

# AMERICAN COLLEGE OF RHEUMATOLOGY

## POSITION STATEMENT

**SUBJECT:** Screening for Hydroxychloroquine Retinopathy

**PRESENTED BY:** Committee on Rheumatologic Care

**FOR DISTRIBUTION TO:** Members of the American College of Rheumatology  
Medical Societies  
Centers for Medicare and Medicaid Services  
Managed Care Organizations/Third-Party Carriers  
Arthritis Foundation

### BACKGROUND:

1 Hydroxychloroquine (Plaquenil) is a commonly used medication in the management of various  
2 rheumatic diseases. Standard doses used by rheumatologists are 200mg to 400mg per day.  
3 Although serious toxicity with hydroxychloroquine is very unusual, the most important is retinal  
4 toxicity. More than forty years of experience in monitoring retinal toxicity has documented that  
5 it is extremely rare. The American Academy of Ophthalmology (AAO) has reviewed the  
6 cumulative experience with hydroxychloroquine and has published updated recommendations  
7 for retinal toxicity monitoring summarized below. *Ophthalmology* 2011;118:415-422.  
8 The purpose of monitoring is to recognize early toxicity, not the prevention of toxicity. Once  
9 abnormalities are observed, toxicity has occurred and it may not be reversible. While there is a  
10 strong suggestion from the literature that toxicity is cumulative with a dose greater than 1000  
11 grams and duration of treatment over 7 years, the majority of cases involved doses of more than  
12 6.5 mg/kg/day and more than 5 years of use. Of more than one million patients using  
13 hydroxychloroquine, fewer than 20 cases have been documented with doses less than 6.5  
14 mg/kg/day, and all occurred after 5 years of use. The AAO is concerned that retinal toxicity,  
15 although rare, may be more common than previously recognized, based on a study by F. Wolfe  
16 et al which found risk exceeded 1% after 5 years. Patients with macular degeneration, retinal  
17 dystrophy, cataracts, or previous exposure to hydroxychloroquine may be more susceptible to  
18 toxicity or at least present more complicated monitoring problems. Since hydroxychloroquine is  
19 cleared by both renal and hepatic systems, patients with severe compromise could theoretically  
20 experience higher drug levels, although there is little evidence for this in practice. Finally,  
21 obesity may cause an overestimation of the safe dose of hydroxychloroquine because the drug  
22 does not accumulate in fat. *Arthritis Care and Research* 2010;62:775-784.

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### POSITION:

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25 Patients beginning hydroxychloroquine therapy should be informed of the possibility, although  
26 extremely rare, of retinal toxicity and that periodic monitoring can limit the toxicity by early  
27 recognition. The AAO recommends that the following factors be taken into consideration when  
28 assessing increased risk for hydroxychloroquine toxicity: cumulative dose of 1000 g, treatment  
29

30 for more than 7 years, obesity, significant liver or kidney disease or advanced age, and pre-  
31 existing retinal, macular disease or cataracts.

32  
33 All individuals starting these drugs should have a complete baseline ophthalmologic examination  
34 within the first year of treatment including examination of the retina through a dilated pupil and  
35 testing of central visual field sensitivity by an automated threshold central visual field testing  
36 (Humphrey 10-2 testing). Examination by Amsler grid is no longer recommended as it is deemed  
37 too dependent on patient interpretation. If available, examination by an objective test such as  
38 multifocal electroretinography (mfERG), spectral domain optical coherence tomography (SD-  
39 OCT), or fundus autofluorescence testing (FAF) is also recommended. If the patient is  
40 considered low risk and these examination results are normal, the AAO recommendation is that  
41 no further special ophthalmologic testing for hydroxychloroquine toxicity is needed for the next  
42 5 years. Some ophthalmologists may elect to screen more often based on the patient's age and  
43 other risk factors. For patients who are considered high risk, annual eye examination is  
44 recommended without the initial 5 year delay. If any abnormality is detected by Humphrey 10-2  
45 testing or retinal examination, follow up with the previously mentioned objective testing is  
46 imperative. The sensitivity and specificity of each of these objective tests for  
47 hydroxychloroquine toxicity is still being determined.

48  
49 If toxicity is suspected or documented, ideally the drug should be stopped. However, there are  
50 situations when this is not an easy decision, e.g., if the impression of toxicity is early or tenuous,  
51 or if the treatment has been very effective. Alternatives to hydroxychloroquine are potentially  
52 more toxic. The rheumatologist, ophthalmologist and patient can make a cooperative decision to  
53 stop the drug or cautiously continue it with close monitoring, with the knowledge that some  
54 vision could be lost.

55  
56 Appropriate standards for children and adolescents have not been sufficiently addressed in the  
57 available literature. Retinal abnormalities or new interference with vision (including color vision)  
58 can be an indication of toxicity and should be discussed with the consulting ophthalmologist on  
59 an urgent basis. Use of hydroxychloroquine in children younger than 7 years of age may be  
60 limited by difficulty in obtaining satisfactory evaluation of color vision in this age group. For this  
61 reason, the pediatric age group should receive an annual examination, as a minimum standard of  
62 care, until definitive studies in children suggest increasing this monitoring interval.

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64 Approved by the Board of Directors: 03/03, 05/06, 8/10 8/11