Oxford University Hospitals NHS
NHS Foundation Trust

NHS
Oxfordshire
Clinical Commissioning Group

HYDROXYCHLOROQUINE FOR USE IN ADULT AND PAEDIATRIC RHEUMATOLOGY AND DERMATOLOGY
Shared Care Protocol

This protocol provides prescribing and monitoring guidance for hydroxychloroquine therapy. It should be read in conjunction with the Summary of Product Characteristics (SPC) available on www.medicines.org.uk/emc and the BNF.

Shared Care Protocol – Responsibilities

Shared care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. See Rheumatology Shared Care Responsibilities document for further information.

Rheumatology or Dermatology Specialist Team

At the start of treatment:

- Complete pre-treatment assessments, including baseline tests, in accordance to the specific shared care protocol
- Determine whether patient is high risk for ocular toxicity and advise patient and GP on monitoring required (see flow chart)
- Initiate treatment by prescribing the first 56 days
- Ensure that patients understand the nature and complications of drug therapy and their role in reporting adverse effects promptly, as part of obtaining informed agreement to shared care
- Provide a copy of the drug-specific patient information leaflet (or direct patient to Versus Arthritis website https://www.versusarthritis.org/about-arthritis/treatments/drugs/ or British Association of Dermatologists website)
- Provide a copy of contact details for the rheumatology advice line (rheumatology patients only)
- Send a letter to the GP requesting shared care once dose is stable, confirming the above has been completed. Include any results from pre-treatment assessments if appropriate. Provide details of the dose to be continued. Outline shared care protocol criteria and/or direct them to the relevant document on the Oxfordshire CCG website

Unless any concerns are raised by the GP within 14 days, shared care will be assumed and the patient will collect the next prescription from the GP. [9]

During treatment:

- Liaise with GP regarding changes in disease management, drug dose, missed clinic appointments
- Be available to give advice to GP and patient

GP

- Prescribe medication once the dose is stable or shared care is agreed
- Ensure that the patient is attending regular eye tests at the optometrist OR at the eye hospital (high risk or long-term treatment only) as determined by specialist.
- Notify the specialist to any changes in patient's condition, any adverse drug reactions or failure to attend tests

Patient and/or carer

- Agree to treatment and monitoring after making an informed decision
- Agree to being under the shared care of the GP and specialist
- Attend all hospital and GP appointments as scheduled
- Attend all eye tests as advised (see ongoing monitoring below)
- Report any side effects to the GP or a member of the specialist team

BACKGROUND FOR USE

Hydroxychloroquine (HCQ) is a disease modifying anti-rheumatic drug (DMARD). It is used to treat a number of inflammatory conditions, including:

- Cutaneous and Systemic Lupus Erythematosus (SLE)
- Rheumatoid Arthritis
- Juvenile Cutaneous and Systemic Lupus Erythematosus
- Juvenile Idiopathic Arthritis
- Juvenile Dermatomyositis
- Sarcoidosis
- Photosensitive skin disorders such as Polymorphic Light Eruption and Porphyria Cutanea Tarda
- Inflammatory skin disorders such as Lichen Planus and Granuloma Annulare (unlicensed)
- Hair disorders such as Lichen Planopilaris and Frontal Fibrosing Alopecia (unlicensed)
- Vasculitis (unlicensed)

DOSAGE

Adult Indications:

- Typical regimen 200 – 400 mg orally daily [1,2] (keep doses less than 5mg/kg to minimise risk of retinopathy) [3]
- Maximum dose 6.5 mg/kg daily (but not exceeding 400 mg daily) [1,2]
- Doses should be calculated using ideal body weight for obese patients
- Photosensitive skin conditions may allow a break in treatment during Winter months, and Porphyria Cutanea Tarda may only require low doses of 200 mg once to twice per week
- Time to response is up to 3 months
- Each dose should be taken with a meal or glass of milk [1]

Paediatric Indications:

- Prescribed according to weight: 5-6.5mg/kg/day (maximum dose 400mg daily).[1,2,4] Prescribe according to ideal body weight to reduce risk of ocular toxicity. A 200mg daily dose is therefore not suitable for use in children with an ideal body weight of less than 31kg.[2] Adjust weekly dose and frequency accordingly to provide an appropriate dose, e.g. 200mg five times a week.
- Benefit is seen after 6 to 8 weeks, improvement may continue over a further 4 to 6 months
- Hydroxychloroquine is available as 200mg tablets. Tablets may be halved or crushed and dispersed in water [4,5]
- Each dose should be taken with a meal or glass of milk [1]

PRE-TREATMENT ASSESSMENT BY SPECIALIST

- FBC, LFTs, U&Es, CRP [6]
- Complete hydroxychloroquine retinopathy risk stratification [3]

Hydroxychloroquine Retinopathy Risk Stratification

- **See flow chart below for the following information in diagrammatic form**
- Assess patient for risk of ocular toxicity using the risk stratification advice produced by the Royal College of Ophthalmologists (RCO). Consider whether the patient possesses any of the risk factors below or belongs to a high-risk group:
    - Patients with renal insufficiency (eGFR less than 60ml/min/1.73m^2)
    - Patients on doses of hydroxychloroquine greater than 5mg/kg
    - Patients on concomitant tamoxifen therapy
- For **high-risk** patients, consider whether an alternative treatment is indicated. If not, refer to ophthalmology for baseline hydroxychloroquine retinal monitoring within 6 months of starting treatment (which includes fundus photography and SD-OCT scans of the macula). Counsel the patient on the need for annual ophthalmology monitoring while on hydroxychloroquine treatment. Hydroxychloroquine monitoring does not replace routine eye care e.g. testing for glasses or glaucoma screening, which is performed in the community, nor other assessments e.g. diabetic retinopathy screening or other hospital eye services
- For **paediatric patients,** retinal monitoring is important as these patients are likely to be on long term treatment. There are no reports of hydroxychloroquine retinopathy in patients under the age of 18, or evidence for screening paediatric patients for drug toxicity.[3] Long-term users of hydroxychloroquine under the age of 18 who otherwise satisfy the criteria should be referred for baseline monitoring at onset of treatment.
- For **all other patients**, consider whether patient will need to be on treatment for more than 5 years:
    - If patient will require more than 5 years of treatment, refer to ophthalmology for hydroxychloroquine baseline monitoring. Counsel patient to attend community optometrist regular eye checks for visual acuity and that they will require annual hospital monitoring after 5 years of being on hydroxychloroquine treatment.
    - For patients expected to be on treatment for less than 5 years, no baseline monitoring is required, but patients are kept under regular follow-up. Counsel patient to attend community optometrist for visual acuity tests at baseline and regularly thereafter. Ask the patient to bring these test results to their GP and next Specialist appointment. At each follow-up appointment, re-assess patient for risk factors. After 3 to 4 years, review clinical need to continue hydroxychloroquine. If treatment is to be continued, refer to ophthalmology for monitoring (be aware that baseline results will not be available for this patient group). Counsel the patient on the need for annual monitoring after 5 years of being on hydroxychloroquine treatment. Please note that this is a deviation from RCO guidance. There has been local agreement that baseline screening is not required in this group of patients.
- Where a patient cannot undergo monitoring (e.g. unable to undergo visual field testing), discuss with the patient/carer to determine whether hydroxychloroquine treatment should be continued without retinal monitoring. Ensure this discussion is documented.

ONGOING MONITORING

More information available in separate guideline; 'Recommended Monitoring Schedule for patients taking disease-modifying anti-rheumatic drugs (DMARDs)'

No routine blood monitoring is required for hydroxychloroquine. [6]

All patients on hydroxychloroquine are recommended to have regular eye tests at the optometrist **OR** at the eye hospital (high risk or long-term treatment only). See flowchart to determine frequency and type of monitoring required.

The GP should ensure that the patient is attending these appointments annually and refer if any risk factors for ocular toxicity (see above) develop while on treatment during shared care. The GP and Specialist team have joint responsibility to refer these patients for monitoring. However, the GP should be aware of how frequently the patient is being followed up by the Specialist team and may choose to refer the patient directly to ophthalmology to avoid any delays.

For existing patients on hydroxychloroquine, while the retinal monitoring service is being set up, please see the hydroxychloroquine and retinal screening position statement for further information

CONTRAINDICATIONS AND PRECAUTIONS

CONTRAINDICATION	
Pre-existing maculopathy	Avoid

PRECAUTIONS	
Epilepsy	May reduce threshold for convulsions
Severe gastro-intestinal disorders	Use with caution
Psoriasis	May exacerbate skin symptoms
Moderate to severe hepatic and renal impairment and drugs which cause renal and hepatic toxicity	Use with caution
Myasthenia gravis	May aggravate symptoms

SIDE EFFECTS AND ACTIONS TO BE TAKEN

Side Effect	**Action**
Change in visual acuity, development of blurred vision , reduced colour vision, and retinal damage	Withhold treatment. Discuss with specialist who may arrange a review by ophthalmologist.
Gastrointestinal disturbance	If severe, drug may have to be discontinued.
Skin rashes	Stop in all but the mildest of cases. Please seek specialist advice as appropriate.
Over dosage	HCQ is very toxic in over dosage. Immediate advice from the National Poisons Information Service is essential. Adults or children presenting within 1 hour of ingesting doses greater than 10mg/kg should be considered for activated charcoal 1g/kg to a maximum dose of 50g.[4]
Cardiomyopathy	Discontinue treatment if cardiomyopathy develops. Seek specialist advice.

Notes:
Hydroxychloroquine can be withheld for 2-3 weeks without inducing a flare.

NOTABLE DRUG INTERACTIONS

(Please note that this is not an extensive list. Refer to BNF and SPC for any specific drug interaction queries)

Some of these drug interactions have been extrapolated from known interactions with chloroquine.

Drug	Interaction
Antacids	Reduce absorption of hydroxychloroquine and should be avoided within 4 hours of dose.
Cimetidine	Cimetidine inhibits metabolism of hydroxychloroquine so plasma concentration of hydroxychloroquine is increased.
Digoxin, Ciclosporin	Hydroxychloroquine may increase plasma concentration of these drugs. Please monitor closely.
Drugs that lower the seizure threshold e.g. Mefloquine	Increased risk of convulsions if used with hydroxychloroquine and should be used with caution.
Neostigmine, Pyridostigmine	Diminished effect with hydroxychloroquine, causing increased symptoms of myasthenia gravis. Avoid concomitant use.
Drugs that prolong the QT interval e.g. Moxifloxacin, amiodarone, quinine.	Increase risk of cardiac arrhythmias if used with hydroxychloroquine and should be used with caution.
Tamoxifen	Increases risk of toxic effects of the retina and should be avoided. If unavoidable, annual retinal monitoring is recommended.
Anti-epileptics	Activity of antiepileptic drugs may be impaired if co-administered with hydroxychloroquine.
Anti-diabetics	As hydroxychloroquine may enhance the effects of a hypoglycaemic treatment, a decrease in doses of insulin or antidiabetic drugs may be required

FAMILY PLANNING

Follow advice from secondary care

VACCINATIONS

Check Department of Health green book guidance and if not covered, discuss with secondary care

BACK-UP INFORMATION AND ADVICE

Contact Details	Oxford University Hospitals NHS Foundation Trust	
Rheumatology	Rheumatology Helpline (Adult and Paediatric) Adult - Option 1 (Monday to Friday 8am - 2pm, answerphone service) Paediatric - Option 2 (Monday to Friday, answerphone service) Closed on weekends and bank holidays	Tel: 01865 737656 Email: Adult - Rheumatology.NOC@nhs.net Paediatric - cnspaedrheumatology@ouh.nhs.uk
	Rheumatology Registrar/Consultant on call Registrar on site Monday to Friday 9am-8pm Weekends and bank holidays 9am-5pm	OUH switchboard number: 0300 304 7777, ask for Rheumatology on call

Dermatology	Dermatology Helpline (Adult and Paediatric) Dermatology Registrar On Call	Email: oxon.dermatologyadvice@nhs.net OUH switchboard number: 0300 304 7777, ask for Dermatology On Call, Bleep 5044
Medicines Information	Tel: 01865 221505 (Monday to Friday 9am - 5pm) Email: Medicines.information@ouh.nhs.uk	

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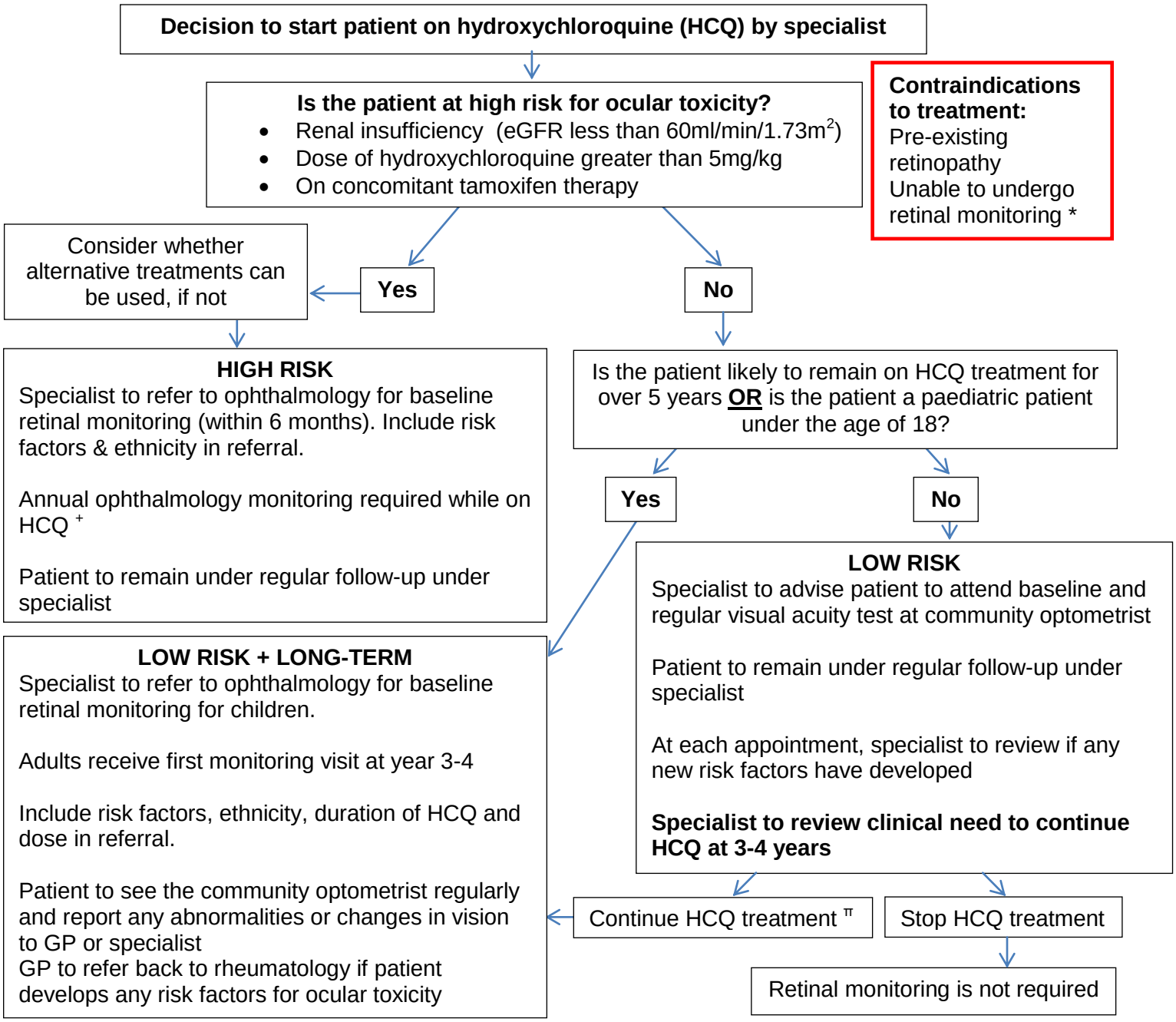

* Where a patient cannot undergo monitoring (e.g. cannot undergo visual field testing), discuss with the patient/carer to determine whether HCQ treatment should be continued without retinal monitoring. Ensure this discussion is documented. Do not start HCQ in these patients unless there are no alternative treatments. For high-risk patients, do not treat for more than 3 years. In all other patients, do not treat for more than 5 years.

+ HCQ monitoring does not replace routine eye care e.g. testing for glasses or glaucoma screening, which is performed in the community, nor other assessments e.g. diabetic retinopathy screening or other hospital eye services.

ᵀᵀ Be aware that baseline retinal monitoring results will not be available for this patient group.

The aim of monitoring is not to prevent HCQ toxicity but to detect the earliest definitive signs of pre-symptomatic toxicity. This will facilitate an informed discussion between the patient and prescribing physician on treatment options (continuing HCQ vs seeking alternative treatment). The less severe the visual deficits are at the point of detection, the less likely they are to progress.

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