HYDROXYCHLOROQUINE SULFATE (Plaquenil®) (Adults) – Prescribing Support (March 2017)

- Hydroxychloroquine 200mg tablets (Plaquenil) are licensed for the treatment of rheumatoid arthritis, discoid and systemic lupus erythematosus, and dermatological conditions caused or aggravated by sunlight in adults.
- Treatment should be initiated only under hospital or specialist supervision.
- Hydroxychloroquine is generally well tolerated but skin rashes and gastrointestinal effects sometimes occur.
- All patients should have an annual eye test by an optometrist. Formal ophthalmological examination should be considered if patients continue hydroxychloroquine beyond 5 years.

Licensed Indication
Licensed for the treatment of rheumatoid arthritis, discoid and systemic lupus erythematosus, and dermatological conditions caused or aggravated by sunlight. Treatment should be initiated only under hospital or specialist supervision.

Dosage
Hydroxychloroquine 200mg twice daily (or as advised by Rheumatology or Dermatology specialists, once daily). The maximum dosage should not exceed 6.5mg/kg/day ideal body weight

Contraindications
- known hypersensitivity to 4-aminoquinoline compounds
- pre-existing maculopathy of the eye

Drug interactions (summary of significant interactions)\(^{(1)}\)
- Anti-arrhythmics: increased risk of ventricular arrhythmias when hydroxychloroquine administered with amiodarone – avoid concomitant use
- Digoxin: Hydroxychloroquine sulfate has been reported to increase plasma digoxin levels: serum digoxin levels should be closely monitored in patients receiving concomitant therapy
- Antibacterials: increased risk of ventricular arrhythmias when hydroxychloroquine administered with moxifloxacin – avoid concomitant use
- Ciclosporin: hydroxychloroquine increases plasma concentration of ciclosporin (increased risk of toxicity)
- Antacids: as with chloroquine, antacids may reduce absorption of hydroxychloroquine so it is advised that a 4 hour interval be observed between hydroxychloroquine and antacid dosaging.
- Antidiabetic medicines: As hydroxychloroquine may enhance the effects of hypoglycaemic treatment, a decrease in doses of insulin or antidiabetic drugs may be required
- Tamoxifen may enhance the adverse/toxic effect of Hydroxychloroquine. Specifically, concomitant use of tamoxifen and hydroxychloroquine may increase the risk of retinal toxicity.

For full details, please consult the latest edition of the British National Formulary or Summary of Product Characteristics (SmPC), see references.

Recommendations for hydroxychloroquine in pregnancy and breastfeeding\(^{(2,3)}\)
Hydroxychloroquine remains the treatment of choice in women planning a pregnancy with rheumatic disease in need of treatment and should be continued during pregnancy. Hydroxychloroquine is compatible with breastfeeding. Men should not be discouraged from taking hydroxychloroquine while trying to conceive.
Please note this advice is taken from evidence-based recommendations from the British Society of Rheumatology and is not directly in line with the manufacturer product information.

Adverse Effects

Very Common
- Abdominal pain, nausea

Common (≥ 1 in 100 and < 1 in 10)
- Anorexia
- Affect lability, Headache
- Diarrhoea, vomiting
Skin rashes, pruritis

**Uncommon (≥ 1 in 1000 and < 1 in 100)**
- Dizziness
- Nervousness
- Dizziness
- Vertigo, tinnitus
- Abnormal LFTs
- Pigmentation disorders
- Sensory motor disorders

**Unknown frequency**
- Bone-marrow depression, anaemia, aplastic anaemia, agranulocytosis, leucopenia and thrombocytopenia
- Urticaria, angioedema, bronchospasm
- Hypoglycemia
- Hydroxychloroquine may precipitate or exacerbate porphyria.
- Convulsions have been reported with this class of drugs
- Extrapyramidal disorders such as dystonia, dyskinesia, tremor
- Bullous eruptions including erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis, Drug Rash with Eosinophilia and Systemic Symptoms (DRESS syndrome) photosensitivity, exfoliative dermatitis, acute generalised exanthematous pustulosis (AGEP).
- AGEP has to be distinguished from psoriasis, although hydroxychloroquine may precipitate attacks of psoriasis. It may be associated with fever and hyperleukocytosis. Outcome is usually favourable after drug withdrawal.
- Cardiomyopathy
- Fulminant hepatic failure
- Myopathy

**Ocular effects**

Ocular side effects include retinal toxicity, which can lead to permanent vision loss and deposition of the drug in the cornea. The mechanism of retinal toxicity is poorly understood. All patients should have an annual eye test by an optometrist. Formal ophthalmological examination should be considered if patients continue hydroxychloroquine beyond 5 years.

The SmPC states: The occurrence of retinopathy is very uncommon if the recommended daily dose is not exceeded. The administration of doses in excess of the recommended maximum is likely to increase the risk of retinopathy, and accelerate its onset. All patients should have an ophthalmological examination by an optometrist within 6-12 months of initiating treatment with hydroxychloroquine. Thereafter, ophthalmological examinations must be repeated at least every 12 months. The examination should include testing visual acuity, careful ophthalmoscopy, fundoscopy, central visual field testing with a red target, and colour vision. This examination should be more frequent and adapted to the patient in the following situations:
- daily dosage exceeds 6.5mg/kg lean body weight. Absolute body weight used as a guide to dosage could result in an overdosage in the obese;
- renal insufficiency;
- visual acuity below 6/8;
- age above 65 years old;
- cumulative dose more than 200g

Hydroxychloroquine should be discontinued immediately in any patient who develops a pigmentary abnormality, visual field defect, or any other abnormality not explainable by difficulty in accommodation or presence of corneal opacities. Patients should continue to be observed for possible progression of the changes. Patients should be advised to stop taking the drug immediately and seek the advice of their prescribing doctor if any disturbances of vision are noted, including abnormal colour vision.

For full details of all of the above, please consult the latest edition of the British National Formulary or SmPC

**Monitoring**

See for ocular adverse effects above. We suggest the Royal College of Ophthalmologists Guidelines should be followed (Appendix 1).

**References**


**APPENDIX 1**

Hydroxychloroquine and Ocular Toxicity recommendations on screening 2009