Mefloquine (Lariam) Long-term Adverse Effects Pocket Guide for Clinicians

What is Mefloquine?

Mefloquine (Larium) is an FDA-approved medication for the prevention of malaria and for treatment of falciparum and vivax malarial infections. This medication is particularly useful in locations where chloroquine resistance is a problem. Like all antimalarials, mefloquine produces some side effects, and the manufacturer's (Roche USA) product label describes reported side effects. The newest label (May 2004) indicates it should not be prescribed to individuals with active or recent depression or with a psychiatric disorder. The Air Force has issued a policy directing that mefloquine not be prescribed for their air crews. Some Service members and veterans have expressed concerns about mefloquine side effects.

Helping Your Patients:

Attempt to confirm if they took mefloquine (see "Background" below). Discuss their current and past use of antimalarials. Listen carefully to their concerns when evaluating symptoms, and assure them they will be appropriately evaluated and treated.

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Clinical trials and epidemiological studies suggest that reported side effects are *not common*, and *usually resolve when the drug is discontinued.* Reported side effects associated with prophylactic doses of mefloquine (per manufacture's product label) include:

In *up to* 3%:	In *less than* 1%:
Vomiting	Dizziness, Fainting, Heart Arrhythmias (extrasystoles)

Other side effects reported by the US Centers for Disease Control and Prevention (CDC) that may occur with prophylactic doses of mefloquine include: gastrointestinal disturbances, headache, insomnia, abnormal dreams, visual disturbances, depression, and anxiety disorder.

Background:

Mefloquine (Lariam) is approved by FDA and recommended by CDC for malaria prevention. Since the late 1980s, DoD has prescribed mefloquine to Service members in areas where chloroquine-resistant malaria is a threat. The beginning of Operation Iraqi Freedom (OIF) saw some mefloquine use, but Service members deployed to Iraq since mid-2003 are generally not prescribed antimalarials as malaria risk is very low. For Operation Enduring Freedom (Afghanistan, Horn of Africa, and some surrounding countries), antimalarials continue to be prescribed, with either doxycycline or mefloquine required for all personnel. The surrounding countries where malarial prophylaxis is required include: Yemen, Pakistan, Kazakhstan, Kyrgyzstan, Uzbekistan, Somalia, Djibouti, Ethiopia, Eritrea, Kenya, and Sudan.

Media reports in 2002 linked mefloquine to rare but serious mental problems, including violent and suicidal behavior and post-traumatic stress disorder (PTSD).

In 2004, VA conducted an exhaustive literature review on mefloquine health effects to produce the Under Secretary for Health Information Letter (IL) 10-2004-007, (www.va.gov/EnvironAgents), which provides guidance to clinicians on diagnosis and treatment for possible long-term mefloquine health effects. This review identified 47 cases contained in 34 case reports, which described various rare but potentially serious conditions noted in people taking mefloquine. **None of these conditions were observed in the clinical and epidemiological studies on mefloquine and must be very rare**, if they are related to the use of mefloquine, given the background of millions of doses used worldwide over the decades following this drug's introduction.

The reported conditions included:

- Paranoia, hallucinations, suicidal ideation, cognitive and other neuropsychiatric symptoms
- Acute and paranoid psychosis
- Convulsions, grand mal seizures, coma and abnormal electroencephalography (EEG)
- High frequency sensorineural hearing loss and tinnitus, with partial or no remission
- Acute lung injury with diffuse alveolar damage
- Elevated liver function tests or fatty liver
- Multifocal myoclonus
- Fatal toxic epidermal necrolysis
- Trigeminal sensory neuropathy
- Atrial flutter
- Mefloquine overdose induced encephalopathy

Additional Mefloquine Facts:

- Side effects always begin while the person is taking the drug but may persist temporarily after stopping because of mefloquine's long half-life (15-30 days)
- Patients with a history of psychiatric illness may be more vulnerable to mefloquine-related psychiatric symptoms
- Mefloquine should not be taken by persons with active depression or recent depression, or a history of major psychiatric disorder such as psychosis, anxiety disorder, schizophrenia, seizures (except febrile) or cardiac conduction abnormalities
- Persons with a known allergy to mefloquine, quinine, or quinidine should not use mefloquine

Management of Symptoms:

No practical tests for past mefloquine use exist. Medical care should focus on taking a thorough military and medical history, along with a basic medical examination and appropriate laboratory tests relating to the veteran's complaints and medical findings.

For Further Information:

- Online information from the VA on mefloquine (Lariam), at www.va.gov/EnvironAgents
- The DoD index of fact sheets for clinicians, servicemembers, and unit leaders, that cover topics including mefloquine at: http://deploymenthealthlibrary.fhp.osd.mil/
- National Institutes for Health information is at: www.nlm.nih.gov/medlineplus/druginfo/medmaster/a603030.html
- Centers for Disease Control and Prevention (CDC) at: http://wwwn.cdc.gov/travel/contentMalariaDrugsHC.aspx