

# Mefloquine: contraindicated in patients with mood, psychotic or seizure disorders

**Reason for posting:** Increases in global travel and the prevalence of drug-resistant malaria put travellers at risk of serious and often fatal malaria infections. Mefloquine is an effective first-line agent for preventing malaria in areas of chloroquine resistance,<sup>1,2</sup> but it has known neuropsychiatric adverse effects ranging from anxiety and paranoia to depression, hallucinations, psychotic behaviour and possibly suicide.<sup>3,4</sup> In order to reduce the risk of serious neuropsychiatric events, the drug's manufacturer recently strengthened warnings in its US product monograph, making it clear that mefloquine is contraindicated for people with a recent history of depression, generalized anxiety disorder, or a psychotic or seizure disorder.<sup>5</sup>

**The drug:** Mefloquine, a compound structurally related to quinine,<sup>6</sup> is indicated for the prophylaxis and treatment of *Plasmodium falciparum* and *Plasmodium vivax* malaria.<sup>7</sup> The recommended adult prophylactic dose is 250 mg once a week, starting 1 week before entering an area where chloroquine-resistant malaria is endemic and continuing until 4 weeks after departing it. Mild, transient adverse effects such as nausea and dizziness occur in about 40% of patients.<sup>8</sup> Serious neuropsychiatric adverse events (e.g., psychosis, encephalopathy and convulsions) occur in about 4 to 7 patients in 1000 given mefloquine to treat malaria<sup>7,8</sup> and about 1 in 13 000 patients taking it for prophylaxis.<sup>7</sup> Other possible adverse effects<sup>5-7,9</sup> include confusion, depressed mood, panic attacks, sleep disturbances, anorexia, tremor, ataxia, fatigue and, rarely, suicide (although no firm correlation has been established). Younger patients often tolerate the drug better than older patients, and men better than women.<sup>6</sup> Long-term safety data are lacking. Serious adverse events are noted 75% of the time within a month after starting treatment<sup>6</sup> and may persist for months after the drug is stopped. Mefloquine augments the prolongation of QT inter-

vals caused by halofantrine (another antimalarial agent), and it should not be combined with digoxin, calcium-channel blockers or  $\beta$ -blockers.<sup>7</sup> The drug should not be prescribed for women in the first trimester of pregnancy.

**What to do:** The US Centers for Disease Control and Prevention maintain updated information about antimalarial prophylaxis for specific destinations ([www.cdc.gov/travel](http://www.cdc.gov/travel)). Prophylaxis has benefits that often outweigh the risks,<sup>1,10</sup> and it complements the use of insect repellants and bed nets, reduced skin exposure, and restricted evening and nighttime outdoor activity.<sup>11</sup> Unfortunately poor compliance often limits the effectiveness of prophylactic regimens.<sup>1,10</sup> Patients with a recent history of neuropsychiatric illness, including depression, generalized anxiety disorder, or psychotic or seizure disorder, should be prescribed an alternative regimen (e.g., doxycycline).<sup>2</sup>

If mefloquine is indicated, patients should be warned to stop the drug and seek medical attention if they experience anxiety, depression, restlessness, irritability or confusion. A well-informed and balanced discussion of the risks and benefits of mefloquine prophylaxis for malaria is needed to avoid problems such as the reduction in mefloquine use (and 10-fold increase in imported malaria cases and some deaths) that oc-

curred in the past in the United Kingdom following negative media hype about the drug's adverse effects.<sup>10</sup>

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## References

1. Croft A, Garner P. Mefloquine to prevent malaria: a systematic review of trials [review]. *BMJ* 1997;315:1412-6.
2. Kain KC, MacPherson DW, Kelton T, Keystone JS, Mendelson J, MacLean JD. Malaria deaths in visitors to Canada and in Canadian travellers: a case series. *CMAJ* 2001;164(5):654-9.
3. Stuijver PC, Ligthelm RJ, Goud TJ. Acute psychosis after mefloquine. *Lancet* 1989;2:282.
4. Wittes RC, Saginur R. Adverse reaction to mefloquine associated with ethanol ingestion. *CMAJ* 1995;152(4):515-7.
5. 2002 Safety Alert — Lariam (mefloquine hydrochloride) [Dear Doctor Letter]. Nutley (NJ): Roche Laboratories Inc; Sept 2002. Available: [www.fda.gov/medwatch/SAFETY/2002/liariam\\_deardoc.htm](http://www.fda.gov/medwatch/SAFETY/2002/liariam_deardoc.htm) (accessed 2002 Oct 16).
6. White NJ. Mefloquine [editorial]. *BMJ* 1994;308:286-7.
7. Lariam (mefloquine) [product monograph]. *Compendium of Pharmaceuticals and Specialties*. Ottawa: Canadian Pharmacists Association; 2002. p. 876-7.
8. Barrett PJ, Emmins PD, Clarke PD, Bradley DJ. Comparison of adverse events associated with use of mefloquine and combination chloroquine and proguanil as antimalarial prophylaxis: postal and telephone survey of travellers. *BMJ* 1996; 313:525-8.
9. Potasman I, Beny A, Seligmann H. Neuropsychiatric problems in 2500 long-term young travellers to the tropics. *J Travel Med* 2000;7:5-9.
10. Reid AJC, Whitty CJM, Ayles HM, Jennings RM, Bovill BA, Felton JM, et al. Malaria at Christmas: risks of prophylaxis versus risks of malaria. *BMJ* 1998;317:1506-7.
11. Ryan ET, Kain KC. Health advice and immunizations for travelers [review]. *N Engl J Med* 2000;342:1716-25.

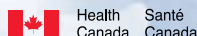
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