LINCOLNSHIRE CLINICAL COMMISSIONING GROUPS in association with UNITED LINCOLNSHIRE HOSPITALS TRUST

SHARED CARE GUIDELINE: Hydroxychloroquine for treatment of active rheumatoid arthritis including juvenile idiopathic arthritis and systemic and discoid lupus erythematosus.

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 74, September 2017 – March 2018, 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 members of the Optum Medicines Management and Optimisation Team.

Date of Issue: November 2018
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Principles of shared care

NHS England published Guidance - Responsibility for Prescribing between primary, secondary and tertiary care – January 2018.
Key recommendations from guidance:

1.0 Introduction

1.1 Shared Care Prescribing guidelines are local policies to enable General Practitioners to accept responsibility for the prescribing and monitoring of medicines/ treatments in primary care in agreement with the initiating service.
1.4 Where possible shared acre should be disease specific rather than medicine specific and link into complement local integrated care pathways and shared acre policies. Medicines and conditions suitable for shared care will be identified by local medicines committees and will be classified as AMBER (AMBER 1 for Lincolnshire) through the traffic light system. … However it should be remembered that the provision of shared care prescribing guidelines does not necessarily mean that the GP has to agree to accept clinical and legal responsibility for prescribing; that they should only do so if they feel clinically confident in managing that condition.

2.3 reasonable predictable clinical situation

2.3.1 Transfer of clinical responsibility to primary care should only be considered where the person's clinical condition is stale or predictable.

2.4 Agreement of shared care between consultant and GP

2.4.1 Referral to the GP should only take place once the GP has agreed in each individual case and the hospital or specialist will continue to provide prescriptions until a successful transfer of responsibilities. The GP should confirm the agreement and acceptance of the shared care prescribing arrangement and that the supply arrangements have been finalised. The secondary/ tertiary provider must supply an adequate amount of the medication to cover the transition period. The patiet should then be informed to obtain further prescriptions from the GP.

2.7 Clear definition of responsibility

2.7.1 The areas of care for which each clinician has responsibility should be clearly defined.

2.8 Clinical responsibility

2.8.1 Clinical responsibility for prescribing is held by the person signing the prescription who must also ensure adequate monitoring.

2.9 Communication network & emergency support

2.9.1.Telephone details and (if appropriate) secure email addresses of both parties should be exchanged and recorded. This will enable the practice to access timely advice, guidance and information if problems arise, and will also enable secondary care clinicians to easily contact the GP if necessary. This should include out of hours contact numbers, how to access the on-call duty doctor. Patients and their carers should also be provided with contact details for support and help if required both in and out of hours.
2.9.2 People who are being treated on the advice of a secondary acre team, but are no longer being seen in that setting , may still need a review should problems arise. The appropriate level of care or advice should be available from the secondary care team in a timely manner without necessarily requiring a new referral.

6.0 Monitoring

6.0.1 All appropriate monitoring arrangements must be fulfilled. The person delivering that aspect of the shared care agreement should ensure that the resources to do this are in place in the clinical setting in which they are delivered.

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 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 within 6 months of starting therapy to have a colour retinal photograph and spectral domain optical coherence tomography (SD-OCT) scans of the macula. All patients will receive a list of the high street opticians in their area that provide this examination.
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, if receiving concomitant therapy with other DMARDS.
9. Undertake monitoring at appropriate intervals, if clinically indicated, until dose stabilised and GP has agreed to undertake routine monitoring. More frequent ophthalmic monitoring may be considered if additional risk factors exist e.g. on a dose exceeding 5mg/kg, concomitant tamoxifen therapy or renal insufficiency.
10. Periodically review the patient's clinical condition and communicate promptly to the GP any changes in dose or monitoring requirements.
11. Review all patients who have received five years of treatment, All patients who have received five years or more treatment should be advised to undergo 10-2 Humphrey visual field testing followed by pupillary dilation and imaging with both SD-OCT and wide field fundus autoflurorescence imaging(FAF).
12. Advise the GP on when to adjust dose, stop treatment or consult with specialist. dosage alterations where appropriate.
13. 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 as requested by rheumatology team.
6. Act promptly on the results of all tests and adjust or stop the dose if appropriate.
7. Notify specialist immediately if patient requires treatment with or is receiving tamoxifen or if their renal function deteriorates.

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, dose should not normally exceed 5mg/kg daily based on ideal body weight.
To avoid excessive doses in obese patients, the dose of hydroxychloroquine should be calculated on the basis of ideal body weight.
Doses above 5mg/kg to the BNF maximum dose 6,5mg/kg should only be used in exceptional circumstances and patients on this dose may require additional monitoring due to risk of ocular toxicity.

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

For further information on adverse effects please refer to the online BNF which can be accessed via
https://bnf.nice.org.uk/
or from the Summary of Product Characteristics which can be accessed via:
www.medicines.org.uk

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.
The Royal College of Opthalmologists issued a the Clinical Guideline. Hydroxychloroquine and chloroquine retinopathy recommendations on screening in February 2018. This replaced guidance previously issued in 2009.
Key recommendations:
All patients planning to take hydroxychloroquine long term i.e over five years have a baseline assessment in a hospital eye department ideally within 6 months , but definitely within 12 months, of starting therapy with a colour retinal photograph and spectral domain optical coherence tomography (SD-OCT) cans of the macula.
Patients should be referred for annual screening after 5 years of therapy and be reviewed annually thereafter whist on therapy.
At each screening visit patients should undergo 10-2 Humphrey visual field testing followed by pupillary dilation and imaging with both SD-OCT and wide field fundus autoflurorescence imaging(FAF).
Patients with abnormalities on widefield FAF with 10-2 visual filed tests should undergo 30-2 visual field testi ng on another date. Patients with persistant and significant visual field defects consistent with hydroxychloroquine retinopathy, but without evidence of structural defcets on SD-OCT or FAF may be considered for multifocal electroretinography. Screening may be commenced before five years of therapy if additional risk factors exisit e.g. very high dose of drug therapy, concomitant therapy with tamoxifen therapy or renal insufficiency. Adequate screening may not be possible with retinal co-pathology.

Common adverse effects
Gastrointestinal disturbances e.g.– nausea, diarrhoea, appetite decreased, abdominal pain, vomiting. Headache and skin reactions – rashes and pruritus, emotional lability.
Uncommon adverse effects
Alopecia, corneal oedema, dizziness, eye disorders,hair colour changes,haing impairment, nervousness, neuromuscular dysfunction, retinopathy, seizure, vertigo.
Frequency not known
Hepatic failure, agranulocytosis, anaemia, angioedema, bone marrow disorders, bronchospasm, cardiac conduction disorders, cardiomyopathy, hypoglycaemia, leucopenia, movement disorders, muscle weakness, myopathy, photosensitivity reaction, psychosis, reflexes absent, severe cutaneous adverse reactions (SCARs) , thrombocytopenia, tremor, ventricular hypertrophy.
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 detailed information on drug interactions, please refer to the online BNF which can be accessed via
https://bnf.nice.org.uk/
or from the Summary of Product Characteristics which can be accessed via:
www.medicines.org.uk
Below is a summary of some of the key interactions.

Amiodarone
Avoid- increased risk of ventricular arrhythmias.

Antacids
Avoid concurrent administration separate doses by 4 hours

Anticonvulsants
Avoid- antagonism of anticonvulsant effect.

Ciclosporin
Caution. May cause a rise in serum ciclosporin. Increased risk of toxicity.

Cimetidine
Caution. May cause a rise in serum hydroxychloroquine.

Digoxin
Caution.. May cause rise in serum digoxin.

Droperidol
Avoid. Increased risk of ventricular arrhythmias.

Lanthanum
Avoid concurrent use administration. May reduce absorption of hydroxychloroquine. Separate doses by at least 2 hours.

Neostigmine
Caution. May antagonise effect and increase myasthenic symptoms.

Mefloquine
Avoid. Increased risk of convulsions.

Methotrexate
Caution. May cause rise in serum methotrexate, but drugs are often used in combination.

Moxifloxacin
Avoid. Increased risk ventricular arrhythmias.

Pyridostigmine
Caution. May antagonise effect and increase myasthenic symptoms.

Typhoid vaccine oral
Avoid. Inactivated by hydroxychloroquine.

Quinine
Avoid.

Penicillamine
Hydroxychloroquine is predicted to increase the risk of haematological toxicity when given by penicillamine. Manufacturer advises avoid.

Vaccines
Hydroxychloroquine predicted to decrease efficacy of rabies and cholera vaccine.

Precautions and Contraindications

For further information on contraindications and cautions in use, please refer to the online BNF which can be accessed via
https://bnf.nice.org.uk/
or from the Summary of Product Characteristics which can be accessed via:
www.medicines.org.uk

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 AGIANST THE SMALL POSSIBLE RISK TO THE UNBORN CHILD. Hydroxychloroquine crosses the placenta. Is 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 hydroxychoroquine
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 with a sensitivity to quinine.
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.
Instruct patient to see optometrist/ophthalmologist within 6 months of starting therapy to have a colour retinal photograph and spectral domain optical coherence tomography (SD-OCT) scans of the macula. All patients will receive a list of the high street opticians in their area that provide this examination.

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).
Specialist advice should be sought if patient commences on or requires concomitant treatment with tamoxifen.
Specialist advice should be sought if renal function deteriorates.
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 £3.96 (60 tabs)
Hydroxychloroquine (Plaquenil) 200mg tablets £5.15 (60 tabs)

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 Pilgrim (01205) 445730

Dr Joshi's secretary (01522) 573036
Dr Obaid's secretary (01522) 573413
Dr Chikura's secretary (01522) 573413
Dr Palkonyai's 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. British Society Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR) Non - Biologic disease-modifying anti-rheumatic drug (DMARD) Guidelines. Rheumatology Updated 2016.
4. 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.
8. Drug Tariff January2015

Additional references – November 2018 update

9. The Royal College of Opthalmologists - Clinical Guideline. Hydroxychloroquine and chloroquine retinopathy recommendations on screening. February 2018.
10. Online BNF- Hydroxychloroquine sulphate, accessed 31/10/18

Summary of product characteristics Paquenil

11. Shared Care Guideline for Hydroxychloroquine. NHS Basingstoke, Southampton & Winchester District prescribing Committee. Review date May 2019.

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