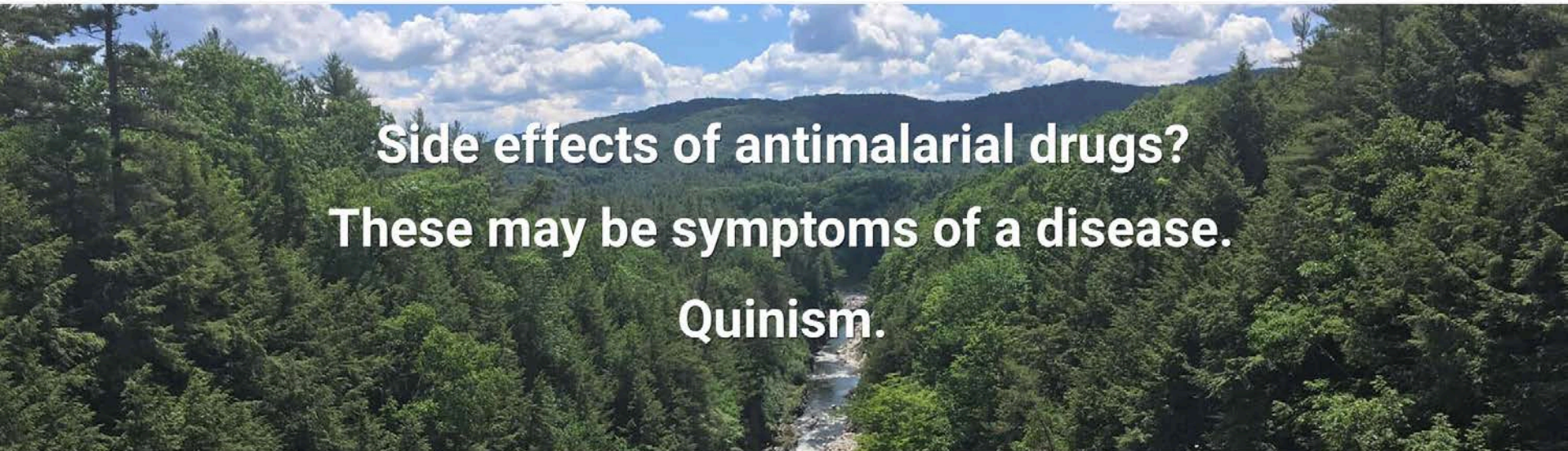


# Identifying and Evaluating Sources of Evidence of Quinism: A Novel Disease Affecting U.S. Veterans

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# Side effects of antimalarial drugs? These may be symptoms of a disease. Quinism.

The Quinism Foundation is a 501(c)(3) nonprofit charitable organization established January 1, 2018 in White River Junction, Vermont.

The Quinism Foundation promotes and supports education and research on quinism, the family of medical disorders caused by poisoning by mefloquine, tafenoquine, and related quinoline drugs.

Symptoms of neuropsychiatric quinism (also known as chronic quinoline encephalopathy) can mimic those of several psychiatric and neurologic disorders including PTSD and TBI.

# Neuropsychiatric Quinism

- Significant empirical evidence of a common set of symptoms and signs developing after exposure to quinoline drugs
  - Quinine, quinacrine, clioquinol, primaquine, chloroquine, mefloquine, tafenoquine, and others
  - 100+ years of case reports, pharmacovigilance reports, and accumulated clinical observations
- Significant *in vitro* and *in vivo* evidence of a common pathophysiology
  - Chronic encephalopathy from focal brainstem and limbic neurotoxicity
  - Idiosyncratic effects at prophylactic doses

## Checklist for the prescription, supply or recommendation of Lariam® (mefloquine) for malaria chemoprophylaxis

### Always use this checklist when prescribing and supplying Lariam:

- considering if Lariam is the most appropriate medicine for malaria chemoprophylaxis;
- issuing a prescription for Lariam as malaria chemoprophylaxis;
- supplying Lariam as malaria chemoprophylaxis under a Patient Group Direction;
- dispensing Lariam for malaria chemoprophylaxis.

For further information the Lariam Summary of Product Characteristics can be found at [www.medicines.org.uk/emc](http://www.medicines.org.uk/emc).

Official guidelines and local information on the prevalence of resistance to antimalarial drugs should be taken into consideration. The National Travel Health Network and Centre should be consulted for current advice on geographical resistance patterns, appropriate chemoprophylaxis and current guidelines which can be found at [www.travelhealthpro.org.uk/disease/113/malaria](http://www.travelhealthpro.org.uk/disease/113/malaria).

Contraindications	Yes	No
<b>1 Hypersensitivity:</b> Is the patient hypersensitive to mefloquine or related compounds (e.g. quinine, quinidine), or to any of the excipients contained in the formulation?	<input type="checkbox"/>	<input type="checkbox"/>
<b>2 Neuropsychiatric disorders:</b> Does the patient currently suffer from, or at any time had a history of depression, generalised anxiety disorder, psychosis, suicide attempts & suicidal ideations, self-endangering behaviour, schizophrenia or other psychiatric disorders, or with a history of convulsions of any origin?	<input type="checkbox"/>	<input type="checkbox"/>
<b>3 Blackwater fever:</b> Does the patient have a history of Blackwater fever?	<input type="checkbox"/>	<input type="checkbox"/>
<b>4 Liver function:</b> Does the patient have severe liver function impairment?	<input type="checkbox"/>	<input type="checkbox"/>
<b>5 Halofantrine use:</b> Is the patient currently receiving halofantrine?	<input type="checkbox"/>	<input type="checkbox"/>
<b>If one or more of the contraindication questions (1-5) is answered with "Yes", then the patient is ineligible for prescription with Lariam (mefloquine) for malaria chemoprophylaxis</b>		
Precautions	Yes	No
<b>1 Have you informed the patient about the neuropsychiatric symptoms to look out for?</b> Mefloquine may induce psychiatric symptoms such as anxiety disorders, paranoia, depression, hallucinations and psychosis. Psychiatric symptoms such as insomnia, abnormal dreams/nightmares, acute anxiety, depression, restlessness or confusion have to be regarded as prodromal for a more serious event. Cases of suicide, suicidal thoughts and self-endangering behaviour such as attempted suicide have been reported.	<input type="checkbox"/>	<input type="checkbox"/>
<b>2 Have you informed the patient when to stop taking mefloquine?</b> Patients on malaria chemoprophylaxis with mefloquine should be informed that if they experience any psychiatric symptoms or changes to their mental state during mefloquine use, to stop taking mefloquine and seek medical advice immediately so that mefloquine can be replaced by alternative malaria prevention medication.	<input type="checkbox"/>	<input type="checkbox"/>
<b>3 Have you informed the patient of the potential for neuropsychiatric reactions to occur after discontinuing of the drug?</b> Adverse reactions may also occur after discontinuation of the drug. In a small number of patients, it has been reported that neuropsychiatric reactions (e.g. depression, dizziness or vertigo and loss of balance) may persist for months or longer, even after discontinuation of the drug.	<input type="checkbox"/>	<input type="checkbox"/>
<b>4 Have you informed the patient to read the Patient Information Leaflet as well as highlighting the importance of reading the Patient Alert Card (enclosed in the pack) and keeping it on themselves?</b>	<input type="checkbox"/>	<input type="checkbox"/>

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

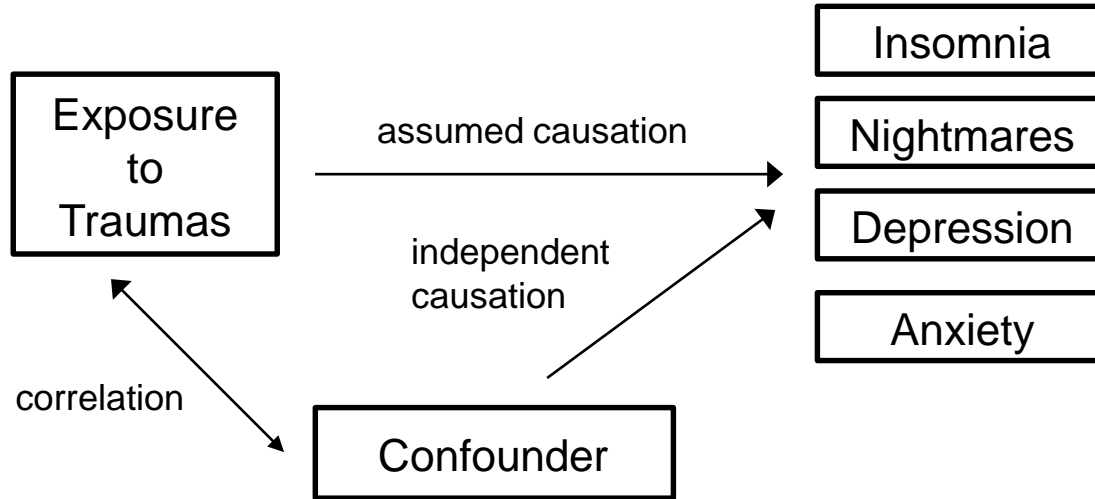
Adverse events should be reported. Reporting forms and information can be found at [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

Adverse events should also be reported to Roche Products Ltd. Please contact Roche Drug Safety Centre by emailing [drs@roche.com](mailto:drs@roche.com) or calling +44 (0)1707 367554. This educational material is provided by Roche Products Limited and is mandatory as a condition of the Marketing Authorisation in order to further minimise important selected risks.

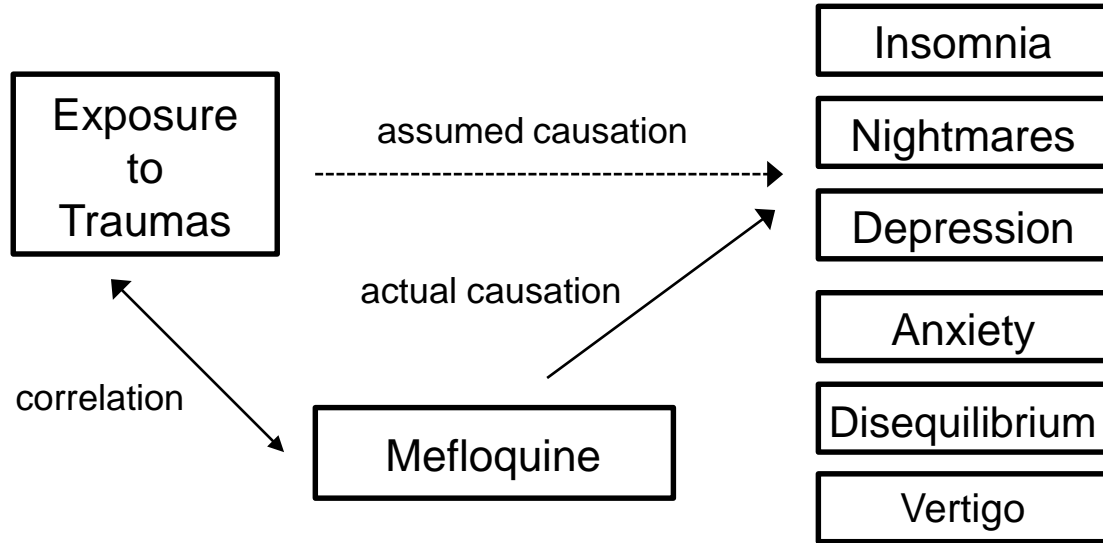
“Psychiatric symptoms such as insomnia, abnormal dreams/nightmares, acute anxiety, depression, restlessness or confusion have to be regarded as prodromal for a more serious event.”

Roche UK. Lariam product documentation, June 2018. Emphasis added.

# Confounding



# Confounding



# WRMI-2

- “Have you ever taken the weekly drug mefloquine (also known as Lariam®) to prevent malaria?”
- If yes, “At any time while taking the drug, did you experience abnormal dreams or nightmares, insomnia, anxiety, depression, restlessness, or confusion?”



# DSM-5 PTSD Criterion H

- The 2012 revision to the DSM added a diagnostic exclusion (“Criterion H”)
- Per Criterion H, the symptoms that would otherwise contribute to a PTSD diagnosis cannot be due to the effects of a medication
- Should symptoms such as nightmares or insomnia that first begin with mefloquine use and prior to any trauma contribute towards PTSD diagnostic criteria?



# Conflicts of Interest

- Centers for Disease Control and Prevention (CDC)
- Peace Corps
- Department of Veterans Affairs
- Department of Defense

“Malaria is a deadly disease”



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