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IMPORTANT
DRUG
WARNING

Date: August 16, 2012

**Subject: Risk of Serious and Life-Threatening hematologic reactions, including thrombocytopenia, hemolytic uremic syndrome/thrombotic thrombocytopenic purpura with Qualaquin® (quinine sulfate) Capsules, 324 mg**

Dear Healthcare Provider:

AR Scientific, Inc. would like to inform you of important safety information regarding the use of Qualaquin® (quinine sulfate) capsules, 324 mg. Qualaquin Capsules are approved only for the treatment of uncomplicated Plasmodium falciparum malaria.

**Qualaquin capsules are not approved for treatment or prevention of nocturnal leg cramps.** No evidence documenting the efficacy of quinine sulfate in the treatment or prevention of this condition has been submitted to the FDA for review, and because of the risks associated with the use of quinine sulfate, the risk versus benefit assessment does not favor the use of quinine sulfate for this indication.

**The Warnings section of the product labeling has been updated to include the following:**

1. **Addition of BOXED WARNING:**

> **WARNING**
> Qualaquin use for the treatment or prevention of nocturnal leg cramps may result in serious and life-threatening hematologic reactions, including thrombocytopenia and hemolytic-uremic syndrome/thrombotic thrombocytopenic purpura (HUS/TTP). Chronic renal impairment associated with the development of TTP has been reported. The risk associated with Qualaquin use in the absence of evidence of its effectiveness in the treatment or prevention of nocturnal leg cramps outweighs any potential benefit (see **WARNINGS)**

2. **Revision to Warnings/Thrombocytopenia subsection of the Qualaquin labeling as follows:**

**Use of Qualaquin for Treatment or Prevention of Nocturnal Leg Cramps**
Qualaquin may cause unpredictable serious and life-threatening hematologic reactions including thrombocytopenia and hemolytic-uremic syndrome/thrombotic thrombocytopenic purpura (HUS/TTP) in addition to hypersensitivity reactions, QT prolongation, serious cardiac arrhythmias including torsades de pointes, and other serious adverse events requiring medical intervention and hospitalization. Chronic renal impairment associated with the development of TTP, and fatalities have also been reported. The risk associated with the use of Qualaquin in the absence of evidence of its effectiveness for treatment or prevention of nocturnal leg cramps outweighs any potential benefit in treating and/or preventing this benign, self-limiting condition.

**Thrombocytopenia**
Quinine-induced thrombocytopenia is an immune-mediated disorder. Severe cases of thrombocytopenia that are fatal or life threatening have been reported, including cases of HUS/TTP. Chronic renal impairment associated with the development of TTP has also been reported. Thrombocytopenia usually resolves within a week upon discontinuation of quinine. If quinine is not stopped, a patient is at risk for fatal hemorrhage. Upon re-exposure to quinine from any source, a patient with quinine-dependent antibodies could develop thrombocytopenia that is more rapid in onset and more severe than the original episode.

3. **The patient package insert for Qualaquin has been replaced with a Medication Guide. Patients should be advised to read the Medication Guide that is dispensed with each Qualaquin prescription.**

**To report adverse patient experiences please contact AR Scientific, Inc's Medical Information by telephone at 1-888-351-3786. Alternatively, adverse events may be reported to FDA's MedWatch reporting system:**

- **By phone (1-800-FDA-1088)**
- **By facsimile (1-800-FDA-0178)**
- **Online (https://www.accessdata.fda.gov/scripts/medwatch/)**

If you wish further information, please contact AR Scientific, Inc.'s Medical Information by telephone at 1-888-351-3786.

Sincerely,

Matthew W Davis, MD, RPh
Senior Vice President
Chief Medical Officer
AR Scientific, Inc

Enclosure