Roche

Pharmaceuticals

September 2002

Dear Pharmacist:

Important changes and additions to the prescribing information for LARIAM® (mefloquine hydrochloride) TABLETS are described in the enclosed complete product information.

Lariam is indicated for the treatment of mild to moderate acute malaria caused by mefloquine-susceptible strains of *Plasmodium falciparum* (both chloroquine-susceptible and resistant strains) or by *P. vivax*. Lariam is also indicated for the prophylaxis of *P. falciparum* and *P. vivax* malaria infections, including prophylaxis of chloroquine-resistant strains of *P. falciparum*.

CONTRAINDICATIONS

The new label includes additional contraindications in patients with a recent history of depression, generalized anxiety disorder, psychosis, or schizophrenia or other major psychiatric disorders. The section now reads:

> "Use of Lariam is contraindicated in patients with a known hypersensitivity to mefloquine or related compounds (eg, quinine and quinidine). Lariam should not be prescribed for prophylaxis in patients with active depression, a recent history of depression, generalized anxiety disorder, psychosis, or schizophrenia or other major psychiatric disorders, or with a history of convulsions."

WARNINGS

The section now includes two additional paragraphs stating:

> "Mefloquine may cause psychiatric symptoms in a number of patients, ranging from anxiety, paranoia, and depression to hallucinations and psychotic behavior. On occasions, these symptoms have been reported to continue long after mefloquine has been stopped. Rare cases of suicidal ideation and suicide have been reported though no relationship to drug administration has been confirmed. To minimize the chances of these adverse events, mefloquine should not be taken for prophylaxis in patients with active depression or with a recent history of depression, generalized anxiety disorder, psychosis, or schizophrenia or other major psychiatric disorders. Lariam should be used with caution in patients with a previous history of depression."

> "During prophylactic use, if psychiatric symptoms such as acute anxiety, depression, restlessness or confusion occur, these may be considered prodromal to a more serious event. In these cases, the drug must be discontinued and an alternative medication should be substituted."

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PRECAUTIONS

In the *Information for Patients* subsection the following information (fifth bullet point) has been restated as "Patients should be advised:

> that if the patients experience psychiatric symptoms such as acute anxiety, depression, restlessness or confusion, these may be considered prodromal to a more serious event. In these cases, the drug must be discontinued and an alternative medication should be substituted;"

ADVERSE REACTIONS

The *Postmarketing* subsection has been redrafted. The changes include the addition of the following:

- occasional reports of more severe neuropsychiatric disorders (tremor, ataxia, mood changes, panic attacks)
- rare cases of suicide (though no relationship to drug administration has been confirmed)
- infrequent reports of chest pain, edema and dyspepsia

Please see the enclosed prescribing information for the complete list of adverse reactions.

Enclosed is a copy of the complete product information that incorporates the changes described in this letter. If you have any questions about Lariam, we encourage you to call the toll-free number for the Roche Pharmaceuticals Service Center at 1-800-526-6367. Also, if you are aware of any serious adverse experiences potentially associated with the use of Lariam, please report such information to Roche at the above number or to the Food and Drug Administration MedWatch program at 1-800-FDA-1088.

Sincerely,

Iris Kingma, MD, PhD
Medical Science Leader
Medical Affairs