Hydroxychloroquine (All Populations Monograph)

Indications/Dosage

expand all | collapse all

Labeled

- malaria
- malaria prophylaxis
- rheumatoid arthritis
- systemic lupus erythematosus (SLE)

Off-Label, Recommended

- coronavirus disease 2019 (COVID-19) †
- lupus nephritis †
- polymorphous light eruption †
- severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection †

† Off-label indication

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]

- **Children and Adolescents weighing 31 kg or more**
  
  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 (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 hydroxychloroquine as an alternative to chloroquine.[63990]

- **Children and Adolescents weighing 31 kg or more**
  
  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 hydroxychloroquine as an alternative to chloroquine.[63990]

For the treatment of systemic lupus erythematosus (SLE)
• 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. 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.

• Children† and Adolescents†

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

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 hydroxychloroquine maintenance is achieved. 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. 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. 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. 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.

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, hydroxychloroquine, 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**

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]

• **Infants, Children, and Adolescents**

Efficacy in pediatric patients and optimal dosing 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]

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**Maximum Dosage Limits**

- **Adults**

  800 mg (620 mg base) PO as a single dose for malaria with 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 (620 mg base) PO as a single dose for malaria with 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 (10 mg base/kg) or 800 mg (620 mg base) PO as a single dose for malaria up to a total of 2 g (1.55 g base) PO in 48 hours; 6.5 mg/kg/week (5 mg base/kg/week) or 400 mg/week (310 mg base/week) PO for malaria prophylaxis.

- **Children**

  13 mg/kg (10 mg base/kg) or 800 mg (620 mg base) PO as a single dose for malaria up to a total of 2 g (1.55 g base) PO in 48 hours; 6.5 mg/kg/week (5 mg base/kg/week) or 400 mg/week (310 mg base/week) PO for malaria prophylaxis.

- **Infants**

  Safety and efficacy have not been established.

- **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

Revision Date: 03/24/2020 09:37:21 AM

References


### How Supplied

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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. 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**
  - **Antiparasitic Agents, Insecticides, and Repellants**
    - Antiprotozoals
    - Antimalarials
  - **Musculo-Skeletal System**
    - Antiinflammatory Agents and Antirheumatic Agents
      - Antiinflammatory and Antirheumatic Agents
      - Other Antiinflammatory and Antirheumatic Agents

References


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 at least 90 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 20°C with swirling, even when halved.

References

Anon. Manufacturer's information and labeling. (Package insert and bulk material data sheet).


2. General Stability Info

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

References


3. Oral Liquid

Pesko reported on an extemporaneous suspension of hydroxychloroquine. 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.

References

Pesko LJ. Compounding: hydroxychloroquine. Am Druggist. 1993; 207:57
References


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 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]

Allergic and dermatologic reactions have been reported with the use of hydroxychloroquine. These include urticaria, angioedema, bronchospasm, rash (unspecified), pruritus, pigmentation 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 4-aminoquinolines.[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 life-threatening 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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References


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

https://www.clinicalkey.com/pharmacology/monograph/print?cpnum=300&type=0&printSections=monindi&printSections=monsup&printSections=mo...
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 hydroxychloroquine for systemic lupus erythematosus and juvenile idiopathic arthritis in children and infants have not been established. Children are especially sensitive to the 4-aminooquinoline 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. 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. In infants monitored for up to at least 1 year of age, careful follow-up found no adverse effects on growth, vision, or hearing. Previous American Academy of Pediatrics (AAP) recommendations considered hydroxychloroquine as usually compatible with breast-feeding.

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.

Hydroxychloroquine prolongs the QT interval. Use hydroxychloroquine 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. 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 life-threatening cardiac complications.

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.

References


48474 – Cimaz R, Brucato A, Meregalli E et al. Electroretinograms of children born to mothers treated with hydroxychloroquine during pregnancy and breast-feeding: comment on the article by Costedoat-Chalumeau et
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]

References


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: CYP2D6

Hydroxychloroquine appears to inhibit the CYP2D isoenzyme.[29396]

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 (RA) 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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References
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. Guidelines recommend hydroxychloroquine as an alternative to chloroquine as a treatment option for acute malaria and for prophylaxis in pregnant women during all trimesters. Hydroxychloroquine may also be appropriate for pregnancies complicated by lupus.

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. 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. In infants monitored for up to at least 1 year of age, careful follow-up found no adverse effects on growth, vision, or hearing. Previous American Academy of Pediatrics (AAP) recommendations considered hydroxychloroquine as usually compatible with breast-feeding.

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References


Interactions

Level 1 (Severe)

- Cisapride
- Dronedarone
- Pimozide
- Thioridazine

Level 2 (Major)

- Alfuzosin
- Amiodarone
- Amoxicillin; Clarithromycin; Lansoprazole
- Amoxicillin; Clarithromycin; Omeprazole
- Anagrelide
- Antacids
- Apomorphine
- Aripiprazole
- Arsenic Trioxide
- Artemether; Lumefantrine
- Asenapine
- Aspirin, ASA; Citric Acid; Sodium Bicarbonate
- Atomoxetine
- Azithromycin
- Bedaquiline
- Bismuth Subcitrate Potassium; Metronidazole; Tetracycline
- Bismuth Subsalicylate; Metronidazole; Tetracycline
- Botulinum Toxins
- Buprenorphine
- Buprenorphine; Naloxone
- Calcium Carbonate
- Calcium Carbonate; Magnesium Hydroxide
- Calcium Carbonate; Risedronate

https://www.clinicalkey.com/pharmacology/monograph/print?cpnum=300&type=0&printSections=monindi&printSections=monsup&printSections=mos... 25/88
• Calcium Carbonate; Simethicone
• Ceritinib
• Chlorpromazine
• Ciprofloxacin
• Citalopram
• Clarithromycin
• Clofazimine
• Clozapine
• Codeine; Phenylephrine; Promethazine
• Codeine; Promethazine
• Crizotinib
• Dasatinib
• Degarelix
• Desflurane
• Deutetrabenazine
• Dextromethorphan; Promethazine
• Dextromethorphan; Quinidine
• Disopyramide
• Dofetilide
• Dolasetron
• Dolutegravir; Rilpivirine
• Donepezil
• Donepezil; Memantine
• Doxorubicin
• Droperidol
• Efavirenz
• Efavirenz; Emtricitabine; Tenofovir
• Efavirenz; Lamivudine; Tenofovir Disoproxil Fumarate
• Eliglustat
• Emtricitabine; Rilpivirine; Tenofovir alafenamide
• Emtricitabine; Rilpivirine; Tenofovir disoproxil fumarate
• Encaïnide
• Encorafenib
• Enflurane
• Entrectinib
• Eribulin
• Erythromycin
• Erythromycin; Sulfisoxazole
• Escitalopram
• Ezogabine
• Fingolimod
• Flecaïnide
• Fluconazole
• Fluoxetine
• Fluoxetine; Olanzapine
• Fluvoxamine
• Foscartern
• Gemifloxacin
• Gemtuzumab Ozogamicin
• Gilteritinib
• Glasdegib
• Goserelin
• Granisetron
• Halogenated Anesthetics
• Haloperidol
• Halothane
• Histrelin
• Hydroxyzine
• Ibutilide
• Iloperidone
• Inotuzumab Ozogamicin
• Isoflurane
• Itraconazole
• Ivosidenib
• Ketoconazole
• Lanthanum Carbonate
• Lapatinib
• Lefamulin
• Lenvatinib
• Leuprolide
• Leuprolide; Norethindrone
• Levofloxacin
• Lithium
• Lofexidine
• Loperamide
• Loperamide; Simethicone
• Lopinavir; Ritonavir
• Macimorelin
• Maprotiline
• Mefloquine
• Meperidine; Promethazine
• Methadone
• Metronidazole
• Midostaurin
• Mifepristone
• Mirtazapine
• Moxifloxacin
• Nilotinib
• Norfloxacine
• Octreotide
• Oflaxacin
• Olanzapine
• Omeprazole; Sodium Bicarbonate
• Ondansetron
• Osimertinib
• Oxaliplatin
• Paliperidone
• Panobinostat
• Pasireotide
• Pazopanib
• Penicillamine
• Pentamidine
• Phenylephrine; Promethazine
• Pimavanserin
• Pitolisant
Level 3 (Moderate)

- Acarbose
- Acetaminophen; Butalbital; Caffeine; Codeine
- Acetaminophen; Caffeine; Dihydrocodeine
- Acetaminophen; Codeine
- Acetaminophen; Hydrocodone
- Acetazolamide
- Acetohexamide
- Acidinium; Formoterol
- Albiglutide
- Alogliptin
- Alogliptin; Metformin
- Alogliptin; Pioglitazone
- Alpha-glucosidase Inhibitors
- Amobarbital
- Ampicillin
- Arformoterol
- Aspirin, ASA; Butalbital; Caffeine; Codeine
- Aspirin, ASA; Caffeine; Dihydrocodeine
- Aspirin, ASA; Carisoprodol; Codeine
- Atazanavir; Cobicistat
- Atropine; Hyoscyamine; Phenobarbital; Scopolamine
- Belladonna Alkaloids; Ergotamine; Phenobarbital
- Brivaracetam
- Brompheniramine; Guaifenesin; Hydrocodone
- Brompheniramine; Hydrocodone; Pseudoephedrine
- Budesonide; Formoterol
- Canagliflozin
- Canagliflozin; Metformin
- Carbamazepine
- Carbinoxamine; Hydrocodone; Phenylephrine
- Carbinoxamine; Hydrocodone; Pseudoephedrine
- Chlorpheniramine; Codeine
- Chlorpheniramine; Dihydrocodeine; Phenylephrine
- Chlorpheniramine; Dihydrocodeine; Pseudoephedrine
- Chlorpheniramine; Guaifenesin; Hydrocodone; Pseudoephedrine
- Chlorpheniramine; Hydrocodone
- Chlorpheniramine; Hydrocodone; Phenylephrine
- Chlorpheniramine; Hydrocodone; Pseudoephedrine
- Chlorpropamide
- Cimetidine
- Clobazam
- Clonazepam
- Clorazepate
- Cobicistat
- Codeine
- Codeine; Guaifenesin
- Cyclosporine
- Dapagliflozin
- Dapagliflozin; Metformin
- Dapagliflozin; Saxagliptin
- Darunavir; Cobicistat
- Darunavir; Cobicistat; Emtricitabine; Tenofovir alafenamide
- Diazepam
- Digoxin
- Dihydrocodeine; Guaifenesin; Pseudoephedrine
- Dipeptidyl Peptidase-4 Inhibitors
- Diphenhydramine; Hydrocodone; Phenylephrine
- Dulaglutide
- Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Alafenamide
- Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Disoproxil Fumarate
- Empagliflozin
- Empagliflozin; Linagliptin
- Empagliflozin; Linagliptin; Metformin
- Empagliflozin; Metformin
- Ertugliflozin
- Ertugliflozin; Metformin
- Ertugliflozin; Sitagliptin
- Eslicarbazepine
- Ethosuximide
- Ethotoin
- Exenatide
- Felbamate
- Fluticasone; Salmeterol
- Fluticasone; Umeclidinium; Vilanterol
- Fluticasone; Vilanterol
- Formoterol
- Formoterol; Mometasone
- Fosphenytoin
- Gabapentin
- Gefitinib
- Glimepiride
- Glimepiride; Pioglitazone
- Glimepiride; Rosiglitazone
- Glipizide
- Glipizide; Metformin
- Glyburide
- Glyburide; Metformin
- Glycopyrrolate; Formoterol
- Guaifenesin; Hydrocodone
- Guaifenesin; Hydrocodone; Pseudoephedrine
- Homatropine; Hydrocodone
- Hydrochlorothiazide, HCTZ; Metoprolol
- Hydrocodone
- Hydrocodone; Ibuprofen
- Hydrocodone; Phenylephrine
- Hydrocodeone; Potassium Guaiacolsulfonate
- Hydrocodeone; Potassium Guaiacolsulfonate; Pseudoephedrine
- Hydrocodone; Pseudoephedrine
- Incrin Mimetics
- Indacaterol
- Indacaterol; Glycopyrrolate
- 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
- Long-acting beta-agonists
- Lorazepam
- Meglitinides
- Mephobarbital
- Metformin
- Metformin; Pioglitazone
- Metformin; Repaglinide
- Metformin; Rosiglitazone
- Metformin; Saxagliptin
- Metformin; Sitagliptin
- Methotrexate
- Methsuximide
- Metoprolol
- Mexiletine
- Migliitol
- Nateglinide
- Nebivolol
- Nebivolol; Valsartan
- Olodaterol
- Pentobarbital
- Perampanel
- Phenobarbital
- Phentermine; Topiramate
- Phenytoin
- Pioglitazone
- Pramlintide
- Pregabalin
- Primidone
- Regular Insulin
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]

Acetaminophen; Butalbital; Caffeine; Codeine: (Moderate) Concomitant use of codeine with hydroxychloroquine may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If hydroxychloroquine is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [33654] [34883]

Acetaminophen; Caffeine; Dihydrocodeine: (Moderate) Concomitant use of dihydrocodeine with hydroxychloroquine may increase dihydrocodeine plasma concentrations, but decrease the plasma concentration of the active metabolite, dihydromorphine, resulting in reduced efficacy or symptoms of opioid withdrawal. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of

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<th>Compound/Drug Class</th>
<th>Level 4 (Minor)</th>
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<td>Acarbose</td>
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dihydrocodeine until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease dihydrocodeine plasma concentrations and increase dihydromorphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If hydroxychloroquine is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Dihydrocodeine is primarily metabolized by CYP2D6 to dihydromorphine, and by CYP3A4. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30282]

Acetaminophen; Codeine: (Moderate) Concomitant use of codeine with hydroxychloroquine may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If hydroxychloroquine is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [33654] [34883]

Acetaminophen; Hydrocodone: (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]

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: (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

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: (Minor) Use caution with coadministration of hydroxychloroquine and short-acting beta-agonists. Hydroxychloroquine 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. 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]

**Albuterol; Ipratropium:** (Minor) Use caution with coadministration of hydroxychloroquine and short-acting beta-agonists. Hydroxychloroquine 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. 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]

**Alfuzosin:** (Major) Avoid coadministration of hydroxychloroquine and alfuzosin. Hydroxychloroquine 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. Based on electrophysiology studies performed by the manufacturer, alfuzosin may prolong the QT interval in a dose-dependent manner. [28261] [41806] [65157]

**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]

**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]

**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 hydroxychloroquine and amiodarone. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Amiodarone, a Class III antiarrhythmic agent, is associated with a well-established risk of QT prolongation and 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]
Amitriptyline: (Minor) Use hydroxychloroquine and tricyclic antidepressants together with caution due to a potential risk of QT prolongation. 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).

Amitriptyline; Chlordiazepoxide: (Minor) Use hydroxychloroquine and tricyclic antidepressants together with caution due to a potential risk of QT prolongation. 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).

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.

Amoxicillin; Clarithromycin; Lansoprazole: (Major) Avoid coadministration of hydroxychloroquine and clarithromycin. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Clarithromycin is associated with an established risk for QT prolongation and TdP.

Amoxicillin; Clarithromycin; Omeprazole: (Major) Avoid coadministration of hydroxychloroquine and clarithromycin. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Clarithromycin is associated with an established risk for QT prolongation and TdP.

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.

Anagrelide: (Major) Avoid coadministration of hydroxychloroquine and anagrelide. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. 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. A cardiovascular examination, including an ECG, should be obtained in all patients prior to initiating anagrelide therapy. Monitor patients during anagrelide therapy for cardiovascular effects and evaluate as necessary.

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).

Apomorphine: (Major) Avoid coadministration of hydroxychloroquine and apomorphine. Hydroxychloroquine 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. 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.

Arformoterol: (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

Aripiprazole: (Major) Hydroxychloroquine has been associated with ventricular arrhythmias and torsade de pointes and generally should not be administered with other drugs known to prolong the QT interval such as aripiprazole. In addition, because aripiprazole is partially metabolized by CYP2D6, patients should be carefully monitored for aripiprazole-related adverse reactions during concurrent use of a CYP2D6 inhibitor such as hydroxychloroquine. Because aripiprazole is also metabolized by CYP3A4, patients receiving a combination of a CYP3A4 and CYP2D6 inhibitor should have their oral aripiprazole dose reduced to one-quarter (25%) of the usual dose with subsequent adjustments based upon clinical response. Adult patients receiving a combination of a CYP3A4 and CYP2D6 inhibitor for more than 14 days should have their Abilify Maintena dose reduced from 400 mg/month to 200 mg/month or from 300 mg/month to 160 mg/month, respectively. There are no dosing recommendations for Aristada or Aristada Initio during use of a mild to moderate CYP2D6 inhibitor. [41806] [42845] [53394] [60196] [63328] [65157]

Arsenic Trioxide: (Major) Avoid coadministration of hydroxychloroquine and arsenic trioxide.
Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. TdP, QT interval prolongation, and complete atrioventricular block have been reported with arsenic trioxide use. If concomitant drug use is unavoidable, frequently monitor electrocardiograms. [41806] [59438] [65157]

Artemether; Lumefantrine: (Major) Avoid coadministration of hydroxychloroquine and artemether; lumefantrine. Hydroxychloroquine 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. Artemether; lumefantrine is associated with prolongation of the QT interval and should be avoided in combination with other QT prolonging drugs. Consider ECG monitoring if other QT prolonging drugs must be used with or after artemether; lumefantrine treatment. In addition, other antimalarial agents, such as hydroxychloroquine, should not be given with artemether unless there is no other treatment option because limited safety data are available. [34501] [41806] [65157] (Major) Avoid coadministration of hydroxychloroquine and artemether; lumefantrine. Hydroxychloroquine 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. Artemether; lumefantrine is associated with prolongation of the QT interval and should be avoided in combination with other QT prolonging drugs. Consider ECG monitoring if other QT prolonging drugs must be used with or after artemether; lumefantrine treatment. In addition, other antimalarial agents, such as hydroxychloroquine, should not be given with artemether unless there is no other treatment option because limited safety data are available. [35401] [41806] [65157]

Asenapine: (Major) Avoid coadministration of hydroxychloroquine and asenapine. Hydroxychloroquine 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. Asenapine has been associated with QT prolongation. [36343] [41806] [65157]

Aspirin, ASA; Butalbital; Caffeine; Codeine: (Moderate) Concomitant use of codeine with hydroxychloroquine may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If hydroxychloroquine is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6.
to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [33654] [34883]

**Aspirin, ASA, Caffeine, Dihydrocodeine:** (Moderate) Concomitant use of dihydrocodeine with hydroxychloroquine may increase dihydrocodeine plasma concentrations, but decrease the plasma concentration of the active metabolite, dihydromorphine, resulting in reduced efficacy or symptoms of opioid withdrawal. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of dihydrocodeine until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease dihydrocodeine plasma concentrations and increase dihydromorphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If hydroxychloroquine is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Dihydrocodeine is primarily metabolized by CYP2D6 to dihydromorphine, and by CYP3A4. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30282]

**Aspirin, ASA, Carisoprodol, Codeine:** (Moderate) Concomitant use of codeine with hydroxychloroquine may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If hydroxychloroquine is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30282] [34883]

**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 = 495). [30284] [30285] [41806] [61758]

**Atazanavir, Cobicistat:** (Moderate) Caution is warranted when cobicistat is administered with hydroxychloroquine as there is a potential for elevated cobicistat concentrations. Hydroxychloroquine is a CYP2D6 inhibitor, while cobicistat is a substrate of CYP2D6. [29396] [51664]

**Atomoxetine:** (Major) Avoid coadministration of hydroxychloroquine and atomoxetine. Hydroxychloroquine 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. QT prolongation has occurred during therapeutic use of atomoxetine and following overdose. In addition, atomoxetine is primarily metabolized by CYP2D6. Concurrent use of CYP2D6 inhibitors such as hydroxychloroquine may theoretically increase the risk of atomoxetine-induced adverse effects. [28405] [29396] [41806] [65157]

**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, perform an ECG at baseline and monitor closely throughout therapy, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances prior to initiation. Hydroxychloroquine prolongs the QT interval. Qt prolongation and torsade de pointe (TdP) have been spontaneously reported during azithromycin postmarketing surveillance. [28855] [41806] [43974] [65157]
**Bedaquiline:** (Major) Avoid coadministration of hydroxychloroquine and bedaquiline. Hydroxychloroquine 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. Bedaquiline has been reported to prolong the QT interval. Coadministration with other QT prolonging drugs may result in additive or synergistic prolongation of the QT interval. If coadministration is unavoidable, obtain serum electrolyte concentrations and a baseline ECG prior to initiating bedaquiline. An ECG should also be performed at least 2, 12, and 24 weeks after starting bedaquiline therapy. [41806] [52746] [65157]

**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 hydroxychloroquine and metronidazole. Hydroxychloroquine 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. Potential QT prolongation has been reported in limited case reports with metronidazole. [41806] [57377] [57378]

**Bismuth Subsalicylate; Metronidazole; Tetracycline:** (Major) Avoid coadministration of hydroxychloroquine and metronidazole. Hydroxychloroquine 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. Potential QT prolongation has been reported in limited case reports with metronidazole. [41806] [57377] [57378]

**Botulinum Toxins:** (Major) One study reported that chloroquine antagonized the actions of botulinum toxins. The study suggested that chloroquine may prevent internalization by inhibiting toxin binding at the cell membrane or inhibit lysosomal processing of the toxin in the cell interior. Hydroxychloroquine, a related quinoline agent, may also interfere with the actions of botulinum toxins. [26411]

**Brimonidine; Timolol:** (Minor) Timolol is significantly metabolized by CYP2D6 isoenzymes. CYP2D6 inhibitors, such as hydroxychloroquine, could theoretically impair timolol metabolism; the clinical significance of such interactions is unknown. [4718] [6134]

**Brivaracetam:** (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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]

**Brompheniramine; Guaifenesin; Hydrocodone:** (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]

**Brompheniramine; Hydrocodone; Pseudoephedrine:** (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydroxychloroquine...
hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]

**Budesonide; Formoterol:** (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

**Buprenorphine:** (Major) Avoid coadministration of hydroxychloroquine and buprenorphine. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Buprenorphine has been associated with QT prolongation and has a possible risk of TdP. FDA-approved labeling for some buprenorphine products recommend avoiding use with Class 1A and Class III antiarrhythmic medications while other labels recommend avoiding use with any drug that has the potential to prolong the QT interval. [41235] [41806] [59321] [60270] [65157]

**Buprenorphine; Naloxone:** (Major) Avoid coadministration of hydroxychloroquine and buprenorphine. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Buprenorphine has been associated with QT prolongation and has a possible risk of TdP. FDA-approved labeling for some buprenorphine products recommend avoiding use with Class 1A and Class III antiarrhythmic medications while other labels recommend avoiding use with any drug that has the potential to prolong the QT interval. [41235] [41806] [59321] [60270] [65157]

**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 = 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]

**Calcium Carbonate; Simethicone:** (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]

**Carbamazepine:** (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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]

**Carbinoxamine; Hydrocodone; Phenylephrine:** (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]

**Carbinoxamine; Hydrocodone; Pseudoephedrine:** (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]

**Carvedilol:** (Minor) Inhibitors of the hepatic CYP450 isozyme CYP 2D6, such as hydroxychloroquine, may inhibit the hepatic oxidative metabolism of carvedilol. Clinicians should use these drugs cautiously in patients stabilized on carvedilol. [5267] [6134]

**Ceritinib:** (Major) Hydroxychloroquine prolongs the QT interval and should not be administered with other drugs known to prolong the QT interval, such as ceritinib which causes concentration-dependent QT prolongation. [41806] [57094] [65157]

**Chlorpheniramine; Codeine:** (Moderate) Concomitant use of codeine with hydroxychloroquine may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If hydroxychloroquine is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine,
and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Hydroxychloroquine is a moderate inhibitor of CYP2D6. \[29396\] [33654] [34883]

**Chlorpheniramine; Dihydrocodeine; Phenylephrine:** (Moderate) Concomitant use of dihydrocodeine with hydroxychloroquine may increase dihydrocodeine plasma concentrations, but decrease the plasma concentration of the active metabolite, dihydromorphine, resulting in reduced efficacy or symptoms of opioid withdrawal. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of dihydrocodeine until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease dihydrocodeine plasma concentrations and increase dihydromorphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If hydroxychloroquine is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Dihydrocodeine is primarily metabolized by CYP2D6 to dihydromorphine, and by CYP3A4. Hydroxychloroquine is a moderate inhibitor of CYP2D6. \[29396\] [30282]

**Chlorpheniramine; Dihydrocodeine; Pseudoephedrine:** (Moderate) Concomitant use of dihydrocodeine with hydroxychloroquine may increase dihydrocodeine plasma concentrations, but decrease the plasma concentration of the active metabolite, dihydromorphine, resulting in reduced efficacy or symptoms of opioid withdrawal. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of dihydrocodeine until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease dihydrocodeine plasma concentrations and increase dihydromorphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If hydroxychloroquine is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Dihydrocodeine is primarily metabolized by CYP2D6 to dihydromorphine, and by CYP3A4. Hydroxychloroquine is a moderate inhibitor of CYP2D6. \[29396\] [30282]

**Chlorpheniramine; Guaifenesin; Hydrocodone; Pseudoephedrine:** (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. \[29396\] [30379] [56303]

**Chlorpheniramine; Hydrocodone:** (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. \[29396\] [30379] [56303]

**Chlorpheniramine; Hydrocodone; Phenylephrine:** (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. \[29396\] [30379] [56303]
opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]

Chlorpheniramine; Hydrocodone; Pseudoephedrine: (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If concomitant use is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]

Chlorpromazine: (Major) Avoid coadministration of hydroxychloroquine and chlorpromazine. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Chlorpromazine is associated with an established risk of QT prolongation and TdP. [28415] [41806] [43065] [65157]

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 hydroxychloroquine and ciprofloxacin. Hydroxychloroquine 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. Rare cases of QT prolongation and torsade de pointes (TdP) have been reported with ciprofloxacin during postmarketing surveillance. Ciprofloxacin should be used with caution in patients receiving other drugs that prolong the QT interval. [28432] [28457] [29833] [33144] [33145] [33146] [41806] [43411] [48869] [48871] [65157]

Cisapride: (Severe) QT prolongation and ventricular arrhythmias, including torsade de pointes (TdP) and death, have been reported with cisapride. Because of the potential for TdP, use of hydroxychloroquine with cisapride is contraindicated. [28978] [41806] [47221]

Citalopram: (Major) Avoid coadministration of hydroxychloroquine and citalopram. Hydroxychloroquine 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. Citalopram causes dose-dependent QT interval prolongation. According to the manufacturer, concurrent use of citalopram with other drugs that prolong the QT interval is not recommended. If concurrent therapy is considered essential, ECG monitoring is recommended. [28269] [41806] [65157]

Clarithromycin: (Major) Avoid coadministration of hydroxychloroquine and clarithromycin. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Clarithromycin is associated with an established risk for QT prolongation and TdP. [28225] [28238] [41806] [65157]
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]

Clomipramine: (Minor) Use hydroxychloroquine and tricyclic antidepressants together with caution due to a potential risk of QT prolongation. 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]

Clonazepam: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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 hydroxychloroquine 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 hydroxychloroquine and clozapine. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Treatment with clozapine has been associated with QT prolongation, TdP, cardiac arrest, and sudden death. In addition, hydroxychloroquine is an inhibitor of CYP2D6, one of the isoenzymes responsible for the metabolism of clozapine. Elevated plasma concentrations of clozapine occurring through inhibition of CYP2D6 may potentially increase the risk of life-threatening arrhythmias or other adverse effects. If coadministration is unavoidable, a decrease in clozapine dose may be required. [28262] [29396] [41806] [65157]

Cobicistat: (Moderate) Caution is warranted when cobicistat is administered with hydroxychloroquine as there is a potential for elevated cobicistat concentrations. Hydroxychloroquine is a CYP2D6 inhibitor, while cobicistat is a substrate of CYP2D6. [29396] [51664]

Codeine: (Moderate) Concomitant use of codeine with hydroxychloroquine may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If hydroxychloroquine is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [33654] [34883]

Codeine; Guaifenesin: (Moderate) Concomitant use of codeine with hydroxychloroquine may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease codeine plasma concentrations and increase morphine plasma concentrations.
concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If hydroxychloroquine is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [33654] [34883]

Codeine; Phenylephrine; Promethazine: (Major) Avoid coadministration of hydroxychloroquine and promethazine. Hydroxychloroquine 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. Promethazine is associated with a possible risk for QT prolongation. [28225] [41806] [55578] (Moderate) Concomitant use of codeine with hydroxychloroquine may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If hydroxychloroquine is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [33654] [34883]

Codeine; Promethazine: (Major) Avoid coadministration of hydroxychloroquine and promethazine. Hydroxychloroquine 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. Promethazine is associated with a possible risk for QT prolongation. [28225] [41806] [55578] (Moderate) Concomitant use of codeine with hydroxychloroquine may increase codeine plasma concentrations, but decrease the plasma concentration of the active metabolite, morphine, resulting in reduced efficacy or symptoms of opioid withdrawal. It is recommended to avoid this combination when codeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of codeine until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease codeine plasma concentrations and increase morphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If hydroxychloroquine is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Codeine is primarily metabolized by CYP2D6 to morphine, and by CYP3A4 to norcodeine; norcodeine does not have analgesic properties. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [33654] [34883]

Crizotinib: (Major) Do not administer hydroxychloroquine with crizotinib due to the risk of QT prolongation. Both drugs have been associated with QT prolongation. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. [41806] [45458] [65157]

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]

Dapagliflozin: (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]

Dapagliflozin; 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]

Dapagliflozin; 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] (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]

Darunavir; Cobicistat: (Moderate) Caution is warranted when cobicistat is administered with hydroxychloroquine as there is a potential for elevated cobicistat concentrations. Hydroxychloroquine is a CYP2D6 inhibitor, while cobicistat is a substrate of CYP2D6. [29396] [51664]

Darunavir; Cobicistat; Emtricitabine; Tenofovir alafenamide: (Moderate) Caution is warranted when cobicistat is administered with hydroxychloroquine as there is a potential for elevated cobicistat concentrations. Hydroxychloroquine is a CYP2D6 inhibitor, while cobicistat is a substrate of CYP2D6. [29396] [51664]

Dasatinib: (Major) Avoid coadministration of hydroxychloroquine and dasatinib. Hydroxychloroquine 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. In vitro studies have shown that dasatinib has the potential to prolong the QT interval. [32387] [41806] [65157]

Degarelix: (Major) Avoid coadministration of hydroxychloroquine and degarelix. Hydroxychloroquine 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. QTc prolongation has been reported with the use of degarelix. [41806] [46869] [65157]

Desflurane: (Major) Avoid coadministration of hydroxychloroquine and halogenated anesthetics. Hydroxychloroquine 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. Halogenated anesthetics can prolong the QT interval. [28457] [28458] [28754] [28755] [28756] [41806]

Desipramine: (Minor) Use hydroxychloroquine and tricyclic antidepressants together with caution due to a potential risk of QT prolongation. 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]

Deutetrabenazine: (Major) Hydroxychloroquine prolongs the QT interval and should not be administered with other drugs known to prolong the QT interval. Clinically relevant QTc prolongation may occur with deutetrabenazine. [41806] [61845] [65157]

Dextromethorphan; Promethazine: (Major) Avoid coadministration of hydroxychloroquine and promethazine. Hydroxychloroquine 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. Promethazine is associated with a possible risk for QT prolongation. [28225] [41806] [55578]

Dextromethorphan; Quinidine: (Major) Avoid coadministration of hydroxychloroquine and quinidine. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to
prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Quinidine administration is associated with QT prolongation and TdP. [41806] [42280] [47357]

**Diazepam:** (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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) Digoxin serum concentrations have been reported to increase when hydroxychloroquine was added. Hydroxychloroquine may inhibit P-glycoprotein (P-gp). Digoxin is a substrate for P-gp transport. For patients on a stable digoxin regimen and initiating hydroxychloroquine, no initial dose adjustment of either drug has been advised; however, serum digoxin concentrations should be monitored and used for digoxin dose titration as clinically necessary. [28272] [30287] [60957]

**Dihydrocodeine; Guaifenesin; Pseudoephedrine:** (Moderate) Concomitant use of dihydrocodeine with hydroxychloroquine may increase dihydrocodeine plasma concentrations, but decrease the plasma concentration of the active metabolite, dihydromorphine, resulting in reduced efficacy or symptoms of opioid withdrawal. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage increase of dihydrocodeine until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease dihydrocodeine plasma concentrations and increase dihydromorphine plasma concentrations resulting in prolonged opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. If hydroxychloroquine is discontinued, monitor the patient carefully and consider reducing the opioid dosage if appropriate. Dihydrocodeine is primarily metabolized by CYP2D6 to dihydromorphine, and by CYP3A4. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30282]

**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]

**Diphenhydramine; Hydrocodone; Phenylephrine:** (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]

**Disopyramide:** (Major) Avoid coadministration of hydroxychloroquine and disopyramide. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Disopyramide administration is also associated with QT prolongation and TdP. [28228] [41806] [65157]

**Dofetilide:** (Major) Coadministration of dofetilide and hydroxychloroquine is not recommended as concurrent use may increase the risk of QT prolongation. Dofetilide, a Class III antiarrhythmic agent, is associated with a well-established risk of QT prolongation and torsade de pointes (TdP). Hydroxychloroquine prolongs the QT interval. [28221] [28432] [28457] [41806] [65157]

**Dolasetron:** (Major) Avoid coadministration of hydroxychloroquine and dolasetron. Hydroxychloroquine 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.
Dolasetron has been associated with a dose-dependent prolongation in the QT, PR, and QRS intervals on an electrocardiogram. [41806] [42844]

Dolutegravir; Rilpivirine: (Major) Avoid coadministration of hydroxychloroquine and rilpivirine. Hydroxychloroquine 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. Supratherapeutic doses of rilpivirine (75 to 300 mg/day) have caused QT prolongation. [41806] [44376]

Donepezil: (Major) Avoid coadministration of hydroxychloroquine and donepezil. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Case reports indicate that QT prolongation and TdP can occur during donepezil therapy. Donepezil is considered a drug with a known risk of TdP. [41806] [59321] [59322] [65157]

Donepezil; Memantine: (Major) Avoid coadministration of hydroxychloroquine and donepezil. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Case reports indicate that QT prolongation and TdP can occur during donepezil therapy. Donepezil is considered a drug with a known risk of TdP. [41806] [59321] [59322] [65157]

Dorzolamide; Timolol: (Minor) Timolol is significantly metabolized by CYP2D6 isoenzymes. CYP2D6 inhibitors, such as hydroxychloroquine, could theoretically impair timolol metabolism; the clinical significance of such interactions is unknown. [4718] [6134]

Doxepin: (Minor) Use hydroxychloroquine and tricyclic antidepressants together with caution due to a potential risk of QT prolongation. 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]

Doxorubicin: (Major) Hydroxychloroquine is an inhibitor of CYP2D6 and doxorubicin is a major CYP2D6 substrate. Clinically significant interactions have been reported when doxorubicin was coadministered with inhibitors of CYP2D6, resulting in increased concentration and clinical effect of doxorubicin. Avoid coadministration of hydroxychloroquine and doxorubicin if possible. If not possible, closely monitor for increased side effects of doxorubicin including myelosuppression and cardiotoxicity. [29396] [56361]

Dronedarone: (Severe) 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. Because of the potential for torsade de pointes, use of hydroxychloroquine with dronedarone is contraindicated. [36101] [41806]

Droperidol: (Major) Avoid coadministration of hydroxychloroquine and droperidol. Hydroxychloroquine 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. Droperidol administration is associated with an established risk for QT prolongation and torsade de pointes (TdP). [28235] [28236] [28737] [41806] [51289] [65157]

Dulaglutide: (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 hydroxychloroquine and efavirenz. Hydroxychloroquine 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. QTc prolongation has been observed with the use of efavirenz. [28442] [41806] [65157]

Efavirenz; Emtricitabine; Tenofovir: (Major) Avoid coadministration of hydroxychloroquine and efavirenz. Hydroxychloroquine 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. QTc prolongation has been observed with the use of efavirenz. [28442] [41806] [65157]

Efavirenz; Lamivudine; Tenofovir Disoproxil Fumarate: (Major) Avoid coadministration of hydroxychloroquine and efavirenz. Hydroxychloroquine 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. QTc prolongation has been observed with the use of efavirenz. [28442] [41806] [65157]

Eliglustat: (Major) Avoid coadministration of hydroxychloroquine and eliglustat. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Eliglustat is predicted to cause PR, QRS, and/or QT prolongation at significantly elevated plasma concentrations. Additionally, hydroxychloroquine is a moderate CYP2D6 inhibitor; eliglustat is a CYP2D6 substrate. Coadministration with CYP2D6 inhibitors may increase eliglustat exposure and the risk of serious adverse events (e.g., QT prolongation and cardiac arrhythmias). If coadministration is necessary in extensive or intermediate CYP2D6 metabolizers (EMS or IMs), a dose reduction of eliglustat to 84 mg PO once daily is necessary; however, coadministration of eliglustat with both hydroxychloroquine and a strong or moderate CYP3A inhibitor is contraindicated. [41806] [57803] [65157]

Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Alafenamide: (Moderate) Caution is warranted when cobicistat is administered with hydroxychloroquine as there is a potential for elevated cobicistat concentrations. Hydroxychloroquine is a CYP2D6 inhibitor, while cobicistat is a substrate of CYP2D6. [29396] [51664]

Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Disoproxil Fumarate: (Moderate) Caution is warranted when cobicistat is administered with hydroxychloroquine as there is a potential for elevated cobicistat concentrations. Hydroxychloroquine is a CYP2D6 inhibitor, while cobicistat is a substrate of CYP2D6. [29396] [51664]

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 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. 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.

**Empagliflozin; Metformin:** 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.

**Empagliflozin; Rilpivirine; Tenofovir alafenamide:** 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.

**Emtricitabine; Rilpivirine; Tenofovir alafenamide:** 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.

**Emtricitabine; Rilpivirine; Tenofovir disoproxil fumarate:** 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.

**Encainide:** Encainide is significantly metabolized by CYP2D6 isoenzymes. Caution is recommended when administering encainide with CYP2D6 inhibitors, such as hydroxychloroquine, since encainide exhibits a narrow therapeutic range and large increases in serum concentrations may be associated with severe adverse reactions.

**Encorafenib:** Avoid coadministration of encorafenib and hydroxychloroquine due to QT prolongation. Encorafenib is associated with dose-dependent prolongation of the QT interval. Hydroxychloroquine prolongs the QT interval and should not be administered with other drugs known to prolong the QT interval.

**Enflurane:** Avoid coadministration of hydroxychloroquine and halogenated anesthetics. Hydroxychloroquine 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. Supratherapeutic doses of rilpivirine (75 to 300 mg/day) have caused QT prolongation.

**Entrectinib:** Avoid coadministration of entrectinib with hydroxychloroquine due to the risk of QT prolongation. Entrectinib has been associated with QT prolongation. Hydroxychloroquine also prolongs the QT interval.

**Eribulin:** Avoid coadministration of hydroxychloroquine and eribulin. Hydroxychloroquine 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. Eribulin has been associated with QT prolongation. If eribulin and another drug that prolongs the QT interval must be coadministered, ECG monitoring is recommended; closely monitor the patient for QT interval prolongation.

**Ertugliflozin:** 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; 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]

**Erythromycin:** (Major) Avoid coadministration of hydroxychloroquine and erythromycin. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Erythromycin is associated with QT prolongation and TdP. [41806] [43258] [65157]

**Erythromycin; Sulfisoxazole:** (Major) Avoid coadministration of hydroxychloroquine and erythromycin. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Erythromycin is associated with QT prolongation and TdP. [41806] [43258] [65157]

**Escitalopram:** (Major) Avoid coadministration of hydroxychloroquine and escitalopram. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Escitalopram has been associated with a risk of QT prolongation and TdP. [28270] [41806] [65157]

**Eslicarbazepine:** (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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 hydroxychloroquine 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 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]

**Ezogabine:** (Major) Avoid coadministration of hydroxychloroquine and ezogabine. Hydroxychloroquine 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.
Ezogabine has 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]

Felbamate: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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]

Fingolimod: (Major) Avoid coadministration of hydroxychloroquine and fingolimod. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Fingolimod initiation results in decreased heart rate and may prolong the QT interval. 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 TdP. 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]

Flecainide: (Major) Avoid coadministration of hydroxychloroquine and flecainide. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. 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. [23774] [28752] [41806] [65157]

Fluconazole: (Major) Avoid coadministration of hydroxychloroquine and fluconazole. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Fluconazole has been associated with QT prolongation and rare cases of TdP. [28674] [41806] [65157]

Fluoxetine: (Major) Avoid coadministration of hydroxychloroquine and fluoxetine. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. QT prolongation and TdP have been reported in patients treated with fluoxetine. [32127] [41806] [65157]

Fluoxetine; Olanzapine: (Major) Avoid coadministration of hydroxychloroquine and fluoxetine. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. QT prolongation and TdP have been reported in patients treated with fluoxetine. [32127] [41806] [65157]

Fluphenazine: (Minor) Use caution with the coadministration of hydroxychloroquine and fluphenazine. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Fluphenazine is associated with a possible risk for QT prolongation. Theoretically, fluphenazine may increase the risk of QT prolongation if coadministered with other drugs that have a risk of QT prolongation, such as hydroxychloroquine. [28514] [41806]

Fluticasone; Salmeterol: (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

**Fluticasone; Umeclidinium; Vilanterol:** (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

**Fluticasone; Vilanterol:** (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

**Fluvoxamine:** (Major) There may be an increased risk for QT prolongation and torsade de pointes (TdP) during concurrent use of fluvoxamine and hydroxychloroquine. Cases of QT prolongation and TdP have been reported during postmarketing use of fluvoxamine. Hydroxychloroquine prolongs the QT interval and should not be administered with other drugs known to prolong the QT interval. [41806] [50507]

**Formoterol:** (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

**Formoterol; Mometasone:** (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

**Fosphenytoin:** (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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 hydroxychloroquine 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]
Galsulfase: (Minor) Theoretically, there is a possible drug interaction between galsulfase and medications which may impact lysosomal efficacy. Both chloroquine and hydroxychloroquine are weak bases that accumulate in acidic lysosomes because of ion trapping. The subsequent elevation of lysosomal pH results in lysosomal enzyme inhibition. Although these drugs have been clinically shown to interact with other MPS treatments, it is unknown if they will have any effect on the efficacy of galsulfase. [4144]

Gefitinib: (Moderate) Monitor for an increase in gefitinib-related adverse reactions if coadministration with hydroxychloroquine is necessary; the risk is increased in CYP2D6 poor metabolizers. Based on in vitro data, gefitinib is metabolized to O-desmethyl gefitinib by CYP2D6 and hydroxychloroquine is a CYP2D6 inhibitor. In healthy CYP2D6 poor metabolizers, the concentration of O-desmethyl gefitinib was not measurable and mean exposure to gefitinib was 2-fold higher compared to extensive metabolizers. The impact of CYP2D6 inhibitors on gefitinib pharmacokinetics has not been evaluated; however, the manufacturer recommends precautions based on exposure in patients with poor CYP2D6 metabolism. [29396] [45935]

Gemifloxacin: (Major) Avoid coadministration of hydroxychloroquine and gemifloxacin. Hydroxychloroquine 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. 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, if coadministration is necessary, 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]

Gemtuzumab Ozogamicin: (Major) Avoid coadministration of gemtuzumab ozogamicin with hydroxychloroquine due to the potential for additive QT interval prolongation and risk of torsade de pointes (TdP). If coadministration is unavoidable, obtain an ECG and serum electrolytes prior to the start of and as needed during treatment. Although QT interval prolongation has not been reported with gemtuzumab ozogamicin, it has been reported with other drugs that contain calicheamicin. Hydroxychloroquine may cause QT interval prolongation. [41806] [62292] [65157]

Gilteritinib: (Major) Do not administer hydroxychloroquine and gilteritinib together due to the potential for additive QT prolongation. Both drugs have been associated with QT prolongation; coadministration has the potential for additive effects. [41806] [63787] [65157]

Glasdegib: (Major) Glasdegib and hydroxychloroquine should not be coadministered due to additive risk of QT prolongation. Hydroxychloroquine prolongs the QT interval. Glasdegib therapy may result in QT prolongation and ventricular arrhythmias including ventricular fibrillation and ventricular tachycardia. [41806] [63777] [65157]

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:** (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

**Goserelin:** (Major) Avoid coadministration of hydroxychloroquine and goserelin due to the risk of QT prolongation. Hydroxychloroquine prolongs the QT interval. Androgen deprivation therapy (e.g., goserelin) also may prolong the QT/QTc interval. [28592] [41806]

**Granisetron:** (Major) Avoid coadministration of hydroxychloroquine and granisetron. Hydroxychloroquine 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. Granisetron has been associated with QT prolongation. [31723] [41806]

**Guaifenesin; Hydrocodone:** (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodeine is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and
potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]

Guaifenesin; Hydrocodone; Pseudoephedrine: (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]

Halogenated Anesthetics: (Major) Avoid coadministration of hydroxychloroquine and halogenated anesthetics. Hydroxychloroquine 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. Halogenated anesthetics can prolong the QT interval. [28457] [28458] [28754] [28755] [28756] [41806]

Haloperidol: (Major) Avoid coadministration of hydroxychloroquine and haloperidol. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. QT prolongation and 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. Additionally, hydroxychloroquine is an inhibitor of CYP2D6, one of the isoenzymes responsible for the metabolism of haloperidol. Mild to moderate increases in haloperidol plasma concentrations have been reported during concurrent use of haloperidol and inhibitors of CYP2D6. Elevated haloperidol concentrations occurring through inhibition of CYP2D6 may increase the risk of adverse effects, including QT prolongation. [23500] [23779] [28225] [28307] [28415] [28416] [41806]

Halothane: (Major) Avoid coadministration of hydroxychloroquine and halogenated anesthetics. Hydroxychloroquine 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. Halogenated anesthetics can prolong the QT interval. [28457] [28458] [28754] [28755] [28756] [41806]

Histrelin: (Major) Avoid coadministration of hydroxychloroquine and histrelin due to the risk of QT prolongation. Hydroxychloroquine prolongs the QT interval. Androgen deprivation therapy (e.g., histrelin) also may prolong the QT/QTc interval. [30369] [41806]

Homatropine; Hydrocodone: (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]
Hydrochlorothiazide, HCTZ; Metoprolol: (Moderate) Monitor for increased metoprolol adverse reactions including bradycardia and hypotension during coadministration. A dosage reduction for metoprolol may be needed based on response. Concurrent use may increase metoprolol exposure. Metoprolol is a CYP2D6 substrate; hydroxychloroquine is a moderate CYP2D6 inhibitor. In the presence of another moderate CYP2D6 inhibitor, the AUC of metoprolol was increased by 3.29-fold with no effect on the cardiovascular response to metoprolol. [29396] [32916] [62643]

Hydrochlorothiazide, HCTZ; Propranolol: (Minor) Propranolol is significantly metabolized by CYP2D6 isoenzymes. CYP2D6 inhibitors, such as hydroxychloroquine, could theoretically impair propranolol metabolism; the clinical significance of such interactions is unknown. [4718] [6134]

Hydrocodone: (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]

Hydrocodone; Ibuprofen: (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]

Hydrocodone; Phenylephrine: (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]

Hydrocodone; Potassium Guaiacolsulfonate: (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]
**Hydrocodone; Potassium Guaiacolsulfonate; Pseudoephedrine:** (Moderate) Concomitant use of hydrocodone with hydroxychloroquine may increase hydrocodone plasma concentrations and prolong opioid adverse reactions, including hypotension, respiratory depression, profound sedation, coma, and death. It is recommended to avoid this combination when hydrocodone is being used for cough. If coadministration is necessary, monitor patients closely at frequent intervals and consider a dosage reduction of hydrocodone until stable drug effects are achieved. Discontinuation of hydroxychloroquine could decrease hydrocodone plasma concentrations, decrease opioid efficacy, and potentially lead to a withdrawal syndrome in those with physical dependence to hydrocodone. If hydroxychloroquine is discontinued, monitor the patient carefully and consider increasing the opioid dosage if appropriate. Hydrocodone is a substrate for CYP2D6. Hydroxychloroquine is a moderate inhibitor of CYP2D6. [29396] [30379] [56303]

**Hydroxyzine:** (Major) Avoid coadministration of hydroxychloroquine and hydroxyzine. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Postmarketing data indicate that hydroxyzine causes QT prolongation and TdP. [41806] [47129]

**Ibutilide:** (Major) Avoid coadministration of hydroxychloroquine and ibutilide. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Ibutilide administration can cause QT prolongation and TdP; proarrhythmic events should be anticipated. The potential for proarrhythmic events with ibutilide increases with the coadministration of other drugs that prolong the QT interval. [41806] [41830]

**Iloperidone:** (Major) Avoid coadministration of hydroxychloroquine and iloperidone. Hydroxychloroquine 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. Iloperidone has been associated with QT prolongation. [36146] [41806]

**Imipramine:** (Minor) Use hydroxychloroquine and tricyclic antidepressants together with caution due to a potential risk of QT prolongation. 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]

**Incretin Mimetics:** (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]

**Indacaterol:** (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

**Indacaterol; Glycopyrrolate:** (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

**Inotuzumab Ozogamicin:** (Major) Avoid coadministration of inotuzumab ozogamicin with hydroxychloroquine due to the potential for additive QT interval prolongation and risk of torsade de pointes (TdP). If coadministration is unavoidable, obtain an ECG and serum electrolytes prior to the start of treatment, after treatment initiation, and periodically during treatment. Both inotuzumab and hydroxychloroquine have been associated with QT prolongation. [41806] [62245]

**Insulin Aspart:** (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]

**Insulin Aspart; Insulin Aspart Protamine:** (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]

**Insulin Degludec:** (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]

**Insulin Degludec; Liraglutide:** (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]

**Insulin Detemir:** (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]

**Insulin Glargine:** (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]

**Insulin Glargine; Lixisenatide:** (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]
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]

**Insulin Glulisine:** (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]

**Insulin Lispro:** (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]

**Insulin Lispro; Insulin Lispro Protamine:** (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]

**Insulin Inhaled:** (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]

**Insulins:** (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]

**Isoflurane:** (Major) Avoid coadministration of hydroxychloroquine and halogenated anesthetics. Hydroxychloroquine 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. Halogenated anesthetics can prolong the QT interval. [28457] [28458] [28754] [28755] [28756] [41806]

**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]

**Itraconazole:** (Major) Avoid coadministration of hydroxychloroquine and itraconazole. Hydroxychloroquine 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. Itraconazole has been associated with prolongation of the QT interval. [40233] [41806] [57441]

**Ivosidenib:** (Major) Avoid coadministration of ivosidenib with hydroxychloroquine due to an increased risk of QT prolongation. If concomitant use is unavoidable, monitor ECGs for QTc prolongation and monitor electrolytes; correct any electrolyte abnormalities as clinically appropriate. An interruption of therapy and dose reduction of ivosidenib may be necessary if QT prolongation occurs. Prolongation of the QTc interval and ventricular arrhythmias have been reported in patients treated with ivosidenib. Hydroxychloroquine prolongs the QT interval. [41806] [63368]

**Ketoconazole:** (Major) Avoid coadministration of hydroxychloroquine and ketoconazole. Hydroxychloroquine 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. Ketoconazole has been associated with prolongation of the QT interval. [27982] [41806]
Lacosamide: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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]

Lamotrigine: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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]

Lanthanum Carbonate: (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]

Lapatinib: (Major) Hydroxychloroquine should not be administered with lapatinib. 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]

Lefamulin: (Major) Avoid coadministration of lefamulin with hydroxychloroquine as concurrent use may increase the risk of QT prolongation. If coadministration cannot be avoided, monitor ECG during treatment. 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. Hydroxychloroquine prolongs the QT interval. [41806] [64576]

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 with hydroxychloroquine due to the risk of QT prolongation. Prolongation of the QT interval has been reported with lenvatinib therapy. Hydroxychloroquine also prolongs the QT interval and should not be administered with other drugs known to prolong the QT interval. [41806] [58782]

Leuprolide: (Major) Avoid coadministration of hydroxychloroquine and leuprolide due to the risk of QT prolongation. Hydroxychloroquine prolongs the QT interval. Androgen deprivation therapy (e.g., leuprolide) also may prolong the QT/QTc interval. [41806] [43800]

Leuprolide; Norethindrone: (Major) Avoid coadministration of hydroxychloroquine and leuprolide due to the risk of QT prolongation. Hydroxychloroquine prolongs the QT interval. Androgen deprivation therapy (e.g., leuprolide) also may prolong the QT/QTc interval. [41806] [43800]

Levalbuterol: (Minor) Use caution with coadministration of hydroxychloroquine and short-acting beta-agonists. Hydroxychloroquine 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. 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]

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 hydroxychloroquine and levofloxacin. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and TdP have been reported with the use of hydroxychloroquine. Levofloxacin has been associated with a risk of QT prolongation and TdP. Although extremely rare, TdP has been reported during postmarketing surveillance of levofloxacin. [28421] [28432] [28457] [29833] [33144] [33145] [33146] [41806] [48869] [48871]

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]

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]

Liraglutide: (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]

Lithium: (Major) Avoid coadministration of hydroxychloroquine and lithium. Hydroxychloroquine 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. Lithium has been associated with QT prolongation. [41806] [59809] [59810] [59811]

Lixisenatide: (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 the potential for additive QT prolongation and torsade de pointes (TdP). Monitor ECG for QT prolongation if coadministration is required. Lofexidine may prolong the QT interval, and TdP has been reported during postmarketing use. Hydroxychloroquine increases the QT interval. Ventricular arrhythmias and TdP have also been reported with the use of hydroxychloroquine. [41806] [63161]

Long-acting beta-agonists: (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

Loperamide: (Major) Avoid coadministration of hydroxychloroquine and loperamide. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. At high doses, loperamide has been associated with serious cardiac toxicities, including syncope, ventricular tachycardia, QT prolongation, TdP, and cardiac arrest. Additionally, the plasma concentration of loperamide, a CYP2D6 substrate, may be increased when administered concurrently with hydroxychloroquine, a CYP2D6
inhibitor. If these drugs are used together, monitor for loperamide-associated adverse reactions, such as CNS effects and cardiac toxicities. [29396] [30106] [41806] [60864]

**Loperamide; Simethicone:** (Major) Avoid coadministration of hydroxychloroquine and loperamide. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. At high doses, loperamide has been associated with serious cardiac toxicities, including syncope, ventricular tachycardia, QT prolongation, TdP, and cardiac arrest. Additionally, the plasma concentration of loperamide, a CYP2D6 substrate, may be increased when administered concurrently with hydroxychloroquine, a CYP2D6 inhibitor. If these drugs are used together, monitor for loperamide-associated adverse reactions, such as CNS effects and cardiac toxicities. [29396] [30106] [41806] [60864]

**Lopinavir; Ritonavir:** (Major) Avoid coadministration of hydroxychloroquine and lopinavir; ritonavir due the risk of additive QT prolongation. If use together is necessary, perform an ECG at baseline and monitor closely throughout therapy, avoid any non-essential QT prolonging drugs, and correct electrolyte imbalances prior to initiation. Hydroxychloroquine prolongs the QT interval. Lopinavir; ritonavir is also associated with QT prolongation. [28341] [41806] [65157]

**Lorazepam:** (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 concurrent administration of macimorelin with drugs that prolong the QT interval, such as hydroxychloroquine. Use of these drugs together may increase the risk of developing 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. Treatment with macimorelin has been associated with an increase in the corrected QT (QTc) interval. Hydroxychloroquine prolongs the QT interval. [41806] [62723]

**Maprotiline:** (Major) Avoid coadministration of hydroxychloroquine and maprotiline. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. 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 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]

**Mefloquine:** (Major) Avoid coadministration of hydroxychloroquine and mefloquine. Hydroxychloroquine 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. 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]

**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 hydroxychloroquine and promethazine. Hydroxychloroquine 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. Promethazine is associated with a possible risk for QT prolongation. [28225] [41806] [55578]
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: (Minor) Use caution with coadministration of hydroxychloroquine and short-acting beta-agonists. Hydroxychloroquine 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. 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]

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 hydroxychloroquine and an antidiabetic agent. [41806]

**Methadone**: (Major) Avoid coadministration of hydroxychloroquine and methadone. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. 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] [33136] [41806]

**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]

**Metoprolol**: (Moderate) Monitor for increased metoprolol adverse reactions including bradycardia and hypotension during coadministration. A dosage reduction for metoprolol may be needed based on response. Concurrent use may increase metoprolol exposure. Metoprolol is a CYP2D6 substrate; hydroxychloroquine is a moderate CYP2D6 inhibitor. In the presence of another moderate CYP2D6 inhibitor, the AUC of metoprolol was increased by 3.29-fold with no effect on the cardiovascular response to metoprolol. [29396] [32916] [62643]

**Metronidazole**: (Major) Avoid coadministration of hydroxychloroquine and metronidazole. Hydroxychloroquine 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. Potential QT prolongation has been reported in limited case reports with metronidazole. [41806] [57377] [57378]

**Mexiletine**: (Moderate) Mexiletine is significantly metabolized by CYP2D6 isoenzymes. CYP2D6 inhibitors, such as hydroxychloroquine, could theoretically impair mexiletine metabolism; the clinical significance of such interactions is unknown. [5007]

**Midostaurin**: (Major) The concomitant use of midostaurin and hydroxychloroquine may lead to additive QT interval prolongation. If these drugs are used together, perform electrocardiogram monitoring during hydroxychloroquine therapy. In clinical trials, QT prolongation has been reported in patients who received midostaurin as single-agent therapy or in combination with cytarabine and daunorubicin. Ventricular arrhythmias (i.e., ventricular fibrillation and ventricular tachycardia) and torsade de pointes have been reported in patients taking hydroxychloroquine. [41806] [61906]

**Mifepristone**: (Major) Avoid coadministration of hydroxychloroquine and mifepristone. Hydroxychloroquine 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. Mifepristone has been associated with dose-dependent prolongation of the QT interval. To minimize the risk of QT prolongation, the lowest effective dose of mifepristone should always be used. [41806] [48697]

**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) There may be an increased risk for QT prolongation and torsade de pointes (TdP) during concurrent use of mirtazapine and hydroxychloroquine. Hydroxychloroquine prolongs the QT interval and should not be administered with other drugs known to prolong the QT interval. Cases of QT prolongation, 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, including concomitant use of other medications associated with QT prolongation. [40942] [41806]

**Moxifloxacin:** (Major) Avoid coadministration of hydroxychloroquine and moxifloxacin. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Quinolones have been associated with a risk of QT prolongation and 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]

**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]

**Nebivolol:** (Moderate) Monitor for increased toxicity as well as increased therapeutic effect of nebivolol if coadministered with hydroxychloroquine. Nebivolol is metabolized by CYP2D6. Although data are lacking, CYP2D6 inhibitors, such as hydroxychloroquine, could potentially increase nebivolol plasma concentrations via CYP2D6 inhibition; the clinical significance of this potential interaction is unknown, but an increase in adverse effects is possible. [29396] [60860] [60986] [60987]

**Nebivolol; Valsartan:** (Moderate) Monitor for increased toxicity as well as increased therapeutic effect of nebivolol if coadministered with hydroxychloroquine. Nebivolol is metabolized by CYP2D6. Although data are lacking, CYP2D6 inhibitors, such as hydroxychloroquine, could potentially increase nebivolol plasma concentrations via CYP2D6 inhibition; the clinical significance of this potential interaction is unknown, but an increase in adverse effects is possible. [29396] [60860] [60986] [60987]

**Nilotinib:** (Major) Avoid the concomitant use of nilotinib and hydroxychloroquine; significant prolongation of the QT interval may occur. Sudden death and QT prolongation have been reported in patients who received nilotinib therapy. Ventricular arrhythmias and torsade de pointes have been reported with the use of hydroxychloroquine. [41806] [58766]

**Norfloxacin:** (Major) Avoid coadministration of hydroxychloroquine and norfloxacin. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Quinolones have been associated with a risk of QT prolongation and TdP. Although extremely rare, TdP 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. [29818] [41806]

**Nortriptyline:** (Minor) Use hydroxychloroquine and tricyclic antidepressants together with caution due to a potential risk of QT prolongation. 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]

**Octreotide:** (Major) Avoid coadministration of hydroxychloroquine and octreotide. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Arrhythmias, sinus bradycardia, and conduction disturbances have occurred during octreotide therapy. Since bradycardia is a risk factor for development of 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]

**Ofloxacin:** (Major) Avoid coadministration of hydroxychloroquine and ofloxacin. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Quinolones have been associated with a risk of QT prolongation and TdP. Although extremely rare, TdP 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]

**Olanzapine:** (Major) Avoid coadministration of hydroxychloroquine and olanzapine. Hydroxychloroquine 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. 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]

**Olodaterol:** (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

**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 hydroxychloroquine and ondansetron. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Ondansetron has been associated with a dose-related increase in the QT interval and postmarketing reports of TdP. ECG monitoring is recommended. [31266] [41806]

**Osimertinib:** (Major) Hydroxychloroquine prolongs the QT interval and should not be administered with other drugs known to prolong the QT interval such as osimertinib. Concentration-dependent QTc prolongation occurred during clinical trials of osimertinib. Concomitant use may increase the risk of QT prolongation. [41806] [60297]

**Oxaliplatin:** (Major) Avoid coadministration of hydroxychloroquine and oxaliplatin. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. QT prolongation and ventricular arrhythmias including fatal TdP have been reported with oxaliplatin use in postmarketing experience. [41806] [41958]

**Paliperidone:** (Major) Avoid coadministration of hydroxychloroquine and paliperidone if possible. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Paliperidone has been associated with QT prolongation; TdP and ventricular fibrillation have been reported in the setting of overdose. If coadministration is necessary and the patient has known risk factors for cardiac disease or arrhythmias, close monitoring is essential. [40936] [41806]
Panobinostat: (Major) Avoid coadministration of hydroxychloroquine and panobinostat. Hydroxychloroquine 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. QT prolongation has been reported with panobinostat therapy in patients with multiple myeloma in a clinical trial. If coadministration cannot be avoided, obtain an electrocardiogram at baseline and periodically during treatment. Hold panobinostat if the QTcF increases to ≥ 480 milliseconds during therapy; permanently discontinue if QT prolongation does not resolve. [41806] [58821]

Pasireotide: (Major) Avoid coadministration of hydroxychloroquine and pasireotide. Hydroxychloroquine 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. Pasireotide is associated with QT prolongation. [41806] [52611]

Pazopanib: (Major) Avoid coadministration of hydroxychloroquine and pazopanib. Hydroxychloroquine 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. Pazopanib has been reported to prolong the QT interval. If pazopanib and the other drug must be continued, closely monitor the patient for QT interval prolongation. [37098] [41806]

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 hydroxychloroquine and systemic pentamidine. Hydroxychloroquine 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. Systemic pentamidine has been associated with QT prolongation. [23620] [23778] [28419] [28879] [41806]

Pentobarbital: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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]

Perampanel: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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: (Minor) Use perphenazine and hydroxychloroquine together with caution. Hydroxychloroquine 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. Perphenazine is associated with a possible risk for QT prolongation. Theoretically, perphenazine may increase the risk of QT prolongation if coadministered with other drugs that have a risk of QT prolongation. [28514] [41806]

Perphenazine; Amitriptyline: (Minor) Use hydroxychloroquine and tricyclic antidepressants together with caution due to a potential risk of QT prolongation. 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] (Minor) Use perphenazine and hydroxychloroquine together with caution. Hydroxychloroquine 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. Perphenazine is associated with a possible risk for QT prolongation. Theoretically, perphenazine may increase the risk of QT prolongation if coadministered with other drugs that have a risk of QT prolongation. [28514] [41806]
**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]

**Phentermine; Topiramate:** (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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 hydroxychloroquine and promethazine. Hydroxychloroquine 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. Promethazine is associated with a possible risk for QT prolongation. [28225] [41806] [55578]

**Phenytoin:** (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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]

**Pimavanserin:** (Major) Avoid coadministration of hydroxychloroquine and pimavanserin. Hydroxychloroquine 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. Pimavanserin may cause QT prolongation and should generally be avoided in patients receiving other medications known to prolong the QT interval. [41806] [60748]

**Pimozide:** (Severe) Pimozide is associated with a well-established risk of QT prolongation and torsade de pointes (TdP). Because of the potential for TdP, use of hydroxychloroquine with pimozide is contraindicated. [28225] [41806] [43463]

**Pioglitazone:** (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:** (Minor) Use caution with coadministration of hydroxychloroquine and short-acting beta-agonists. Hydroxychloroquine 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. 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]

**Pitolisant:** (Major) Avoid coadministration of pitolisant with hydroxychloroquine as concurrent use may increase the risk of QT prolongation. Both pitolisant and hydroxychloroquine prolong the QT interval. [41806] [64562]

**Posaconazole:** (Major) Avoid coadministration of hydroxychloroquine and posaconazole. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Posaconazole has been associated with QT prolongation and TdP. [32723] [41806]

**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]

**Praziquantel:** (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]

Pregabalin: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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 hydroxychloroquine and primaquine. Hydroxychloroquine 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. Primaquine is associated with the potential for QT prolongation. [41806] [41984]

Primidone: (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 hydroxychloroquine and procainamide. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Procainamide is associated with a well-established risk of QT prolongation and TdP. [28250] [41806]

Prochlorperazine: (Minor) Use caution with the coadministration of hydroxychloroquine and prochlorperazine. Hydroxychloroquine 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. 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, such as hydroxychloroquine. [28514] [41806]

Promethazine: (Major) Avoid coadministration of hydroxychloroquine and promethazine. Hydroxychloroquine 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. Promethazine is associated with a possible risk for QT prolongation. [28225] [41806] [55578]

Propafenone: (Major) Avoid coadministration of hydroxychloroquine and propafenone. Hydroxychloroquine 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. Propafenone is a Class IC antiarrhythmic which increases the QT interval, but largely due to prolongation of the QRS interval. [28287] [41806]

Propranolol: (Minor) Propranolol is significantly metabolized by CYP2D6 isoenzymes. CYP2D6 inhibitors, such as hydroxychloroquine, could theoretically impair propranolol metabolism; the clinical significance of such interactions is unknown. [4718] [6134]

Protriptyline: (Minor) Use hydroxychloroquine and tricyclic antidepressants together with caution due to a potential risk of QT prolongation. 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]

Quetiapine: (Major) Avoid coadministration of hydroxychloroquine and quetiapine. Hydroxychloroquine 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. 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]
Quinidine: (Major) Avoid coadministration of hydroxychloroquine and quinidine. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Quinidine administration is associated with QT prolongation and TdP. [41806] [42280] [47357]

Quinine: (Major) Avoid coadministration of hydroxychloroquine and quinine. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Quinine has also been associated with QT prolongation and rare cases of TdP. [31403] [41806]

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 hydroxychloroquine and ranolazine. Hydroxychloroquine 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. Ranolazine is associated with dose- and plasma concentration-related increases in the QTc interval. Although there are no studies examining the effects of ranolazine in patients receiving other QT prolonging drugs, coadministration of such drugs may result in additive QT prolongation. Additionally, ranolazine is metabolized mainly by CYP3A and to a lesser extent by CYP2D6. Hydroxychloroquine is a known CYP2D6 inhibitor; coadministration with ranolazine may result in increased plasma concentrations of ranolazine. [31938] [41806]

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 with hydroxychloroquine due to an increased risk for QT prolongation. Ribociclib has been shown to prolong the QT interval in a concentration-dependent manner. Hydroxychloroquine has also been associated with QT prolongation. Concomitant use may increase the risk for QT prolongation. [41806] [61816]

Ribociclib; Letrozole: (Major) Avoid coadministration of ribociclib with hydroxychloroquine due to an increased risk for QT prolongation. Ribociclib has been shown to prolong the QT interval in a concentration-dependent manner. Hydroxychloroquine has also been associated with QT prolongation. Concomitant use may increase the risk for QT prolongation. [41806] [61816]

Rilpivirine: (Major) Avoid coadministration of hydroxychloroquine and rilpivirine. Hydroxychloroquine 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. Supratherapeutic doses of rilpivirine (75 to 300 mg/day) have caused QT prolongation. [41806] [44376]
**Risperidone:** (Major) Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine and coadministration with other drugs having a risk of QT prolongation and TdP, such as risperidone, should be avoided if possible. If coadministration is required and the patient has known risk factors for cardiac disease or arrhythmias, close monitoring is recommended. [22256] [28225] [28414] [28416] [41806]

**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 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]

**Romidepsin:** (Major) Avoid coadministration of hydroxychloroquine and romidepsin. Hydroxychloroquine 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. Romidepsin has been reported to prolong the QT interval. If romidepsin must be coadministered with another drug that prolongs the QT interval, appropriate cardiovascular monitoring precautions should be considered, such as the monitoring of electrolytes and ECGs at baseline and periodically during treatment. [37292] [41806]

**Rosiglitazone:** (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]

**Rufinamide:** (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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:** (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

**Saquinavir:** (Major) Avoid administering saquinavir boosted with ritonavir concurrently with other drugs that may prolong the QT interval. Saquinavir boosted with ritonavir increases the QT interval in a dose-dependent fashion, which may increase the risk for serious arrhythmias such as torsade de pointes (TdP). If no acceptable alternative therapy is available, perform a baseline ECG prior to initiation of concomitant therapy and carefully follow monitoring recommendations. Ventricular arrhythmias and TdP have been reported with the use of hydroxychloroquine. [28995] [41806]

**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 hydroxychloroquine and sertraline as concurrent use may increase the risk of QT prolongation. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. QTc prolongation and torsade de pointes (TdP) have been reported during postmarketing use of sertraline; most cases had confounding risk factors. 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 m/sec), 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]

**Sevoflurane:** (Major) Avoid coadministration of hydroxychloroquine and halogenated anesthetics. Hydroxychloroquine 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. Halogenated anesthetics can prolong the QT interval. [28457] [28458] [28754] [28755] [28756] [41806]

**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:** (Minor) Use caution with coadministration of hydroxychloroquine and short-acting beta-agonists. Hydroxychloroquine 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. 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]

**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 the potential for additive QT prolongation. Consult a cardiologist regarding appropriate monitoring if siponimod use is required. Siponimod therapy prolonged the QT interval at recommended doses in a clinical study. Hydroxychloroquine 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. [41806] [64031]

**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 hydroxychloroquine and solifenacin. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Solifenacin has been associated with dose-dependent prolongation of the QT interval. TdP has been reported with postmarketing use, although causality was not determined. This should be taken into consideration when prescribing solifenacin to patients taking other drugs that are associated with QT prolongation. [30515] [41806]

Sorafenib: (Major) Hydroxychloroquine and sorafenib should not be administered together due to the risk of QT prolongation. Both drugs have been associated with QT prolongation. [31832] [41806]

Sotalol: (Major) Avoid coadministration of hydroxychloroquine and sotalol. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Sotalol administration is associated with QT prolongation and TdP. Proarrhythmic events should be anticipated after initiation of sotalol therapy and after each upward dosage adjustment. [28234] [41806]

Sulfonlureas: (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 hydroxychloroquine and sunitinib. Hydroxychloroquine 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. Sunitinib can cause dose-dependent QT prolongation, which may also increase the risk for ventricular arrhythmias, including torsades de points (TdP). [31970] [41806]

Tacrolimus: (Major) Avoid coadministration of hydroxychloroquine and tacrolimus. Hydroxychloroquine 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. Tacrolimus causes QT prolongation. [27954] [28611] [41806]

Tamoxifen: (Major) Hydroxychloroquine should not be administered with tamoxifen due to the risk of QT prolongation. Hydroxychloroquine prolongs the QT interval. Tamoxifen has also 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]

Telavancin: (Major) Avoid coadministration of hydroxychloroquine and telavancin. Hydroxychloroquine 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 hydroxychloroquine and telithromycin. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Telithromycin is associated with QT prolongation and TdP. [28156] [41806]

Terbutaline: (Minor) Use caution with coadministration of hydroxychloroquine and short-acting beta-agonists. Hydroxychloroquine 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. Beta-agonists may be associated with adverse cardiovascular effects including QT interval prolongation. [30985] [41806]
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]

**Tetrabenazine:** (Major) Avoid coadministration of hydroxychloroquine and tetrabenazine. Hydroxychloroquine 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. Tetrabenazine causes a small increase in the corrected QT interval (QTc). [34389] [41806]

**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) Thioridazine is associated with a well-established risk of QT prolongation and torsade de pointes (TdP). Thioridazine is considered contraindicated for use along with agents that may prolong the QT interval and increase the risk of TdP, and/or cause orthostatic hypotension. Because of the potential for TdP, use of hydroxychloroquine with thioridazine is contraindicated. [28225] [28293] [41806]

**Tiagabine:** (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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]

**Timolol:** (Minor) Timolol is significantly metabolized by CYP2D6 isoenzymes. CYP2D6 inhibitors, such as hydroxychloroquine, could theoretically impair timolol metabolism; the clinical significance of such interactions is unknown. [4718] [6134]

**Tiotropium; Olodaterol:** (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

**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 hydroxychloroquine and tolterodine. Hydroxychloroquine 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. Tolterodine has been associated with dose-dependent prolongation of the QT interval, especially in poor CYP2D6 metabolizers. [31112] [41806]

**Topiramate:** (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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 hydroxychloroquine and toremifene. Hydroxychloroquine 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. Toremifene has been shown to prolong the QTc interval in a dose- and concentration-related manner. [28822] [41806]

Trazodone: (Major) Avoid coadministration of hydroxychloroquine and trazodone. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Trazodone can prolong the QT/QTc interval at therapeutic doses. In addition, there are postmarketing reports of TdP with trazodone. [38831] [41806]

Tricyclic antidepressants: (Minor) Use hydroxychloroquine and tricyclic antidepressants together with caution due to a potential risk of QT prolongation. 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]

Trifluoperazine: (Minor) Use caution with the coadministration of hydroxychloroquine and trifluoperazine. Hydroxychloroquine 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. Trifluoperazine is associated with a possible risk for QT prolongation. Theoretically, trifluoperazine may increase the risk of QT prolongation if coadministered with other drugs that have a risk of QT prolongation, such as hydroxychloroquine. [28514] [41806]

Trimipramine: (Minor) Use hydroxychloroquine and tricyclic antidepressants together with caution due to a potential risk of QT prolongation. 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]

Triptorelin: (Major) Avoid coadministration of hydroxychloroquine and triptorelin due to the risk of QT prolongation. Hydroxychloroquine prolongs the QT interval. Androgen deprivation therapy (e.g., triptorelin) also may prolong the QT/QTc interval. [41806] [45411]

Ultralente 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]

Umeclidinium; Vilanterol: (Moderate) Use caution with coadministration of hydroxychloroquine and long-acting beta-agonists. Hydroxychloroquine 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. 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. [32901] [41806]

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) Hydroxychloroquine prolongs the QT interval and should not be administered with other drugs known to prolong the QT interval. Vandetanib can prolong the QT interval in a concentration-dependent manner; TdP and sudden death have been reported in patients receiving vandetanib. [41806] [43901]
Vardenafil: (Major) Avoid coadministration of hydroxychloroquine and vardenafil. Hydroxychloroquine 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. Vardenafil is associated with QT prolongation. Both therapeutic and supratherapeutic doses of vardenafil produce an increase in QTc interval (e.g., 4 to 6 msec calculated by individual QT correction). [28216] [41806]

Vemurafenib: (Major) Avoid coadministration of hydroxychloroquine and vemurafenib. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Vemurafenib has been associated with QT prolongation. If vemurafenib and another drug that is associated with a possible risk for QT prolongation and TdP must be coadministered, ECG monitoring is recommended; closely monitor the patient for QT interval prolongation. [41806] [45335]

Venlafaxine: (Major) Avoid coadministration of hydroxychloroquine and venlafaxine. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Venlafaxine administration is associated with a possible risk of QT prolongation; TdP has been reported with postmarketing use. [33715] [41806]

Vigabatrin: (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 hydroxychloroquine and voriconazole. Hydroxychloroquine increases the QT interval and should not be administered with other drugs known to prolong the QT interval. Ventricular arrhythmias and torsade de pointes (TdP) have been reported with the use of hydroxychloroquine. Voriconazole has been associated with QT prolongation and rare cases of TdP. [28158] [41806]

Vorinostat: (Major) Avoid coadministration of hydroxychloroquine and vorinostat. Hydroxychloroquine 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. Vorinostat therapy is associated with a risk of QT prolongation. [32789] [41806]

Ziprasidone: (Major) Concomitant use of ziprasidone and hydroxychloroquine should be avoided due to the potential for additive QT prolongation. Clinical trial data indicate that ziprasidone causes QT prolongation; there are postmarketing reports of torsade de pointes (TdP) in patients with multiple confounding factors. Hydroxychloroquine prolongs the QT interval and should not be administered with other drugs known to prolong the QT interval. [28233] [41806]

Zonisamide: (Moderate) Caution is warranted with the coadministration of hydroxychloroquine 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]

References


28262 – Clozaril (clozapine) tablets package insert. Rosemont, PA: HLS Therapeutics (USA), Inc. (Clozaril is a registered trademark of Novartis AG); 2017 Feb.


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<tr>
<th>Code</th>
<th>Drug Name</th>
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47221 – Propulsid (cisapride) package insert. Titusville, NJ; Janssen Pharmaceutica; 2006 Oct. NOTE: As of May 2000; Propulsid has only been available in the United States via an investigational limited access program to ensure proper patient screening and prescribing.


51664 – Stribild (elvitegravir; cobicistat; emtricitabine; tenofovir disoproxil fumarate) package insert. Foster City, CA: Gilead Sciences, Inc; 2019 Jan.


57094 – Zy kadia (ceritinib) package insert. Indianapolis, IN: Novartis; 2019 March.


57803 – Cerdelga (eliglustat) capsules. Waterford, Ireland: Genzyme Ireland, Ltd.;2018 Sept.


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

- Plaquenol - (Sanofi-Aventis)
- Reuquinol - (Apsen)

Canada

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

Chile

- Ilinol - (Pharma Investi)
- Parenquil - (Recalcine)
- Plaquenol - (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
- Plaquinel - (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
- Plaquenol - (Sanofi-Aventis)

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