

ISSUE BRIEF: Long-Term Health Effects of Anti-Malarial Medications

The Situation

- Malaria is a serious infectious disease transmitted by mosquitoes and is found in Iraq, Afghanistan, and many areas in Africa, South America, and Asia. Mefloquine, an antimalarial drug, was approved by the Food and Drug Administration (FDA) in May 1989 and was widely prescribed to U.S. military service members until 2009. However, the Department of Defense (DOD) is still using mefloquine in cases when other antimalarials are ineffective.
- The *Journal of the Royal Society of Medicine* reported on three randomized controlled trials between 2001-2003 and the studies confirmed mefloquine's potential for causing psychological illness, and all three study reports described an excess of neuropsychiatric adverse effects in the mefloquine arm.
- In 2013, the FDA published a safety alert on mefloquine and added a black box warning (its strongest warning) to the drug label and pointed out that neurologic side effects can include dizziness, loss of balance (vestibular problems), tinnitus and psychiatric side effects, which can include anxiety, paranoia, depression, or hallucinations. Furthermore, it was noted that the neurologic or psychiatric side effects may occur at any time during drug use, and may last for months to years after the drug is stopped.
- In the 2015 clinicians book, "*Posttraumatic Stress Disorder and Related Diseases in Combat Veterans*," mefloquine intoxication is noted to be a potentially life-threatening condition marked by changes in affect, behavior, cognition, and thought that may be associated with a risk of central nervous system (CNS) neuronal injury as well as chronic neurological and psychiatric sequelae. The acute symptoms of mefloquine intoxication may mimic and be mistaken for a number of acute psychiatric disorders including posttraumatic stress disorder (PTSD).
- The study, "*Neuropsychiatric Outcomes After Mefloquine Exposure Among U.S. Military Service Members*," published in January 2017, found that relative risks for adjustment disorder, anxiety, insomnia, and PTSD were higher for mefloquine when compared with doxycycline, another antimalarial drug.

The Challenge

- The Department of Veterans Affairs (VA) does not recognize an association between mefloquine and negative mental health outcomes. In the joint VA-DOD study, "*Associations between Use of Antimalarial Medications and Health among U.S. Veterans of the Wars in Iraq and Afghanistan*," published in 2019, it is noted that there are no significant associations between mefloquine and mental health issues.

The Solution

- In January 2019 an ad hoc committee of the National Academies of Sciences, Engineering, and Medicine started a VA-contracted study to assess the long-term health effects that might result from the use of antimalarial drugs by adults, in particular mefloquine, for the prophylaxis of malaria.
- Based on the outcomes of the study, Congress must establish presumptive service connection for any diseases or disorders found to be associated with the use of antimalarials to include mefloquine.