

**LINCOLNSHIRE CLINICAL COMMISSIONING GROUPS in association
with UNITED LINCOLNSHIRE HOSPITALS TRUST**

SHARED CARE GUIDELINE: Hydroxychloroquine

General Principles

Shared Care Responsibilities:

In its guidelines on responsibility for prescribing (circular EL (91) 127) between hospitals and general practitioners, the Department of Health has advised that legal responsibility for prescribing lies with the doctor who signs the prescription. (*BNF 68*, September 2014 -March 2015, pg.5)

Aims:

- (1) The aim of shared care guidelines is to provide information and/or guidance to GPs and hospital staff relating to the potentially complex implications of sharing patient care for a specific drug between primary and secondary/tertiary care.
- (2) Specific shared care guidance should be available for any high cost drug, high-risk drug therapy or device that may be prescribed for a patient following specialist referral. Such guidance will only be produced where shared care is considered an appropriate option.
- (3) Each guideline will include a clear statement of the responsibilities of both the GP and the specialist unit within the overall provision of the treatment to the patient.
- (4) Shared care guidelines will ensure that the GP has sufficient information available to undertake to prescribe a specialist treatment if s/he so wishes. It is not the intention of these guidelines to insist that GPs prescribe such treatment and any doctor who does not wish to accept clinical or legal responsibility to prescribe such a drug is under no obligation to do so. Nonetheless the development of a shared care guideline will only be undertaken within the context of a broad acceptance between the Lincolnshire Prescribing and Clinical Effectiveness Forum (PACEF) and secondary/tertiary care that GP prescribing of such a treatment is appropriate within the constraints of formal shared care. Any drug approved for the development of a shared care guideline will automatically be classified as amber on the Lincolnshire Traffic Lights List and, if high-cost, will be supported financially through the High Cost Drugs Reserve. Thus there should be no financial reason why a GP should be deterred from prescribing a high cost drug under a shared care guideline.

Further copies

Further copies of any guidelines in this series are available from Greater East Midlands Commissioning Support Unit (GEMCSU) Prescribing and Medicines Optimisation Service (PMOS) .

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Principles of shared care

The General Medical Council published their Good Practice In Prescribing And Managing Medicines and which came into effect 25th February 2013. A section of the guidance provides recommendations for the sharing of care which applies to any instance when care is shared between different services.

Good practice recommendation 35.

- Decisions about who and who should take responsibility for continuing care or treatment after initial diagnosis or assessment should be based on patients best interest rather than on convenience or the cost of the medicine and associated monitoring or follow-up

Good practice recommendation 36.

- Shared care requires the agreement of all parties including the patient. Effective communication and continuing liaison between all parties to a shared care agreement is essential.

Good practice recommendation 37.

- If you prescribe at the recommendation of another doctor, nurse or other healthcare professional, you must satisfy yourself that the prescription is needed, appropriate for the patient and within the limits of your competence.

Good practice recommendation 38.

- If you delegate assessment of a patients' suitability for a medicine, you must be satisfied that the person to whom you delegate has the qualifications, experience, knowledge and skills to make the assessment. You must give them enough information about the patient to carry out the assessment required

Good practice recommendation 39.

- In both cases, you will be responsible for any prescription you sign.

Good practice recommendation 40.

- If you recommend that a colleague, for example a junior doctor or general practitioner, prescribes a particular medicine for a patient, you must consider their competence to do so. You must satisfy yourself that they have sufficient knowledge of the patient and the medicine, experience (especially in the case of junior doctors) and information to prescribe. You should be willing to answer their questions and otherwise assist them in caring for the patient, as required

Good practice recommendation 41

- If you share responsibility for a patient's care with a colleague , you must be competent to exercise your share of clinical responsibility.

You should:

- a) Keep yourself informed about the medicines that are to be prescribed for the patient
- b) Be able to recognise serious and frequently occurring adverse side effects
- c) Make sure appropriate clinical monitoring arrangements are in place and that the patient and the healthcare professionals involved understand them
- d) Keep up to date with relevance guidance on the use of the medicines and on the management of the patient's condition

Good practice recommendation 42

- In proposing a shared care arrangement, specialists may advise the patient's general practitioner which medicine to prescribe. If you are recommending a new or rarely prescribed medicine you should specify the dosage and means of administration and agree a protocol for treatment. You should explain the use of unlicensed medicines and departures from authoritative guidance or recommended treatments and provide both the general practitioner and the patient with sufficient information to permit the safe management of the patient's condition.

Good practice recommendation 43

- If you are uncertain about your competence to take responsibility for the patient's continuing care you should seek further information or advice from the clinician with whom the patient's care is shared or from another experienced colleague. If you are still not satisfied you should explain this to the other clinician and to the patient and make appropriate arrangements for their continuing care.

Drug Details

Approved Name: **Hydroxychloroquine**

Brand Name: generic formulations and Paquenil®

Form and Strength: 200mg film coated tablets

Specialist Responsibilities

The specialist secondary/tertiary care service will:

1. Send a letter to the GP requesting that the GP participates in shared care. As part of the communication the GP should be signposted to where they can find a copy of the shared care protocol e.g. the PACEF website <http://lincolnshire-pacef.nhs.uk/lincolnshire-prescribing-and-clinical-effectiveness-forum-pacef>
2. Ensure that, where prescribing has been initiated by the specialist, the patient will receive supplies of hydroxychloroquine from the hospital or prescribed from the hospital on FP10 until the GP formally agrees to shared care.
3. Conduct initial tests of complete and differential blood counts, U& E's, creatinine, LFTs and CRP.
4. If impairment or eye disease exists refer to an optometrist/ ophthalmologist for advice before initiating treatment.
5. Provide patient with information as to the ocular toxicity of hydroxychloroquine and advise patients to see an optometrist/ophthalmologist urgently if they develop a reduction in visual acuity or any other visual problems.
6. Initiate and stabilise patient on hydroxychloroquine therapy.
7. Assess the patient's response to hydroxychloroquine.
8. Liaise with the GP regarding conducting and interpreting future monitoring tests.
9. Undertake monitoring at appropriate intervals until dose stabilised and GP has agreed to undertake routine monitoring.
10. Periodically review the patient's clinical condition and communicate promptly to the GP any changes in dose or monitoring requirements.
11. Advise the GP on when to adjust dose, stop treatment or consult with specialist. dosage alterations where appropriate.

12. Be available to give advice to the GP and ensure that clear backup arrangements exist for GPs to obtain advice and support. (See contact details)

GP Responsibilities

The GP will:

1. Notify the consultant in writing that s/he agrees to participate in shared care.
2. Monitor the patient's overall health and wellbeing.
3. Monitor for adverse effects and drug interactions.
4. Prescribe the medication once shared care has been agreed.
5. Carry out monitoring tests if requested by rheumatology team.
6. Act promptly on the results of all tests and adjust or stop the dose if appropriate.

If in doubt STOP the treatment and contact the Specialist – within 7 days.

Referral Criteria

1. Patients will have received at least 3 months of hydroxychloroquine therapy on hospital prescription.
2. Patients will have been stabilised on a suitable dose of hydroxychloroquine. During this time it may be more convenient for the patient to have blood tests conducted at the GP surgery, but the responsibility for ensuring that the monitoring is done and the interpretation of the results remains with the specialist until the GP has agreed to shared care.
3. The specialist will have carried out an assessment of efficacy.

Licensed Indications

Treatment of active rheumatoid arthritis including juvenile idiopathic arthritis and systemic and discoid lupus erythematosus.

Recommended Dosage and Administration

The minimum effective dose should be used. Dose is 200-400mg daily, but dose should not exceed 6.5mg/kg daily based on ideal body weight.

Background Pharmacology

Rheumatoid arthritis is common and affects over 1% of the population. The disease runs a variable and unpredictable course. Research has shown that early intervention with disease specific disease-modifying antirheumatic drugs (DMARDs) is the cornerstone of treatment. Used in the early stages they may curb or arrest the progressive synovitis and joint destruction and therefore limit joint disability.

Preparations Available

Hydroxychloroquine is available as film coated tablets containing 200mg of hydroxychloroquine sulphate.

Adverse Effects

Ocular – visual changes and retinal damage.

Retinopathy with changes in pigmentation and visual field defects may occur.

Corneal changes including oedema and opacities. Blurred vision.

Royal College of Ophthalmologists have issued guidance on Hydroxychloroquine and ocular toxicity in October 2009. In their review they have concluded that although

there is a link between hydroxychloroquine use and retinal toxicity there is not enough evidence to support a programme of systematic screening, as clinically significant maculopathy is very rare. There is also no reliable test for detecting it at a reversible stage.

The guidance recommends that a baseline check is made on reading performance with reading spectacles if required and that an annual review is conducted. If visual impairment is suspected patients should be advised to consult an optometrist in the first instance.

The guidance also recommends that the maximum dose of hydroxychloroquine is not exceeded.

If treatment is required long term (5 years) this should be discussed with the ophthalmologist.

Common adverse effects

Gastrointestinal disturbances e.g.– nausea, diarrhoea, anorexia, abdominal pain, vomiting. Headache and skin reactions – rashes and pruritus.

Less frequent adverse effects

ECG changes (conduction disorders), convulsions visual changes and retinal damage (see above), keratopathy, ototoxicity, hair depigmentation, hair loss and discoloration of skin, nails and mucous membranes.

Rare adverse effects

Blood disorders –including thrombocytopenia, agranulocytosis and aplastic anaemia. Mental changes – emotional disturbances and psychosis.

Myopathy including cardiomyopathy and neuromyopathy.

Acute generalised exanthematous pustulosis, exfoliative dermatitis, Stevens-Johnson syndrome and photosensitivity.

Liver - abnormal liver function tests, hepatic failure.

May also cause bronchospasm so care should be taken in those with existing respiratory conditions.

Risk of hypoglycaemia.

Hydroxychloroquine has been shown to cause severe hypoglycaemia including loss of consciousness that could be life threatening in patients treated with and without antidiabetic medications. Patients treated with hydroxychloroquine should be warned about the risk of hypoglycaemia and the associated clinical signs and symptoms.

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

IMPORTANT – very toxic in overdose – seek immediate advice from specialist poison centres.

Drug Interactions

For complete list of drug interactions please refer to current edition of BNF and the summary of product characteristics (SPC)

Amiodarone – avoid concomitant use as increased risk of ventricular arrhythmias.

Digoxin – concomitant administration may cause an increase in plasma concentration of digoxin.

Methotrexate – concomitant administration may increase plasma concentration of methotrexate although methotrexate and hydroxychloroquine are often used in combination.

Anticonvulsants – may antagonise anticonvulsant effect. In creasing risk of convulsions

Antidepressants – risk of ventricular arrhythmias manufacturers advise avoid use with citalopram and escitalopram.

Antipsychotics increased risk of ventricular arrhythmias when hydroxychloroquine given with droperidol, avoid concomitant use.
Ciclosporin – concomitant administration may increase plasma concentration of ciclosporin leading to increased risk of toxicity.
Antibacterials – increased risk of ventricular arrhythmias when hydroxychloroquine given with moxifloxacin – avoid concomitant use.
Cytotoxics – increased risk of ventricular arrhythmias when given with bosutinib.
Avoid concomitant use of mefloquine, and other antimalarials
Oral typhoid vaccine may inactivate vaccine.
Lanthanum – absorption possibly reduced give at least 2 hours apart.
Cimetidine – may inhibit metabolism of hydroxychloroquine leading to increased plasma levels.
Parasympathomimetics – antagonising the effect of neostigmine & pyridostigmine diminishing effectiveness of treatments and increasing the symptoms of myasthenia gravis.
Antacids the absorption of hydroxychloroquine is reduced by antacids, it is recommended that antacids should not be taken for at least four hours before or after hydroxychloroquine to reduce possible interference with the absorption of hydroxychloroquine.

Precautions and Contraindications

Contraindications

Pre-existing maculopathy.

Pregnancy – The manufacturer of hydroxychloroquine advises avoid use in pregnancy however the British Society of Rheumatologists and British Health Professionals in Rheumatology state that THE RISKS OF STOPPING TREATMENT SHOULD BE WEIGHED UP AGAINST THE SMALL POSSIBLE RISK TO THE UNBORN CHILD. Hydroxychloroquine crosses the placenta. It should be noted that 4 aminoquinolones in therapeutic dose have been associated with central nervous system damage, including ototoxicity (auditory and vestibular toxicity, congenital deafness) retinal haemorrhage and abnormal retinal pigmentation.

Breast feeding – avoid due to risk of toxicity in the infant.

Known hypersensitivity to hydroxychloroquine & 4-aminoquinoline compounds

Use with caution

Patients with renal impairment, manufacturer advises caution and monitoring of plasma hydroxychloroquine concentration in severe impairment.

Patients with liver impairment, hydroxychloroquine should be used with caution in moderate to severe hepatic impairment.

Patients with neurological disorders particularly epilepsy as may reduce threshold for convulsions.

Patients with blood disorders. Although the risk of bone marrow depression is low, periodic blood counts are advisable as anaemia, aplastic anaemia, agranulocytosis, a decrease in white blood cells, and thrombocytopenia have been reported. Hydroxychloroquine should be discontinued if abnormalities develop.

Patients with porphyria cutanea tarda which can be exacerbated by hydroxychloroquine

Patients with psoriasis as may exacerbate condition

Patients receiving treatment with antacids -avoid administration of antacids within four hours of each dose of hydroxychloroquine

Patients who are sensitive to quinine.

Patients with severe gastrointestinal disorders
Patients with G6PD deficiency, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
Patients taking medication that may cause adverse ocular reactions
Risk of hypoglycaemia.
Hydroxychloroquine has been shown to cause severe hypoglycaemia including loss of consciousness that could be life threatening in patients treated with and without antidiabetic medications. Patients treated with hydroxychloroquine should be warned about the risk of hypoglycaemia and the associated clinical signs and symptoms.
Patients presenting with clinical symptoms suggestive of hypoglycaemia during treatment with hydroxychloroquine should have their blood glucose level checked and treatment reviewed as necessary.
All patients on long-term therapy should undergo periodic examination of skeletal muscle function and tendon reflexes. If weakness occurs, the drug should be withdrawn.

Monitoring

Baseline monitoring

FBC, U&E, creatine, LFT, CRP prior to commencing treatment.
Ophthalmoscopy to assess for maculopathy.
Visual acuity & visual fields assessment. Refer to optometrist or ophthalmology clinic if pre-existing visual impairment.

Ongoing monitoring

Routine monitoring of FBC, U&E's, liver and renal functions is not required providing the baseline tests have been carried out. However the majority of patients will be receiving regular monitoring as they will be receiving other DMARD therapies or if they are being treated for Systemic Lupus Erythematosus (SLE).
Patients are advised to report any visual disturbance such as changes in visual acuity to an optician or an ophthalmologist (if they are already under review for an existing eye condition).

Treatment should be stopped and specialist advice sought if:

Development of blurred vision or changes to visual acuity

Remember: if in doubt STOP the hydroxychloroquine and contact the specialist (within 7 days).

Indication of Likely Cost of Therapy in Primary Care

Hydroxychloroquine 200mg tablets £5.15 (60 tabs)
Hydroxychloroquine (Plaquenil) 200mg tablets £5.15 (60 tabs)

Cost annual treatment 200mg-400mg daily - £31.24- £62.48pa.
Drug Tariff price currently that for branded Plaquenil .

Information Given to the Patient

ARC leaflet.

Contact Details

ULHT Rheumatology Team:

First contact the nurse's helpline

Rheumatology Nurses Lincoln (01522) 573828 (Helpline)

Rheumatology Nurses Louth (01522) 597972

Rheumatology Nurses Pilgrim (01205) 445730

Dr Joshi's secretary (01522) 573036

Dr Obaid's secretary (01522) 573413

Dr Chikura's secretary (01522) 573413

Dr James secretary (01522) 573036

Note:

ULHT do not provide care for all patients on hydroxychloroquine for arthritis in Lincolnshire. The ULHT rheumatology team cannot provide advice and guidance for patients under the care of other units.

References

1. BNF 68 September 2014 – March 2015 BNF.org.
2. British Society Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR) Guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatologists. Rheumatology 2008
3. Quick reference guideline for monitoring of disease modifying anti-rheumatic drug (DMARD) therapy. Updated November 2009.
4. Peterborough and Stamford hospitals NHS Foundation Trust Shared Care guideline Hydroxychloroquine.
5. Shared care information on the prescribing of hydroxychloroquine – Plymouth Area Joint Formulary
6. NHS Lothian Shared care protocol – hydroxychloroquine for the treatment of rheumatological inflammatory diseases.
7. Summary of Product Characteristics. Plaquenil Tablets. Sanofi-Aventis. Last updated 10.01.14.
7. Drug Tariff January 2015

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