prolongation. [36101] [41806]

<u>Droperidol:</u> (Major) Avoid coadministration of droperidol and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Initiate droperidol at a low dose and increase the dose as needed to achieve the desired effect. Hydroxychloroquine prolongs the QT interval. Droperidol administration is associated with an established risk for QT prolongation and torsade de pointes (TdP). [28235] [28236] [28737] [41806] [51289] [65157] [65170]

<u>Dulaglutide</u>: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the incretin mimetics, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Efavirenz: (Major) Avoid coadministration of efavirenz and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. QTc prolongation has been observed with the use of efavirenz. [28442] [41806] [65157] [65170]

Efavirenz; Emtricitabine; Tenofovir: (Major) Avoid coadministration of efavirenz and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. QTc prolongation has been observed with the use of efavirenz. [28442] [41806] [65157] [65170]

Efavirenz; Lamivudine; Tenofovir Disoproxil Fumarate: (Major) Avoid coadministration of efavirenz and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any nonessential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. QTc prolongation has been observed with the use of efavirenz. [28442] [41806] [65157] [65170]

Eliglustat: (Major) Avoid coadministration of eliglustat and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Eliglustat is predicted to cause PR, QRS, and/or QT prolongation at significantly elevated plasma concentrations. [41806] [57803] [65157] [65170]

Empagliflozin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the SGLT2 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Empagliflozin; Linagliptin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the SGLT2 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Empagliflozin; Linagliptin; Metformin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the SGLT2 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Empagliflozin; Metformin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the SGLT2 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Emtricitabine; Rilpivirine; Tenofovir alafenamide: (Major) Avoid coadministration of rilpivirine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any nonessential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Supratherapeutic doses of rilpivirine (75 to 300 mg/day) have caused QT prolongation. [41806] [44376] [65157] [65170]

Emtricitabine; Rilpivirine; Tenofovir disoproxil fumarate: (Major) Avoid coadministration of rilpivirine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any nonessential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Supratherapeutic doses of rilpivirine (75 to 300 mg/day) have caused QT prolongation. [41806] [44376] [65157] [65170]

Encorafenib: (Major) Avoid coadministration of encorafenib and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Encorafenib is associated with dose-dependent prolongation of the QT interval. [41806] [63317] [65157] [65170]

Enflurane: (Major) Avoid coadministration of halogenated anesthetics and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Both hydroxychloroquine and halogenated anesthetics can prolong the QT interval. [28457] [28458] [28754] [28755] [28756] [41806] [65157] [65170]

Entrectinib: (Major) Avoid coadministration of entrectinib and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Entrectinib has also been associated with QT prolongation. [41806] [64567] [65157] [65170]

Eribulin: (Major) Avoid coadministration of eribulin and hydroxychloroguine due to the risk of increased OT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Both hydroxychloroquine and eribulin have been associated with QT prolongation. [41806] [42449] [65157] [65170]

Ertugliflozin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the SGLT2 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroguine and an antidiabetic agent. [41806]

Ertugliflozin; Metformin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the SGLT2 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Ertugliflozin; Sitagliptin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the SGLT2 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroguine and an antidiabetic agent. [41806]

Erythromycin: (Major) Avoid coadministration of erythromycin and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Erythromycin is associated with QT prolongation and torsade de pointes (TdP). [41806] [43258] [65157] [65170]

Erythromycin; Sulfisoxazole: (Major) Avoid coadministration of erythromycin and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Erythromycin is associated with QT prolongation and torsade de pointes (TdP). [41806] [43258] [65157] [65170]

Escitalopram: (Major) Avoid coadministration of escitalopram and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and

correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Escitalopram has been associated with a risk of QT prolongation and torsade de pointes (TdP). [28270] [41806] [65157] [65170]

Eslicarbazepine: (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as eslicarbazepine. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Ethosuximide: (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as ethosuximide. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Ethotoin: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine and antiepileptic drugs, such as ethotoin. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Exenatide: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroguine and antidiabetic agents, including the incretin mimetics, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Ezogabine: (Major) Avoid coadministration of ezogabine and hydroxychloroquine due to the risk of increased QT prolongation and seizures. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine and ezogabine have both been associated with QT prolongation. Additionally, hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806] [44800] [65157] [65170]

<u>Felbamate:</u> (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as felbamate. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

<u>Fingolimod:</u> (Major) Avoid coadministration of fingolimod and hydroxychloroquine due to the risk of increased QT prolongation. If coadministration cannot be avoided, overnight monitoring with continuous ECG in a medical facility is advised after the first fingolimod dose for patients taking QT prolonging drugs with a known risk of torsade de pointes (TdP). Also, avoid any non-essential QT prolonging drugs and correct electrolyte imbalances. Monitor ECG throughout therapy. Hydroxychloroquine prolongs the QT interval. Fingolimod initiation results in decreased heart rate and may prolong the QT interval. Fingolimod has not been studied in patients treated with drugs that prolong the QT interval, but drugs that prolong the QT interval have been associated with cases of TdP in patients with bradycardia. [41806] [41823] [65157] [65170]

Flecainide: (Major) Avoid coadministration of flecainide and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Flecainide is a Class IC antiarrhythmic associated with a possible risk for QT prolongation and/or TdP; flecainide increases the QT interval, but largely due to prolongation of the QRS interval. Although causality for TdP has not been established for flecainide, patients receiving concurrent drugs which have the potential for QT prolongation may have an increased risk of developing proarrhythmias. Hydroxychloroquine also prolongs the QT interval. [23774] [28752] [41806] [65157] [65170]

Fluconazole: (Major) Avoid coadministration of fluconazole and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Fluconazole has been associated with QT prolongation and rare cases of torsade de pointes (TdP). [28674] [41806] [65157] [65170]

Fluoxetine: (Major) Avoid coadministration of fluoxetine and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. QT prolongation and torsade de pointes (TdP) have been reported in patients treated with fluoxetine. [32127] [41806] [65157] [65170]

Fluoxetine; Olanzapine: (Major) Avoid coadministration of fluoxetine and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. QT prolongation and torsade de pointes (TdP) have been reported in patients treated with fluoxetine. [32127] [41806] [65157] [65170] (Major) Avoid coadministration of olanzapine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Limited data, including some case reports, suggest that olanzapine may be associated with a significant prolongation of the QTc interval. [28785] [32732] [32734] [32745] [32746] [41806] [65157] [65170]

Fluphenazine: (Major) Avoid coadministration of fluphenazine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Fluphenazine is associated with a possible risk for QT prolongation. [28514] [41806] [65157] [65170]

Fluticasone; Salmeterol: (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Betaagonists may be associated with adverse cardiovascular effects including OT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

Fluticasone; Umeclidinium; Vilanterol: (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any nonessential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Beta-agonists may be associated with adverse cardiovascular effects including OT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

Fluticasone; Vilanterol: (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Betaagonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

Fluvoxamine: (Major) Avoid coadministration of fluvoxamine and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and

correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Cases of QT prolongation and torsade de pointes (TdP) have been reported during postmarketing use of fluvoxamine. [41806] [50507] [65157] [65170]

Formoterol: (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

Formoterol; Mometasone: (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Betaagonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

<u>Foscarnet:</u> (Major) Avoid coadministration of foscarnet and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Foscarnet has been associated with postmarketing reports of both QT prolongation and torsade de pointes (TdP). [28377] [41806] [65157] [65170]

Fosphenytoin: (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as fosphenytoin. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Gabapentin: (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as gabapentin. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Gemifloxacin: (Major) Avoid coadministration of gemifloxacin and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Gemifloxacin may prolong the QT interval in some patients. The maximal change in the QTc interval occurs approximately 5 to 10 hours following oral administration of gemifloxacin. The likelihood of QTc prolongation may increase with increasing dose of the drug; therefore, the recommended dose should not be exceeded especially in patients with renal or hepatic impairment where the Cmax and AUC are slightly higher. [28424] [28432] [28457] [29833] [33144] [33145] [33146] [41806] [48869] [49971] [65157] [65170]

Gemtuzumab Ozogamicin: (Major) Avoid coadministration of gemtuzumab and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Although QT interval prolongation has not been reported with gemtuzumab ozogamicin, it has been reported with other drugs that contain calicheamicin. [41806] [62292] [65157] [65170]

Gilteritinib: (Major) Avoid coadministration of gilteritinib and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and

determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Both drugs have been associated with QT prolongation. [41806] [63787] [65157] [65170]

Glasdegib: (Major) Avoid coadministration of glasdegib and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Glasdegib therapy may result in QT prolongation and ventricular arrhythmias including ventricular fibrillation and ventricular tachycardia. [41806] [63777] [65157] [65170]

Glimepiride: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including sulfonylureas, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Glimepiride; Pioglitazone: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including sulfonylureas, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the thiazolidinediones, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Glimepiride; Rosiglitazone: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including sulfonylureas, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the thiazolidinediones, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Glipizide: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including sulfonylureas, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Glipizide; Metformin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including sulfonylureas, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Glyburide: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including sulfonylureas, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Glyburide; Metformin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is

recommended when hydroxychloroquine and antidiabetic agents, including sulfonylureas, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Glycopyrrolate; Formoterol: (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any nonessential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

Goserelin: (Major) Avoid coadministration of goserelin and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Androgen deprivation therapy (e.g., goserelin) also may prolong the QT/QTc interval. [28592] [41806] [65157] [65170]

Granisetron: (Major) Avoid coadministration of granisetron and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Both drugs have been associated with QT prolongation. [31723] [41806] [65157] [65170]

Halogenated Anesthetics: (Major) Avoid coadministration of halogenated anesthetics and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Both hydroxychloroquine and halogenated anesthetics can prolong the QT interval. [28457] [28458] [28754] [28755] [28756] [41806] [65157] [65170]

Haloperidol: (Major) Avoid coadministration of haloperidol and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. QT prolongation and torsade de pointes (TdP) have been observed during haloperidol treatment. Excessive doses (particularly in the overdose setting) or IV administration of haloperidol may be associated with a higher risk of QT prolongation. [23500] [23779] [28225] [28307] [28415] [28416] [41806] [65157] [65170]

Halothane: (Major) Avoid coadministration of halogenated anesthetics and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Both hydroxychloroquine and halogenated anesthetics can prolong the QT interval. [28457] [28458] [28754] [28755] [28756] [41806] [65157] [65170]

Histrelin: (Major) Avoid coadministration of histrelin and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Androgen deprivation therapy (e.g., histrelin) also may prolong the QT/QTc interval. [30369] [41806] [65157] [65170]

Hydroxyzine: (Major) Avoid coadministration of hydroxyzine and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and

correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Postmarketing data indicate that hydroxyzine causes QT prolongation and torsade de pointes (TdP). [41806] [47129] [65157] [65170]

<u>Ibutilide</u>: (Major) Avoid coadministration of ibutilide and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Ibutilide administration can cause QT prolongation and torsade de pointes (TdP). [41806] [41830] [65157] [65170]

<u>Iloperidone</u>: (Major) Avoid coadministration of iloperidone and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine and iloperidone have been associated with QT prolongation. [36146] [41806] [65157] [65170]

<u>Imipramine</u>: (Major) Avoid coadministration of tricyclic antidepressants and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). [28225] [28415] [28416] [41806] [65157] [65170]

<u>Incretin Mimetics</u>: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the incretin mimetics, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Indacaterol:</u> (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

<u>Indacaterol</u>; <u>Glycopyrrolate</u>: (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any nonessential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

Inotuzumab Ozogamicin: (Major) Avoid coadministration of inotuzumab and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Both inotuzumab and hydroxychloroquine have been associated with QT prolongation. [41806] [62245] [65157] [65170]

<u>Insulin Aspart:</u> (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be

necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Insulin Aspart; Insulin Aspart Protamine:</u> (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Insulin Degludec:</u> (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Insulin Degludec</u>; <u>Liraglutide</u>: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the incretin mimetics, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Insulin Detemir:</u> (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Insulin Glargine:</u> (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Insulin Glargine</u>; <u>Lixisenatide</u>: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the incretin mimetics, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Insulin Glulisine:</u> (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Insulin Lispro:</u> (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Insulin Lispro</u>; <u>Insulin Lispro Protamine</u>: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Insulin</u>, <u>Inhaled</u>: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Insulins:</u> (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroguine and an antidiabetic agent. [41806]

<u>Isoflurane:</u> (Major) Avoid coadministration of halogenated anesthetics and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Both hydroxychloroquine and halogenated anesthetics can prolong the QT interval. [28457] [28458] [28754] [28755] [28756] [41806] [65157] [65170]

<u>Isophane Insulin (NPH):</u> (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Itraconazole: (Major) Avoid coadministration of itraconazole and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine and itraconazole have been associated with prolongation of the QT interval. [40233] [41806] [57441] [65157] [65170]

Ivosidenib: (Major) Avoid coadministration of ivosidenib and hydroxychloroguine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Dose reduce or interrupt ivosidenib therapy if QT prolongation occurs. Prolongation of the QTc interval and ventricular arrhythmias have been reported in patients treated with ivosidenib. Hydroxychloroquine also prolongs the QT interval. [41806] [63368] [65157] [65170]

Ketoconazole: (Major) Avoid coadministration of ketoconazole and hydroxychloroquine due to the increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Ketoconazole and hydroxychloroquine have been associated with prolongation of the QT interval. [27982] [41806] [65157] [65170]

<u>Lacosamide:</u> (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as lacosamide. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

<u>Lamotrigine</u>: (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as lamotrigine. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

<u>Lanthanum Carbonate:</u> (Major) Oral compounds known to interact with antacids, like hydroxychloroquine, may interact with lanthanum carbonate. Hydroxychloroquine absorption may be reduced by antacids as has been observed with the structurally similar chloroquine. Administer hydroxychloroquine and lanthanum carbonate at least 4 hours apart. Of note, a study demonstrated no significant difference in hydroxychloroquine serum concentration in patients taking concomitant antacids (n = 14) compared to those not taking antacids (n = 495). [30284] [30285] [41806] [44406] [61758]

<u>Lapatinib</u>: (Major) Avoid coadministration of lapatinib and hydroxychloroquine due to the increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Lapatinib has also been associated with concentration-dependent QT prolongation; ventricular arrhythmias and torsade de pointes (TdP) have been reported in postmarketing experience with lapatinib. [33192] [41806] [65157] [65170]

Lefamulin: (Major) Avoid coadministration of lefamulin and hydroxychloroguine due to the increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Lefamulin has a concentration dependent QTc prolongation effect. The pharmacodynamic interaction potential to prolong the QT interval of the electrocardiogram between lefamulin and other drugs that effect cardiac conduction is unknown. [41806] [64576] [65157] [65170]

Lente Insulin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Lenvatinib: (Major) Avoid coadministration of lenvatinib and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine and lenvatinib are both associated with QT prolongation. [41806] [58782] [65157] [65170]

<u>Leuprolide</u>: (Major) Avoid coadministration of leuprolide and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Androgen deprivation therapy (e.g., leuprolide) also may prolong the QT/QTc interval. [41806] [43800] [65157] [65170]

<u>Leuprolide</u>; <u>Norethindrone</u>: (Major) Avoid coadministration of leuprolide and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Androgen deprivation therapy (e.g., leuprolide) also may prolong the QT/QTc interval. [41806] [43800] [65157] [65170]

Levalbuterol: (Major) Avoid coadministration of short-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [33925] [41806] [49951] [51793] [59321] [65157] [65170]

Levetiracetam: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine and antiepileptic drugs, such as levetiracetam. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Levofloxacin: (Major) Avoid coadministration of levofloxacin and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Levofloxacin has been associated with a

risk of QT prolongation and torsade de pointes (TdP). Although extremely rare, TdP has been reported during postmarketing surveillance of levofloxacin. [28421] [28432] [28457] [29758] [29833] [33144] [33145] [33146] [41806] [48869] [48871] [61195] [63729] [65157] [65170]

<u>Linagliptin:</u> (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Linagliptin</u>; <u>Metformin</u>: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Liraglutide</u>: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the incretin mimetics, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Lithium:</u> (Major) Avoid coadministration of lithium and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine and lithium have both been associated with QT prolongation. [41806] [59809] [59810] [59811] [65157] [65170]

<u>Lixisenatide</u>: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the incretin mimetics, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Lofexidine: (Major) Avoid coadministration of lofexidine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Lofexidine may prolong the QT interval, and torsade de pointes (TdP) has been reported during postmarketing use. [41806] [63161] [65157] [65170]

Long-acting beta-agonists: (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Betaagonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

Loperamide: (Major) Avoid coadministration of loperamide and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. At high doses, loperamide has been associated with serious cardiac toxicities, including syncope, ventricular tachycardia, QT prolongation, torsade de pointes (TdP), and cardiac arrest. [29396] [30106] [41806] [60864] [65157] [65170]

Loperamide; Simethicone: (Major) Avoid coadministration of loperamide and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. At high doses, loperamide has been associated with serious cardiac toxicities, including syncope, ventricular tachycardia, QT prolongation, torsade de pointes (TdP), and cardiac arrest. [29396] [30106] [41806] [60864] [65157] [65170]

<u>Lopinavir</u>; <u>Ritonavir</u>: (Major) Avoid coadministration of hydroxychloroguine and lopinavir; ritonavir due the risk of additive QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Lopinavir; ritonavir is also associated with QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Monitor ECG and electrolytes and avoid other non-essential QT prolonging drugs if use together is required. [28341] [41806] [65157] [65170]

<u>Lorazepam:</u> (Moderate) Caution is warranted with the coadministration of hydroxychloroquine and antiepileptic drugs, such as lorazepam. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Macimorelin: (Major) Avoid coadministration of macimorelin and hydroxychloroquine due to an increased risk of QT prolongation and torsade de pointes-type ventricular tachycardia. Sufficient washout time of drugs that are known to prolong the QT interval prior to administration of macimorelin is recommended. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Treatment with macimorelin has been associated with an increase in the corrected QT (QTc) interval. Hydroxychloroquine prolongs the QT interval. [41806] [62723] [65157] [65170]

Maprotiline: (Major) Avoid coadministration of maprotiline and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Maprotiline has been reported to prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). Cases of long QT syndrome and torsade de pointes (TdP) tachycardia have been described with maprotiline use, but rarely occur when the drug is used alone in normal prescribed doses and in the absence of other known risk factors for QT prolongation. Limited data are available regarding the safety of maprotiline in combination with other QT-prolonging drugs. [28225] [28759] [41806] [65157] [65170]

Mefloquine: (Major) Avoid coadministration of mefloquine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. There is evidence that the use of halofantrine after mefloquine causes a significant lengthening of the QTc interval. Mefloquine alone has not been reported to cause QT prolongation. However, due to the lack of clinical data, mefloquine should be used with caution in patients receiving drugs that prolong the QT interval. Additionally, both drugs may lower the seizure threshold. [28301] [41806] [65157] [65170]

Meglitinides: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the meglitinides, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Meperidine; Promethazine: (Major) Avoid coadministration of promethazine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Promethazine, a phenothiazine, is associated with a possible risk for QT prolongation. [28225] [41806] [55578] [65157] [65170]

Mephobarbital: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine and antiepileptic drugs, such as mephobarbital. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Metaproterenol: (Major) Avoid coadministration of short-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [33925] [41806] [49951] [51793] [59321] [65157] [65170]

Metformin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Metformin; Pioglitazone: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the thiazolidinediones, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Metformin; Repaglinide: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the meglitinides, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Metformin; Rosiglitazone: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the thiazolidinediones, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Metformin; Saxagliptin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Metformin; Sitagliptin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including metformin, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806] (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroguine and an antidiabetic agent. [41806]

Methadone: (Major) Avoid coadministration of methadone and hydroxychloroguine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Methadone is considered to be associated with an increased risk for QT prolongation and TdP, especially at higher doses (more than 200 mg/day but averaging approximately 400 mg/day in adult patients). Most cases involve patients being treated for pain with large, multiple daily doses of methadone, although cases have been reported in patients receiving doses commonly used for maintenance treatment of opioid addiction. [28319] [28320] [28321] [28322] [33136] [41806] [65157] [65170]

Methotrexate: (Moderate) Hydroxychloroquine may reduce the renal clearance of methotrexate; the exact mechanism of this interaction is unknown. The mean AUC of methotrexate was increased 52% and the mean Cmax was reduced 17% when a single dose of methotrexate was given with a dose of hydroxychloroquine (200 mg oral). Close monitoring for evidence of methotrexate toxicity should be done in patients receiving this combination, especially in those with reduced renal function. [31335] [40129]

Methsuximide: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine and antiepileptic drugs, such as methsuximide. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Metronidazole: (Major) Avoid coadministration of metronidazole and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Potential QT prolongation has been reported in limited case reports with metronidazole. [41806] [57377] [57378] [65157] [65170]

Midostaurin: (Major) Avoid coadministration of midostaurin and hydroxychloroquine due to an increased risk of OT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial OT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. In clinical trials, QT prolongation has been reported in patients who received midostaurin. [41806] [61906] [65157] [65170]

Mifepristone: (Major) Avoid coadministration of mifepristone and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Mifepristone has been associated with dose-dependent prolongation of the QT interval. [41806] [48697] [65157] [65170]

Miglitol: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the alpha-glucosidase inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Mirtazapine: (Major) Avoid coadministration of mirtazapine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Cases of QT prolongation, torsade de pointes (TdP), ventricular tachycardia, and sudden death have been reported during postmarketing use of

mirtazapine, primarily following overdose or in patients with other risk factors for QT prolongation. [40942] [41806] [65157] [65170]

Moxifloxacin: (Major) Avoid coadministration of moxifloxacin and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Quinolones have been associated with a risk of QT prolongation and torsade de pointes (TdP). Although extremely rare, TdP has been reported during postmarketing surveillance of moxifloxacin. These reports generally involved patients with concurrent medical conditions or concomitant medications that may have been contributory. [28423] [28432] [28457] [29833] [33144] [33145] [33146] [41806] [48869] [48871] [65157] [65170]

Nateglinide: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the meglitinides, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Nilotinib: (Major) Avoid coadministration of nilotinib and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Sudden death and QT prolongation have been reported in patients who received nilotinib therapy. [41806] [58766] [65157] [65170]

Norfloxacin: (Major) Avoid coadministration of norfloxacin and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, perform an ECG at baseline and monitor closely throughout therapy. Hydroxychloroquine prolongs the QT interval. Quinolones have been associated with a risk of QT prolongation and torsade de pointes (TdP). Although extremely rare, torsade de pointes has been reported during postmarketing surveillance of norfloxacin. These reports generally involved patients with concurrent medical conditions or concomitant medications that may have been contributory. Norfloxacin should be used cautiously with other agents that may prolong the QT interval or increase the risk of TdP. [29818] [41806] [65157] [65170]

Nortriptyline: (Major) Avoid coadministration of tricyclic antidepressants and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). [28225] [28415] [28416] [41806] [65157] [65170]

Octreotide: (Major) Avoid coadministration of octreotide and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Arrhythmias, sinus bradycardia, and conduction disturbances have occurred during octreotide therapy. Since bradycardia is a risk factor for development of torsade de pointes (TdP), the potential occurrence of bradycardia during octreotide administration could theoretically increase the risk of TdP in patients receiving drugs that prolong the QT interval. [28432] [29113] [30624] [41806] [65157] [65170]

Ofloxacin: (Major) Avoid coadministration of ofloxacin and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Quinolones have been associated with a risk of QT prolongation and torsade de pointes (TdP). Although extremely rare, torsade de pointes has been reported during postmarketing surveillance of ofloxacin. These reports generally involved patients with concurrent medical

conditions or concomitant medications that may have been contributory. [28432] [28457] [29833] [30738] [33144] [33145] [33146] [41806] [48869] [48871] [65157] [65170]

Olanzapine: (Major) Avoid coadministration of olanzapine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Limited data, including some case reports, suggest that olanzapine may be associated with a significant prolongation of the QTc interval. [28785] [32732] [32734] [32745] [32746] [41806] [65157] [65170]

Olodaterol: (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

Omeprazole; Sodium Bicarbonate: (Major) Hydroxychloroquine absorption may be reduced by antacids as has been observed with the structurally similar chloroquine. Administer hydroxychloroquine and antacids at least 4 hours apart. Of note, a study demonstrated no significant difference in hydroxychloroquine serum concentration in patients taking concomitant antacids (n = 14) compared to those not taking antacids (n = 495). [30284] [30285] [41806] [61758]

Ondansetron: (Major) Avoid coadministration of ondansetron and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Ondansetron has been associated with a dose-related increase in the QT interval and postmarketing reports of torsade de pointes (TdP). [31266] [41806] [65157] [65170]

Osimertinib: (Major) Avoid coadministration of osimertinib and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. An interruption of osimertinib therapy with dose reduction or discontinuation may be necessary if QT prolongation occurs. Concentration-dependent QTc prolongation occurred during clinical trials of osimertinib. Hydroxychloroquine prolongs the QT interval. [41806] [60297] [65157] [65170]

Oxaliplatin: (Major) Avoid coadministration of oxaliplatin and hydroxychloroguine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. QT prolongation and ventricular arrhythmias including fatal torsade de pointes (TdP) have been reported with oxaliplatin use in postmarketing experience. Hydroxychloroquine prolongs the QT interval. [41806] [41958] [65157] [65170]

<u>Paliperidone:</u> (Major) Avoid coadministration of paliperidone and hydroxychloroguine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Paliperidone has been associated with QT prolongation; Torsade de pointes (TdP) and ventricular fibrillation have been reported in the setting of overdose. [40936] [41806] [65157] [65170]

Panobinostat: (Major) Avoid coadministration of panobinostat and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and

determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. QT prolongation has also been reported with panobinostat. [41806] [58821] [65157] [65170]

Pasireotide: (Major) Avoid coadministration of pasireotide and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. QT prolongation has occurred with pasireotide at therapeutic and supra-therapeutic doses. [41806] [52611] [65157] [65170]

<u>Pazopanib</u>: (Major) Avoid coadministration of pazopanib and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential OT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine and pazopanib both prolong the QT interval. [37098] [41806] [65157] [65170]

Penicillamine: (Major) Do not use penicillamine concurrently with antimalarials due to an increased risk of severe hematologic and renal adverse reactions. [28834]

Pentamidine: (Major) Avoid coadministration of pentamidine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Systemic pentamidine has been associated with QT prolongation. [23620] [23778] [28419] [28879] [41806] [65157] [65170]

Pentobarbital: (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as pentobarbital. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

<u>Perampanel:</u> (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as perampanel. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Perphenazine: (Major) Avoid coadministration of perphenazine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Perphenazine is associated with a possible risk for OT prolongation. [28514] [41806] [65157] [65170]

Perphenazine; Amitriptyline: (Major) Avoid coadministration of perphenazine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Perphenazine is associated with a possible risk for QT prolongation. [28514] [41806] [65157] [65170] (Major) Avoid coadministration of tricyclic antidepressants and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). [28225] [28415] [28416] [41806] [65157] [65170]

Phenobarbital: (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as phenobarbital. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

<u>Phentermine</u>; <u>Topiramate</u>: (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as topiramate. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Phenylephrine; Promethazine: (Major) Avoid coadministration of promethazine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Promethazine, a phenothiazine, is associated with a possible risk for QT prolongation. [28225] [41806] [55578] [65157] [65170]

<u>Phenytoin:</u> (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as phenytoin. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

<u>Pimavanserin:</u> (Major) Avoid coadministration of pimavanserin and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine and pimavanserin both prolong the QT interval. [41806] [60748] [65157] [65170]

<u>Pimozide:</u> (Severe) Coadministration of pimozide and hydroxychloroquine is contraindicated due to an increased risk of QT prolongation. Hydroxychloroquine prolongs the QT interval. Pimozide is associated with a well-established risk of QT prolongation and torsade de pointes (TdP). [28225] [41806] [43463]

<u>Pioglitazone:</u> (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the thiazolidinediones, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Pirbuterol: (Major) Avoid coadministration of short-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the OT interval. Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [33925] [41806] [49951] [51793] [59321] [65157] [65170]

<u>Pitolisant:</u> (Major) Avoid coadministration of pitolisant and hydroxychloroguine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Both pitolisant and hydroxychloroquine prolong the QT interval. [41806] [64562] [65157] [65170]

<u>Posaconazole:</u> (Major) Avoid coadministration of posaconazole and hydroxychloroquine due to an increased risk of OT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial OT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Posaconazole has been associated with prolongation of the QT interval as well as rare cases of torsade de pointes. [32723] [41806] [65157] [65170]

Pramlintide: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including pramlintide, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Praziquantel:</u> (Minor) Hydroxychloroquine may reduce praziquantel bioavailability and maximum serum concentrations as was observed with the structurally similar chloroquine. The mechanism of the interaction is not certain. Clinicians should be alert to the possibility of praziquantel failure if hydroxychloroquine is used. [27846] [41806]

<u>Pregabalin:</u> (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as pregabalin. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Primaquine: (Major) Avoid coadministration of primaquine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Primaquine is associated with the potential for QT prolongation. [41806] [41984] [65157] [65170]

<u>Primidone:</u> (Moderate) Caution is warranted with the coadministration of hydroxychloroquine and antiepileptic drugs, such as primidone. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Procainamide: (Major) Avoid coadministration of procainamide and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the OT interval. Procainamide is associated with a wellestablished risk of QT prolongation and torsade de pointes (TdP). [28250] [41806] [65157] [65170]

Prochlorperazine: (Major) Avoid coadministration of prochlorperazine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Prochlorperazine is associated with a possible risk for QT prolongation. Theoretically, prochlorperazine may increase the risk of QT prolongation if coadministered with other drugs that have a risk of QT prolongation. [28514] [41806] [65157] [65170]

<u>Promethazine:</u> (Major) Avoid coadministration of promethazine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Promethazine, a phenothiazine, is associated with a possible risk for QT prolongation. [28225] [41806] [55578] [65157] [65170]

Propafenone: (Major) Avoid coadministration of propafenone and hydroxychloroguine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Propafenone is a Class IC antiarrhythmic which increases the QT interval, but largely due to prolongation of the QRS interval. [28287] [41806] [65157] [65170]

Protriptyline: (Major) Avoid coadministration of tricyclic antidepressants and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). [28225] [28415] [28416] [41806] [65157] [65170]

Quetiapine: (Major) Avoid coadministration of quetiapine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Limited data, including some case reports, suggest that quetiapine may be associated with a significant prolongation of the QTc interval in rare instances. [29118] [33068] [33072] [33074] [41806] [65157] [65170]

Quinidine: (Major) Avoid coadministration of quinidine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Quinidine administration is associated with QT prolongation and torsade de pointes (TdP). [41806] [42280] [47357] [65157] [65170]

Quinine: (Major) Avoid coadministration of quinine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Quinine has been associated with QT prolongation and rare cases of torsade de pointes (TdP). [31403] [41806] [65157] [65170]

Rabies Vaccine: (Major) If administered concurrently, antimalarials can impair the immunologic response to the rabies vaccine, thereby, decreasing its protective effect. If possible, administration of antimalarials should be avoided during use of the rabies vaccine for postexposure prophylaxis. When antimalarials must be administered to persons also receiving the rabies vaccine for postexposure prophylaxis, a serum rabies antibody titer should be obtained on day 14 (day of the 4th vaccination) to ensure an acceptable antibody response has been induced. [40848] [40849]

Ranolazine: (Major) Avoid coadministration of ranolazine and hydroxychloroguine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Ranolazine is associated with dose- and plasma concentration-related increases in the QTc interval. [31938] [41806] [65157] [65170]

Regular Insulin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Regular Insulin; Isophane Insulin (NPH): (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Repaglinide: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the meglitinides, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Ribociclib: (Major) Avoid coadministration of ribociclib and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Ribociclib has been shown to prolong the QT interval in a concentration-dependent manner. [41806] [61816] [65157] [65170]

Ribociclib; Letrozole: (Major) Avoid coadministration of ribociclib and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and

determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Ribociclib has been shown to prolong the QT interval in a concentration-dependent manner. [41806] [61816] [65157] [65170]

Rilpivirine: (Major) Avoid coadministration of rilpivirine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Supratherapeutic doses of rilpivirine (75 to 300 mg/day) have caused QT prolongation. [41806] [44376] [65157] [65170]

Risperidone: (Major) Avoid coadministration of risperidone and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Risperidone has been associated with a possible risk for QT prolongation and/or torsade de points (TdP), primarily in the overdose setting. [22256] [28225] [28414] [28416] [41806] [65157] [65170]

Rituximab: (Moderate) The concomitant use of rituximab with other disease modifying anti-rheumatic drugs (DMARDs), such as hydroxychloroquine, may result in an increased risk of infection. Hydroxychloroquine itself does not increase immunosuppression or infection risk, but, is often used in DMARD regimens where infection risk is increased. Monitor patients closely for signs or symptoms of infection. [41806] [49773] [56233]

Rituximab; Hyaluronidase: (Moderate) The concomitant use of rituximab with other disease modifying antirheumatic drugs (DMARDs), such as hydroxychloroquine, may result in an increased risk of infection. Hydroxychloroquine itself does not increase immunosuppression or infection risk, but, is often used in DMARD regimens where infection risk is increased. Monitor patients closely for signs or symptoms of infection. [41806] [49773] [56233]

Romidepsin: (Major) Avoid coadministration of romidepsin and hydroxychloroquine due to an increased risk of OT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial OT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Romidepsin has been reported to prolong the QT interval. [37292] [41806] [65157] [65170]

Rosiglitazone: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroguine and antidiabetic agents, including the thiazolidinediones, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Rufinamide: (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as rufinamide. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Salmeterol: (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

Saquinavir: (Major) Avoid coadministration of saquinavir and hydroxychloroquine due to an increased risk of OT prolongation. If no acceptable alternative therapy is available, obtain an ECG at baseline to assess initial OT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Saquinavir boosted with ritonavir increases the QT interval in a dosedependent fashion, which may increase the risk for serious arrhythmias such as torsade de pointes (TdP). Hydroxychloroguine prolongs the OT interval. [28995] [41806] [65157] [65170]

Saxagliptin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Semaglutide: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the incretin mimetics, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Sertraline: (Major) Avoid coadministration of sertraline and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Sertraline's FDA-approved labeling recommends avoiding concomitant use with drugs known to prolong the QTc interval; however, the risk of sertraline-induced QT prolongation is generally considered to be low in clinical practice. Its effect on QTc interval is minimal (typically less than 5 msec), and the drug has been used safely in patients with cardiac disease (e.g., recent myocardial infarction, unstable angina, chronic heart failure). [28343] [41806] [64391] [64392] [64394] [64395] [64396] [65157] [65170]

Sevoflurane: (Major) Avoid coadministration of halogenated anesthetics and hydroxychloroquine due to the risk of increased QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Both hydroxychloroquine and halogenated anesthetics can prolong the QT interval. [28457] [28458] [28754] [28755] [28756] [41806] [65157] [65170]

SGLT2 Inhibitors: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the SGLT2 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Short-acting beta-agonists: (Major) Avoid coadministration of short-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any nonessential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [33925] [41806] [49951] [51793] [59321] [65157] [65170]

Simvastatin; Sitagliptin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Siponimod: (Major) Avoid coadministration of siponimod and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Siponimod therapy prolonged the QT interval at recommended doses in a clinical study. Hydroxychloroquine prolongs the QT interval. [41806] [64031] [65157] [65170]

Sitagliptin: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the dipeptidyl peptidase-4 inhibitors, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Sodium Bicarbonate: (Major) Hydroxychloroquine absorption may be reduced by antacids as has been observed with the structurally similar chloroquine. Administer hydroxychloroquine and antacids at least 4 hours apart. Of note, a study demonstrated no significant difference in hydroxychloroquine serum concentration in patients taking concomitant antacids (n = 14) compared to those not taking antacids (n = 495). [30284] [30285] [41806] [61758]

Solifenacin: (Major) Avoid coadministration of solifenacin and hydroxychloroquine due to an increased risk of OT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial OT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Solifenacin has been associated with dose-dependent prolongation of the QT interval. Torsade de pointes (TdP) has been reported with postmarketing use, although causality was not determined. [30515] [41806] [65157] [65170]

Sorafenib: (Major) Avoid coadministration of sorafenib and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Interrupt or discontinue sorafenib if QT prolongation occurs. Hydroxychloroquine and sorafenib both prolong the QT interval. [31832] [41806] [65157] [65170]

Sotalol: (Major) Avoid coadministration of sotalol and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Sotalol administration is associated with QT prolongation and torsade de pointes (TdP). Proarrhythmic events should be anticipated after initiation of therapy and after each upward dosage adjustment. [28234] [41806] [65157] [65170]

Sulfonylureas: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including sulfonylureas, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Sunitinib: (Major) Avoid coadministration of sunitinib and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine and sunitinib can prolong the QT interval. [31970] [41806] [65157] [65170]

Tacrolimus: (Major) Avoid coadministration of tacrolimus and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tacrolimus may prolong the QT interval and cause torsade de pointes (TdP). [27954] [28611] [41806] [65157] [65170]

<u>Tamoxifen:</u> (Major) Avoid coadministration of tamoxifen and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tamoxifen has been reported to prolong the QT interval, usually in overdose or when used in high doses. Rare case reports of QT prolongation have also been described when tamoxifen is used at lower doses. [41806] [61870] [61871] [61872] [63589] [65157] [65170]

<u>Telavancin:</u> (Major) Avoid coadministration of hydroxychloroguine and telavancin. Hydroxychloroguine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes have been reported with the use of hydroxychloroquine. Telavancin has been associated with QT prolongation. [36615] [41806]

Telbivudine: (Moderate) The risk of myopathy may be increased if hydroxychloroquine is coadministered with telbivudine. Monitor patients for any signs or symptoms of unexplained muscle pain, tenderness, or weakness, particularly during periods of upward dosage titration. [9671]

Telithromycin: (Major) Avoid coadministration of telithromycin and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the OT interval. Telithromycin is associated with OT prolongation and torsade de pointes (TdP). [28156] [41806] [65157] [65170]

Terbutaline: (Major) Avoid coadministration of short-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Beta-agonists may be associated with adverse cardiovascular effects including OT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [33925] [41806] [49951] [51793] [59321] [65157] [65170]

Tetrabenazine: (Major) Avoid coadministration of tetrabenazine and hydroxychloroguine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tetrabenazine causes a small increase in the corrected QT interval (QTc). [34389] [41806] [65157] [65170]

Thiazolidinediones: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including the thiazolidinediones, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Thioridazine: (Severe) Coadministration of thioridazine and hydroxychloroquine is contraindicated due to an increased risk of QT prolongation. Hydroxychloroquine prolongs the QT interval. Thioridazine is associated with a well-established risk of QT prolongation and torsade de pointes (TdP). [28225] [28293] [41806]

Tiagabine: (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as tiagabine. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

<u>Tiotropium</u>; <u>Olodaterol</u>: (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Betaagonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

Tolazamide: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including sulfonylureas, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Tolbutamide: (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including sulfonylureas, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

Tolterodine: (Major) Avoid coadministration of tolterodine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tolterodine has been associated with dose-dependent prolongation of the QT interval, especially in poor CYP2D6 metabolizers. [31112] [41806] [65157] [65170]

<u>Topiramate:</u> (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as topiramate. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Toremifene: (Major) Avoid coadministration of toremifene and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Toremifene has been shown to prolong the QTc interval in a dose- and concentrationrelated manner. Hydroxychloroquine prolongs the QT interval. [28822] [41806] [65157] [65170]

<u>Trazodone:</u> (Major) Avoid coadministration of trazodone and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential OT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are postmarketing reports of torsade de pointes (TdP), [38831] [41806] [65157] [65170]

Tricyclic antidepressants: (Major) Avoid coadministration of tricyclic antidepressants and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). [28225] [28415] [28416] [41806] [65157] [65170]

<u>Trifluoperazine:</u> (Major) Avoid coadministration of trifluoperazine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Trifluoperazine is associated with a possible risk for QT prolongation. [28514] [41806] [65157] [65170]

<u>Trimipramine:</u> (Major) Avoid coadministration of tricyclic antidepressants and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Tricyclic antidepressants (TCAs) share pharmacologic properties similar to the Class IA antiarrhythmic agents and may prolong the QT interval, particularly in overdose or with higher-dose prescription therapy (elevated serum concentrations). [28225] [28415] [28416] [41806] [65157] [65170]

<u>Triptorelin:</u> (Major) Avoid coadministration of triptorelin and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Androgen deprivation therapy (e.g., triptorelin) also may prolong the QT/QTc interval. [41806] [45411] [65157] [65170]

<u>Ultralente Insulin:</u> (Moderate) Careful monitoring of blood glucose is recommended when hydroxychloroquine and antidiabetic agents, including insulins, are coadministered. A decreased dose of the antidiabetic agent may be necessary as severe hypoglycemia has been reported in patients treated concomitantly with hydroxychloroquine and an antidiabetic agent. [41806]

<u>Umeclidinium; Vilanterol:</u> (Major) Avoid coadministration of long-acting beta-agonists and hydroxychloroquine due to an increased risk of OT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Betaagonists may be associated with adverse cardiovascular effects including QT interval prolongation, usually at higher doses, when associated with hypokalemia, or when used with other drugs known to prolong the QT interval. This risk may be more clinically significant with long-acting beta-agonists as compared to short-acting beta-agonists. [28229] [32901] [41231] [41806] [44026] [44063] [44979] [59321] [65157] [65170]

Valproic Acid, Divalproex Sodium: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine and antiepileptic drugs, such as valproic acid. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

Vandetanib: (Major) Avoid coadministration of vandetanib and hydroxychloroguine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Interrupt or dose reduce vandetanib for QT prolongation. Vandetanib can prolong the QT interval in a concentration-dependent manner; torsade de pointes (TdP) and sudden death have been reported in patients receiving vandetanib. Hydroxychloroquine also prolongs the QT interval. [41806] [43901] [65157] [65170]

Vardenafil: (Major) Avoid coadministration of vardenafil and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Both therapeutic and supratherapeutic doses of vardenafil produce an increase in QTc interval. [28216] [41806] [65157] [65170]

Vemurafenib: (Major) Avoid coadministration of vemurafenib and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Vemurafenib and hydroxychloroquine have both been associated with QT prolongation. [41806] [45335] [65157] [65170]

Venlafaxine: (Major) Avoid coadministration of venlafaxine and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Venlafaxine administration is associated with a possible risk of QT prolongation; torsade de pointes (TdP) has been reported with postmarketing use. [33715] [41806] [65157] [65170]

<u>Vigabatrin:</u> (Major) Vigabatrin should not be used with hydroxychloroquine, which is associated with serious ophthalmic effects (e.g., retinopathy or glaucoma) unless the benefit of treatment clearly outweighs the risks. Additionally, hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [36250] [41806]

Voriconazole: (Major) Avoid coadministration of voriconazole and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Voriconazole has been associated with OT prolongation and rare cases of torsade de pointes (TdP). [28158] [41806] [65157] [65170]

Vorinostat: (Major) Avoid coadministration of vorinostat and hydroxychloroquine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial OT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Vorinostat therapy is also associated with a risk of QT prolongation. [32789] [41806] [65157] [65170]

Ziprasidone: (Major) Avoid coadministration of ziprasidone and hydroxychloroguine due to an increased risk of QT prolongation. If use together is necessary, obtain an ECG at baseline to assess initial QT interval and determine frequency of subsequent ECG monitoring, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances. Hydroxychloroquine prolongs the QT interval. Clinical trial data indicate that ziprasidone causes OT prolongation; there are postmarketing reports of torsade de pointes (TdP) in patients with multiple confounding factors. [28233] [41806] [65157] [65170]

Zonisamide: (Moderate) Caution is warranted with the coadministration of hydroxychloroguine and antiepileptic drugs, such as zonisamide. Hydroxychloroquine can lower the seizure threshold; therefore, the activity of antiepileptic drugs may be impaired with concomitant use. [41806]

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Monitoring Parameters

- blood glucose
- CBC
- ECG
- glucose-6-phosphate dehydrogenase (G6PD) activity
- ophthalmologic exam

US Drug Names

- Plaquenil
- Quineprox

Global Drug names

Argentina

- Axokine (Rontag)
- Evoquin (Ivax)
- Metirel (Rontag)
- Narbon (Buxton)
- Plaquenil (Sanofi-Aventis)
- Polirreumin (TRB)

Australia

- Hequinel (Aspen)
- Plaquenil (Sanofi-Aventis)
- Rusquen (Ipca)

Austria

• Plaquenil - (Sanofi Synthelabo)

Belgium

• Plaquenil - (Sanofi-Aventis)

Brazil

- Plaquinol (Sanofi-Aventis)
- Reuquinol (Apsen)

Canada

- Apo-Hydroxyquine (Apotex)
- Plaquenil (Sanofi-Aventis)
- Pro-Hydroxyquine (Pro Doc)

Chile

- Ilinol (Pharma Investi)
- Parenquil (Recalcine)
- Plaquinol (Sanofi-Aventis)
- Quinilen (Royal)
- Reumazine (Sanitas)

China

- Fen Le (ZhongXi)
- Plaquenil (Abbott)

Czech Republic

• Plaquenil - (Sanofi-Aventis)

Denmark

- Ercoquin (Medic)
- Plaquenil (Sanofi-Aventis)

Finland

- Oxiklorin (Orion)
- Plaquenil (Sanofi Synthelabo)

France

• Plaquenil - (Sanofi-Aventis)

Germany

• Quensyl - (Sanofi-Aventis)

Greece

• Plaquenil - (IFET (ΙΦΕΤ))

Hong Kong

• Plaquenil - (Sanofi-Aventis)

India

- HCQS (Ipca)
- HQTor (Torrent)
- Hydrocad (Cadila)
- Hydroquin (Sun)
- Oxcq (Wallace)
- Oxy-Q (Daffohils)

Ireland

• Plaquenil - (Sanofi-Aventis)

Israel

• Plaquenil - (Sanofi-Aventis)

Italy

• Plaquenil - (Sanofi-Aventis)

Japan

• Plaquenil - (Sanofi)

Malaysia

• Plaquenil - (Sanofi-Aventis)

Mexico

• Plaquenil - (Sanofi-Aventis)

Netherlands

• Plaquenil - (Sanofi-Aventis)

New Zealand

• Plaquenil - (Sanofi-Aventis)

Norway

- Ercoquin (Nycomed)
- Plaquenil (Sanofi-Aventis)

Philippines

• Plaquenil - (Sanofi-Aventis)

Portugal

• Plaquinol - (Alfa Wassermann)

Russian Federation

- Immard (Ipca)
- Plaquenil (Sanofi-Aventis)

Singapore

- Haloxin (Hanlim)
- Plaquenil (Sanofi-Aventis)

Spain

• Dolquine - (Products & Technology)

Sweden

• Plaquenil - (Sanofi-Aventis)

Switzerland

• Plaquenil - (Sanofi-Aventis)

Thailand

- HCQS (Ipca)
- Hydroquin (Sun)
- Plaquenil (Sanofi-Aventis)

Turkey

• Plaquenil - (Sanofi-Aventis)

Ukraine

- Immard (Ipca)
- Plaquenil (Sanofi-Aventis)

United Kingdom

- Plaquenil (Zentiva)
- Quinoric (Bristol)

Venezuela

• Plaquinol - (Sanofi-Aventis)

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