

# New recommendations for retinal monitoring in hydroxychloroquine users:

## Baseline testing is no longer supported

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The Royal College of Ophthalmologists (RCOphth) has published new recommendations for retinal monitoring for hydroxychloroquine and chloroquine users in the United Kingdom (2020).<sup>1</sup> The recommendations aim to protect both patients and prescribers by reducing the risk of irreversible visual loss from hydroxychloroquine retinopathy. Importantly, as a consequence of new evidence, baseline retinal testing is no longer required and an updated monitoring timetable is recommended.

The General Medical Council stipulates that the prescriber of a drug is responsible for drug monitoring arrangements.<sup>2</sup> Therefore if this medication is prescribed by a hospital physician, monitoring should be supervised by secondary care until the prescribing is taken over by their General Practitioner. Dermatologists should assess the factors associated with a high risk of hydroxychloroquine retinal toxicity at the time of prescribing. These risk factors include a high daily dose of hydroxychloroquine (>5mg per kg per day, absolute body weight), concurrent tamoxifen therapy and renal impairment (eGFR <60ml/min/1.73m<sup>2</sup>). Chloroquine users are at high risk for retinal toxicity and prescribers should follow the high-risk pathway, but this treatment is rarely prescribed by UK dermatologists. Annual retinal monitoring should begin after 1 year of drug therapy if any high risk factor is present, or after 5 years if not (**Figure I**). This guideline does not apply to mepacrine or quinine as there is insufficient evidence that these drugs cause retinal toxicity.

The joint recommendations were developed according to prespecified methodology to ensure alignment with the strength of the evidence, as outlined in the full guideline.<sup>3</sup> The PICO framework was used to identify key questions relevant to hydroxychloroquine retinopathy. A systematic review of the literature was undertaken in collaboration with the Cochrane Eyes and Vision Group. Embase, Medline and the Cochrane library were searched for literature

published from 2000-2017. Literature relevant to the scope of the guideline was identified. The strength of evidence underpinning each recommendation was graded according to the Scottish Intercollegiate Guidelines Network framework (SIGN 50). In 2020, the literature was reassessed (2017-2020) to update guidance relating to the timing and nature of monitoring tests using the same methodology.

Two large U.K. audits<sup>4, 5</sup> undertaken since the 2018 RCOphth recommendations<sup>6</sup> found that the clinical benefit of baseline testing was considered insufficient to justify the significant resources required to deliver it. Referral for retinal monitoring should be made 3-6 months after treatment initiation for those individuals at high-risk of retinopathy (i.e. for monitoring at 1 year). For individuals at low-risk for whom monitoring begins at 5 years, a clear note of the date at which monitoring is due should be made in the clinical record to prompt referral at the appropriate time. The full clinical guideline contains a referral proforma<sup>3</sup> which may be customised for electronic medical record systems, if relevant.

The new recommendations aim to increase the efficiency and reduce the cost of delivering monitoring services (**Figure 1**). It is recommended that all patients receive retinal imaging with optical coherence tomography and fundus autofluorescence as first line tests. Most will have no abnormalities and annual follow-up will be arranged by the eye service. The outcome of every monitoring visit will be communicated to the patient, G.P. and prescribing physician. The RCOphth definition of retinal toxicity aims to reduce the risk of inappropriate treatment cessation; individuals with “possible retinopathy” who have one abnormal test are advised to continue using hydroxychloroquine and are seen annually. Two abnormal test results are required for a diagnosis of “definite retinopathy”. Ophthalmologists will provide a description of the severity of retinopathy in order to help inform the discussion between the patient and

dermatologist regarding treatment cessation. Individuals with mild retinopathy who derive significant clinical benefit from hydroxychloroquine may decide to continue therapy following discussion with the prescribing dermatologist.

- 80 There are several further considerations that may impact on the decision and timing of referral for retinal monitoring by dermatology. For individuals receiving seasonal prescriptions (i.e. for photosensitive dermatoses such as polymorphic light eruption), an approximation of the cumulative duration of drug therapy may be used to determine the timing of referral for monitoring (i.e. after 2 years for those on 6 monthly prescriptions for a high-risk individual).
- 85 Earlier monitoring is unnecessary for those individuals on combined therapies (i.e. hydroxychloroquine and mepacrine) as the recommendations relate only to the use of hydroxychloroquine and chloroquine.

- Hydroxychloroquine is not contraindicated in those with visual symptoms, although they
- 90 should be encouraged to see their community optometrist. However, annual optometry assessments are no longer recommended for hydroxychloroquine users, on the basis of hydroxychloroquine use. The British Association of Dermatologists, in collaboration with the RCOphth, has produced an updated patient information leaflet, which reflects the new guideline, available at [https://www.bad.org.uk/for-the-public/patient-information-](https://www.bad.org.uk/for-the-public/patient-information-leaflets/hydroxychloroquine)
- 95 [leaflets/hydroxychloroquine](https://www.bad.org.uk/for-the-public/patient-information-leaflets/hydroxychloroquine).

## Key words

Hydroxychloroquine retinopathy; retinopathy; monitoring; screening; chloroquine; discoid lupus erythematosus; dermatomyositis; photosensitive dermatoses; quinacrine; mepacrine

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## Figure legend

115 **Figure 1. Hydroxychloroquine retinopathy monitoring protocol.** Risk factors for hydroxychloroquine retinopathy should be assessed by the dermatologist at treatment initiation to determine the interval to the first monitoring visit (blue shade). Note that if monitoring is first due at 5 years, a referral should be made nearer the time. Once referred, annual monitoring visits will be arranged by the hospital eye service (green shade). Two  
120 abnormal test results consistent with hydroxychloroquine retinopathy are needed for “definite toxicity”. For individuals with confirmed retinopathy, a discussion between the patient and prescriber is recommended to determine whether treatment cessation is appropriate (blue shade). SD-OCT - spectral-domain optical coherence tomography; FAF – fundus autofluorescence imaging; ERG – electroretinography.

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