



DEPARTMENT OF THE ARMY
OFFICE OF THE SURGEON GENERAL
5109 LEESBURG PIKE
FALLS CHURCH, VA 22041-3258

REPLY TO
ATTENTION OF

02 FEB 2009

DASG-PPM-NC

MEMORANDUM FOR SEE DISTRIBUTION

SUBJECT: Updated Guidance on Use of Mefloquine (Lariam®) for Malaria Prophylaxis

1. References.

a. Memorandum, MCPO-NCR, 20 Nov 03, subject: Additional Patient Information to Accompany Each Prescription of Mefloquine (Lariam®).

b. Memorandum, DASG-PPM-NC, 3 Oct 02, subject: Updated Health Care Provider Information on Use of Mefloquine Hydrochloride (Lariam®) for Malaria Prophylaxis.

c. Mefloquine (Lariam®) package insert
<http://www.rocheusa.com/products/lariam/pi.pdf>.

d. Mefloquine (Lariam®) medication guide
http://rocheusa.com/products/lariam/lariam_medguide.pdf (encl1).

e. DoD Medical Material Quality Control (MMQC) Message 31 Oct 08, subject: MMQC-08-1525, Mefloquine (Lariam®)/Important Drug Information.

f. DoD Medical Material Quality Control (MMQC) Message 161253SEP02, subject: MMQC-02-1302. Important Label Changes/Lariam (Mefloquine Hydrochloride)/Update Information Bulletin.

g. AR 40-3, Medical, Dental, and Veterinary Care. 22 Feb 08.

h. AR 40-66, Medical Records Administration and Healthcare Documentation, 17 Jun 08.

2. This memorandum replaces the guidance provided in references 1.a. and 1.b.

3. Malaria remains one of the deadliest infectious disease threats to Soldiers deployed around the world. Use of appropriate prophylactic medication, in addition to the Department of Defense (DoD) repellent system and barriers such as bed nets, provides optimal force health protection against this threat.

4. In many areas of the world where chloroquine-resistant malaria is found, especially Africa and South America, doxycycline, 100 mg per day or mefloquine (Lariam®), 250 mg per week, provides safe and effective prophylaxis against susceptible strains of malaria. In areas where doxycycline and mefloquine are equally efficacious in preventing malaria, doxycycline is the drug of choice. Mefloquine should only be used for personnel with contraindications to doxycycline and do not have any contraindications to the use of mefloquine (active depression, a recent history of depression, generalized anxiety disorder, psychosis, or schizophrenia or other major psychiatric disorders, or a history of convulsions). Mefloquine should not be given to Soldiers with recent history of Traumatic Brain Injury (TBI) or have symptomatic TBI. Malarone would be the treatment of choice for these Soldiers who cannot take doxycycline or mefloquine.

5. Mefloquine (Lariam®) has been used successfully to protect thousand of individuals against malaria. It is well tolerated by most people and has been a preferred alternative to doxycycline because it has the advantage of a weekly dosing regimen. However, it is contraindicated in some persons who have certain medical conditions or are taking other medications.

6. It is critically important that all Army healthcare providers be familiar with the proper use, contraindications, warnings, and precautions for prescribing mefloquine, especially with respect neurobehavioral effects. Providers must refer to the package insert (paragraph 1.c.) for complete prescribing information and the full clinical profile of this medication.

a. Contraindications. Use of mefloquine (Lariam®) is contraindicated in patients with known hypersensitivity to mefloquine or related compounds (e.g., quinine and quinidine). Mefloquine (Lariam®) should not be prescribed for prophylaxis in patients with active depression or recent history of depression; generalized anxiety disorder, psychosis or schizophrenia or other major psychiatric disorders; or a history of seizure disorders or epilepsy. Mefloquine should not be given to Soldiers with recent history of TBI or have symptomatic TBI. Providers should ask patients to identify all medications they are taking including prescriptions and non-prescription medicines, vitamins, and herbal supplements. Some medications may give patients a higher chance of having serious side effects from mefloquine (Lariam®).

b. Warnings and Precautions. When used for prophylaxis, mefloquine may cause psychiatric symptoms at a rate of one per 2,000-13,000 persons. These symptoms include anxiety, paranoia, depression, hallucination and psychotic behavior. Rarely, these symptoms have been reported to continue after mefloquine has been stopped. Rare cases of suicidal ideation and suicide have been reported although no relationship to drug administration has been confirmed.

c. Patient Information. Patients should be advised that if they experience psychiatric symptoms such as excessive acute anxiety, depression, restlessness, or

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confusion, these may be considered prodromal to a more serious event related to mefloquine. In these cases, the drug must be discontinued and an alternative medication should be substituted.

d. The manufacturer of Lariam® revised the Lariam Medication Guide in Sep 08 (paragraph 1.d.). It provides important information that patients should know about the drug. This guide contains an information wallet-card that addresses the need to take the medication, provides information on side effects that may necessitate discontinued use. This information card, which may be reproduced locally, must be provided to each person who is prescribed Lariam® or generic forms of mefloquine.

7. Additional information is available from the Deployment Health Clinical Center website, <http://www.pdhealth.mil/mefloquine.asp>.

8. Adverse event reporting. In accordance with (IAW) AR 40-3 (reference 1.g), paragraph 11.9, all known or suspected adverse events related to the administration of mefloquine will be reported to the appropriate Pharmacy and Therapeutics Committee for further review and consideration for forward to the US Food and Drug Administration.

9. Prescriptions for mefloquine, like all prescriptions products, will be appropriately dispensed and documented IAW AR 40-3, Chapter 11, and AR 40-66.

10. Points of contact are COL Scott Stanek, Office of The Surgeon General, DSN 761-3130, commercial (703) 681-3130, or e-mail Scott.Stanek@amedd.army.mil and COL Robert Mott, DSN 761-3160, commercial (703) 681-3160, or e-mail Robert.Mott@amedd.army.mil.

Encl



ERIC B. SCHOOMAKER
Lieutenant General
The Surgeon General

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MEDICATION GUIDE
LARIAM (LAH-ree-am)
(mefloquine hydrochloride) Tablets
to Prevent Malaria

R_x only

This Medication Guide is intended only for travelers who are taking Lariam to prevent malaria. The information may not apply to patients who are sick with malaria and who are taking Lariam to treat malaria.

An information wallet card is provided with this Medication Guide. Carry it with you when you are taking Lariam.

This Medication Guide was revised in September 2008. Please read it before you start taking Lariam and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking with your prescriber (doctor or other health care provider) about Lariam and malaria prevention. Only you and your prescriber can decide if Lariam is right for you. If you cannot take Lariam, you may be able to take a different medicine to prevent malaria.

What is the most important information I should know about Lariam?

1. **Take Lariam exactly as prescribed to prevent malaria.**
Malaria is an infection that can cause death and is spread to humans through mosquito bites. If you travel to parts of the world where the mosquitoes carry the malaria parasite, you must take a malaria prevention medicine. Lariam is one of a small number of medications approved to prevent and to treat malaria. If taken correctly, Lariam is effective at preventing malaria but, like all medications, it may produce side effects in some patients.
2. **Lariam can rarely cause serious mental problems in some patients.**
The most frequently reported side effects with Lariam, such as nausea, difficulty sleeping, and bad dreams are usually mild and do not cause people to stop taking the medicine. However, people taking Lariam occasionally experience severe anxiety, feelings that people are against them, hallucinations (seeing or hearing things that are not there, for example), depression, unusual behavior, or feeling disoriented. There have been reports that in some patients these side effects continue after Lariam

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37 is stopped. Some patients taking Lariam think about killing themselves,
38 and there have been rare reports of suicides. It is not known whether
39 Lariam was responsible for these suicides.

40 **3. You need to take malaria prevention medicine before you travel to a**
41 **malaria area, while you are in a malaria area, and after you return**
42 **from a malaria area.**

43 Medicines approved in the United States for malaria prevention include
44 Lariam, doxycycline, atovaquone/proguanil, hydroxychloroquine, and
45 chloroquine. Not all of these drugs work equally as well in all areas of the
46 world where there is malaria. The chloroquines, for example, do not work
47 in areas where the malaria parasite has developed resistance to
48 chloroquine. Lariam may be effective against malaria that is resistant to
49 chloroquine or other drugs. All drugs to treat malaria have side effects that
50 are different for each one. For example, some may make your skin more
51 sensitive to sunlight (Lariam does not do this). However, if you use
52 Lariam to prevent malaria and you develop a sudden onset of anxiety,
53 depression, restlessness, confusion (possible signs of more serious mental
54 problems), or you develop other serious side effects, contact a doctor or
55 other health care provider. It may be necessary to stop taking Lariam and
56 use another malaria prevention medicine instead. If you can't get another
57 medicine, leave the malaria area. However, be aware that leaving the
58 malaria area may not protect you from getting malaria. You still need to
59 take a malaria prevention medicine.

60 Who should not take Lariam?

61 Do not take Lariam to prevent malaria if you

- 62 • **have depression or had depression recently**
- 63 • **have had recent mental illness or problems**, including anxiety disorder,
64 schizophrenia (a severe type of mental illness), or psychosis (losing touch
65 with reality)
- 66 • **have or had seizures (epilepsy or convulsions)**
- 67 • **are allergic to quinine or quinidine (medicines related to Lariam)**

68 **Tell your prescriber about all your medical conditions.** Lariam may not be
69 right for you if you have certain conditions, especially the ones listed below:

- 70 • **Heart disease.** Lariam may not be right for you.
- 71 • **Pregnancy.** Tell your prescriber if you are pregnant or plan to become
72 pregnant. It is dangerous for the mother and for the unborn baby (fetus) to
73 get malaria during pregnancy. Therefore, ask your prescriber if you should
74 take Lariam or another medicine to prevent malaria while you are
75 pregnant.

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76 • **Breast-feeding.** Lariam can pass through your milk and may harm the
77 baby. Therefore, ask your prescriber whether you will need to stop breast-
78 feeding or use another medicine.

79 • **Liver problems.**

80 **Tell your prescriber about all the medicines you take, including**
81 **prescription and non-prescription medicines, vitamins, and herbal**
82 **supplements. Some medicines may give you a higher chance of having**
83 **serious side effects from Lariam.**

84 **How should I take Lariam?**

85 **Take Lariam exactly as prescribed. If you are an adult or pediatric**
86 **patient weighing 45 kg (99 pounds) or less, your prescriber will tell you**
87 **the correct dose based on your weight.**

88 **To prevent malaria**

89 • **For adults and pediatric patients weighing over 45 kg, take 1 tablet of**
90 **Lariam at least 1 week before you travel to a malaria area (or 2 to 3 weeks**
91 **before you travel to a malaria area, if instructed by your prescriber). This**
92 **starts the prevention and also helps you see how Lariam affects you and**
93 **the other medicines you take. Take 1 Lariam tablet once a week, on the**
94 **same day each week, while in a malaria area.**

95 • **Continue taking Lariam for 4 weeks after returning from a malaria**
96 **area. If you cannot continue taking Lariam due to side effects or for other**
97 **reasons, contact your prescriber.**

98 • **Take Lariam just after a meal and with at least 1 cup (8 ounces) of water.**

99 • **For children. Lariam can be given with water or crushed and mixed with**
100 **water or sugar water. The prescriber will tell you the correct dose for**
101 **children based on the child's weight.**

102 • **If you are told by a doctor or other health care provider to stop taking**
103 **Lariam due to side effects or for other reasons, it will be necessary to take**
104 **another malaria medicine. You must take malaria prevention medicine**
105 **before you travel to a malaria area, while you are in a malaria area,**
106 **and after you return from a malaria area. If you don't have access to**
107 **a doctor or other health care provider or to another medicine besides**
108 **Lariam and have to stop taking it, leave the malaria area. However, be**
109 **aware that leaving the malaria area may not protect you from getting**
110 **malaria. You still need to take a malaria prevention medicine.**

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111 What should I avoid while taking Lariam?

- 112 • **Halofantrine (marketed under various brand names)**, a medicine used
113 to treat malaria. Taking both of these medicines together can cause serious
114 heart problems that can cause death.
- 115 • **Do not become pregnant.** Women should use effective birth control
116 while taking Lariam.
- 117 • **Quinine, quinidine, or chloroquine (other medicines used to treat**
118 **malaria).** Taking these medicines with Lariam could cause changes in
119 your heart rate or increase the risk of seizures.

120 In addition:

- 121 • **Be careful driving or in other activities** needing alertness and careful
122 movements (fine motor coordination). Lariam can cause dizziness or loss
123 of balance. even after you stop taking Lariam (see “**What are the possible**
124 **side effects of Lariam?**”).
- 125 • **Be aware that certain vaccines may not work if given while you are**
126 **taking Lariam.** Your prescriber may want you to finish taking your
127 vaccines at least 3 days before starting Lariam.

128 What are the possible side effects of Lariam?

129 Lariam, like all medicines, may cause side effects in some patients. The most
130 frequently reported side effects with Lariam when used for prevention of
131 malaria include nausea, vomiting, diarrhea, dizziness, loss of balance,
132 difficulty sleeping, and bad dreams. These side effects are usually mild and do
133 not cause people to stop taking the medicine. However, in a small number of
134 patients, it has been reported that dizziness and loss of balance may continue
135 for months after stopping Lariam.

136 Lariam may cause serious mental problems in some patients (see “**What is the**
137 **most important information I should know about Lariam?**”).

138 Lariam may affect your liver and your eyes if you take it for a long time. Your
139 prescriber will tell you if you should have your eyes and liver checked while
140 taking Lariam.

141 Call your doctor for medical advice about side effects. You may report side
142 effects to FDA at 1-800-FDA-1088.

143 What else should I know about preventing malaria?

- 144 • **Find out whether you need malaria prevention.** Before you travel, talk
145 with your prescriber about your travel plans to determine whether you
146 need to take medicine to prevent malaria. Even in those countries where
147 malaria is present, there may be areas of the country that are free of
148 malaria. In general, malaria is more common in rural (country) areas than

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149 in big cities. and it is more common during rainy seasons. when
150 mosquitoes are most common. You can get information about the areas of
151 the world where malaria occurs from the Centers for Disease Control and
152 Prevention (CDC) and from local authorities in the countries you visit. If
153 possible, plan your travel to reduce the risk of malaria.

154 • **Take medicine to prevent malaria infection.** Without malaria prevention
155 medicine. you have a higher risk of getting malaria. Malaria starts with
156 flu-like symptoms. such as chills. fever, muscle pains, and headaches.
157 However. malaria can make you very sick or cause death if you don't seek
158 medical help immediately. These symptoms may disappear for a while.
159 and you may think you are well. But. the symptoms return later and then it
160 may be too late for successful treatment.

161 Malaria can cause confusion, coma, and seizures. It can cause kidney
162 failure. breathing problems, and severe damage to red blood cells.
163 However. malaria can be easily diagnosed with a blood test, and if
164 caught in time. can be effectively treated.

165 **If you get flu-like symptoms (chills, fever, muscle pains, or**
166 **headaches) after you return from a malaria area, get medical help**
167 **right away and tell your prescriber that you may have been exposed to**
168 **malaria.**

169 People who have lived for many years in areas with malaria may have
170 some immunity to malaria (they do not get it as easily) and may not
171 take malaria prevention medicine. This does not mean that you don't
172 need to take malaria prevention medicine.

173 • **Protect against mosquito bites.** Medicines do not always completely
174 prevent your catching malaria from mosquito bites. So protect yourself
175 very well against mosquitoes. Cover your skin with long sleeves and long
176 pants. and use mosquito repellent and bednets while in malaria areas. If
177 you are out in the bush. you may want to pre-wash your clothes with
178 permethrin. This is a mosquito repellent that may be effective for weeks
179 after use. Ask your prescriber for other ways to protect yourself.

180 **General information about the safe and effective use of Lariam.**

181 Medicines are sometimes prescribed for conditions not listed in Medication
182 Guides. If you have any concerns about Lariam, ask your prescriber. This
183 Medication Guide contains certain important information for travelers visiting
184 areas with malaria. Your prescriber or pharmacist can give you information
185 about Lariam that was written for health care professionals. Do not use
186 Lariam for a condition for which it was not prescribed. Do not share Lariam
187 with other people.

188 This Medication Guide has been approved by the U.S. Food and Drug
189 Administration.

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191 Revised: September 2008

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193 Reprint of information wallet card:

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 Lariam (mefloquine hydrochloride) Tablets Carry this information wallet card with you when you are taking Lariam.	
<p>You need to take malaria prevention medicine before you travel to a malaria area, while you are in a malaria area, and after you return from a malaria area.</p> <p>If taken correctly, Lariam is effective at preventing malaria but, like all medications, it may produce side effects in some patients.</p> <p>If you use Lariam to prevent malaria and you develop a sudden onset of anxiety, depression, restlessness, confusion (possible signs of more serious mental problems), or you develop other serious side effects, contact a doctor or other health care provider. It may be necessary to stop taking Lariam and use another malaria prevention medicine instead.</p>	<p>Other medicines approved in the United States for malaria prevention include: doxycycline, atovaquone/proguanil, hydroxychloroquine, and chloroquine. Not all malaria medicines work equally well in malaria areas. The chloroquines, for example, do not work in many parts of the world. If you can't get another medicine, leave the malaria area. However, be aware that leaving the malaria area may not protect you from getting malaria. You still need to take a malaria prevention medicine.</p> <p>Please read the Medication Guide for additional information on Lariam.</p> <p>Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.</p> <p style="text-align: right;">Card Revised: September 2008</p>

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Manufactured by:
F. HOFFMANN-LA ROCHE LTD
Basel, Switzerland

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LARIAM (mefloquine hydrochloride)



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