Hydroxychloroquine AMBER 0

For Treatment of rheumatoid arthritis, discoid and systemic lupus erythematosus, and dermatological conditions caused or aggravated by sunlight in adults

Information for prescribers - to be read in conjunction with the SPC

Background

Hydroxychloroquine has several pharmacological actions which may be involved in the therapeutic effect in the treatment of rheumatic disease, but the role of each is not known. [1]

Dosage and administration

The minimum effective dose should be employed. Each dose should be taken orally with a meal or glass of milk.

This dose should not exceed 6.5mg/kg/day (**calculated from ideal body weight NOT actual body weight**) and will be either 200mg or 400mg per day. [1] Alternate dosing schedules may be recommended by the specialist service i.e. 200mg and 400mg on alternate days.

In patients able to receive 400mg daily:
Initially 400mg daily in divided doses. The dose can be reduced to 200mg when no further improvement is evident. The maintenance dose should be increased to 400mg daily if the response lessens. [1]

Hydroxychloroquine is cumulative in action and will require several weeks to exert its beneficial effects, whereas minor side effects may occur relatively early. For rheumatic disease treatment requires review with the specialist consultant if no improvement by 6 months. In light-sensitive diseases, treatment should only be given during periods of maximum exposure to light. [1]

Monitoring

No routine laboratory drug monitoring is required for hydroxychloroquine. [2]

All individuals who have taken hydroxychloroquine for greater than five years should receive annual screening for retinopathy. [3]

Please note: it is the specialist secondary care clinician that is responsible for making the referral for retinopathy screening.

All individuals taking hydroxychloroquine who have additional risk factors for retinal toxicity (see below) should be screened annually from the baseline visit or annual screening may be commenced before five years of treatment completed. This is to be decided by a consultant ophthalmologist following the baseline visit. [3]

Additional risk factors:

- Concomitant Tamoxifen use.
- Impaired renal function (estimated glomerular filtration rate of less than 60ml/min/1.73m^2).
- Dose of hydroxychloroquine greater than 5mg/kg/day or cumulative dose >200gram. [3]

- Age above 65 years. [1]
- Visual acuity below 6/8

The specialist referring clinician should be encouraged to complete a standardised referral proforma specifying the key clinical details relevant to screening for retinal toxicity. This will allow a
determination of risk toxicity and interpretation of test results (see appendix 1). [3]

Please note: The current version of the SPC (October 2018) for hydroxychloroquine states that patients taking hydroxychloroquine need a baseline and annual ophthalmology test.

Contraindications

Hydroxychloroquine is contraindicated in:

- Patients with hypersensitivity to 4-aminoquinoline compounds
- Pre-existing maculopathy of the eye
- Pregnancy
    - The SPC contraindicates hydroxychloroquine in pregnancy. However, use in pregnancy is supported by the BSR Guidelines and under these circumstances prescribing should be the responsibility of the specialist.
    - Therefore, female patients that become pregnant whilst receiving hydroxychloroquine in primary care should continue their prescription and be referred back to the specialist service for review and on-going management.
- 200mg tablets in children with an ideal body weight less than 31kg

Cautions for use [4]

- The administration of doses in excess of the recommended maximum is likely to increase the risk of retinopathy and accelerate its onset.
- Hydroxychloroquine should be discontinued immediately in any patient who develops a pigmentary abnormality, visual field defect, disturbances of vision (including abnormal colour vision) 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.
- Cases of cardiomyopathy resulting in cardiac failure, in some cases with fatal outcome, have been reported in patients treated with hydroxychloroquine. Clinical monitoring for signs and symptoms of cardiomyopathy is advised and hydroxychloroquine should be discontinued if cardiomyopathy develops. Chronic toxicity should be considered when conduction disorders (bundle branch block / atrio-ventricular heart block) as well as biventricular hypertrophy are diagnosed.
- Acute porphyrias; diabetes (may lower blood glucose); elderly; G6PD deficiency; may aggravate myasthenia gravis; may exacerbate psoriasis; neurological disorders (especially in those with a history of epilepsy); severe gastro-intestinal disorders.

Side effects [4]

Common or very common

Abdominal pain; appetite decreased; diarrhoea; emotional lability; headache; nausea; skin reactions; vision disorders; vomiting

Uncommon

Alopecia; corneal oedema; dizziness; eye disorders; hair colour changes; hearing impairment; nervousness; neuromuscular dysfunction; retinopathy; seizure; vertigo

Frequency not known

Acute hepatic failure; agranulocytosis; anaemia; angioedema; bone marrow disorders; bronchospasm; cardiac conduction disorders; cardiomyopathy; hypoglycaemia; leucopenia; movement disorders; muscle weakness; myopathy; photosensitivity reaction; psychosis; reflexes absent; severe cutaneous adverse reactions (SCARs); thrombocytopenia; tremor; ventricular hypertrophy

Drug interactions

- Antacids may reduce the absorption of hydroxychloroquine, a 4-hour interval is advised between hydroxychloroquine and antacids.
- As hydroxychloroquine may enhance the effects of a hypoglycaemic treatment, a decrease in doses of insulin or antidiabetic drugs may be required.
- Hydroxychloroquine can lower the convulsive threshold. Co-administration of hydroxychloroquine with other antimalarials known to lower the convulsion threshold (e.g. mefloquine) may increase the risk of convulsions. Also, the activity of antiepileptic drugs might be impaired if co-administered with hydroxychloroquine.
- Hydroxychloroquine has been reported to increase plasma ciclosporin and digoxin levels: serum digoxin levels should be closely monitored in patients receiving concomitant treatment.
- Cimetidine may increase the plasma concentration of hydroxychloroquine.
- There may be an increased risk of inducing ventricular arrhythmias if hydroxychloroquine is used concomitantly with other arrhythmogenic drugs, such as amiodarone and moxifloxacin.

This is not an exhaustive list of side effects, cautions, contra-indications or interactions please refer to the BNF or Summary of Product Characteristics for more information.

References

[1] Electronic Medicines Compendium, "Summary of Product Characteristics for Plaquenil-Hydroxychloroquine 200mg tablets," Zentiva, July 2018. [Online]. Available: https://www.medicines.org.uk/emc/product/1764/smpc. [Accessed October 2018].

[2] J Ledingham et al, "BSR and BHPR guideline for the prescription and monitoring of non-biological disease-modifying anti-rheumatic drugs," *Rheumatology,* vol. 56, no. 6, pp. 865-868, 2017.

[3] The Royal College of Ophthalmologists, "Hydroxychloroquine and Chloroquine Retinopathy," February 2018. [Online]. Available: https://www.rcophth.ac.uk/wp-content/uploads/2018/07/Hydroxychloroquine-and-Chloroquine-Retinopathy-Screening-Guideline-Recommendations.pdf. [Accessed October 2018].

[4] Joint Formulary Committee, "British National Formulary (online)," London BMJ Group and Pharmaceutical Press, [Online]. Available: http://www.medicinescomplete.com. [Accessed October 2018].

15. Referral form for specialists/general practitioners to complete when referring to the ophthalmology service for hydroxychloroquine screening

Date:

Referring Consultant Clinician

Name:

Contact email:

Specialty (*please circle*):

Rheumatology / Dermatology

Patient Details (sticker)

Name:

D.O.B:

NHS:

GP Details

Name:

Address:

Postcode:

Essential Information

- Date hydroxychloroquine (or chloroquine) commenced: ...../...../.....
  OR
  Total Duration of treatment if non-continuous: ____/____ (*years/months*)
- Daily Dose: _____mg
- Body weight: _____kg
- Tamoxifen use (past or present): Yes/No (*please circle*)
- Renal Function (please give most recent):

  GFR _____

  Date recorded: ...../...../.....
- Other medication (*please list all*)
- Any known eye condition: Yes/No
  - If Yes please give details