795FM.3.1 HYDROXYCHLOROQUINE FOR USE IN RHEUMATOLOGY AND DERMATOLOGY Shared Care Protocol

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

BACKGROUND FOR USE

Hydroxychloroquine (HCQ) is a disease modifying anti-rheumatic drug (DMARD). It is used to treat:

- Systemic lupus erythematosus (SLE) (licensed)
- Rheumatoid arthritis (licensed)
- Dermatological conditions caused or aggravated by sunlight (licensed)

Its use in this protocol includes the above three indications.

In rheumatology it is often used in combination with other DMARDs, such as methotrexate or sulfasalazine.

CONTRAINDICATIONS AND PRECAUTIONS

CONTRAINDICATIONS	
Pre-existing retinal disease	
Known hypersensitivity to 4-aminoquinoline compounds	
PRECAUTIONS	
Epilepsy	May reduce threshold for convulsions
Severe gastrointestinal disorders	Use with caution
Psoriasis	Exacerbation
Glucose-6-phosphate dehydrogenase deficiency	Exacerbation
Porphyria cutanea tarda	Exacerbation
Renal impairment and drugs which cause renal toxicity	Use with caution eGFR <60 requires annual retinal screening due to increased risk of toxicity Reduce the dose as below
Hepatic impairment and drugs which can cause hepatic toxicity	Use with caution in moderate to severe hepatic impairment
Myasthenia gravis	Avoid - may aggravate symptoms
Diabetes	May enhance the effects of hypoglycaemic treatment - decrease doses of insulin or anti-diabetic medication may be required

PREGNANCY AND BREASTFEEDING

HCQ can be continued in pregnancy and is compatible with breastfeeding. Men can continue taking HCQ while trying to conceive[4].

PRECAUTIONS DUE TO RISK OF OCULAR TOXICITY

Royal College of Ophthalmologists (RCOpth) recommendations

Antimalarials can cause retinal damage, but recent studies show that this occurs less frequently with hydroxychloroquine than chloroquine. The risk increases with dose and after 5 years of treatment. The RCOphth has produced guidance for screening to prevent ocular toxicity on long-term treatment with chloroquine and hydroxychloroquine[1]. Screening is recommended for all patients who:

1. are **planning to take HCQ long term i.e. more than five years.** They should be referred for a baseline examination in a hospital eye department ideally within six months, but definitely within 12 months, of starting therapy with a colour retinal photograph and spectral domain optical coherence tomography (SD-OCT) scans of the macula.
2. **have received treatment for five years**. After five years, they should be referred for annual screening and be reviewed annually thereafter whilst on therapy.
3. are taking HCQ **and have additional risk factors for retinal toxicity**. They may be screened annually from the baseline visit or annually if treatment commenced before five years of treatment was completed. This is to be decided by a consultant ophthalmologist following the baseline visit.

Additional risk factors:

- Concomitant tamoxifen use
- Impaired renal function (estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73 m^2)
- Dose of HCQ >5 mg/kg/day

Steps being taken to implement the RCOphth guidance by specialists

Rheumatoid arthritis (RA)* represents the largest patient group to be treated with HCQ. The following actions reduce the risks and hence the need for ocular screening of HCQ patients:

- When starting HCQ in RA patients, a shorter course (<5 years) of combination therapy is planned. (A shorter course is generally not possible for other conditions.)
- Attention is paid to the body weight and eGFR at the start of the treatment and at follow up/annual review clinics.
- HCQ withdrawal is started once low disease activity/remission is achieved.
- It is aimed to reduce the number of patients with RA who remain on HCQ at 5 years.

* RCOphth guidance refers to Kings College Hospital data which confirms that 55% of rheumatology patients use HCQ for RA. It is recognised that a teaching hospital, may be an outlier as they may see proportionately more connective tissue disease (and less RA) than district general hospitals.

DOSAGE[1]

Rheumatology and dermatology indications:

- Maximum 5 mg/kg of actual body weight (usually 200 mg once or twice daily).
- Dose adjustment is required in renal impairment due to increased risk of retinal toxicity.

HCQ dosing in renal impairment

HCQ dose adjustment	CKD stage	eGFR
75%	3	30 - 60 ml/min
25 - 50%	4	15 - 29 ml/min
25%	5	<15 ml/min

TIME TO RESPONSE

3 to 6 months

PRE-TREATMENT RESPONSIBILITIES OF SPECIALIST

Assessment

- Height and weight
- Full blood count (FBC), liver function tests (LFTs), creatinine and eGFR, erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)
- History of previous eye disease and family history of eye disease

Patient advice

- Written information about HCQ, including the risk of retinal damage, should be given to the patient
- Advise patients 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.

Ophthalmology referral

- Refer the patient for baseline ophthalmology assessment if treatment is intended for >5 years or if risk factors are present (see Screening for Ocular Toxicity above). Inform GP and patient if ophthalmology referral is being made.

ONGOING MONITORING RESPONSIBILITIES of the Specialist

Parameter	Frequency and Result
Blood tests	Review renal function results annually and consider repeat renal function monitoring if required.
Body weight	Body weight monitored annually.
Monitoring of the disease and need/dose adjustment for HCQ	Ongoing monitoring undertaken in accordance with clinical need. The need for continuing HCQ is reviewed regularly by the specialist.
Ocular toxicity	Patients who meet RCOphth criteria for ongoing ocular toxicity screening are identified by the specialist and referred to ophthalmology. Patient and GP will be informed of the referral.

ONGOING MONITORING RESPONSIBILITIES of the GP

Parameter	Frequency and Result
Blood tests: renal function	Annual renal function (to assess risk of ocular toxicity and the need for ocular screening and dose adjustment). In addition, if renal function declines e.g. due to comorbidities, the specialist should be informed so that HCQ dose adjustment and ophthalmology referral can be considered.

ACTIONS TO BE TAKEN

Side Effect/Need for Action	Action
Change in visual acuity or development of blurred vision	Stop and discuss with specialist who will arrange a **review by ophthalmologist.**
Allergic reactions: urticaria, angioedema and bronchospasm	Stop and inform specialist.
Gastrointestinal disturbance	If severe, drug may have to be discontinued.
Skin rashes	Often photosensitive. Stop in all but the mildest of cases.
Skin pigmentation, hair thinning	Stop if significant.
Headaches and less frequently dizziness, vertigo, tinnitus, hearing loss, nervousness, emotional lability, toxic psychosis	Stop if significant and discuss with specialist.
Cardiomyopathy has been rarely reported. New conduction disorders (bundle branch block/atrioventricular heart block), biventricular hypertrophy.	Stop and discuss with specialist.
Overdose	HCQ is very toxic in overdose. Immediate advice from the Poisons Centre is essential.

NOTABLE DRUG INTERACTIONS

- **Antacids:** Reduce absorption of HCQ and should be avoided within 4 hours of HCQ dose.
- **Moxifloxacin, amiodarone, quinine:** Increase risk of cardiac arrhythmias if used with HCQ and should be avoided.
- **Mefloquine:** Increased risk of convulsions if used with HCQ and should be avoided.
- **Digoxin, ciclosporin, methotrexate:** HCQ may increase plasma concentration of these drugs.
- **Neostigmine** and **pyridostigmine** effects are diminished by HCQ, causing increased symptoms of myasthenia gravis. Avoid concomitant use.
- **Penicillamine:** increased risk of haematological toxicity. Avoid concomitant use.
- **Tamoxifen increases the risk of retinopathy.**

BACK-UP INFORMATION AND ADVICE

Contact Details	Wycombe and Amersham	Stoke Mandeville
Rheumatology	01296 315960 (specialist nurse helpline – may take 48 hours for response; not for urgent queries) In an emergency contact consultant rheumatologist of the week 01296 316664 Rheumatology Reg: Bleep 905/907 via switchboard E-mail: bht.rheumatology@nhs.net	
Dermatology	09:00 – 17:00 contact on-call registrar or consultant via switchboard 01494 526161	09:00 – 17:00 contact on-call registrar or consultant via switchboard 01296 315000
Medicines Resource Centre	01494 425355 Bucks.medicinesresourcecentre@nhs.net	

Shared Care Agreement Form

Available on DocGen. When not available, use the Word version linked here.

REFERENCES

1. RCOphth Hydroxychloroquine and chloroquine recommendations on screening Feb 2018 https://www.rcophth.ac.uk/wp-content/uploads/2018/07/Hydroxychloroquine-and-Chloroquine-Retinopathy-Screening-Guideline-Recommendations.pdf
2. BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs, February 2017
3. Hydroxychloroquine 200 mg tablets Quinoric® SPC last updated 07/11/2017 https://www.medicines.org.uk/emc/product/477/smpc#DOCREVISION
4. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding - Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids, September 2016

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