



Guide for Healthcare Professionals

LARIAM[®] (mefloquine) FOR MALARIA CHEMOPROPHYLAXIS

This guide is intended to provide you with information regarding some of the side effects – especially neuropsychiatric adverse reactions – under chemoprophylactic use of Lariam (mefloquine).

For the complete prescribing and safety information, please refer to the Lariam Summary of Product Characteristics which is enclosed and available at www.medicines.ie

About Lariam

Lariam (mefloquine hydrochloride) is an antimalarial agent available as 250-mg tablets for oral administration. The quantity of mefloquine hydrochloride (mefloquine HCl) in one tablet is 274.09 mg, equivalent to 250 mg mefloquine base.

Therapeutic indication

Therapy: Mefloquine is especially indicated for therapy of *P. falciparum* malaria in which the pathogen has become resistant to other antimalarial agents.

- Following treatment of *P. vivax* malaria with Lariam, relapse prophylaxis with an 8-amino-quinoline derivative, for example primaquine, should be considered in order to eliminate parasites in the hepatic phase.

Chemoprophylaxis: with mefloquine is particularly recommended for travellers to malarious areas in which multiple resistant *P. falciparum* strains occur.

In order to ensure, before arrival in endemic area, that mefloquine administration is well tolerated, it is recommended to start chemoprophylaxis with mefloquine 10 days before departure (i.e. first intake 10 days before departure and 2nd intake 3 days before departure). Subsequent doses should be taken once a week (at a fixed day).

For current advice on geographical resistance patterns and appropriate chemoprophylaxis, current guidelines or competent national expert centres should be consulted.

Please follow the associated prescriber's contraindications checklist to decide if your patient is eligible for Lariam chemoprophylaxis.

Before prescribing Lariam for malaria chemoprophylaxis

As Lariam may induce neuropsychiatric side effects, there are important contraindications for its use. These include any previous or past conditions that may predispose the patient to neuropsychiatric side effects (*please refer to sections - Contraindications and Special Warnings and Precautions for Use*).

Counselling your patient

As part of your discussions with patients or their carers, please ensure that:

- You provide a full description of the neuropsychiatric profile of mefloquine (Lariam);
- You instruct the patient to read the patient information leaflet;
- You hand out a patient alert card.

Additional information can be found in the Summary of Product Characteristics (SmPC).

Please advise patients that, should neuropsychiatric reactions or changes to their mental state occur during mefloquine chemoprophylaxis, they should stop taking mefloquine, and seek medical advice immediately so that mefloquine can be replaced by alternative malaria prevention medication.

Undesirable effects

Lariam may cause long lasting serious mental health problems. Due to the long half-life of mefloquine, adverse reactions may occur and persist up to several months after discontinuation of the drug.

Some people who have taken Lariam developed serious mental health problems, including:

- suicidal behaviour
- committing suicide
- severe anxiety
- **paranoia**
- **hallucinations**
- depression
- feeling restless
- **unusual behaviour**
- **amnesia**

Contraindications

- Mefloquine is **contraindicated** for chemoprophylaxis in patients with active or a history of the following conditions: depression, generalized anxiety disorder, psychosis, suicide attempts, suicidal ideations and self-endangering behaviour, schizophrenia or other psychiatric disorders or convulsions of any origin.
- Mefloquine **must not** be prescribed for chemoprophylaxis in patients with severe impairment of liver function.
- Mefloquine **must not** be prescribed in patients who currently receive halofantrine treatment.
- Mefloquine is **contraindicated** in patients with a history of Blackwater fever.
- Lariam **must not be** administered to patients with a known hypersensitivity to mefloquine or related compounds or to any of the excipients contained in the formulation.

Special warnings and precautions for use

Neuropsychiatric Adverse Reactions/Suicidality

Mefloquine may induce psychiatric symptoms such as anxiety disorders, paranoia, depression, hallucinations and psychosis. Psychiatric symptoms such as 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.

Patients on malaria chemoprophylaxis with mefloquine should be informed that **if these reactions or changes to their mental state occur during mefloquine use, to stop taking mefloquine and seek medical advice immediately** so that mefloquine can be replaced by alternative malaria prevention medication.

Due to the long half-life of mefloquine, adverse reactions may occur and persist up to several months after discontinuation of the drug. In a small number of patients it has been reported that dizziness or vertigo and loss of balance continued for months after discontinuation of the drug.

To minimise the risk for these adverse reactions, mefloquine must not be used for chemoprophylaxis in patients with active or a history of psychiatric disturbances such as depression, anxiety disorders, schizophrenia or other psychiatric disorders.

Cardiac toxicity

Concomitant administration of mefloquine and other related compounds (e.g. quinine, quinidine and chloroquine) may produce electrocardiographic abnormalities.

Due to the risk of a potentially fatal prolongation of the QTc interval, halofantrine must not be used during mefloquine chemoprophylaxis or treatment of malaria or within 15 weeks after the last dose of mefloquine. Due to increased plasma concentrations and elimination half-life of mefloquine following co-administration with ketoconazole, the risk of QTc prolongation may also be expected if ketoconazole is taken during mefloquine chemoprophylaxis or treatment of malaria or within 15 weeks after the last dose of mefloquine.

Patients should be advised to consult a doctor if signs of arrhythmia or palpitations occur during mefloquine chemoprophylaxis. These symptoms might in rare cases precede severe cardiologic side effects.

Eye disorders

Any patient presenting with a visual disorder should be referred to a physician as certain conditions (such as retinal disorders or optic neuropathy) may require stopping treatment with mefloquine.

Seizure disorders

In patients with epilepsy, mefloquine may increase the risk of convulsions. Therefore in such cases, mefloquine should be used only for curative treatment (i.e. not for stand-by therapy) and only if compelling reasons exist.

Concomitant administration of mefloquine and anticonvulsants (e.g. valproic acid, carbamazepine, phenobarbital or phenytoin) may reduce seizure control by lowering the plasma levels of anticonvulsant. Therefore, patients concurrently taking anti-seizure medication, including valproic acid, carbamazepine, phenobarbital, and phenytoin, and mefloquine should have the blood level of their anti-seizure medication monitored and the dosage adjusted as necessary.

Concomitant administration of mefloquine and drugs known to lower the epileptogenic threshold (antidepressants such as tricyclic or selective serotonin reuptake inhibitors (SSRIs); bupropion, antipsychotics, tramadol, chloroquine or some antibiotics) may increase the risk of convulsions.

Neuropathy

Cases of polyneuropathy (based on neurological symptoms such as pain, burning, sensory disturbances or muscle weakness, alone or in combination) have been reported in patients receiving mefloquine.

Mefloquine should be discontinued in patients experiencing symptoms of neuropathy, including pain, burning, tingling, numbness, and/or weakness in order to prevent the development of an irreversible condition.

Pneumonitis

Pneumonitis of possible allergic etiology has been reported in patients receiving mefloquine. Patients who develop signs of dyspnoea, dry cough or fever etc. while receiving mefloquine should be advised to contact a doctor to undergo medical evaluation.

Long-term use

During clinical trials, this drug was not administered for longer than one year. If the drug is to be administered for a prolonged period, periodic evaluations including liver function tests and periodic ophthalmic examinations should be performed.

For information on **renal impairment** and **pregnancy and breastfeeding**, refer to the Lariam Summary of Product Characteristics which is enclosed and available at www.medicines.ie



In the event of a suspected adverse event, please report it to the Drug Surveillance Centre at Roche Products (Ireland) Limited, 3004 Lake Drive, Citywest, Naas Road, Dublin 24 by mail, telephone (01 4690700), fax (01 4690793), or email (Ireland.drug_surveillance_centre@roche.com). Alternatively, suspected adverse events should be reported to the Irish Medicines Board using the online form at www.imb.ie or by using the freepost yellow card system. The IMB can also be contacted on 01 6764971.

For the complete prescribing and safety information, please refer to the Lariam Summary of Product Characteristics which is enclosed and available at www.medicines.ie

Should you have any questions or require additional information regarding the use of Lariam (mefloquine), or if you require additional copies of any of the Lariam educational materials, please contact Medical Information at Roche Products (Ireland) Limited, 3004 Lake Drive, Citywest, Naas Road, Dublin 24 by mail, telephone (01 4690700), fax (01 4690751), or email (Ireland.druginfo@roche.com).

Contraindications checklist for the prescription of Lariam (mefloquine) chemoprophylaxis in your patients

The following checklist provides a brief guide to conditions and medications that are contraindicated in mefloquine chemoprophylaxis. The checklist is designed to assist you in determining your patient's suitability for chemoprophylaxis with mefloquine and all items should be checked in the presence of the patient or his/her carer. If **one** of the checklist questions 1-6 is answered with "**Yes**" then the prescription of mefloquine is **contraindicated** for this patient. Please find additional information regarding mefloquine in the associated educational Guide for Healthcare Professionals.

Please complete the checklist, ticking the appropriate answers.

Contraindications	Yes	No
1 Is the patient known to be hypersensitive to mefloquine or related compounds (e.g. quinine, quinidine) or excipients?	<input type="checkbox"/>	<input type="checkbox"/>
2 Does the patient currently suffer, or has he/she suffered at any time from depression, generalized anxiety disorder, psychosis, schizophrenia, suicide attempts, suicidal thoughts, self-endangering behaviour or any other psychiatric disorder?	<input type="checkbox"/>	<input type="checkbox"/>
3 Does the patient currently suffer, or has he/she suffered at any time from convulsions of any origin?	<input type="checkbox"/>	<input type="checkbox"/>
4 Does the patient have a history of Blackwater fever?	<input type="checkbox"/>	<input type="checkbox"/>
5 Does the patient have severe impairment of liver function?	<input type="checkbox"/>	<input type="checkbox"/>
6 Is the patient currently receiving halofantrine?	<input type="checkbox"/>	<input type="checkbox"/>



If **one** of the checklist items 1-6 is answered with "**Yes**", then the prescription of mefloquine is **contraindicated** for this patient.



Counselling your patient

As part of your discussions with patients or their carers, please ensure that:

- You provide a full description of the neuropsychiatric profile of mefloquine (Lariam);
- You instruct the patient to read the patient information leaflet;
- You hand out a patient alert card.

Please advise patients that, should neuropsychiatric reactions or changes to their mental state occur during mefloquine chemoprophylaxis, they should stop taking mefloquine, and seek medical advice immediately so that mefloquine can be replaced by alternative malaria prevention medication.

Consult the product information (available at www.medicines.ie) for the complete prescribing and safety information before prescribing Lariam (mefloquine).

This material is provided as a licence requirement for this medicine, as part of the Lariam Risk Management Plan.

For additional copies of the Contraindications Checklist, please contact Medical Information at Roche Products (Ireland) Limited, 3004 Lake Drive, Citywest, Naas Road, Dublin 24 by mail, telephone (01 4690700), fax (01 4690791), or email (Ireland.druginfo@roche.com).

