The Advisory Committee on Malaria Prevention (ACMP) meetings 2010 to 2015: Discussions in the minutes relating to the potential side-effects of mefloquine

1 Overview of the ACMP

The Advisory Committee on Malaria Prevention (ACMP) is an expert advisory committee of Public Health England (PHE) established in 1998 to formulate evidence-based guidelines on malaria prevention in the United Kingdom. The ACMP is chaired by a leading international expert in malaria and tropical medicine and membership includes medical/non-medical professionals who have expertise in i) antimalarial drug resistance, ii) the use of antimalarial drugs, iii) malaria prevention/treatment methods and iv) the behaviour of UK travellers. This includes representation from the Ministry of Defence (MOD).

The ACMP regularly reviews data on safety and efficacy of all antimalarials. Whenever new evidence about antimalarials appears the ACMP considers this as part of its continuous process of developing advice.

Mefloquine is one of the three prescription-only anti-malarials recommended for chemoprophylaxis in most parts of the tropics. Its use is therefore considered at every ACMP meeting. Between 2010 and 2015, the potential side effects of mefloquine, including neuropsychiatric, were reviewed regularly by the committee and discussed specifically in response to changes in international guidance and the manufacturer's SPC. The relevant sections in the minutes from the ACMP meetings during this time are outlined below.

2 Relevant sections from the minutes

2.1 ACMP meeting September 2010

- Section 7. Prophylaxis for the armed forces

The Surgeon General had officially requested that AG bring to the attention of the Committee, a paper derived from a Cochrane review of randomized controlled trials of malaria chemoprophylactic drugs. Members agreed that although the data analysis was correct, the conclusions were inappropriate and appeared to reflect personal opinion rather than being supported by the data. The ACMP saw no reason to change their opinion on the role of mefloquine in chemoprophylaxis

Action: DL/Sec will write to the Surgeon General to say that the Committee has read the paper and does not support the conclusions drawn. The article does not change current policy.

2.2 ACMP meeting: August 2012

- Section 6. Mefloquine and Traumatic Brain Injury

AG reported that some military physicians in the UK had commented on US military policy that recommends avoiding mefloquine in patients with traumatic brain injury where there are alternative drugs. The Committee felt that this was no evidence to support this and no need for the ACMP to change its policy. A risk assessment of an individual patient was key in determining the suitability of an antimalarial for a particular patient.

- Section 9: AOB

Adverse events

The CSM reporting of adverse events is available for all to access online. RB asked if the Committee should be concerned at reports that potentially suggest higher suicide rate with mefloquine than with other drugs. MP will discuss how best to analyse these data with colleagues at the MRHA

2.3 ACMP meeting: December 2013

- Section 5. Mefloquine adverse events

- US FDA have changed mefloquine to become a black box warning drug. The basis for this decision is uncertain; no new data are available in the public domain. CDC has not changed their recommendations.
- Roche has made changes to the SPC for mefloquine in the UK about timing of initiation of mefloquine before travel and periodic liver function and ophthalmic tests after prolonged use.
- It was agreed that the ACMP 2014 malaria prevention guidelines will emphasise the importance of stringent risk assessment before mefloquine use. No changes will be made to the current recommendations about timing of initiation as current recommendations are already more conservative than those suggested by the manufacturer. The new guidelines will also not reflect changes about periodic testing of individuals on prolonged mefloquine until some data emerges about the basis of these concerns

Action 5.1 (DL): To write formally to the European Medicines Agency with regard to the data transparency surrounding the increased stringency of mefloquine risk assessment (ASAP).

Action 5.2 (DL): To write formally to Roche requesting the data that underpinned their recommendation for periodic testing in prolonged use

- Section 8. BNF questions

BNF documentation on mefloquine will reflect the 2013 Malaria Prevention Guidelines with respect to administration of mefloquine e.g. starting mefloquine 2-3 weeks before entering a malarious area.

2.4 ACMP meeting: January 2015

- Section 2. Minutes of last meeting / actions

The minutes were accepted as accurate, with updates on the outstanding actions listed below:

- *Action 5.1* – DL requested clarification on the purpose of this action. It was agreed that the committee wanted to see the evidence (published or unpublished) that had led to the raising of a second level concern about mefloquine by the MHRA.
- *Action 5.2* – A response is yet to be received from Roche to DL's request to share the data that underpinned their recommendation for periodic testing in the prolonged use of mefloquine

ACTION 2.2 (DL): To write formally to the MHRA to request view of the data that the raising of a second level concern on mefloquine (ASAP)
ACTION 2.3 (DL): Update the group on any response to the request for Roche for data to support their recommendation for periodic testing in long term use of mefloquine

- Section 5d. Mefloquine evidence review

- No additional data on Mefloquine has been published

2.5 ACMP meeting: June 2015

The ACMP met this week (24.06.2015) to finalise the 2015 revision of the ACMP guidelines. The minutes of this meeting are not yet available.