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Defence Committee

An acceptable risk? The use of Lariam for military personnel: Government Response to the Committee's Fourth Report of Session 2015–16

Third Special Report of Session 2016–17

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The Defence Committee

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Third Special Report

The Defence Committee published its Fourth Report of Session 2015–16, entitled *An acceptable risk? The use of Lariam for military personnel* on 24 May 2016. The Government's response was received on 21 July 2016 and is appended to this report.

Appendix: Government Response

The Government's formal response to the HCDC's conclusions and recommendations is set out below. The HCDC's findings are highlighted in bold, with the Government response in plain text. For ease of reference, paragraph numbering follows that in the 'Conclusions and Recommendations' section of the HCDC's report.

Introduction

1. We welcome the Minister's apology to former and current Service personnel who believed that they were prescribed Lariam without the necessary individual risk assessments. This is a timely acknowledgement of the concerns raised about the use of Lariam. We look to the Minister to build on his opening statement by engaging positively with the recommendations we make in this Report. The prescription of a drug known to have 'neuropsychiatric side effects and vestibular disorders' without face-to-face interviews shows a lamentable weakness in the MoD's Duty of Care towards service personnel. (Paragraph 5)

The Government welcomes the HCDC's report and has considered its conclusions and recommendations carefully. Malaria is a deadly disease and we have a duty to protect our deployed personnel from it. Mefloquine (commercially known as Lariam) continues to be recommended as a safe and effective form of malaria prevention by Public Health England, the World Health Organisation and other respected bodies who take account of the body of global evidence.

Adverse reactions to any drug can be experienced by some, so we will continue to keep our policies and procedures under review to ensure that the anti-malarial being prescribed can be tolerated by the individual patient.

We take seriously the claims made to the Committee that Lariam has been inappropriately prescribed to Service personnel and that serious and long-lasting adverse drug effects have been experienced. We continue to encourage anyone with such concerns to raise them with the MoD so they can be investigated fully and in confidence.

MoD use of Lariam

2. While the ACMP may be able to give general medical advice on the use of Lariam, it does not tailor its advice for use by the Armed Forces. We believe this to be a serious deficiency. Given the clear concerns about the use of Lariam for military personnel, this must be addressed as a matter of urgency. We recommend that the MoD, and its

representative on the ACMP, work with the ACMP to develop guidelines on Lariam and other anti-malarials specific to their use by military personnel, along similar lines to the US Centre for Disease Control and Protection's Yellow Book. (Paragraph 23)

A revised malaria prevention policy is currently going through the internal MoD approval process. Once finalised, the MoD has agreed with the ACMP to pass the document to them for review, in order to provide an objective assessment of the revised policy.

3. The Government's assertion that geographical deployment was part of the assessment for using Lariam has been disputed. For the sake of clarity we recommend that the MoD should set out which geographical areas, if any, it believes to have resistance to each anti-malarial drug which it uses, and any accompanying evidence it has to support its view. (Paragraph 27)

The MoD relies on authoritative external advice on the global distribution of anti-malarial resistance. The MoD follows the UK guidance provided in Table 7 of 'Country Recommendations' in the 'Guidelines for malaria prevention in travellers from the United Kingdom, 2015' by Public Health England, dated September 2015.[1] These guidelines are updated on a regular basis (usually at least annually).

4. Publishing evidence pertinent to our inquiry on the day of a Ministerial oral evidence session, and without prior notice, is not an acceptable way to engage with the Committee. In its response to our Report, we shall expect a clear undertaking from the Ministry of Defence that this will not happen again. (Paragraph 29)

The MoD apologised about the timing of the release of information at the oral evidence session. The information was made available to HCDC as soon as it was ready and released in line with the Code of Practice for Official Statistics. That is why the publication was released at short notice as an ad hoc publication. There was no intention to delay or withhold information from the Committee, the publication was to ensure transparency and so that any statements MoD Ministers or officials made at the Committee were supported by an Official Statistics publication. In future MoD will ensure that HCDC is aware of any planned ad hoc publications relevant to the session so that they may be anticipated.

Individual risk assessments

5. The clear guidance from Roche is for individual risk assessments to be conducted before Lariam is prescribed. It is the MoD's policy to adhere to that guidance, but the MoD appears to have interpreted the guidance to include the option of 'desk-based' risk assessments using patients' medical records. We do not believe that to be an adequate alternative to face-to-face interviews. We therefore recommend that the MoD cease conducting risk assessments based solely on patients' records and prescribe Lariam, if at all, only after detailed face-to-face individual risk assessments. Records of face-to-face assessments should be recorded in individual's medical notes and a signature obtained confirming that risks have been explained and advice notes provided. (Paragraph 38)

1 Table 7 'Country recommendations', Public Health England 'Guidelines for malaria prevention in travellers from the United Kingdom 2015', September 2015, pp 36–45

On the prevention of malaria in military personnel, the revised malaria prevention policy will direct that all anti-malaria drugs are only supplied after a face-to-face travel health risk assessment performed by an appropriately trained and regulated healthcare professional. Where this is physically not possible (for example, a ship at sea that may not have a doctor or nurse on board) the risk assessment will be undertaken by a suitably trained Medical Assistant or Medical Technician following endorsed protocols, with the drugs authorised by a doctor before supply. In either case, travel health risk assessments are to be recorded on the patients' electronic health record.

6. We are concerned that the records held by the MoD are insufficient to give certainty that the policy of conducting individual risk assessments has been fully adhered to. While we understand that it would be more difficult to produce records before 2013, it should be a straightforward exercise to provide that detail for the past three years. We recommend that the Ministry of Defence conduct an audit of all prescriptions of Lariam since responsibility was moved to the Surgeon General. As part of that audit, we will expect the MoD to provide figures on the number of face-to-face assessments alongside the number of prescriptions based solely on patients' records. (Paragraph 39)

The purpose of audit is to measure performance against a prescribed standard, to introduce measures to address any perceived failure to meet the standard, and then to re-measure to determine if the standard has been achieved after intervention. The MoD will undertake prospective audit of returning travellers to examine the impact of the new strategy, once the revised policy is approved. Given the high rate of adverse effects of anti-malaria drugs, it will be extended to include all anti-malarial drugs.

Undertaking a retrospective audit of all Armed Forces personnel prescribed Lariam since 2013 is neither straightforward nor practicable. For the two years 2013–2015 it is estimated that this would require the review of more than 6,500 case records requiring more than 2,000 man hours of manual raw data compilation: this would principally be by doctors in individual medical centres examining individual electronic medical records, which could have a significant impact on the delivery of healthcare. Additional staff time would also be required to collate and analyse the results. The results would not alter the MoD intent to ensure that all future prescriptions for Lariam are following an individual face-to-face consultation. Individual units are responsible for carrying out a number of mandatory pre-deployment administrative checks before an individual can deploy, one of which includes checking that a face-to face consultation has been conducted. If the new policy is found not to have been followed, the individual will be referred back to a Medical Officer.

7. It is not clear how the MoD would provide individual risk assessments prior to the prescription of Lariam in the event of a significant deployment. In its response to our Report, the MoD should set out how this would be done and an estimation of the time it would take to conduct face-to-face individual risk assessments at both company and battalion level. (Paragraph 43)

The MoD agrees that it can be difficult to undertake individual risk assessments if military personnel deploy at short notice. In order to address this difficulty, the revised malaria prevention policy will direct a robust risk assessment strategy based upon three elements.

First, at around the time they complete their initial training and enter the trained strength, all new Armed Forces personnel will undergo a malaria chemoprophylaxis contra-

indications check. This will involve a face-to-face consultation with an appropriately trained and regulated healthcare professional to identify any contraindications to the five commonly used anti-malaria drugs. The results will be recorded in the patients' electronic health record. This will highlight any Armed Forces personnel who have a fixed contra-indication to any anti-malarial both on their medical record and to the individual.

Second, depending upon individual circumstances, after posting into a deployable role, or before they enter a period of high readiness, Armed Forces personnel will undertake a generic face-to-face travel health risk assessment with an appropriately trained and regulated healthcare professional and the results recorded in their electronic health record. It is estimated that this will take up to 20 minutes per individual, or approximately 33 hours for a company (or any military unit of around 100 personnel) or approximately 200 hours for a battalion.

Finally, once individuals are warned for a deployment they will normally undertake a deployment-specific face-to-face travel health risk assessment with an appropriately trained and regulated healthcare professional, with the results recorded in their electronic health record. When the operational imperative means that time does not allow this additional face-to-face interview, an appropriately trained and regulated healthcare professional will review individual electronic health records and confirm that there are no contraindications to the recommended anti-malaria drug. It is estimated that this will take up to 5 minutes per individual, or approximately 8 hours for a company, or approximately 50 hours for a battalion.

8. We further recommend that the MoD sets out a comparative assessment of the practicalities of prescribing Lariam with face-to-face interviews and prescribing other anti-malarial protections in the event of a large deployment at short notice. (Paragraph 44)

All anti-malaria drugs have the potential to cause adverse effects and the revised malaria prevention policy will direct that all anti-malaria drugs are only to be supplied after face-to-face travel health risk assessments. If the choice of anti-malaria drug is known beforehand there will be no significant difference in the time needed to supply Lariam when compared to any other anti-malaria drug.

However, should a nurse or pharmacist identify that a traveller requires Lariam during a travel health risk assessment, the traveller will need to be referred to a doctor. This will add at least 10 minutes to the time required per individual.

9. Whilst the extent of non-reporting of contra-indications is not clear, all of our witnesses acknowledged that there was a risk that some military personnel may hide symptoms in the belief that to do otherwise could jeopardise their careers. Doctors are well placed to spot this, but they cannot be guaranteed to do so in every case. This reinforces the need for detailed face-to-face individual risk assessments rather than implied risk assessments based on patients' records. (Paragraph 50)

As outlined in the answer to recommendation 7, the revised malaria prevention policy will direct a robust risk assessment strategy for face to face assessments.

10. The anecdotal evidence we received suggesting that some military personnel preferred to throw away their Lariam rather than use it is deeply disturbing. If true, it is an indication that some in the Armed Forces have completely lost confidence in Lariam. In its response, we shall expect the Ministry of Defence to set out how it monitors compliance rates among military personnel who have been prescribed Lariam. (Paragraph 54)

Compliance with a prescribed course of drugs is a matter of personal choice that is influenced by informed consent. The importance of taking anti-malaria drugs is stated during pre-deployment health briefings delivered to personnel before overseas deployment, and reinforced during deployment. All cases of malaria are reported to the Surgeon General's Headquarters and each case is investigated to determine compliance with the malaria prevention policy in order to identify lessons.

The only absolutely reliable way of measuring compliance with anti-malaria drug regimens would be by blood testing. Except as part of formally approved research, the widespread use of blood testing to assess compliance is considered to be impractical with a disproportionate logistic burden, and ethically unacceptable to mandate an invasive test and enforce any failure to detect an adequate drug level through punitive measures.

The MoD undertakes ad hoc surveys of personnel returning from overseas, that include questions on compliance with malarial chemoprophylaxis. Following the approval of a revised malaria prevention policy, the MoD intends to continue to undertake post-deployment surveys to enhance the understanding of compliance.

11. In addition to the need for a face-to-face interview, we recommend that the MoD ensures that each individual, when made aware of the risks of Lariam, must be offered the option of receiving an alternative anti-malarial drug. (Paragraph 56)

The revised MoD policy is currently going through the internal MoD approval process and specific wording is not yet finalised. However, the revised policy will direct that all anti-malaria drugs are only to be supplied after face-to-face travel health risk assessments.

Travel health assessments will be performed by an appropriately trained and regulated healthcare professional. This will determine the existing contraindications and known intolerances to all relevant anti-malarial drugs (including Lariam) for the specified geographic deployment. The traveller will then be offered the most suitable drug on both safety and efficacy grounds, taking into account patient preference.

All anti-malaria drugs have the potential to cause adverse effects and the revised Anti-Malaria Prophylaxis Protocol, introduced in February this year, on the Defence Medical Information Capability Programme (DMICP) ensures that travellers are informed of these during the travel health risk assessment. If Lariam is to be supplied the prescribing doctor will be required to actively check a box to confirm that alternative drugs have been offered to the traveller.

12. The risk of severe side-effects of using Lariam have been highlighted by both Roche and our witnesses. The evidence we have received has emphasised the specific risks that such side-effects can place on military personnel when deployed and the belief that the military environment has the potential to exacerbate those side-effects. While

the majority of users will not experience them, we do not believe Lariam, and its risk profile, is compatible with the duties required of military personnel on operations. (Paragraph 73)

The MoD acknowledges and respects the opinion of the Committee that was based on the evidence provided to them. However, the MoD is not aware of any peer-reviewed evidence that any of the anti-malaria drugs recommended by ACMP are incompatible with the duties required of military personnel on operations.

It is well known that all anti-malaria drugs have the potential to cause adverse effects (see Table 1 below) and it is acknowledged that these can, on occasion, be severe.

	Very Common (more than 1 in 10)	Common (more than 1 in 100)
Atovaquone/Proguanil[2]	Abdominal pain Diarrhoea Headache Vomiting	Abnormal dreams Allergic reactions Anaemia Anorexia Cough Depression Dizziness Fever Insomnia Pruritus Rash
Chloroquine & Proguanil[3]	**Chloroquine** Gastro Intestinal Disturbances Headache Pruritus Rashes Skin Reactions **Proguanil** Constipation Diarrhoea Mild Gastric intolerance	
Doxycycline[4]	Anorexia Anxiety Dry mouth Flushing Fungal superinfection Tinnitus	

2 Atovaquone & Proguanil Summary of Product Characteristics (http://www.medicines.org.uk/emc/medicine/756) accessed 10 Nov 15

3 BNF 70 Sept 2015–March 2016 pp 536–538 www.medicinescomplete.com accessed 04 Feb 16

4 BNF 70 Sept 2015–March 2016 pp 496–497 www.medicinescomplete.com accessed 04 Feb 16

	Very Common (more than 1 in 10)	Common (more than 1 in 100)
Mefloquine[5]	Abnormal dreams Insomnia	Abdominal pain Anxiety Depression Diarrhoea Dizziness Headache Nausea Pruritus Vertigo Visual impairment Vomiting

Table 1: Common and Very Common Adverse Effects of anti-malaria drugs

The MoD considers Lariam to be an appropriate drug for chloroquine resistant regions of the world if the traveller wishes to take it in preference to atovaquone/proguanil or doxycycline and accepts the side-effect profile.

13. Strong anecdotal evidence suggests that a body of current and former Service personnel have been adversely affected by the use of Lariam. The MoD acknowledges its duty of care to support them, but the current arrangements for doing so appear to be inadequate. We recommend that the MoD establishes a single point of contact for all current and former Service personnel who have concerns about their experience of Lariam. This point of contact should be publicised widely though the Chain of Command, veterans organisations, the MoD website and military and forces magazines and publications. Discussions should also be held with the Department of Health on possible ways of advising GPs of potential risks to veterans who may have been prescribed Lariam. (Paragraph 77)

Work is in hand to recruit into a team that will be the point of contact for both current and former Service personnel who have concerns about their experience of Lariam. It is anticipated that the team will be manned by 1 September 2016. We will work with others to ensure the team contact details are publicised widely.

Research undertaken on Lariam

14. There is a body of evidence which indicates that Lariam has a significant risk profile. This has been acknowledged by Roche in the guidance it issues with the drug. However, most of this research has focussed on the civilian population. We welcome the Government's forthcoming audit of both Lariam and its alternatives but recommend that these audits are widened in scope to provide a more detailed understanding of the risks attached to the use of Lariam by military personnel. Such research should then be evaluated alongside research conducted by other nations' militaries. (Paragraph 86)

5 Mefloquine Summary of Product Characteristics (http://www.medicines.org.uk/emc/medicine/1701) accessed 10 Nov 15.

The revised malaria prevention policy will reduce the need for, and value of, future research, by limiting the ability to randomise drug allocation and by explicitly influencing patient acceptability. In order to counter this, the MoD is simplifying and routinising data collection through DMICP that will facilitate future audits of anti-malaria drug use.

A research proposal for a wider study into the impact of adverse effects of anti-malaria drugs on the performance of military personnel exercising in Kenya is currently being considered by the MoD Research Ethics Committee (MoDREC). This study will add to our understanding of the risks associated with the use of anti-malaria drugs by military personnel. In addition, MoD will continue to share its research and to monitor research into anti-malaria drugs by other nations.

Comparisons with the use of Lariam by other States

15. The Ministry of Defence asserts that its use of Lariam is not out of step with that of our allies. To support this, it has provided evidence on which of our allies offers Lariam as an anti-malarial drug. However, a number of our witnesses told us that our allies take a far more restrictive approach to the use of the drug. We recommend that the MoD updates its information on the use of Lariam by our allies to include the extent to which Lariam is used and under what circumstances it is prescribed. (Paragraph 96)

The MoD will continue to update the information held on the use by our allies of Lariam and other anti-malaria drugs. This includes the extent to which Lariam is used, and the circumstances in which it is supplied.

Conclusion

16. The Ministry of Defence has a duty of care to protect military personnel on operations overseas. It includes ensuring that they are adequately inoculated against disease. This will never be without the risk of detrimental side-effects, and we understand that the MoD must balance those risks against the health of our Armed Forces. However, in the case of malaria, we conclude that the MoD's current policy has got that balance wrong. (Paragraph 97)

17. While it is clear to us that there are significant risks attached to the use of Lariam for military personnel, we accept that there are a very limited number of occasions when its prescription may be necessary. However, we conclude that the MoD should designate Lariam as a 'drug of last resort' and that prescribing it should be restricted by the following conditions:

- **Only to those who are unable to tolerate any of the available alternatives;**
- **Only after a face-to-face Individual Risk Assessment has been conducted; and**
- **Only after the patient has been made aware of the alternatives and has been given the choice between Lariam and another suitable anti-malarial drug. (Paragraph 98)**

18. Lariam is a drug whose own manufacturers have laid down stringent conditions which must be met if it is to be prescribed safely. We see no reason to disbelieve the very strong anecdotal evidence that such conditions have been ignored in dispensing it to large numbers of troops about to be deployed. Indeed, it is hard to see how they could ever be met except when the numbers to be individually assessed are few and far between. (Paragraph 99)

19. It is our firm conclusion that there is neither the need, nor any justification for continuing to issue this medication to Service personnel except when the three conditions listed above have been met. (Paragraph 100)

As stated in the introduction to this response, malaria is a deadly disease and the MoD has a duty to protect its deployed personnel from it. This includes the supply of malaria chemoprophylaxis.

In 2015 the World Health Organisation estimated that there were 214 million new cases of malaria worldwide, resulting in the death of around 438,000 people. Despite tens of thousands of UK Armed Forces personnel deploying to malaria risk areas, there has not been a death from malaria resulting from an operational deployment since 1992. In addition, cases of severe malaria are now rare in the Armed Forces.

The Government has set out in this response how the MoD will proactively address the HCDC's recommendations. This will include liaising with the ACMP on Armed Forces guidelines; developing and implementing a revised malaria prevention policy (that will include a robust risk assessment strategy including that if Lariam is to be supplied the prescribing doctor will be required to actively check a box to confirm that alternative drugs have been offered to the traveller); and undertaking audits on returning travellers. In addition, new Armed Forces personnel will have a face-to-face consultation with an appropriately trained and regulated healthcare professional to identify any contraindications to the five commonly used anti-malaria drugs These measures will further strengthen the MoD's existing policies and procedures for the use of anti-malarials.

21 July 2016