

**Revised July 2009**

## **Use of mefloquine in pregnancy**

Malaria is a more serious illness in pregnancy, both for the mother and the foetus. Pregnant women should be advised against travel to malaria risk areas. There is little data on the use of mefloquine (Lariam®) during pregnancy. The documented studies are outlined below together with a summary of advice from authoritative sources.

### **Research Studies**

The data available from studies on the prophylactic use of mefloquine in pregnancy is generally reassuring. Four studies, three prospective [1, 2, 3] and one based on passive reporting [4] found that mefloquine given for malaria prevention during pregnancy was not associated with any increased risk of adverse foetal outcome compared with other anti-malarials studied or the general population. One of the prospective studies followed women who were given mefloquine in the first trimester [3], and in the passive surveillance study most exposures to mefloquine occurred in the 2 months prior to pregnancy or during the first trimester [4]. A study in US service women given mefloquine during first trimester pregnancy found a high level of spontaneous abortion, but there were likely to be complicating features in these women [5].

A study in Thai women treated for malaria with mefloquine demonstrated an increased rate of stillbirth [(6]. However, a study in Malawi did not demonstrate an association between treatment or prophylactic doses of mefloquine with stillbirth [7], nor did another small treatment study in Thailand [8]. A small study in Nigeria followed pregnant women treated with artemether and mefloquine and found that all babies were normal at birth and remained so at follow up [9].

Animal studies have found mefloquine to be teratogenic in rats and mice; however these results were associated with doses of over 100mg/kg. The prophylactic dose in humans is approximately 5mg/kg.

A summary of the animal and human data relating to the use of mefloquine during pregnancy is available from the [National Teratology Information Service](#) (56KB PDF). They state: '*The available data on mefloquine exposure in pregnancy do not indicate an increased teratogenic risk.*'

**Summary of Product Characteristics (SPC) Lariam® (mefloquine) UK.** Mefloquine use in pregnancy is unlicensed.

The SPC for Lariam® states that '*there is too little clinical experience in humans to assess any possible damaging effects of Lariam during pregnancy*'. It recommends that '*Lariam should be used in pregnancy only if there are compelling medical reasons. In the absence of clinical experience, prophylactic use during pregnancy should be avoided as a matter of principle*' [10].

### **Advisory Committee on Malaria Prevention for UK Travellers (ACMP)**

The ACMP state '*that it now seems unlikely that mefloquine is associated with adverse foetal outcomes*' [11].

They suggest that '*the risk of adverse effects in pregnancy should be balanced against the risk of contracting malaria and the complications this can involve. Women should be reassured that taking mefloquine inadvertently prior to or during the first trimester is not an indication to terminate the pregnancy.*'

In summary, the ACMP state that mefloquine may be advised in the second and third trimesters and that its use may be justified during the first trimester after taking expert advice.

### **World Health Organization (WHO)**

WHO recommends that '*mefloquine prophylaxis may be given during the second and third trimesters but there is limited information on its safety during the first trimester*' [12].

### **US Centers for Disease Control and Prevention (CDC)**

CDC state that '*Evidence suggests that mefloquine prophylaxis causes no significant increase in spontaneous abortions or congenital malformations when taken during the first trimester.*' [13].

### **Conclusion**

Pregnant women planning to travel to areas with chloroquine resistant *P. falciparum* malaria should always be advised that such areas are not suitable destinations. However, there will be occasions when pregnant women are unable to change their travel plans and this decision has to be acknowledged by the health advisor.

UK guidelines consider doxycycline as unsuitable for use during pregnancy, and there remains a lack of evidence regarding the use of atovaquone/proguanil (Malarone®). Chloroquine plus proguanil are considered safe in all trimesters of pregnancy, but parasite resistance to this regimen is widespread, and it will not provide sufficient protection for many areas of the world. Therefore, there are instances when mefloquine is considered.

The lack of conclusive data has led to caution with the use of mefloquine during pregnancy. Women are advised to use contraceptive precautions when taking mefloquine and for 3 months after the last dose [10]. However, women should be reassured that taking mefloquine inadvertently prior to and / or during the first trimester is not considered an indication to terminate the pregnancy.

Most experts recommend that mefloquine is avoided during the first trimester; but can be offered to women during the second and third trimesters. However, if travel during first trimester cannot be avoided, then mefloquine can be considered following expert consultation.

The risk of adverse events of mefloquine use during pregnancy needs to be balanced against the risk of contracting malaria and the possible complications to both mother and foetus. The decision on whether or not to recommend mefloquine should be carefully discussed with the traveller.

All travellers should be advised of the importance of [insect bite precautions](#) and that they need to obtain urgent medical assistance if they develop signs and symptoms of malaria.

Expert advice should be sought for pregnant women who have other medical contraindications to the use of mefloquine.

### **References**

1. Nosten F, Karbwang J, White NJ, et al. Mefloquine antimalarial prophylaxis in pregnancy: dose finding and pharmacokinetic study. *Br J Clin Pharmacol* 1990;30:79-85.
2. Nosten F, ter Kuile F, Maelankiri L, et al. Mefloquine prophylaxis prevents malaria during pregnancy: a double-blind, placebo-controlled study. *J Infect Dis* 1994;169:595-603.

3. Phillips-Howard PA, Steffen R, Kerr L, et al. Safety of mefloquine and other antimalarial agents in the first trimester of pregnancy. *J Travel Med* 1998;5:124-6.
4. Vanhauwere B, Maradit H, Kerr L. Post-marketing surveillance of prophylactic mefloquine (Lariam®) use in pregnancy. *Am J Trop Med Hyg.* 1998;58(1):17-21.
5. Smoak BL, Writer JV, Keep LW, et al. The effects of inadvertent exposure to mefloquine chemoprophylaxis on pregnancy outcomes and infants of US Army servicewomen. *J Infect Dis* 1997;176:831-3.
6. Nosten F, Vincenti M, Simpson J, et al. The effects of mefloquine treatment in pregnancy. *Clin Infect Dis* 1999;28:808-15.
7. Steketee RW, Wirima JJ, Hightower AW, et al. The effect of malaria and malaria prevention in pregnancy in offspring birthweight, prematurity and interuterine growth retardation in rural Malawi. *Am J Trop Med Hyg* 1996;55:33-41.
8. McGready R, Cho T, Hkirijaroen L, et al. Quinine and mefloquine in the treatment of multidrug-resistant *Plasmodium falciparum* malaria in pregnancy. *Ann Trop Med Parasitol* 1998;92:643-53.
9. Sowunmi A, Oduola AM, Ogundahunsi OA et al. Randomised trial of artemether versus artemether and mefloquine for the treatment of chloroquine/sulfadoxine-pyrimethamine-resistant *falciparum* malaria during pregnancy. *J Obstet Gynaecol* 1998; 18:322-7.
10. Roche Products Ltd. Lariam summary of product characteristics. Revised 22 June 2009. [Accessed 3 July 2009]. Available at <http://emc.medicines.org.uk/medicine/1701/SPC/Lariam/#DOCREVISION>
11. Chiodini P, Hill DR, Laloo D, et al. Guidelines for malaria prevention in travellers from the United Kingdom. London, Health Protection Agency, January 2007. Available at [http://www.hpa.org.uk/infections/topics\\_az/malaria/guidelines.htm](http://www.hpa.org.uk/infections/topics_az/malaria/guidelines.htm)
12. World Health Organization. International travel and health, 2009. Geneva, Switzerland; 2009.
13. Centers for Disease Control and Prevention. Health information for international travel 2010. Atlanta: US Department of Health and Human Services, Public Health Service, 2010.