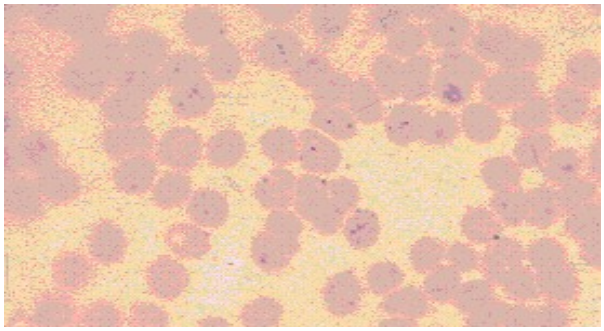
Mefloquine Information Paper

A licensed antimalarial drug developed by DoD and its partners

Product name: Mefloquine
Commercial name: Larium
Application: Antimalarial drug for treatment and prevention
Date of U.S. licensure: May 1989
Type of product: synthetic 4-quinoline methanol (quinine analog)
Company of manufacture: Hoffman-LaRoche
Reasons for development: Mefloquine was developed as a treatment/prophylactic for chloroquine-resistant malaria.

Role of DoD:
The prototype drug for mefloquine was SN 10275, discovered by Americans during the World War II years. The first generation of synthetic quinoline methanols caused unacceptable reactions to skin with sunlight. Mefloquine (WR 149240) was developed by the Division of Experimental Therapeutics at the Walter Army Institute of Research (WRAIR) in the late 1960's by the U.S. Army Medical Research and Development Program in collaboration with the World Health Organization Special Programme for Training and Research in Tropical Diseases (WHO/TDR) and Hoffman-LaRoche, Inc. This division at WRAIR was established in 1961 during the Vietnam War because an increasing burden of malaria was noted among service members. Also, the DoD recognized that there was minimal economic incentive for private pharmaceutical firms to undertake development of antimalarial drugs, since most persons who need such drugs are in developing countries and cannot afford costly pharmaceuticals. The WRAIR program became the lead federal agency for antimalarial drug development, with the expertise and laboratory capability to take a potential antimalarial compound from the chemist's bench through efficacy testing, toxicity testing and clinical trials to licensure by the U.S. Food and Drug Administration (FDA). In recent years, the institute has increasingly formed partnerships with the pharmaceutical industry and WHO and private support groups when possible to help finance and expedite the increasingly expensive and complicated drug development process. No antimalarial has been fully developed by industry, although industry-government collaborations have yielded new agents. Over 300,000 compounds have been tested for antimalarial activity at WRAIR.



P. falciparum malaria parasites can infect red blood cells of all ages, which may result in massive infection.

In August 2003 more than 80 of the 290 service members who landed in Liberia were hospitalized because of P. falciparum malaria. The outbreak was blamed on troops' failure to take preventive drugs.

Mefloquine is effective against both *P. vivax* and P. *falciparum*. A very long half-life permits weekly dosing. Surveillance of service members using mefloquine has provided additional information. Although mefloquine was not approved for use in pregnant women during U.S. military operations in Somalia, some female service members who were unaware they were pregnant inadvertently ingested the drug. Follow-up revealed no congenital defects among the infants. Currently mefloquine is recommended as an antimalarial prophylaxis in pregnant women at risk of multidrug-resistant antimalarial infection.

Current status:
Mefloquine is a relatively low-cost antimalarial, and is still the mainstay antimalarial for the U.S. military. However, the antimalarial action of mefloquine is unknown (as is the case with quinine). Adverse neuropsychiatric effects have been reported, which have a negative impact on compliance. Also, malaria parasites have developed resistance to the drug, especially in southeast Asia and east Africa. The need for new antimalarial drugs is illustrated by the events that occurred during U.S. peacekeeping operations in Africa. Of 290 marines who stepped ashore in Liberia in 2003, 80 developed malaria (28%), and 69(44%) of the 157 who spent at least one night ashore acquired the disease. Five of these malaria-infected marines became extremely ill required intensive care unit support.

Mefloquine References:

Palmer KJ, Holliday SM, Brogden RN. Mefloquine. A review of its antimalarial activity, pharmacokinetic properties and therapeutic efficacy. Drugs 1993;45:430-475.