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.

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. 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.

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.

Monitoring

Patients on long-term therapy should have periodic full blood counts

Retinopathy

Hydroxychloroquine sulfate 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 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.

Annual monitoring (including fundus autofluorescence and spectral domain optical coherence tomography) is recommended in all patients who have taken hydroxychloroquine for longer than 5 years.

Annual monitoring may be started before 5 years of treatment if additional risk factors for retinotoxicity exist, such as concomitant tamoxifen therapy, impaired renal function (eGFR less than 60 mL/minute/1.73 m2), or high-dose therapy (more than 5 mg/kg/day of hydroxychloroquine sulfate.

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]

Baseline monitoring

The Royal College of Ophthalmologists have stated that baseline testing for new initiators of hydroxychloroquine or chloroquine is no longer recommended. However, the SPC for hydroxychloroquine states that patients taking hydroxychloroquine need a baseline and annual ophthalmology test. Whilst it is recommended that prescribers follow guidance from the Royal College of Ophthalmologists, they are remined that this would be an off-label use.

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Contraindications

- 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

MHRA/CHM advice: Hydroxychloroquine, chloroquine: increased risk of cardiovascular events when used with macrolide antibiotics; reminder of psychiatric reactions (February 2022):

Co-administration of azithromycin with hydroxychloroquine in patients with rheumatoid arthritis was associated with an increased risk of cardiovascular events (including angina or chest pain and heart failure) and mortality – see interactions section and below (psychiatric reactions) also.

Retinopathy – see above

QT interval prolongation

Hydroxychloroquine has the potential to prolong the QTc interval in patients with specific risks factors. Hydroxychloroquine should be used with caution in patients with congenital or documented acquired QT prolongation and/or known risk factors for prolongation of the QT interval.

Chronic cardiac toxicity

Clinical monitoring for signs and symptoms of cardiomyopathy is advised and hydroxychloroquine sulfate should be discontinued if cardiomyopathy develops.

Suicidal behaviour and psychiatric disorders

Psychiatric side effects typically occur within the first month after the start of treatment with hydroxychloroquine and have been reported also in patients with no prior history of psychiatric disorders. Patients should be advised to seek medical advice promptly if they experience psychiatric symptoms during treatment.

Severe cutaneous adverse reactions (SCARs)

If signs and symptoms suggestive of severe skin reactions appear, hydroxychloroquine should be withdrawn at once and alternative therapy should be considered.

Excipients

Hydroxychloroquine sulfate contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

The following cautions also apply:

Extrapyramidal disorders may occur with hydroxychloroquine sulfate.

Patients presenting with clinical symptoms suggestive of hypoglycaemia during treatment with hydroxychloroquine should have their blood glucose level checked and treatment reviewed as necessary.

Patients on long-term therapy should have periodic full blood counts, and hydroxychloroquine should be discontinued if abnormalities develop.

Hydroxychloroquine sulfate should be used with caution in patients taking medicines which may cause adverse skin reactions.

Patients with a sensitivity to quinine, those with glucose-6-phosphate dehydrogenase deficiency, those with porphyria cutanea tarda which can be exacerbated by hydroxychloroquine and in patients with psoriasis since it appears to increase the risk of skin reactions. .

Patients with hepatic or renal disease, and in those taking drugs known to affect those organs. Estimation of plasma hydroxychloroquine levels should be undertaken in patients with severely compromised renal or hepatic function and dosage adjusted accordingly.

Side effects

Common or very common
Abdominal pain; appetite decreased; diarrhoea; headache; mood altered; nausea; skin reactions; vision disorders; vomiting

Uncommon
Alopecia; anxiety; corneal oedema; dizziness; eye disorders; hair colour changes; neuromuscular dysfunction; retinopathy; seizure; tinnitus; vertigo

Frequency not known
Acute hepatic failure; agranulocytosis; anaemia; angioedema; bone marrow disorders; bronchospasm; cardiac conduction disorders; cardiomyopathy; confusion; delusions; depression; hallucination; hearing loss; hypoglycaemia; leucopenia; movement disorders; muscle weakness; myopathy; photosensitivity reaction; psychiatric disorder; psychosis; QT interval prolongation; reflexes absent; severe cutaneous adverse reactions (SCARs); sleep disorder; suicidal behaviour; thrombocytopenia; tremor; ventricular hypertrophy

Drug interactions

- Carefully consider the benefits and risks before prescribing hydroxychloroquine for any patients taking azithromycin or other macrolide antibiotics, because of the potential for an increased risk of cardiovascular events and cardiovascular mortality – see MHRA alert detail (above).
- 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.
- Hydroxychloroquine should be used with caution in patients receiving drugs known to prolong the QT interval, e.g., Class IA and III antiarrhythmics, tricyclic antidepressants, antipsychotics, some anti-infectives due to increased risk of ventricular arrhythmia. Halofantrine should not be administered with hydroxychloroquine.
- An increased plasma ciclosporin level was reported when ciclosporin and hydroxychloroquine were co-administered.
- Concomitant use of drugs known to induce retinal toxicity, e.g. tamoxifen and hydroxychloroquine sulfate, is not recommended.
- There is a theoretical risk of inhibition of intra-cellular α-galactosidase activity when hydroxychloroquine is co-administered with agalsidase.

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.

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