National shared care protocol adapted for local use:

Dermatological Conditions: Hydroxychloroquine for patients within adult services.

As well these protocols, please ensure that summaries of product characteristics (SPCs), British national formulary (BNF) or the Medicines and Healthcare products Regulatory Agency (MHRA) or NICE websites are reviewed for up-to-date information on any medicine.

1. Background

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Hydroxychloroquine is an antimalarial and a disease modifying anti-rheumatic drug (DMARD) with several pharmacological actions which may be involved in its therapeutic effect. Hydroxychloroquine can be used to reduce disease activity in patients with dermatological conditions. Clinical benefit may take up to 3 months.

Hydroxychloroquine is not licensed for all indications included in this shared care protocol. Its use for the indications below is however supported by various sources and bodies including the BNF, NICE, British Association of Dermatologists (BAD).

This shared care protocol applies to adults aged 18 and over.

2. Indications

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The licensed indications for hydroxychloroquine include:

- Systemic and discoid lupus erythematosus
- Dermatological conditions caused or aggravated by sunlight.
- Sarcoidosis

This shared care protocol also includes treatment of chronic inflammatory conditions where off-label use of hydroxychloroquine is appropriate, including but not limited to the following conditions:

- Lichen planus, lichen planopilaris, Dermatomyositis, Morphoea, Sjogren's syndrome)

The initiating specialist must specify the indication for each patient when initiating shared care and clearly state when the use is off label.

3. Locally agreed off-label use

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Lichen planus, lichen planopilaris, Dermatomyositis, Morphoea, Sjogren's syndrome

4. Contraindications and cautions

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This information does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Please see BNF & SPC for comprehensive information.

Contraindications:

- Hypersensitivity to hydroxychloroquine or 4-aminoquinoline compounds
- Pre-existing maculopathy

Cautions:

- Concurrent use of medicines which may cause adverse ocular or skin reactions.
- Diabetes mellitus, and those taking anti-diabetic drugs (including SGLT-2 inhibitors) for any indication (hydroxychloroquine treatment may lower blood glucose)
- Glucose-6-phosphate dehydrogenase deficiency
- Increased risk of retinopathy with high doses (>5 mg/kg/day), long-term treatment (>5 years), eGFR <60 mL/min/1.73m^2 or concurrent tamoxifen use.
- Myasthenia gravis or psoriasis (may exacerbate)
- Porphyria cutanea tarda, and other acute porphyria's
- Renal or hepatic disease and concurrent use of drugs known to affect these organs. Dose reduction may be required once GFR <50ml/min.
- Sensitivity to quinine
- Severe gastrointestinal, neurological (especially for those with a history of epilepsy – may lower the seizure threshold), or blood disorders.
- Significant cardiac arrhythmias due to the risk of QT interval prolongation

5. Initiation and ongoing dose regimen

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- Transfer of monitoring and prescribing to primary care is normally after the patient has been treated for at least 12 weeks, the dose has been optimised and with satisfactory investigation results for at least 4 weeks.
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
- Termination of treatment will be the responsibility of the specialist.

Initial stabilisation:

200mg to 400 mg daily (usually 5mg/kg/day, based on actual body weight).

The risk of significant toxicity increases with doses above 5 mg/kg/day (based on actual body weight) as per RCOphth guidelines.

Dose should not exceed 6.5 mg/kg/day (based on actual body weight),

The initial period must be prescribed by the initiating specialist.

Maintenance dose (following initial stabilisation):

200mg to 400 mg daily (usually 5mg/kg/day, based on actual body weight).

The risk of significant toxicity increases with doses above 5 mg/kg/day (based on actual body weight) as per RCOphth guidelines.

The initial maintenance dose must be prescribed by the initiating specialist.

Conditions requiring dose adjustment:

In patients taking 400mg daily, the dose can be reduced to 200mg when no further improvement is evident. The maintenance dose may be increased to 400mg daily if the response lessens.

Dose adjustment and caution are recommended in renal or hepatic impairment (see SPC) .

6. Pharmaceutical aspects

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Route of administration:	Oral
Formulation:	Hydroxychloroquine sulfate 200 mg tablets (Plaquenil® or Quinoric®)
Administration details:	Each dose should be taken with food. If necessary, tablets may be crushed and dispersed in water (unlicensed).
Other important information:	Antacids may reduce absorption of hydroxychloroquine. **Oral antacids should be avoided for 4 hours before and after the dose.**

7. Significant medicine interactions

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The following list is not exhaustive. Please see BNF or SPC for comprehensive information and recommended management.

The following drugs must not be prescribed without consultation with the specialist:

- **Drugs that can prolong the QT interval: for example, amiodarone, azithromycin, moxifloxacin, quinine, citalopram**. Avoid concomitant use; possible increased risk of QT prolongation/ventricular arrhythmias.
- **Antidiabetic drugs and/or insulin**: hypoglycaemic effect may be enhanced, may need dose adjustment of antidiabetic medication.
- **Cimetidine**: possible increase in plasma concentration of hydroxychloroquine.
- **Ciclosporin**: possible increase in plasma concentration of ciclosporin (combination used by some specialists).
- **Digoxin**: possible increase in plasma concentration of digoxin.
- **Mefloquine and other drugs known to lower the convulsion threshold**: possible increased risk of convulsions.
- **Penicillamine**: possible increased risk of haematological toxicity.

- **Tamoxifen**: increased risk of retinal toxicity, necessitates annual ophthalmic monitoring (see section 4).

The following drugs may be prescribed with caution:

- **Antacids and calcium carbonate-containing supplements**: may reduce absorption of hydroxychloroquine; separate administration by **at least four** hours. Other calcium salts do not appear to interact.
- **Antiepileptics**: activity of antiepileptic drugs may be impaired with hydroxychloroquine. Additionally, hydroxychloroquine may lower the seizure threshold.
- **Neostigmine and pyridostigmine**: effects may be antagonised by hydroxychloroquine.
- **Intra-dermal rabies vaccine**: possible reduced antibody response
- **Topiramate** – increased risk of toxicity when co-administered with valproate, monitor for signs and symptoms of encephalopathy or hyperammonaemia

8. Baseline investigations, initial monitoring, and ongoing monitoring to be undertaken by specialist

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Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.

Baseline investigations:

- Urea and electrolytes (U&Es) & creatinine clearance (CrCl)
- Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST), & albumin
- Full blood count (FBC)
- Weight
- Assess for co-morbidities which may influence DMARD choice, including risk factors for retinopathy (e.g., concomitant tamoxifen use, eGFR <60 mL/min)
- Take history of eye disease/symptoms and advise patient to attend a yearly optician review.
- Electrocardiogram (ECG), only if concerns exist regarding the QT-interval, see section 4 and section 7.

Ongoing monitoring:

- No routine ongoing laboratory monitoring is required for hydroxychloroquine. Monitoring may be required if the patient is prescribed an additional DMARD.
- The specialist will retain the responsibility for monitoring the patient's ongoing response to treatment and advise if a dose change or treatment cessation is appropriate. **This should be undertaken annually** and will include a reminder to see local optician.
- After the patient has been on hydroxychloroquine for **five years**, the specialist will refer to ophthalmology (or other commissioned service as appropriate) for annual monitoring for retinopathy. **Patients who are at higher risk of retinal toxicity (on concomitant tamoxifen, impaired renal function, high hydroxychloroquine dose) will need to be referred earlier.** See section 9 below for risk factors.
- After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.

9. Ongoing monitoring requirements to be undertaken by primary care

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See section 10 for further guidance on management of adverse effects/responding to monitoring results.

Monitoring	Frequency
• Discuss with and remind patients that they need to attend annual optician reviews and that they will require referral to ophthalmology for retinal toxicity monitoring when they have been on hydroxychloroquine for five years. Patients who are at higher risk of retinal toxicity will need to be referred earlier. If patients have not been referred to ophthalmology at 5 years, the specialist team must be contacted to organise the referral. See RCOphth guidelines. • Risk factors may change over time; primary care should discuss with specialist if new risk factors that are 'high risk' are identified before the five-year mark.	• Annually after 5 years of treatment, **or** • After 1 year if additional risk factors are present. • **Risk factors include:** ○ concomitant tamoxifen use ○ impaired renal function (eGFR <60mL/min/1.73m^2) ○ hydroxychloroquine dose (>5mg/kg/day)
• Patients aged from 50 years who are severely immunosuppressed and have not received the shingles vaccine before will be eligible for the shingles vaccine (varicella zoster). This will be provided as two doses of the non-live vaccine. If patient is taking additional DMARDs, check advice for all drugs. Refer to Green Book Chapter 6 (Contraindications and special considerations) and Green Book Chapter 28a (Shingles) for further details. • **Annual** influenza (The Green Book, Chapter 19) vaccinations are recommended. • **COVID-19** vaccination is safe and recommended (see The Green Book, Chapter 14a).	• Shingles vaccination: Chapter 28a (Shingles). • Influenza vaccination: annual. It is advisable to add the patient to the influenza vaccine list. • Other vaccinations as per national schedule, e.g., COVID-19.
(If relevant) If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.	

10. Adverse effects and other management

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Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit www.mhra.gov.uk/yellowcard

For a full list of side effects and information on incidence of ADRs, refer to the BNF or see relevant summaries of product characteristics.

IF YOU ARE IN ANY DOUBT ABOUT ANY POTENTIAL ADVERSE REACTION, PLEASE CONTACT THE DERMATOLOGY SPECIALIST TEAM.

Result	Action for primary care
As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance. Other benchmark values may be set by secondary care in specific clinical circumstances. This will be communicated by the specialist.	
Retinopathy monitoring: possible or definite retinal toxicity	• **Possible retinopathy:** Consider whether withholding is in the best interests of the patient (See RCOphth guidelines for recommendations on managing possible retinopathy), specialist to be informed and to determine follow-up plan. • **Definite retinopathy:** primary care to ensure **withheld** pending urgent discussion between patient and specialist/ ophthalmologist / optician.
Vision disturbances including blurred vision, changes in visual acuity or abnormal colour vision	Withhold until discussed with dermatology specialist/ ophthalmologist / optometrist
Symptoms or signs of cardiomyopathy e.g., breathlessness, swelling in the abdomen and ankles, palpitations, cardiac conduction disorders and ECG changes.	Review for reversible causes. Discuss with specialist team urgently and consider withholding. If cardiomyopathy occurs due to hydroxychloroquine treatment, hydroxychloroquine must be withheld.
Headache, gastrointestinal disturbances e.g., abdominal pain, nausea, diarrhoea, vomiting	Review for reversible causes; discuss with specialist team if persistent or severe
Skin and subcutaneous tissue disorders e.g., pruritic erythematous macular rash occurring soon after treatment commenced, blue-black pigmentation of the skin, bleaching of skin & hair	Withhold and discuss with specialist team

Skeletal muscle myopathy or neuromyopathy	Review for reversible causes; withhold and discuss with specialist team
Signs and symptoms of bone marrow suppression e.g., sore throat, oral ulceration, abnormal bleeding/bruising, signs of infection	Review for reversible causes. Be aware that the underlying condition may contribute to bone marrow suppression. Although the risk is low, if bone marrow suppression is suspected, discontinue treatment, and obtain an urgent FBC and other bloods as appropriate. Discuss with specialist team.

11. Advice to patients and carers

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The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.

The patient should be advised to report any of the following signs or symptoms to their primary care prescriber without delay:

- Vision disturbances including blurred vision, changes in visual acuity or abnormal colour vision should be reported **immediately** to an optician/GP for referral to ophthalmology.
- Signs or symptoms of bone marrow suppression, such as a sore throat, oral ulceration, abnormal bleeding or bruising, or other signs of infection.
- Rash
- Muscle weakness
- Symptoms of hypoglycaemia, including dizziness, weakness, or hunger
- Actual or planned pregnancy or breastfeeding

The patient should be advised:

- Avoid over the counter (OTC) and prescribed **antacids for four hours before and after** doses of hydroxychloroquine.
- A number of patients who take hydroxychloroquine may experience some loss of their peripheral and central vision. Patients who drive must inform the DVLA if their eyesight is affected. For further information see: https://www.gov.uk/driving-eyesight-rules
- That vaccination in line with current national advice (e.g., for COVID-19, influenza) is safe and recommended.
- Tell anyone who prescribes them a medicine that they are taking hydroxychloroquine. Always ask a pharmacist before purchasing any medicines over the counter, including herbal remedies, and ask if they are safe.

Patient information:

- British Association of Dermatologists

12. Pregnancy, paternal exposure, and breast feeding

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It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.

Pregnancy:

Hydroxychloroquine can be continued throughout pregnancy.

Information for patients and carers: Hydroxychloroquine in pregnancy (Bumps)

Breastfeeding:

Hydroxychloroquine is compatible with breastfeeding, though does pass into breast milk in small quantities.

Information for healthcare professionals: https://www.sps.nhs.uk/medicines/hydroxychloroquine/.

Paternal exposure:

Hydroxychloroquine is compatible with paternal exposure.

13. Specialist contact information

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Advice on any aspect of DMARD therapy is available Monday to Friday 9-5.

Primary care practitioners should contact the consultant's secretary/specialist nurse's secretary during working hours.

Nottingham Treatment Centre (0115 9194477)

Secretaries for Dermatology Consultants and Nurse Specialists. **Ext 78941**

Sherwood Forest NHS Foundation Trust Contacts (Kings Mill Hospital 01623 622515 ext. 3117/3191)

Consultant Dermatologist and Clinical Nurse Specialists. **01623 672310**

14. Additional information

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Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed. Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.

15. References

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- eBNF accessed via https://bnf.nice.org.uk/drug/hydroxychloroquine-sulfate.html on 22/02/24.
- Hydroxychloroquine sulfate 200 mg film-coated tablets (Quinoric®). Bristol Laboratories. Date of revision of the text: 13/10/2020. Accessed via https://www.medicines.org.uk/emc/product/477/smpc on 09/01/24.

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- Hydroxychloroquine sulfate 200 mg film-coated tablets. Blackrock Pharmaceuticals. Date of revision of the text: 11/11/2020. Accessed via https://www.medicines.org.uk/emc/product/11540/smpc.
- Hydroxychloroquine sulfate 200 mg film-coated tablets. Ipca Laboratories. Date of revision of the text: 07/04/2020. Accessed via https://www.medicines.org.uk/emc/product/11516/smpc.
- Renal Drug Database. Hydroxychloroquine sulphate. Reviewed 20/02/2018. Accessed via https://renaldrugdatabase.com/monographs/hydroxychloroquine-sulphate.
- Royal College of Ophthalmologists. 2020. Hydroxychloroquine and Chloroquine Retinopathy: Recommendations on Monitoring. Accessed via https://www.rcophth.ac.uk/standards-publications-research/clinical-guidelines/.
- Immunisation against infectious diseases (The Green Book). Accessed via https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book.
- NICE Clinical Knowledge Summary. DMARDS: Hydroxychloroquine. Last revised April 2020. Accessed via https://cks.nice.org.uk/topics/dmards/management/hydroxychloroquine/.
- Stockley's Drug Interactions. Accessed via www.medicinescomplete.com.
- NEWT Guidelines. Hydroxychloroquine. Last updated November 2012. Accessed via https://access.newtguidelines.com/H/Hydroxychloroquine.html.
- RMOC Advice on the monitoring requirements for HCQ

16. Other relevant national guidance

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- NHSE guidance – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/
- General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care
- NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/.

17. Local arrangements for referral

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Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.

- The request for shared care should be accompanied by individual patient information, outlining all relevant aspects of the patient's care and which includes direction to the shared care protocols on the APC website.

- Prescribing and monitoring responsibility will only be transferred when it is agreed by the specialist and the patient's primary care prescriber that the patient is stabilised on their medication regimen without adverse effect and with benefits demonstrated.
- The specialist will request shared care with the GP in writing.
- If the GP doesn't agree to shared care, they should inform the specialist of their decision in writing within 14 days, outlining the reason for the decline. The agreement can be assumed if the GP does not provide a written decline.
- In cases where shared care arrangements are not in place or where problems have arisen within the agreement, and patient care may be affected, the responsibility for the patient's management, including prescribing, reverts back to the specialist.
- Should the patient's condition change, the GP should contact the relevant specialist using the details provided with the shared care request letter.