

# Responses to UPI-CNN Lariam investigation

WASHINGTON, Sept. 7 (UPI) -- Here are responses to the two articles about the military's use of the anti-malaria drug Lariam published by United Press International on Sept. 7.

The first article, "Malaria drug links elite soldier suicides," reported a pattern of suicide and violence by Army Special Forces soldiers following their use of Lariam, known generically as mefloquine.

From Terence Hurley, spokesman for Hoffmann-La Roche, which manufactures and markets the drug:

"Roche believes the labeling that accompanies Lariam, and which has been approved by the FDA, is adequate. Information about the use of Lariam and neuropsychiatric events has appeared in the product's label since it was approved by the FDA in 1989. The label has advised for many years that Lariam should be used with caution in patients with psychiatric disturbances and has disclosed, clearly, that depression and other neuropsychiatric events have been reported among patients who have used Lariam. The package insert for Lariam, since its inception, has described adverse events reported in clinical trials and post-marketing surveillance, including neuropsychiatric events. Indeed, since the product's initial launch, the labeling has advised of occasional reports of confusion, hallucinations, anxiety and depression following the use of Lariam.

"Roche takes issues of safety very seriously and works with regulatory authorities on an ongoing basis to ensure recommendations on product use take into account current scientific and medical evidence. Like other pharmaceutical products, the labeling for Lariam has been revised over time, in dialogue with the FDA, to reflect current medical and scientific knowledge. We are diligent in monitoring the safety of all our drugs.

"There is no scientific evidence of a causal link between Lariam and suicide or suicidal ideation. Based on all the data currently available, no cause-and-effect relationship between Lariam and suicide or suicidal ideation has been established. Also, there is no reliable scientific evidence that Lariam is associated with violent acts or criminal conduct. Numerous studies show that the incidence of serious neuropsychiatric events in patients taking Lariam for treatment is very low. And, Roche is not aware of any study, or other reliable scientific evidence, that Lariam causes permanent vestibular dysfunction.

"The United States Army has its own extensive experience with Lariam, including experience in preclinical testing and clinical trials. In fact, Lariam was developed by the Walter Reed Army Institute of Research in its search during the 1960s for drugs active against chloroquine-resistant malaria. In addition, numerous studies of Lariam use by military personnel have been conducted and published in the peer-reviewed medical literature. Thus, the United States Army has its own extensive knowledge base and experience with Lariam. As with all decisions regarding prescription medications, the

decision about whether Lariam is appropriate for any individual patient -- whether soldier or civilian -- is a matter for the independent medical judgment of the prescribing physician.

"Data from well-designed studies have shown Lariam to be safe and well-tolerated. Lariam has been used effectively and safely for treating and preventing malaria by more than 25 million people worldwide over the past 19 years.

"The benefit-risk ratio continues to be favorable for Lariam especially in areas with high-risk exposure to malaria. Lariam is an important and valuable drug that's effective in fighting a life-threatening disease.

"As with all pharmaceutical products, patients should talk to their doctor if they have any concerns and make sure they read the label."

From Army medical officials:

"We have no data that indicate that Lariam was a factor in any Army suicides in Operation Iraqi Freedom or Operation Enduring Freedom (Afghanistan)."

Asked how the Army explained the suicides and violent behavior UPI documented among Special Forces soldiers who took Lariam, they responded:

"Suicide is a very complex tragic phenomenon both in and outside the military. It's often impossible to identify a single cause. Repeated studies (including the Mental Health Advisory Team report completed last spring) show that the associated factors most often found in suicides are failed personal relationships, financial crises, legal difficulties, other similar significant stressors, and the existence of co-morbid psychiatric disorders (depression, psychosis, etc.) as well as ready access to weapons.

"The Army is committed to the health and safety of our people. Where indicated, mefloquine can be used safely to protect soldiers and other travelers against the serious, sometimes fatal, effects of malaria. It is approved by the FDA and recommended by the CDC for travelers worldwide who may be at risk for chloroquine-resistant strains of malaria. Malaria is a potentially fatal disease that kills more than a million people around the world annually. Soldiers deploy around the world, often on short notice, to countries with chloroquine-resistant malaria, and mefloquine is one of the only available, effective countermeasures. Anti-malarial drugs (along with insect repellants, bed nets and protective clothing) are a critical part of our efforts to minimize soldiers' chances of infection from this very serious disease."

In the second article, "Army gave Congress bad data on Iraq suicides," the Army acknowledged in response to questions from UPI that it had given Congress incorrect information about the use of Lariam in units in which suicides in Iraq occurred last year. Army Surgeon General James B. Peake testified in February that no more than four of the deceased soldiers could have been in units taking Lariam. But the Army now says that number may be as high as 11 -- nearly half the total number of suicides the Army said occurred in Iraq during 2003.

Here is the response from Army medical officials, starting with comment about the 3rd Armored Cavalry Regiment, based at Fort Carson, Colo. The Army first told UPI that soldiers in that unit -- where at least one suicide occurred in Iraq -- were taking doxycycline, an alternative malaria drug, not Lariam. The Army now acknowledges the unit was in fact taking Lariam:

"At the time of the surgeon general's testimony, the information provided to him by the 30th Medical Brigade (then the medical headquarters in theater) was that the 3rd Armored Cavalry Regiment (now returned to the U.S.) did not use mefloquine as its primary anti-malarial preventive. We recently obtained information from the 3rd ACR's regimental surgeon that indicates the unit did use mefloquine as its primary anti-malarial.

"The surgeon general's testimony used the most current information available from theater at the time. Since that testimony, our staff has reviewed additional information from these sources:

- Post-mortem testing (which would show evidence of mefloquine in tissue, if present),
- Medical records, either electronic or available written records, or
- Unit surgeon or installation policy for those installations responsible for preparing the troops for deployment.

With regard to the 24 confirmed Army suicides in OIF, more current information indicates:

- Mefloquine was found in only one case, in post-mortem toxicology testing; no mefloquine was found in 23 cases.
- Three additional cases' medical records showed that mefloquine had been prescribed at or near the time of deployment.
- Four cases were assigned or attached to units with the policy of prescribing mefloquine as its preferred anti-malarial drug.
- Three cases were in units with the policy of prescribing either mefloquine or doxycycline.
- Thirteen cases were in units with the policy of prescribing doxycycline as their preferred anti-malarial drug."

Asked by UPI whether the Army believes it is significant that almost half the soldiers who committed suicide in Iraq last year were in units where they could have taken mefloquine, the Army medical officials responded:

"Suicide is a very complex issue especially in military situations when the extraordinary physical and mental stresses of combat and deployment profoundly impact soldiers' emotional well-being. Attributing the cause of a suicide to a single factor when there is little real evidence of its causation does a great disservice to our soldiers and to the general public. In the case of mefloquine, we are convinced that the overall risk of life-

threatening malaria infection posed by chloroquine-resistant malaria requires that we use the best medications available -- including mefloquine --to protect troops against it. ...

"As a reminder, Dr. Winkenwerder (William Winkerwerder Jr., assistant secretary of Defense for health affairs) has two studies on Lariam underway. The first study on attributable risk factors (including mefloquine) for suicide among deployed and recently redeployed Service members is being conducted by Armed Forces Institute of Pathology (AFIP). The second study on comparative rates of adverse events (including neuropsychiatry) among deployed Service members using mefloquine, versus doxycycline, or on (other) antimalarial medications is being conducted by Air Force Research Laboratory (AFRL). Both of these studies include non-Federal scientist investigators who are collaborating with the DoD investigators."

Statement from Sen. Dianne Feinstein, D-Calif., who had previously written key government officials seeking an urgent review of Lariam use:

"I have long been concerned about the use of the drug Lariam for service members and other U.S. government employees deployed abroad. Now, there is an indication that Lariam may have contributed to the suicides of some of our nation's elite troops. The Department of Defense, and all other government agencies that give this drug to their employees, should immediately reassess their decision to use Lariam and look for alternatives that can protect our troops without causing dangerous side effects."

Comment from Steve Robinson, executive director of the National Gulf Resource Center, who has been critical of the Army's handling of Lariam:

"I find it extremely interesting that suicide rates would fall immediately after DoD stops the use of Lariam in theater. It's counter-intuitive to see the suicide rate drop at all while the rate of combat has increased and soldiers were asked to stay longer in Iraq. If the drop in suicide rates is somehow connected to stopping the use of Lariam, then it would provide a significant link in understanding the deleterious effects of the drug. The drop in suicide needs to be investigated further."

Asked for comment about the Army giving Congress incorrect data on Lariam use in units where soldiers committed suicide, Robinson replied:

"Instinctively we knew that the surgeon general was inaccurate and potentially misleading when he claimed only four suicides were from units who took Lariam. We knew his data was wrong because:

- When the question of Lariam was first raised the DoD flatly denied that it was being used in Iraq by any soldier.
- The story has morphed over time to a DoD admission that Lariam was in fact used widely in Iraq and it was used in contravention of the written indications for use prescribed by the FDA.
- DoD Health Affairs ignored public law, and lessons learned, by failing to annotate service members medical records indicating who took Lariam.

"These factors have played out over time. Now we have a potential health care problem that can't be investigated properly because DoD does not know who took the drug, and furthermore they are not referring soldiers who raise the question of Lariam toxicity to follow-on specialized care. Our organization, combined with other non-profits and charitable groups, is having to facilitate air travel and appointments to experts when local commands ignore the soldier's request for help. All of this is eerily similar to the mistakes made in 1991 when veterans returned and complained of health problems only to be told it was in their head.

"If you dont look, you can't find!"

Copyright 2004 by United Press International