CLINICAL UPDATE

Brand Name	Plaquenil®
Generic Name	hydroxychloroquine sulfate
Drug Manufacturer	Accord Healthcare, Inc.

Clinical Update

TYPE OF CLINICAL UPDATE

New Strength

FDA APPROVAL DATE

September 10, 2021

LAUNCH DATE

N/A

REVIEW DESIGNATION

Abbreviated New Drug Application (ANDA): 213342

TYPE OF REVIEW

Standard

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION(S) FOR USE

Hydroxychloroquine sulfate is an antimalarial and antirheumatic indicated for the:

- Treatment of uncomplicated malaria due to Plasmodium falciparum, Plasmodium malariae, Plasmodium ovale, and Plasmodium vivax in adult and pediatric patients.
- Prophylaxis of malaria in geographic areas where chloroquine resistance is not reported in adult and pediatric patients.
- Treatment of rheumatoid arthritis in adults.
- Treatment of systemic lupus erythematosus in adults.
- Treatment of chronic discoid lupus erythematosus in adults.

MECHANISMS OF ACTION

The precise mechanism by which hydroxychloroquine exhibits activity against Plasmodium is not known. Hydroxychloroquine, like chloroquine, is a weak base and may exert its effect by concentrating in the acid vesicles of the parasite and by inhibiting polymerization of heme. It can also inhibit certain enzymes by its interaction with DNA.

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DOSAGE FORM(S) AND STRENGTH(S)

Tablets: 100 mg, 200 mg, 300 mg, and 400 mg of hydroxychloroquine sulfate.

DOSE & ADMINISTRATION

Malaria in Adult and Pediatric Patients:

- Prophylaxis: Begin weekly doses 2 weeks prior to travel to the endemic area, continue weekly doses while in the endemic area, and continue the weekly doses for 4 weeks after leaving the endemic area: – Adults: 400 mg once a week – Pediatric patients ≥ 31 kg: 6.5 mg/kg up to 400 mg, once a week.
- Only for use in individuals traveling to malarious regions without chloroquine resistance

Rheumatoid Arthritis in Adults:

- Initial dosage: 400 mg to 600 mg daily.
- Chronic dosage: 200 mg once daily or 400 mg once daily (or in two divided doses).

Systemic Lupus Erythematosus in Adults:

- 200 mg once daily or 400 mg once daily (or in two divided doses) Chronic Discoid Lupus Erythematosus in Adults.
- 200 mg once daily or 400 mg once daily (or in two divided doses).

EFFICACY

Malaria

With the advantages of high efficacy, good tolerability and low-cost, Chloroquine and hydroxychloroquine were the first-line treatments for malaria for several decades. However, the extensive use of Chloroquine and hydroxychloroquine resulted in the emergence of Chloroquine-resistant P. falciparum strains within 20 years after the introduction of Chloroquine. As the efficacy of Chloroquine/hydroxychloroquine has been clinically certified, it is safer to use it under the strict control of indications and contraindications.

Rheumatoid Arthritis

Review of the records of 108 patients with rheumatoid arthritis who were treated with hydroxychloroquine sulfate for at least six months revealed that 63 percent responded: 12 percent achieved complete remission (no joint pain or tenderness, two or less joints with trace swelling); 14 percent showed a 75 percent response (75 percent or greater reduction in active joint count and 50 percent or greater reduction in morning stiffness); and 37 percent had between 30 percent (30 percent or greater reduction in active joint count and morning stiffness) and 75 percent response. Once response was obtained, flare-up of rheumatoid arthritis was uncommon. Only two of 108 patients developed retinopathy (subclinical); it resolved with drug discontinuation and did not cause visual deficits.

Lupus

In this prospective cohort study, 41 newly diagnosed Systemic lupus erythematosus patients receiving 400 mg HCQ per day were included. Patients requiring statins and immunosuppressive drugs except prednisolone at doses lower than 10 mg/day were excluded. Serum samples of 41 age-matched healthy donors were used as controls.

Median levels of IL-1β ($p < 0.001$), IL-6 ($p = 0.001$), and TNF-α ($p < 0.001$) were significantly higher, whereas median CH50 level was significantly lower ($p < 0.001$) in SLE patients compared with controls. Two-month treatment with HCQ resulted in significant decrease in SLEDAI-2K ($p < 0.001$), anti-dsDNA ($p < 0.001$), IL-1β ($p = 0.003$), IL-6 ($p < 0.001$) and TNF-α ($p < 0.001$) and a significant increase in CH50 levels ($p = 0.012$). The reductions

in SLEDAI-2K and serum levels of IL-1β and TNF-α were significantly greater in the first month compared with the reductions in the second month.

HCQ therapy is effective on clinical improvement of SLE patients through interfering with inflammatory signalling pathways, reducing anti-DNA autoantibodies and normalizing the complement activity.