

**The Lariam Files;** There is compelling evidence that, for a small number of users, this effective antimalarial drug can have devastating psychiatric side effects. So why aren't more people being warned?

*[E copy of article purchased from Washington Post by Lariam Action USA.]*

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Author:	Keith Epstein
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Three stories from the Lariam files.

\* Michael J. Burch, a Washington consultant, had just returned from a visit to his son, a Peace Corps volunteer working in Ghana, and was having dinner at a Capitol Hill restaurant last March. Burch had been feeling dizzy, his legs rubbery. He'd been battling sleeplessness. Now, during dinner, a sudden surge rose in his chest. He feared a heart attack. It was, he recalls, as if "something were taking over my body."

\* Elisa von Joeden-Forgey, an experienced traveler with no history of psychiatric problems, had trouble sleeping within days of her arrival in Cameroon, where she was to conduct postgraduate research. She had vivid nightmares. She grew terrified that if she dozed off she would disappear. Later, after she returned to the United States, she was too frightened to leave the house. She couldn't concentrate or even carry on a conversation very well. Her dissertation stalled. Her marriage faltered.

\* Not even Hope Trachtenberg-Fifer, a Virginia registered nurse and marathon runner who teaches others to recognize symptoms of medical conditions, had any idea what was going on. While serving on a volunteer medical mission to Kenya in 1997, she dreaded the night, sensed doom and thought she'd never see her family again. Though she'd never had mental problems or trouble sleeping back home in Roanoke, she lay balled up in bed, sobbing. She slept only for brief periods and would wake up gasping and sweating. She wouldn't eat or drink. She wouldn't leave her room. Her heart rate soared, her legs wobbled. She was convinced she would die.

"I was a nut. I was psychotic," she says. "And I was clueless. There I was, a nurse and a health educator, and I had no idea what was happening to me."

All of these people say they were suffering side effects of mefloquine, sold in the U.S. under the brand name Lariam. It is the antimalaria medication recommended as the "drug of choice" by the federal Centers for Disease Control and Prevention (CDC) in 79 countries where malaria is resistant to other drugs. Travel clinics and private physicians in the Washington area, including those serving the State Department, the Peace Corps and many public and private groups whose personnel travel between here and Third World locations, prescribe it routinely. American travelers headed for business or pleasure to India, Thailand and Vietnam, on African safaris or on tours of

the Amazon basin typically are given prescriptions for Lariam.

Mefloquine is used to prevent (and sometimes treat) malaria, a devastating disease that kills more than 1 million people worldwide each year, and is the second-most deadly communicable disease in the world, after tuberculosis. Mefloquine is over 90 percent effective when used in prevention, and saves many thousands of lives annually. It is taken by 90 percent of Peace Corps volunteers in Africa and has reduced their infections dramatically since it was introduced. Last year it was prescribed at least half a million times. Most who take it for prevention have only mild side effects or none at all.

But there is convincing evidence that the drug exposes a small number of otherwise healthy travelers to traumatic and sometimes bizarre neuropsychiatric reactions--and that they are often unaware of the risk of such reactions. Reports of side effects from mefloquine exposure include hallucinations, sleeplessness, paranoia, psychotic episodes and suicide attempts. Some users complain of effects persisting for weeks or months, even years.

These reactions are documented in scientific studies, surveys and in thousands of case reports in the files of Lariam's manufacturer, the Swiss firm Hoffmann-LaRoche, and the U.S. Food and Drug Administration (FDA), the agency that regulates pharmaceuticals. Adverse reactions were noticed by the manufacturer and public health officials soon after the drug was approved 11 years ago. The manufacturer twice agreed to revise the label to list more, and more serious, side effects, including psychiatric ones. Regulators in the United Kingdom had already required explicit consumer warnings, and in 1997 the U.K.'s Malaria Advisory Committee stopped recommending mefloquine for travelers headed to malarial regions for two weeks or less.

Even so, U.S. travelers are often unaware of the potential for disturbing effects. Because pharmacies are not required to distribute the complete product label with most drugs, the government-mandated warnings are not routinely circulated to patients. And many physicians--following the advice of the CDC and drawing on their experience prescribing the drug to patients with few serious problems--either downplay or are unaware of the symptoms a minority of people taking mefloquine report. Despite the accumulating facts about side effects, the CDC has continued to support mefloquine as the "drug of choice."

As a consequence, many who take the drug and suffer side effects are less likely to recognize them until considerable mental anguish or physical injury has occurred. Many people continue taking the medication because they do not realize that the puzzling, even debilitating symptoms are associated with the drug they are taking to prevent malaria. Patients often report being treated by doctors who discount the possibility that their problems are related to the drug.

People who have called the CDC to report or gather information about the side effects of Lariam, including several people whose cases were researched for this story, were told by agency staff that their reactions were unlikely to be the result of the drug and were advised to consider other causes, including stress.

While few agree on the number of people who suffer side effects from mefloquine, there is little

question that some of them do.

Andrea Meyerhoff, an FDA medical officer with responsibility for drugs for tropical diseases and a travel medicine clinician at Georgetown University, says that while cause and effect between mefloquine and these symptoms may never be conclusively proven, neuropsychiatric effects are clearly "associated" with the drug.

Raymond Woosley, chairman of the pharmacology department at Georgetown University and an authority on drug side effects, says the reports on mefloquine are sufficiently widespread to eliminate any doubt about the drug's ability to produce these effects at the preventive doses given travelers. "Mefloquine is one of the more troublesome drugs people use, and causes a lot of side effects," he said. "Some of them are quite serious."

Though Lariam can treat a deadly disease, he continued, its use for prevention needs to be carefully considered. Unlike drugs used to treat a patient who has already contracted a serious disease, where even powerful side effects are tolerated in service of the greater good of fighting a life-threatening condition, Lariam is used to prevent a disease in otherwise healthy people who are usually choosing to travel to infected areas.

Says University of Toronto professor Jay Keystone, a leading authority on antimalarials who has served as a consultant to the CDC and to the drug's manufacturer: "I'm not questioning [the CDC's] intentions or integrity, and for most people the drug is safe and effective. But they are trivializing very real and disabling side effects."

Officials at Hoffmann-LaRoche take the position that Lariam has been proven safe and effective, and that labeling changes approved by the FDA provide adequate notice of the side effects.

"Lariam has been used since 1985 by more than 12 million people worldwide for prevention of malaria," said Charles Alfaro, a spokesman for Roche (as Hoffmann-LaRoche is widely known). "The numbers [of side effects] are extremely low. There's a lot of data out there, but if you look at the experts writing about Lariam, the causal association between mefloquine and serious adverse health events is unlikely."

"The pill is well-tolerated by most people, and the drug's really a good drug," said Celia Maxwell, who as an FDA medical officer in 1987 recommended the drug's approval, and who as a travel medicine clinician now frequently prescribes it. Disabling side effects are "very, very rare."

But when they do occur, she adds, "it's 100 percent real--no doubt about it."

The precise odds of having a bad reaction to Lariam are the subject of intense debate, at least partly due to disagreement over what is meant by "bad." Some scientists tally only the most severe reactions requiring hospitalization, while others count users who are unable to continue their daily activities. Others include only those who stop taking the pill due to the side effects, thus exposing themselves to the risk of malaria.

A Roche-sponsored study of 145,000 travelers in 1993 estimated the rate of "serious" side effects--

identified in this study as those causing death or hospitalization--at one in 10,000; this figure is often cited by the CDC and those who support wide use of the drug. In a 1996 English survey of 2,395 users, one in 140 reported problems severe enough to stop them from carrying out their daily activities.

The latest studies, presented last year at a tropical medicine conference but not yet published, suggest that somewhere between 10 and 20 percent of those who take mefloquine suffer side effects ranging from mild to severe. One of these surveys, conducted by the Scripps Travel Clinic of La Jolla, Calif., estimates the ratio of people suffering some side effects at one in five.

Just who is likely to suffer these side effects? One-third of all patients with problems have a history of hypersensitivity to mefloquine or other quinine-related compounds; had been taking beta blockers (a common class of drugs prescribed for hypertension or heart problems); or had been prone to seizure disorders.

The other two-thirds of patients who experience neuropsychiatric and other moderate to severe reactions? They have seemingly solid mental and physical health histories. Medical experts say there is no way of predicting who they will be, and virtually no research is being done to find out.

Beyond the statistics from surveys and studies, there are reports by patients and doctors to various government agencies.

In the United Kingdom, Lariam was suspected of causing 1,505 adverse reactions between 1990 and 1998, according to doctors' reports compiled by health officials there. The government subsequently expanded the drug's warning label. The British press has reported more on Lariam problems than the U.S. press--sometimes sensationally, adding to arguments that fear itself contributes to reports of reactions. Letters to the British Medical Journal have aired disagreements over the proper role of Lariam. Just last week, the New England Journal of Medicine published a similar exchange between doctors about the drug's side effect profile.

In the United States, more than 2,070 reports of adverse reactions have been filed with the FDA in the last 11 years. More than half of those reports--1,288--involved complaints of "neurological events." The Washington Post obtained 130 pages of the reports, covering the period 1997 to 1999, under the federal Freedom of Information Act.

Such data are anecdotally suggestive but statistically unreliable--unreliable because multiple reports may have been filed by a doctor, patient and drug company for the same patient's experience, and because filing a report doesn't prove reactions were linked to mefloquine.

In addition, nobody knows how many other people may have experienced problems they did not report. However, the data do illustrate what some practitioners and patients believe to be happening.

The reports have few details and consist mostly of the date, the source of the report (medical professional or patient), a tally of symptoms, the outcome, a list of drugs reportedly taken and the "primary suspect" of the reaction's cause. Page after page, the list of symptoms repeats: psychosis,

anxiety, panic attack, thoughts of suicide, hallucinations.

\* Report number 3057866-X, filed with the FDA on March 19, 1998, lists the unidentified patient's reactions: "Abnormal behavior, chest pain, hallucinations, hyperventilation, insomnia, suicidal ideation." Outcome: "Required intervention to prevent permanent impairment/ damage." Primary suspect: Lariam.

\* Report 330063-5, filed July 9, 1999. Reactions: "Anxiety, asthma, chest tightness, cough, dehydration, nausea, panic attack." Outcome: Prolonged hospitalization. Primary suspect: Lariam.

\* Report 3413545-8, filed Dec. 3, 1999. Reactions: "Mental disorder. Paranoia. Suicide attempt." Primary suspect: Lariam.

\* Report 3074393-4, filed April 30, 1998. Reactions: "Aortic injury. Facial bone fractures. Successful suicide." Outcome: Death. Primary suspect: Lariam.

During the Vietnam War, the number of malaria infections among American military personnel sometimes exceeded battlefield casualties, and U.S. officials knew something had to be done. Chloroquine, then the drug of choice, wasn't working as well as it once had, and neither were two alternatives. The Walter Reed Army Institute of Research screened a quarter of a million compounds in a quest for a preventive drug.

Army researchers didn't know how mefloquine worked, but it did. Army experiments in the early 1970s on nearly 400 male subjects, mostly hardy men, showed high effectiveness and few symptoms besides dizziness, headaches and insomnia. Hoffmann-LaRoche acquired the rights to develop the drug commercially and submitted the results of the Army's human experiments to the FDA.

Medical officer Celia Maxwell of the FDA, one of many officials involved with the approval process, predicted few adverse reactions other than dizziness, vomiting and nausea. Mefloquine, she concluded in 1987, "appears to be effective and safe." In 1989 the FDA licensed the drug. A year later it was licensed by the United Kingdom. It was immediately popular because malaria was becoming resistant to chloroquine and air travel to the Third World was growing fast.

Around the time the FDA approved Lariam, troubling reports began to appear. In 1989, "serious neurological and psychiatric adverse events attributed to the drug were brought to the attention of the pharmaceutical company and of WHO," the World Health Organization stated in a 1991 report.

A notation on the report states that it was "not issued to the general public" at the time; it was intended only to guide discussions of scientists and policymakers. A copy was obtained by The Washington Post.

"We knew" about adverse reactions, said Maxwell. "That's why we included some language about potential effects in the [original] labeling. But at that time, we just didn't have the numbers of reports" of ill effects that have emerged since.

The list grew. But Maxwell, now a professor of infectious diseases at Howard University and a physician at the university's travel clinic, still favors Lariam, except for use by surgeons or other people engaged in technical work overseas. (The drug's label suggests caution, due to side effects, by those who drive vehicles, pilot planes and operate machinery. Some airlines, hospitals and other companies employing travelers in sensitive, high-risk jobs restrict use of the drug.) She says that, over 16 years of practicing medicine, only one patient reported to her a neuropsychiatric side effect from the drug--psychotic episodes in which the woman heard voices and suspected a plot to murder her.

Even so, the woman instrumental in approving Lariam for the American public never uses it herself--though, she says, not for reasons unique to mefloquine. She opts for doxycycline. Explains Maxwell: "I have a sensitivity to a lot of drugs."

While the number of people who suffer serious side effects from mefloquine is unclear--and while it's difficult to predict who will be affected--it is clear that many people traveling to malarial areas, particularly for the first time, are not well-informed about possible risks.

At Washington-area CVS and Rite-Aid pharmacies, customers do not routinely receive the drug's FDA-approved and twice-revised label--a folded package insert of almost 50 paragraphs of small print that lay out the adverse reactions and contraindications. Instead, customers receive a one-page printout credited to an independent publisher listing milder effects such as lightheadedness and insomnia, and advising patients to "call your doctor if you develop unexplained anxiety, mood changes, depression, restlessness or confusion." It adds: "If you notice other effects not listed above, contact your doctor or pharmacist."

To get the full package insert, customers must ask the pharmacist or look up the drug in the Physicians' Desk Reference, which compiles information on drugs from all manufacturers.

A sampling in August of Washington-area travel clinics resulted in echoes of assertions by CDC officials and the pharmaceutical manufacturer that severe side effects are very rare. And some clinical professionals in the area have little personal experience with travelers' problems with mefloquine.

Intiaz Choudhary, director of Howard University's travel clinic and an infectious disease specialist, offered a common response when asked what drug he prescribes for patients traveling to most malarial regions.

"Mefloquine is the only one we have available," he said. "I strongly suggest people take this because its [side] effects are minimal."

Said Samuel Scott, senior clinical associate of Washington Occupational Health Associates, which functions as a clinic for business travelers and tourists: "[The CDC's] drug of choice is mefloquine, and so that's generally what we use." He added that "I've not found it to be a problem. Bad dreams is the worst of it, and so we warn them about that."

Martin Wolfe, a veteran tropical medicine consultant who advises the State Department, said a few

federal employees have had problems with mefloquine, but he continues to urge its use as the primary defense against malaria. Ill effects are "not unheard of" in his practice, but "we generally follow what the Public Health Service [CDC] recommends."

Meanwhile, other practitioners of travel medicine take a more cautious approach.

"I don't like using mefloquine [on patients] if I can avoid it. I'm not happy with the side effects," said Robert Edelman, director of the travelers' health clinic at the University of Maryland Hospital in Baltimore. He estimates as many as one in four of his patients have a reaction--insomnia, dizziness, feeling lightheaded or nauseated, if not something worse.

"The patients are not happy--and that's bad, because they're going on these trips to get something accomplished or for a good time. They're on business and they need to be alert and quick, and they have enough problems sleeping because of time zones. People on vacation spend thousands of dollars on a trip and suddenly find it ruined. They feel anxious and nervous and have headaches."

Edelman, who is also associate director of the University of Maryland's center for vaccine development, is critical of the CDC's Web site for failing to spell out percentages of patients who have experienced specific categories of symptoms, including the more moderate ones. The Web site says neuropsychiatric events "very rarely" occur, and that statement is deep in the product information. "If it's one in four," Edelman said, "they should put it in there and let the patient decide whether that's too high or not. The problem is, most patients aren't even aware of these side effects unless you tell them."

For those seeking protection from malaria, there are several other options (see box, p. 15). In areas where malaria is not resistant to it, chloroquine is the best choice. In areas where malaria is resistant to chloroquine, the antibiotic doxycycline is cheaper and has milder side effects; indeed, it's the antimalarial favored by President Clinton on foreign forays. (Asked why, former presidential spokesman Joe Lockhart said, "the usual reasons." Lockhart also chose doxycycline, he said, because of "the dreams.")

Doxycycline must be taken daily, which is one argument against it: Patients skipping a single dose can expose themselves to malaria. It's also not safe for pregnant women or children, and creates acute sensitivity to the sun--a tendency to burn faster, a considerable difficulty for many travelers. Like most antibiotics, it can also cause yeast infections.

Malarone (See "Malarone: A New Alternative to Lariam," Page 14) was approved in July and so far shows effectiveness similar to Lariam's but with fewer side effects.

The CDC's preference for Lariam, despite the availability of such options and reports of problems for some users, puzzles some patients and doctors. Hans Lobel, for years the CDC's chief of malaria surveillance, published many articles supporting the drug's use, dismissing reports of side effects as the result of "travel-related stress" or underlying health problems. He encouraged use of the drug for pregnant women and children, despite the fact that the drug's label says sufficient research has not been done on those groups.

In an interview before he retired last fall, Lobel told The Washington Post, "The scientific data showed us there are no side effects that can be attributed to mefloquine. . . . The long and the short of it is that scientific studies have not shown any difference between mefloquine and a placebo."

The CDC's current Yellow Book, a biennial compilation of information on diseases and treatments that is used by doctors, travelers and the media, describes mefloquine as the "drug of choice" and says it is "very rarely" associated with neuropsychiatric reactions.

Jay Keystone, the Canadian authority on antimalarials who has consulted to both the CDC and Roche, calls the language in the Yellow Book "unacceptable and incomplete." The information, he says, should include a range of estimates for people who are expected to experience symptoms such as anxiety, irritability, nightmares and other disturbances that cause them to stop taking the drug.

As this story was being reported, CDC officials repeated the agency's long-standing assertion that the best scientific evidence shows no difference in tolerance between those taking mefloquine and those taking a placebo. Officials also said mefloquine will remain the agency's "drug of choice."

But late last week CDC officials indicated they may review new data on Malarone and suggest its use in cases where mefloquine or doxycycline cannot be used. Monica Parise, a medical epidemiologist of the CDC's infectious disease unit, said it's now possible that the next edition of the Yellow Book, to be published in 2001, will acknowledge that patients and doctors have three options for malaria prevention in chloroquine-resistant areas--creating not a single drug of choice, but three choices.

In January 1999, Charles Perry--a \$160,000-a-year hospital administrator with seven children--had gone downstairs in his Cincinnati home to retrieve a gallon of milk. Instead he got a shotgun, angled the barrel against the base of his skull and pulled the trigger.

He had told his wife, Linda, many times that that was where it hurt the most. The pain at the base of his cranium, the nightmares and the hallucinations--they all had started six months earlier, during a safari trip to Zimbabwe to celebrate their 30th wedding anniversary.

Because of their public health backgrounds, both Perrys had asked about Lariam's safety--at the pharmacy and at the local health department. They were told it was fine--in fact, the "drug of choice."

After a week canoeing the Zambezi River, Charles Perry began imagining there were monkeys in their room.

"I was in bed and Chuck was sitting there just kind of enjoying himself," Linda Perry recalls, "and he jumps up out of the chair and says, 'Hey, there's a monkey under the bed!' " Then he chased "the monkey" into the bathroom.

Back home a few weeks later, he couldn't sleep. He had vivid dreams. He heard voices.

"Chuck went absolutely mad," she says. "He couldn't remember anything. He couldn't write his

name. His eyes were just nuts." He called meetings at work, then forgot why he called them. One night, he called 911--to report that his wife was going crazy. Finally, he checked himself into the psychiatric ward.

Then Linda Perry remembered what an African guide had said about how Lariam can make some people "crazy." The guide said that those who live in Africa know better than to take it.

"Oh God," she remembers thinking. "It's the Lariam."

That may or may not be true--doctors originally were unwilling to blame Lariam for Charles Perry's mental problems, though one physician wrote a letter doing so. And the timing of the suicide, six months after exposure to the drug, is a complicating factor. In many ways, the Perrys' tale is a classic Lariam parable--a dramatic story of personal suffering and tragedy, but one that is very hard to prove, either legally or scientifically, was caused by the drug.

Like many people whose lives have been shattered by what they believe are side effects of Lariam, Linda Perry has become an activist for the cause. She filed a lawsuit in federal court in June charging that the drug was responsible for her husband's suicide. In August, Roche filed a response, denying the allegations, stating it had taken "reasonable care" in making and distributing Lariam, and "any such injuries and/or damages alleged by plaintiff were the result of superseding or intervening causes . . . or caused by the negligence and/or fault of others." No trial date has been set.

A number of such lawsuits have been filed charging the manufacturer with "failure to warn," but none has been successful. An attempt to gather plaintiffs in England for a class action fell apart as legal bills mounted. Similar efforts have stalled in Canada and the United States. One case in New Jersey was settled out of court by Hoffmann-LaRoche, but the case was sealed and the evidence and terms of the settlement remain secret. An Indiana woman received a \$10,000 out-of-court settlement from a pharmacy after suing for "failure to warn" about Lariam's dangers.

Perry is doing her best to provoke government action, so far with only modest results. Ohio senators George Voinovich and Michael DeWine have arranged a conference call for Perry and her husband's doctor with the FDA. The House Commerce Committee is "actively engaged in conversations with the FDA over concerns about the drug," said committee spokesman Pete Sheffield, and is exploring the possibility of holding hearings.

Meanwhile, individuals who believe they are victims of the drug's side effects hope their stories can help the public understand the possible risks of taking the drug.

Michael Burch--whose son contracted malaria while in the Peace Corps and who appreciates the role mefloquine plays in preventing and treating the disease--says he wishes he had known more before taking the pills.

"I wish I'd known what was happening to me" when he experienced the cardiac and psychiatric symptoms in the restaurant and thereafter. "I know we have the best medical system in the world,

and I still believe that. But the system really let me down."

Hope Trachtenberg-Fifer, the nurse and health educator who says she became "psychotic" after taking Lariam, feels "so used and abused." Before taking Lariam, she had consulted solid information sources she often turned to for professional decision-making: the Physicians' Desk Reference and the CDC's Web site.

"I trusted what I'd been told by my government as an American that this was the thing to do to protect me. I'd done my research!" she said. "But the warnings are very minor."

"They only said to be cautious if you have psychiatric problems. I didn't have any--until I took Lariam."

Keith Epstein, a former investigative reporter with the Washington bureau of the Cleveland Plain Dealer, is a frequent contributor to the Health and Travel sections of The Washington Post. Dan Olmsted, a Falls Church writer and editor, contributed reporting to this story.

TO LEARN MORE, CLICK HERE;

For more information on malaria, mefloquine and related topics:

\* Centers for Disease Control and Prevention: [www.cdc.gov](http://www.cdc.gov)

\* Hoffman-LaRoche: [www.rocheusa.com/products/lariam/pi.html](http://www.rocheusa.com/products/lariam/pi.html)

\* Lariam Action USA, a support group for victims: <http://www.lariaminfo.org>,  
[info@lariaminfo.org](mailto:info@lariaminfo.org)

In addition, two high-quality, independently published pages on mefloquine can be found at: [www.indiana.edu/primate/lariam.html](http://www.indiana.edu/primate/lariam.html) and [www.geocities.com/TheTropics/6913/lariam.htm](http://www.geocities.com/TheTropics/6913/lariam.htm)

#### COMMON DRUG CHOICES FOR MALARIA PREVENTION

ARALEN (chloroquine)

Cost/Tablet: \$2.37

Cost for 3-Week Trip: \$7.10

Adult Dose and Schedule: 250 mg; once weekly, only during trip

Applicable Geographic Areas: Chloroquine-sensitive areas only (see p. 17)

Not for People With: Allergies to chloroquine, psoriasis, liver disease, g-6-PD glucose intolerance

Adverse Effects, Listed From Most to Least Frequent: Visual disturbances, hearing loss, muscle

weakness, loss of appetite

VIBRAMYCIN (doxycycline)

Cost/Tablet: \$0.73

Cost for 3-Week Trip: \$15.39

Adult Dose and Schedule: 100 mg; once daily, only during trip

Applicable Geographic Areas: All areas

Not for People With: Age under 8, pregnancy

Adverse Effects, Listed From Most to Least Frequent: Gastrointestinal upset, sensitivity to sunlight, yeast infections, skin rash, diarrhea, headache, vomiting

MALARONE (atovaquone plus proguanil)

Cost/Tablet: \$5.70

Cost for 3-Week Trip: \$171

Adult Dose and Schedule: 350 mg; once daily during, 2 days before and 1 week after trip

Applicable Geographic Areas: All areas, including mefloquine- resistant areas

Not for People With: Hypersensitivity to atovaquone or proguanil

Adverse Effects, Listed From Most to Least Frequent: Stomachache, nausea, vomiting, headache

LARIAM (mefloquine)

Cost/Tablet: \$13.20

Cost for 3-Week Trip: \$105.57

Adult Dose and Schedule: 250 mg; once 1 week before departure, weekly during trip, and for 4 weeks on return

Applicable Geographic Areas: Chloroquine-resistant areas (see p. 17)

Not for People With: Epilepsy, seizure disorders, psychiatric disorders, cardiac conduction abnormalities (little data on pregnancy or children)

Adverse Effects, Listed From Most to Least Frequent: Dizziness, nausea, vomiting, diarrhea,

stomach upset, headaches, nightmares, abnormal dreams, insomnia, forgetfulness, lightheadedness, motor neuropathy, sensory neuropathy, vertigo, visual disturbances, mood alterations, anxiety, restlessness, hypertension, hypotension, flushing, tachycardia, palpitations, confusion, nervous system disturbances, psychotic manifestations, hallucinations

Sources: Drug labels, clinical trials, travel clinics. Cost data from CVS and Rite-Aid pharmacies in the Washington area.

## HOW MALARIA DEVELOPS

1. A female mosquito carrying the malaria parasite bites a person.
2. The parasite reaches liver via bloodstream within 30 minutes.
3. The parasite begins reproducing in the liver. There are usually no symptoms for two to four weeks.
4. Parasites are released from the liver into the bloodstream.
5. Parasites enter red blood cells. The patient usually has flu- like symptoms.
- 6a. If there is no treatment, the parasites reproduce in the red blood cells and eventually burst the cells.
7. The parasites then infect more red blood cells, and symptoms worsen.
- 6b. If the patient has taken the proper dose of mefloquine, the parasites in the red blood cells are killed, preventing transmission of the parasites in the bloodstream and eventually ending the course of the disease.

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