



House of Commons
Defence Committee

An acceptable risk? The use of Lariam for military personnel

Fourth Report of Session 2015–16



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*Report, together with formal minutes
relating to the report*

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The Defence Committee

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Contacts

All correspondence should be addressed to the Clerk of the Defence Committee, House of Commons, London SW1A 0AA. The telephone number for general enquiries is 020 7219 5857; the Committee's email address is defcom@parliament.uk. Media inquiries should be addressed to Alex Paterson on 020 7219 1589.

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Summary

Lariam is one of a number of anti-malarials used by the Ministry of Defence to protect military personnel against malaria. It is not the most widely used anti-malarial drug, but the MoD believes it to be an important part of the defence against malaria for Armed Forces posted to particular locations overseas.

Lariam has a high risk profile and a minority of users experience severe side-effects. These side-effects are clearly highlighted by Roche, the manufacturer of Lariam. Our inquiry considered whether those risks outweigh the benefits of Lariam when other anti-malarial drugs, with a lower risk profile, are available to the MoD.

The evidence we received highlighted some severe examples of the possible side-effects of Lariam in a military setting. While they may be in the minority, we do not believe that the risk and severity of these side-effects are acceptable for our military personnel on operations overseas.

We understand that in very limited instances the prescription of Lariam may be unavoidable. However we believe that it should be considered as a 'drug of last resort' and be prescribed only to those who are unable to take any of the available alternatives.

We also believe that if the MoD continues to prescribe Lariam, this must take place only after a face-to-face Individual Risk Assessment has been conducted. As part of that assessment we believe that each serviceman should be made aware of alternative anti-malarial drugs and be given the choice between Lariam and another suitable anti-malarial drug.

The MoD relies on advice from the Advisory Committee on Malarial Prevention (ACMP), but the ACMP does not tailor its advice for use in a military setting. We consider this to be inadequate and recommend that military specific advice be provided. We are also concerned about the lack of up-to-date research on the impact of the use of Lariam by military personnel, and we expect the MoD to rectify this.

The Minister opened his evidence to us with a clear statement of support to those members of the Armed Forces who believe that they have been affected by the inappropriate prescription of Lariam. We welcome the Minister's statement and look forward to a similar level of engagement by the Government with this Report.

1 Introduction

1. The risks associated with Lariam—an anti-malarial drug used by the MoD—have been the subject of concern and controversy for more than a decade. Since the 1990s, Members of Parliament have regularly highlighted these risks by means of Early Day Motions, written questions and debates. In response to recent media coverage, we wrote to the Secretary of State for Defence on 8 September 2015, requesting an update on MoD policy for using Lariam as an anti-malarial for the Armed Forces.¹ He replied on 21 September 2015,² but we were not convinced by that response and decided to conduct an inquiry into its use for service personnel.

2. Our inquiry concentrated on the prescription of Lariam and the guidelines issued by Roche; the recorded side-effects of Lariam and a comparison with the side-effects of other anti-malarial drugs; the individual risk assessments required before Lariam is prescribed; research into the problems associated with Lariam; and the use of Lariam by other nations' militaries.³

3. We took oral evidence from Roche, the manufacturer of Lariam; Dr Remington Nevin and Dr Ashley Croft, two medical experts; and Trixie Foster and Colonel (Rtd) Andrew Marriott, campaigners against the military's use of Lariam. We concluded our oral evidence with Mark Lancaster TD MP, Minister for Defence Personnel, Welfare and Veterans; Surgeon Vice Admiral Alasdair Walker OBE, Surgeon General; Brigadier Timothy Hodgetts CBE, Medical Director, Defence Medical Services; and Surgeon Captain John Sharpley, Defence Consultant in Psychiatry. We thank our witnesses for their contributions and also those who took the time to write to the Committee setting out their personal experience of Lariam use.

4. In his opening statement, the Minister acknowledged that “anecdotal evidence” submitted to our inquiry “suggests that a limited number of Service personnel believe that their individual risk assessments did not take place”. He apologised to “any former or current Service personnel affected”, should that have been the case.⁴

5. 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.

1 [Letter from the Chairman to the Secretary of State, 8 September 2015](#)

2 [Response from the Secretary of State to the Chairman, 21 September 2015](#)

3 The Terms of Reference for the inquiry can be found [here](#).

4 [Q146](#)

2 MoD use of Lariam

Background

6. Lariam (also known as Mefloquine) is one of a number of anti-malarials used by the Ministry of Defence (MoD) to protect military personnel against malaria. It was developed in the 1970s at the United States Department of Defense and was approved for use in the US and the UK in 1989. The pharmaceutical company Roche holds the licence to supply Lariam in the UK. Under the terms of its licence, the drug is indicated as a treatment for those already suffering from malaria, or as a preventative medicine for those travelling to malarious areas.⁵ Roche does not actively promote Lariam to the MoD, nor supply it directly to any UK customer. Roche has a contract to provide Lariam to a wholesaler, which supplies it to customers including the NHS, MoD and private providers. Around one-fifth of its UK sales are to the MoD.⁶

7. Lariam is one of a number of anti-malarial drugs used by the MoD. In his letter of 21 September 2015 to the Committee, the Secretary of State for Defence explained that Lariam was not “a first line” drug and that Lariam was used “primarily in cases where other drugs would not be effective or appropriate for that person”.⁷

8. On 12 January 2016, the Ministry of Defence published an *Ad Hoc Statistical Bulletin*, produced by Defence Statistics, which provided an update on the use of Lariam by the MoD. According to the Bulletin, a minimum of 17,368 UK Armed Forces personnel were prescribed Lariam at least once between 1 April 2007 and 31 March 2015. The Bulletin compares that to the use of alternative malarial drugs:

Over the same time-period approximately 104,000 UK Armed Forces personnel were prescribed a different anti-malarial drug. Thus of the UK Armed Forces personnel prescribed anti-malarials, approx 86% did not receive Mefloquine in this time period.⁸

9. That Bulletin also set out the level of stocks of anti-malarial drugs held by the MoD: Chemoprophylaxis drugs held by the MoD, August 2015, Tablets and Doses for a Six-Month Deployment

5 Roche ([LAR0001](#))

6 Roche ([LAR0001](#))

7 [Response from the Secretary of State to the Chairman, 21 September 2015](#)

8 Ministry of Defence, [Ad Hoc Statistical Bulletin: Mefloquine Hydrochloride prescribing in the UK Armed Forces, 1 April 2007–31 March 2015, 12 January 2016](#)

Chemoprophylaxis drug	Tablets in Stock %	Doses in Stock for a Six Month Deployment %	Dosage
Chloroquine	1.8	10.8	310 mg once weekly
Chloroquine and proguanil (travel pack)	75.5	56.0	310mg chloroquine once weekly; 200mg proguanil once daily
Proguanil	10.5	—	Not prescribed as individual drug; prescribed with Chloroquine (1)
Mefloquine [Lariam]	1.2	14.0	250mg once weekly
Atorvoquone and Proguanil (Malarone)	1.6	3.0	100mg proguanil/250mg atovaquone daily
Doxycycline	9.4	16.2	100mg once daily

Note: (1) Proguanil is not prescribed on its own as malaria chemoprophylaxis, it is prescribed with Chloroquine. Therefore the amount of Chloroquine tablets has been used to calculate doses.⁹

Roche guidelines and the Advisory Committee on Malarial Prevention

10. Roche, the manufacturer of Lariam, issues guidance which accompanies the drug. In its written evidence, Roche explained that the information includes:

A guide for healthcare professionals; a regular reminder letter about the risk management materials to all relevant healthcare professionals responsible for prescribing Lariam; a prescriber checklist (for example, asking if the patient has ever suffered from any neuropsychological conditions); a patient alert card; and a patient information leaflet (included in every packet).¹⁰

Roche explained to us that the information was provided to “aid compliance with warnings about risks, and to ensure patients are more aware of the neuropsychiatric side-effects and to react promptly when these occur”.¹¹

11. In addition to this guidance, Roche set out clearly in evidence the following conditions for the use of Lariam:

Lariam must not be used in patients with specific pre-existing conditions or ‘contra-indications’.

This includes a clear warning that it must not be used as a prophylactic “in patients with active or a history of psychiatric disturbances such as depression, anxiety disorders,

9 Ministry of Defence, [Ad Hoc Statistical Bulletin: Mefloquine Hydrochloride prescribing in the UK Armed Forces, 1 April 2007–31 March 2015, 12 January 2016](#)

10 Roche ([LAR0001](#))

11 Roche ([LAR0001](#))

schizophrenia or other psychiatric disorders”.¹² Dr Frances Nichol, Head of Drug Safety and Quality at Roche, said that this guidance was “a required document that the prescribing physician should be familiar with”.¹³

12. In addition to these conditions of use, the Roche guidance states that an individual risk assessment is required before Lariam is prescribed. In order to assist the assessment, Dr Nichol told us that the expectation was that a physician would see “every individual prior to prescribing any drug that sits under the legal classification”.¹⁴ Mike Kindell, Lead, Established Products at Roche reiterated the requirement that every individual should have “a proper assessment”.¹⁵ As part of that assessment, Dr Nichol said that the expectation would be that the prescribing doctor would have “a detailed consultation in terms of looking at the patient’s existing medical history, asking them, talking through the risks of any of the products that you would be considering prescribing”.¹⁶

13. According to Dr Nichol, if the individual risk assessment were not conducted, the prescription of Lariam would be “outside of the terms of the summary of product characteristics”.¹⁷ She concluded that if that had not been carried out by an organisation, it fell short of the clear expectation to do so.¹⁸

Advisory Committee for Malarial Prevention

14. In addition to the guidelines set out by Roche, the MoD also takes advice on the use of Lariam from the Advisory Committee for Malarial Prevention (ACMP) through Public Health England.¹⁹ The ACMP is described as an expert committee, established to formulate guidelines on malaria prevention in the UK. Guidelines issued by the ACMP are used by “medical professionals and other travel medicine advisors based in the UK and many other countries”.²⁰ The ACMP regularly updates its guidance to reflect new research. Its most recent guidelines on the use of Lariam, issued in September 2015, state that, in addition to the manufacturer’s advice, a stringent risk assessment is required before Lariam is prescribed and that Lariam should not be provided to individuals with the following conditions:

- Hypersensitivity to quinine or quinidine;
- A current or previous history of depression, generalized anxiety disorder, psychosis, schizophrenia, suicide attempts, suicidal thoughts, self-endangering behaviour or any other psychiatric disorder, epilepsy or convulsions of any origin. The risk of epilepsy and serious mental health disorders is higher in first degree relatives of those in whom these conditions have been diagnosed so they should be considered as part of the risk assessment.
- A history of Blackwater fever; and
- Severe impairment of liver function.²¹

12 Roche ([LAR0001](#))

13 [Q14](#)

14 [Q15](#)

15 [Q79](#)

16 [Q17](#)

17 [Q11](#)

18 [Q16](#)

19 Ministry of Defence ([LAR0013](#))

20 [Advisory committee on malaria prevention \(ACMP\) website](#), Gov.uk, accessed 11 May 2016

21 Public Health England, [Guidelines for malaria prevention in travellers from the UK 2015, September 2015](#)

The ACMP's guidance also highlighted the need to use a checklist to ensure that proper screening is undertaken prior to the prescription of Lariam.²²

15. The ACMP's 2015 guidance stated that it was "not aware of any new data on side-effects" since its 2014 update, but made clear that "attention has focused on neuropsychiatric problems and vestibular disorders" related to Lariam use. It concluded that while there was "no evidence that mefloquine use increases the risk of first-time diagnosis of depression" Lariam could "increase the risk of psychosis and anxiety reactions".²³

Use of guidance on Lariam by the Ministry of Defence

16. While the accuracy of the ACMP guidance was not disputed, some of our witnesses questioned its value in advising for its use in a military setting. Lt. Col. Marriott, a former soldier and campaigner against the MoD's use of Lariam, argued that while the ACMP could provide "very general guidance" it was not appropriate for "the specific conditions under which military forces are required to deploy".²⁴ He went on to argue that, in his opinion, there was "a great deal in the ACMP guidelines that would be quite incompatible with the conduct of military operations".²⁵

17. The MoD does have representation on the ACMP but Trixie Foster, another campaigner against the use of Lariam, cited Dr Hilary Kirkbride, a consultant epidemiologist and Public Health England representative on the Advisory Committee, who cast doubt on the effectiveness of that representation. In response to a letter from Ms Foster, Dr Kirkbride wrote that the ACMP was:

Not responsible for providing advice on malaria prevention to the military, and therefore I regret that we are unable to make specific comments in relation to the use of mefloquine in troops.²⁶

18. That position was confirmed by the MoD in its written evidence:

While there has been a military representative on the ACMP since 1993, the ACMP does not give specific advice to the Armed Forces. The MoD therefore uses ACMP guidance to make a risk assessment for the different areas of the world in which we operate, and prescribes prophylaxis taking into account an individual's medical history and any past history of side-effects.²⁷

19. In oral evidence, Brigadier Timothy Hodgetts CBE, Medical Director, Defence Medical Services, defended the MoD's use of ACMP guidance. He argued that there was "no body of evidence to suggest that a non-immune UK civilian traveller is any different to a non-immune UK military traveller in terms of how they will react to individual drugs".²⁸ The Minister reiterated that view stating that the MoD did not believe that members of the Armed Forces were significantly different from normal travellers.²⁹

22 Public Health England, [Guidelines for malaria prevention in travellers from the UK 2015, September 2015](#)

23 Public Health England, [Guidelines for malaria prevention in travellers from the UK 2015, September 2015](#)

24 [Q98](#)

25 [Q98](#)

26 [Q99](#)

27 Ministry of Defence ([LAR0013](#))

28 [Q165](#)

29 [Q176](#)

20. The MoD also highlighted to us what it believed to be a similar approach by the US Centres for Disease Control (CDC) Yellow Book, which offers public health advice to US citizens. The MoD describes the CDC advice on Lariam as “less proscriptive” than that of the ACMP and cited the following paragraph:

For destinations where chloroquine-resistant malaria is present, in addition to mosquito avoidance measures, chemoprophylaxis options are atovaquone-proguanil, doxycycline, and mefloquine.³⁰

The MoD concluded that Lariam was therefore “considered by US CDC to be equally suitable (with an individual clinical assessment) as each of the other drugs”.³¹

21. This was disputed by a number of our witnesses. Dr Remington Nevin, a consulting physician epidemiologist and former US Army preventive medicine officer, believed that the MoD’s assessment of the CDC advice as a “misinterpretation of CDC’s position”.³² He told us that the CDC stated clearly that “there should be special considerations for US military deployments” and that the continued routine use of Lariam was “less desirable” for military personnel.³³ Dr Jane Quinn, a research neuroscientist and toxicologist at Charles Sturt University, Australia, also highlighted the fact that the CDC distinguished between civilian and military personnel.³⁴ Dr Croft, a consultant public health physician and medical epidemiologist and former Army medical officer, also believed there was a significant difference between military and civilian travellers and concluded that it was “imperative” that anti-malarial policies specific for travelling military populations were developed and that they did not “slavishly follow civilian guidelines”.³⁵

22. Chapter 8 of the CDC—Special Considerations for US Military Deployments—states that the military should be considered “a special population with demographics, destinations, and needs that may differ from those of civilian travelers”. While it is directed at the US military it states that “the concepts may be applicable to other militaries”.³⁶

23. 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 Centers for Disease Control and Protection’s Yellow Book.

Effectiveness of Lariam: Geography

24. In oral evidence, Mark Lancaster MP TD, Minister for Veterans, told us that there was “no single anti-malarial that is effective for all the various and different strains, and nor is there a single anti-malarial that is 100% effective or does not have any side-effects”.³⁷ Surgeon General, Vice Admiral Walker explained that the assessment of which drug to

30 [Response from the Secretary of State to the Chairman, 21 September 2015](#)

31 [Ministry of Defence \(LAR0013\)](#)

32 [Q136](#)

33 [Q136](#)

34 [Dr Quinn \(LAR0025\)](#)

35 [Dr Croft \(LAR0027\)](#)

36 [Centers for Disease Control and Prevention, *Yellow Book*, Chapter 8](#)

37 [Q152](#)

prescribe was based on a variety of factors, including “the person’s ability to take the drug and their geographical location”.³⁸ In its *Ad Hoc Statistical Bulletin*, the MoD confirmed that the choice of which drug was used depended on the region to which personnel were being deployed and the individual’s medical history—for example, past history of side-effects or contra-indications to the drug.³⁹

25. When we took oral evidence from Dr Nevin and Dr Croft, both of them were clear that there were no geographical areas where Lariam would be a more effective drug. Moreover, Dr Nevin stated that Lariam was less effective than the alternatives:

There is no area of the world where mefloquine is, or should be, the preferred drug. There are vast areas of the globe where there is resistance to Lariam. Contrast that with the other two medications that are commonly used—Doxycycline and Malarone. There is no resistance anywhere to doxycycline, and that drug can be administered for deployments worldwide, beginning a few days prior to deployment. The drug is fairly well tolerated. Similarly, there is no reliable, widespread report of resistance to Malarone anywhere.⁴⁰

In its written evidence, Roche confirmed that resistance to Lariam has been identified in areas of Thailand, Myanmar and Cambodia.⁴¹

26. When pressed on the matter, the Surgeon General acknowledged that there was “no geographical area” where Lariam was “absolutely essential” and that it was needed only for those individuals who could not take alternative treatments.⁴²

27. *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.*

Publication of statistics

28. The Ad Hoc Statistical Bulletin referred to earlier in this chapter was published by the Ministry of Defence on 12 January 2016, the morning of our evidence session with the Minister. This gave us no time to consider the information in advance. When questioned on the timing, the Minister stated that it was “simply unfortunate” and was due to the fact that Defence Statistics—an agency of the MoD—enjoyed “a degree of independence”.⁴³ According to the Bulletin, the rationale for the publication was “in response to the recent media coverage on the prescribing of [Lariam] in the UK Armed Forces”.⁴⁴ Given the fact that these media reports included coverage of our inquiry, we would have expected the MoD to provide us with this information in advance of our evidence session.

38 [Q155](#)

39 Ministry of Defence, *Ad Hoc Statistical Bulletin: Mefloquine Hydrochloride prescribing in the UK Armed Forces, 1 April 2007 – 31 March 2015*, 12 January 2016

40 [Q140](#)

41 Roche ([LAR0001](#))

42 [Q157](#)

43 [Q146](#)

44 Ministry of Defence, *Ad Hoc Statistical Bulletin: Mefloquine Hydrochloride prescribing in the UK Armed Forces, 1 April 2007–31 March 2015*, 12 January 2016

29. 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.

3 Individual risk assessments

Guidelines and policy

30. In the previous section we set out Roche’s clear statement that an individual risk assessment was required before Lariam is prescribed. During the course of this inquiry, we explored the extent to which the Ministry of Defence (MoD) has followed this guidance. In its written evidence, the MoD set out its prescribing policy for Lariam and how those guidelines have been implemented:

Since 2004–05 Defence policy has endorsed [Lariam] to be prescribed, with an implied accompanying risk assessment. In 2013, with the formation of the Defence Primary Healthcare (DPHC) organisation, HQ DPHC has been responsible for ensuring that this policy has been followed. Prior to April 2013 the single Services were responsible for the provision of primary care and the procedures for prescribing [Lariam].⁴⁵

31. Brigadier Timothy Hodgetts CBE, Medical Director, Defence Medical Services explained to us that there were two methods of prescribing Lariam. The first was to conduct an “individual face-to-face consultation” which was what the MoD deemed to be a prescription. The second was an “authorised” patient-specific directive, whereby the individual clinician would “conduct a risk assessment from the patient’s notes” which recognised “other safeguards such as the medical employment standards and the fact that we know our people within our individual units”.⁴⁶ In oral evidence the Minister sought to clarify that statement saying that “by following the policy, the implication is that a risk assessment will have been carried out”.⁴⁷ However, Dr Nevin was of the view that an individual risk assessment clearly implied “a lengthy, face-to-face consultation between a patient, and the patient’s prescribing physician”.⁴⁸ He went on to argue that “simply checking the patient’s notes does not constitute an individual risk assessment”.⁴⁹

32. A number of our witnesses painted an altogether different picture of MoD practice. Lt. Col. (Retd) Marriott, a campaigner against Lariam, argued that for many years, the MoD’s policy on Lariam was one of “dispensing a stock drug rather than one of prescription”.⁵⁰ In his written evidence, he argued that, until at least 2012:

Anti-malarials have been administered for deployments to Sub-Saharan Africa, Belize and Afghanistan by medically unqualified personnel such as senior and junior NCOs, and without appropriate reference to individual medical records.⁵¹

He also suggested that anecdotal evidence he had received indicated that “at least until two years ago, the drug was routinely handed out by people such as Company Sergeant Majors who would not be medically qualified at all”.⁵²

45 Ministry of Defence ([LAR0013](#))

46 [Q164](#)

47 [Q168](#)

48 Dr Nevin ([LAR0027](#))

49 Dr Nevin ([LAR0027](#))

50 Lt Col (Retd) Marriott ([LAR0023](#))

51 Lt Col (Retd) Marriott ([LAR0023](#))

52 [Q102](#)

33. Dr Croft, writing in the *Pharmaceutical Journal*, a Royal Pharmaceutical Society publication, argued that rather than being prescribed after an individual risk assessment, Lariam had been “handed out on the parade ground by the medical sergeant, along with other tropical kit”.⁵³ Dr Croft also provided us with the following anecdotal evidence:

We keep hearing from soldiers—there have been some written submissions to this effect—who say, “I turned up for my pre-deployment equipment, which would include the tropical uniform, the mosquito net, the sunscreen and the packet of malaria tablets,” and that was it.⁵⁴

In his opinion, this approach was “pretty much standard, even now”.⁵⁵

34. During our inquiry, we received written evidence from a number of individuals which appears to support this view. Paul Shephard MBE told us that he had been given Lariam on numerous occasions on deployment between May 1996 and Summer 2002. He stated that he “wasn’t provided with any warning on side-effects other than being told to read the instructions enclosed in the tablet box” and that beyond advice on the appropriate length of time to take Lariam he was given “no other information and no risk assessment was undertaken”.⁵⁶

35. In oral evidence, the Surgeon General told us that while he was convinced that the policy of individual risk assessments was being adhered to, he could not give a “100% guarantee” that it had happened in every case.⁵⁷ The reason given was that reviewing every case would require “a disproportionate undertaking, requiring significant diversion of Defence medical resources from existing priorities, and without a clear health benefit outcome”.⁵⁸

36. Of more concern was the fact that the Surgeon General was unable to confirm that individual risk assessments had taken place since he took over responsibility from the single services. While he said that the procedures put in place since 2013 should prevent prescription without an individual risk assessment, he was unable to give “a 100% guarantee about every single person”.⁵⁹

37. When we asked the Minister if one-to-one interviews would be conducted in the future, he gave an equivocal response:

Hopefully, as has been demonstrated, this is always an evolving process, but I am confident, as the Surgeon General has stated, that since 2013 when the Defence Primary Health Care organisation was formed, we have had much stricter guidelines and the electronic system automatically flags up the process. So I am confident that we are in a much better place post-2013 than perhaps we were under the single service regimes. Certainly I am determined to continue to make sure that this process evolves and improves—this is an ongoing process.⁶⁰

53 Dr Croft, ‘Mefloquine, madness and the Ministry of Defence’, *The Pharmaceutical Journal*, 12 November 2015

54 [Q108](#)

55 [Q108](#)

56 Mr Shephard ([LAR0009](#))

57 [Q186](#)

58 Ministry of Defence ([LAR0013](#))

59 [Q187](#)

60 [Q191](#)

38. *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.*

39. *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.*

Obstacles to individual risk assessments

40. During the course of our inquiry, we questioned our MoD witnesses on the practicality of prescribing Lariam—with the required face-to-face interviews—to a large number of troops. Brigadier Hodgetts acknowledged that the preferred way of prescribing anti-malarials was to have such a consultation, but that there remained the opportunity to conduct “a patient-specific directive if at very short notice a large number of people needed to be deployed”.⁶¹

41. A number of our witnesses questioned the practicality of conducting individual risk assessments prior to deployment. Dr Nevin highlighted “numerous challenges” which were encountered by military physicians in prescribing Lariam in a manner that was “fully compliant with the product documentation warnings and precautions”.⁶² Trixie Foster believed that any policy of individual risk assessments for a taskforce of troops was “unrealistic due to the time it would take for a Battalion (approximately 700 personnel) to be assessed individually”.⁶³ This was also the view of Dr Croft, who argued that it was:

wholly implausible that such individual risk assessments could be carried out, because the scale of the operation would be enormous. It would take at least half an hour to conduct a detailed risk assessment, and we are talking about hundreds of troops deploying at short notice. There just would not be the time before a major deployment for such an exercise to occur.⁶⁴

42. Dr Quinn also questioned the practicality of prescribing the drug to a large number of military personnel:

The likelihood of such stringent prescribing practices being adhered to where the workplace requires large numbers of personnel to be administered a drug

61 [Q189](#) and [Q190](#)

62 Dr Nevin ([LAR0007](#))

63 Mrs Foster ([LAR0011](#))

64 [Q104](#)

in a short period of time prior to deployment, and the difficulty of carrying out appropriate health monitoring during deployment and after deployment, make the use of Lariam for military personnel at best highly problematic or worst, simply impossible.⁶⁵

43. *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.*

44. *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.*

Concealing contra-indications

45. Earlier in this Report, we highlighted Roche guidance which included the clear warning that Lariam must not be prescribed to individuals with an “active or a history of psychiatric disturbances such as depression, anxiety disorders, schizophrenia or other psychiatric disorders”.⁶⁶ Face-to-face interviews play a vital part in identifying these contra-indications, but there remains the risk that patients may try to hide aspects of their medical history which would disqualify them from receiving medicine.

46. Dr Nevin told us that this was a clear risk in the military and that, unfortunately, not even the “fairly stringent process” of individual risk assessments had prevented the inappropriate prescribing of Lariam to service members with contra-indicating medical conditions.⁶⁷ Research that he had conducted with the US Army in 2007 had shown that one in seven US Service personnel with contra-indications had still been prescribed Lariam. More disturbingly, Dr Nevin said that the rate of inappropriate prescribing of Lariam had increased “threefold” in subsequent years since restrictions were placed on its use.⁶⁸ Dr Nevin concluded that “service members simply do not want to report or admit that they may have one of the conditions listed in the product insert that is a contra-indication to the use of the drug”.⁶⁹

47. When he gave evidence, Surgeon Captain Sharpley, Defence Consultant in Psychiatry, agreed that non-reporting of contra-indications was a “completely appropriate concern” because individuals reacted to psychiatric side-effects in a different way from physical side-effects. He was also clear that it was not always possible to “stop someone from hiding something if they feel that the risk of revealing this outweighs the risk of hiding it”.⁷⁰ However, he believed that this risk was mitigated by the high level of trust in which doctors—and military doctors in particular—were held. Captain Sharpley concluded that:

65 Dr Quinn ([LAR0025](#))

66 Roche ([LAR0001](#))

67 [Q106](#)

68 [Q106](#)

69 [Q109](#)

70 [Q193](#)

As long as the GPs who are doing the risk assessment ask in an appropriate way for the history—of course they will be looking at the record as well, if the history exists there—we will have done the best we can to make sure that that prescription is safe.⁷¹

48. However, in supplementary evidence, Dr Nevin restated the fact that, in his experience, “service members remain strongly motivated to under-report potentially disqualifying mental health conditions, including those that may be formally undiagnosed or undocumented”.⁷²

49. Dr Quinn, in written evidence, also highlighted a number of studies which, she argued, demonstrated the problems with reliable self-reporting. Dr Quinn argued that non-reporting or under-reporting of mental health issues was “a significant confounding factor in the use of [Lariam] in the military because of “institutional stigma, and/or perceptions of workplace disadvantage” which included not being deployed and possible barriers to promotion. Dr Quinn believed that the available evidence pointed to a higher incidence of under-reporting:

Together this evidence suggests that the incidence of pre-existing conditions which would be clear contra-indications for prescription of [Lariam] are significantly higher in the military than has been previously suggested, with significant implications for the health and wellbeing of those involved.⁷³

50. 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.

Non-use of prescribed Lariam

51. A number of our witnesses reported that some military personnel prescribed Lariam took the decision not to use it. Lt. Col. (Retd) Marriott told us that in his experience, the fear of the side-effects of Lariam was causing personnel to discard their medication with “significant numbers [preferring] the risk of contracting malaria to the risk of Lariam toxicity”.⁷⁴ Mrs Duncan, whose husband Major General A D A Duncan CBE DSO, suffered severely from the side-effects of Lariam, also wrote that she had heard reports of personnel “throwing the tablets away”.⁷⁵

52. John Paul Aisbitt, who was deployed to Sierra Leone, asserted that members of his team had “simply stopped taking [Lariam] during their tour, preferring the risk of malaria to the effects and associated risk of continuing with its use”.⁷⁶ That experience was repeated by Mark Iles during his deployment to Sierra Leone:

71 [Q193](#)

72 Dr Nevin ([LAR0027](#))

73 Dr Jane Quinn ([LAR0010](#))

74 Lt Col (Retd) Marriott ([LAR0006](#))

75 Mrs Duncan ([LAR0014](#))

76 Mr Aisbitt ([LAR0017](#))

I was given Lariam at the RTMC (Chilwell) upon my call-out but like some other Reservists with experience of working overseas I did not take it and used tablets purchased locally in Freetown. I recall that a number of our loan service IMATT personnel in Sierra Leone did similar.⁷⁷

53. The Minister told us that he was aware of such reports and that it was “probably the case that historically, some people may well have thrown away their drugs and not taken them”.⁷⁸ He acknowledged that it is “nigh on impossible” to force military personnel to take the tablets and argued that educating them on the risks of not taking medication was the solution.⁷⁹ Surgeon Vice Admiral Walker explained that this education and information included “posters and signs” on the dangers of malaria and that, once deployed, medical staff would remind personnel of the importance of taking the drugs prescribed to them.⁸⁰

54. 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.

Choice and an opt-out

55. During the evidence session with the Minister, it was suggested that, alongside clearer labelling of the risks associated with Lariam, military personnel should be offered the option of requesting an alternative anti-malarial drug. In response, Surgeon Vice Admiral Walker declared that he was “happy to use that as part of the risk assessment with the patients”.⁸¹ This suggestion also found favour with Dr Nevin who described it as “a low-cost, sensible suggestion” which if implemented would “enhance patient choice, and patient safety”.⁸²

56. 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.

77 Mr Iles ([LAR0002](#))

78 [Q195](#)

79 [Q195](#)

80 [Q196](#)

81 [Q212](#)

82 Dr Nevin ([LAR0027](#))

4 The side-effects of Lariam

Introduction

57. The MoD’s policy for dealing with military personnel who have suffered from detrimental side-effects of using Lariam is threefold. The first is to “recognise and tolerate minor side-effects”,⁸³ and with the patient’s agreement, to continue with the treatment if there is “no other credible pharmaceutical option and the clinical risk of the disease outweighs the side-effect demonstrated”. Should that not prove to be a satisfactory option, then the patient would be prescribed an alternative.⁸⁴

58. Should the side-effects be more severe the prescription would be stopped “immediately” and, a “credible alternative” would be offered. If no alternative were suitable, it would be explained to the patient that providing no therapy was “in the better interests of the patient than experiencing the side-effect”.⁸⁵ This, however, would be “a last resort” because of “the serious nature and the high probability of infection”.⁸⁶

59. In the most extreme cases, the prescription of Lariam would be stopped immediately alongside “life-saving therapy” in the case of anaphylactic reaction to the drug.⁸⁷

Military specific

60. In the previous chapter, we set out the MoD’s assertion that there was “no body of evidence to suggest that a non-immune UK civilian traveller is any different to a non-immune UK military traveller in terms of how either will react to individual drugs”.⁸⁸ However, Dr Nevin and Dr Croft both argue that the specific role of the Armed Forces is incompatible with the use of Lariam.

61. In his paper *Rational Risk-Benefit Decision-Making in the Setting of Military Mefloquine Policy*, Dr Nevin sets out a number of risks attached to the use of Lariam in a military setting. He asserts that, despite the acknowledged importance of sleep hygiene in a military setting, Lariam “adversely alters patterns of dreaming and significantly reduces overall sleep duration”.⁸⁹ Disturbed sleep—including insomnia and abnormal dreaming—was described as “very common” and Dr Nevin cautioned that:

Vivid nightmares, described occasionally as having “technicolor clarity” are not benign and should be considered contra-indications to the drug’s further use.⁹⁰

62. Dr Nevin argued that these side-effects had a “potentially negative impact [...] on military performance and military operations” and cited case reports of deployed Service personnel experiencing “episodes of panic resulting in abnormal behaviour”

83 Ministry of Defence ([LAR0013](#))

84 Ministry of Defence ([LAR0013](#))

85 Ministry of Defence ([LAR0013](#))

86 Ministry of Defence ([LAR0013](#))

87 Ministry of Defence ([LAR0013](#))

88 [Q165](#)

89 Dr Remington Nevin, ‘[Rational Risk-Benefit Decision-Making in the Setting of Military Mefloquine Policy](#)’, *Journal of Parasitology Research*, Volume 2015 (2015)

90 Dr Remington Nevin, ‘[Rational Risk-Benefit Decision-Making in the Setting of Military Mefloquine Policy](#)’, *Journal of Parasitology Research*, Volume 2015 (2015)

and of incidents of Servicemen becoming confused and found “wandering aimlessly”. More disturbingly, Dr Nevin also highlighted subclinical effects among Service personnel including instances of increased “tension” and “anger”.⁹¹

63. A number of contributors to our inquiry described similar symptoms. John Paul Aisbitt, wrote to us about his experience of taking Lariam when he was deployed to Sierra Leone. The side-effects he says he experienced included:

- episodes of severe mental and physical exhaustion and nausea;
- severely broken sleep patterns; nightly periods of insomnia interspersed with hallucinogenic dreams; and
- significant lapses of concentration and short term memory loss.⁹²

Mr Aisbitt also said that he had suffered from “extreme mood swings and episodes of poor judgement” which he described as being “sudden and prolonged events, often resulting in uncharacteristic, unpredictable outbursts of verbally and physically aggressive behaviour”.⁹³

64. In a similar vein, Colin Swift’s written evidence described his experience of taking Lariam while deployed to Kinshasa in 1997. Mr Swift said that he had had “difficulty sleeping and fatigue non-consistent with my duties”, and had experienced “vivid and dark dreams”.⁹⁴ A third example was provided to us by Mrs Ellen Duncan, whose husband Major General A D A Duncan CBE DSO, suffered severely from the side-effects of Lariam. Mrs Duncan wrote of anecdotal evidence that military personnel described the days after taking Lariam as “‘Mad Monday’, or ‘Crazy Tuesday’”.⁹⁵

65. Lt. Col (Retd) Marriott believed that the use of Lariam was “quite incompatible with the conduct of military operations”.⁹⁶ He told us that in his experience “between 25% and 35% of personnel” who had been prescribed Lariam on deployment, experienced side-effects that would not be acceptable in any operational setting.⁹⁷

66. Dr Jane Quinn, has undertaken a number of studies into the use of Lariam by military personnel. In written evidence Dr Quinn stated that “higher rates [of adverse side-effects] have been reported in deployed Service personnel with the suggestion that the unique stressors of military operations may contribute to this effect”.⁹⁸ She concluded that Lariam was “broadly incompatible with military operations due to the reported high incidence of adverse reactions, particularly in military personnel”.⁹⁹

67. In oral evidence, Dr Nevin set out his concerns about the use of Lariam in a military setting:

In military settings there are many reasons why someone may develop insomnia, nightmares, anxiety, so it is very tempting for military clinicians who

91 Dr Remington Nevin, ‘Rational Risk-Benefit Decision-Making in the Setting of Military Mefloquine Policy’, *Journal of Parasitology Research*, Volume 2015 (2015)

92 John Paul Aisbitt (LAR0017)

93 John Paul Aisbitt (LAR0017)

94 Mr Swift (LAR0012)

95 Mrs Duncan (LAR0014)

96 Lt Col (Retd) Marriott (LAR0006)

97 Q121

98 Dr Quinn (LAR0010)

99 Dr Quinn (LAR0010)

are individual Service members to misattribute potentially these symptoms to the situation, to their deployment, to the stresses of traveller combat and not to the drug. The danger is that if a Service member misattributes their symptoms of insomnia, for example, to travel and not to the drug, they may continue taking [Lariam], contrary to the product insert guidance. And if they have a personal susceptibility, the drug may accumulate to what we think are neuro-toxic levels and they risk the more serious event that is alluded to in the product insert, which we think is neuro-toxicity and the risk of permanent disability. The risk is confounding. The particular use of [Lariam] in military settings risks confounding the prodromal symptoms for situational stresses.¹⁰⁰

68. Lt. Col. Marriott also noted that restrictions on the use of Lariam had been placed on aircrew and deep-sea divers and those operating heavy and dangerous machinery. He argued that similar restrictions should therefore be placed on personnel handling weapons.¹⁰¹

Extreme cases

69. A number of our witnesses also highlighted examples of extreme behaviour by military personnel who were using Lariam. In his written evidence, Lt Col (Retd) Marriott wrote that when he was deployed, he had witnessed “many incidents of irrational and ill-disciplined behaviour far in excess of the norm for a deployed force”. This included:

Acts of violence, ill temper, dangerous driving, confusion, expressions of suicide ideation and other behaviours not expected of officers and SNCOs.¹⁰²

70. In his paper *Mefloquine, madness and the Ministry of Defence*, Dr Croft drew attention to a number of “military atrocities” carried out by Service personnel which he attributed to Lariam. They included:

- 1993: Canadian peacekeepers beat, tortured and shot two local teenagers in Somalia;
- 2002: Four US soldiers “killed their wives” at Fort Bragg, North Carolina; and
- 2012: A member of the US Special Forces who “killed 16 Afghan civilians”.¹⁰³

71. In its evidence, the MoD rejected these claims.¹⁰⁴ In respect of the example of Canada, the MoD noted that assertions that Lariam was a “causal factor” in serving personnel accused of War Crimes in Somalia had been “discredited”.¹⁰⁵ The MoD also noted that there was believed to be “no evidence” of association with Lariam use in cases of criminal activity in the US Armed Forces.¹⁰⁶ Furthermore, the MoD claimed that a review in 2015 of extant US policies and findings of DoD [Department of Defense] investigations into putative links between Lariam use and suicides of Servicemen had found “no links”.¹⁰⁷

100 [Q125](#)

101 [Q127](#)

102 Lt Col (Retd) Marriott ([LAR0006](#))

103 Dr Croft, '[Mefloquine, madness and the Ministry of Defence](#)', *The Pharmaceutical Journal*, 12 November 2015

104 Ministry of Defence ([LAR0013](#))

105 Ministry of Defence ([LAR0013](#))

106 [Response from the Secretary of State to the Chairman, 21 September 2015](#)

107 [Response from the Secretary of State to the Chairman, 21 September 2015](#)

72. In supplementary evidence, Dr Nevin challenged the MoD's assessment of these cases. In the example of Canada, he wrote that the mitigation of Lariam had not been "discredited" and that the Commission of Inquiry had stated in its report that it was "not able to explore fully" the possible impact of Lariam as that "would have required additional hearings dedicated specifically to the issue, which time did not permit". Additionally, Dr Nevin highlighted the fact that the Commission concluded that

If [Lariam] did in fact cause or contribute to some of the misbehavior that is the subject of this Inquiry, [Canadian Forces] personnel who were influenced by the drug might be partly or totally excused for their behavior.¹⁰⁸

73. 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.

MoD support for those who have suffered adverse effects

74. Both Roche and the ACMP have acknowledged that for some, the side-effects of Lariam can be severe. Earlier in this Report, we set out the list of contra-indications which must be considered before Lariam is prescribed.¹⁰⁹ The MoD has a stated policy for dealing with military personnel who have suffered severe side-effects of using Lariam. The MoD told us that there were "established processes" by which current and former members of the Armed Forces could have their cases investigated in confidence by the MoD and encouraged those who had not already done so to "request investigation so their specific concerns can be addressed".¹¹⁰ Whilst this may be the case, those processes did not seem clear to us.

75. The Surgeon General told us that veterans were advised either to approach their GPs and ask to be referred back to the MoD for further assessment or to contact the Medicines and Healthcare Products Regulatory Agency, while serving personnel were advised to contact their medical officer.¹¹¹ Surgeon Vice Admiral Alasdair Walker confirmed to us that:

If they are a serving member or a Reservist, it would be through their medical officer and taken that way. If it is a veteran who has left the services, it would be through their GP.¹¹²

76. In written evidence, Dr Quinn, believed that a more systematic approach should be established and recommended the creation of an "outreach programme" to provide information, support and treatment for those affected by exposure to Lariam during military service.¹¹³

108 Dr Nevin ([LAR0022](#))

109 See Chapter 2: MoD use of Lariam.

110 Ministry of Defence ([LAR0013](#))

111 [Q150](#)

112 [Q151](#)

113 Dr Quinn ([LAR0010](#))

77. 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 through 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.

5 Research undertaken on Lariam

General research into Lariam

78. In its response to the Committee’s ‘Topical Letter’ the MoD highlighted the fact that while there have been a number of studies into Lariam in respect of civilian patients, conducting studies of a similar scale on Service personnel would be “unfeasible”.¹¹⁴ The MoD said that, instead, it would continue to rely on the “expert advice and direction” provided by the ACMP and the opinion of international expert bodies including the World Health Organisation and the Centre for Disease Control.¹¹⁵

79. In evidence, the MoD also cited a number of studies of the use of Lariam by military personnel which evaluated the relative occupational impact of side-effects experienced by service personnel. These included:

- a 2012–13 study of soldiers in Kenya, which according to the MoD, identified that more doxycycline users reported that one or more adverse effects had interfered with their ability to do their job than Mefloquine users; and
- a 2015 audit of Lariam during Operation HERRICK,¹¹⁶ which identified that 5.8% of Mefloquine prescriptions were unjustified because of an existing contra-indication, two patients experienced avoidable side-effects requiring the drug to be withdrawn; and 2.46% of personnel experienced documented side-effects.¹¹⁷

80. In both its response to the Committee’s letter to the Secretary of State and in its written evidence, the MoD also refer to a 1997 study on Lariam undertaken by Dr Croft. The MoD highlights Dr Croft’s conclusion which stated that “the incidence of putative side-effects [of Lariam] was not significantly different between the groups” and that the results “support evidence which indicates that mefloquine is no more toxic than chloroquine-proguanil”.¹¹⁸

81. When we took oral evidence from Dr Croft he gave a different view on his work on Lariam in the British Army. Dr Croft told us that he had conducted two successive randomised control trials—double blind trials—of mefloquine in British soldiers which compared mefloquine with the combination of chloroquine and proguanil. In those trials, Dr Croft found that a third of Lariam users reported no side-effects at all; a third had very minor side-effects, and a third had very severe side-effects, which interfered with their daily life and were intolerable.¹¹⁹

82. Dr Croft explained that the second trial had two “extreme, unpredictable events”; one soldier became “psychotic” and another had “committed suicide” as the trial was ending.¹²⁰ Although Dr Croft was not part of the trial at that point he believed the death to be “related” to Lariam. He argued that although Lariam, as with other drugs had a “level

¹¹⁴ [Response from the Secretary of State to the Chairman, 21 September 2015](#)

¹¹⁵ [Response from the Secretary of State to the Chairman, 21 September 2015](#)

¹¹⁶ Operation HERRICK was the name given to British operations in Afghanistan.

¹¹⁷ Ministry of Defence ([LAR0013](#))

¹¹⁸ Ministry of Defence ([LAR0013](#))

¹¹⁹ [Q121](#)

¹²⁰ [Q121](#)

of background traffic noise” the difference was that Lariam had the potential to cause “extreme, unpredictable, completely out-of-character events such as psychoses, violence and disciplinary offences in soldiers who often have unblemished records”.¹²¹

83. A more recent study on Lariam was conducted by the Royal Naval Medical Service in 2013. The study, entitled *The adverse effects of mefloquine in deployed military personnel*, covered 150 deployed military personnel with the objective to assess the rate of adverse reactions. Of the 111 individuals prescribed Lariam who responded, “54% reported at least one adverse effect and 13% required a change in prescription to a second-line anti-malarial due to significant side-effects. All females prescribed [Lariam] reported at least one adverse reaction. There were two cases of clinically significant adverse reactions”. The Report concluded that:

There was a higher rate of adverse events reported amongst deployed military personnel than has been reported among civilian patients. This may be partly due to the stressful environment in which deployed personnel operate.¹²²

84. The MoD noted this research in its written evidence but described it as an “uncontrolled observational study conducted by a junior Medical officer”.¹²³ The MoD concluded that while adverse effects attributed to Lariam were noted, it was “impossible to draw any firm conclusions” from the study in the absence of comparative data from people taking either alternative drugs or a placebo.¹²⁴

85. The MoD have stated that it was planning “a prospective audit” of the side-effect profile of mefloquine;¹²⁵ and was also planning:

an additional study to compare malarone with mefloquine in a similar exercise population in Kenya. The protocol is currently being prepared for ethics submission by the MoD Research Ethics Committee.¹²⁶

86. 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.

121 [Q121](#)

122 [Journal Royal Naval Medical Service 2014, Vol 100.3](#)

123 Ministry of Defence ([LAR0013](#))

124 Ministry of Defence ([LAR0013](#))

125 [Response from the Secretary of State to the Chairman, 21 September 2015](#), para 9

126 [Response from the Secretary of State to the Chairman, 21 September 2015](#), para 10

6 Comparisons with the use of Lariam by other States

87. Our inquiry also covered the use of Lariam in comparison with other nations' Armed Forces. In written evidence, the MoD provided the following table setting out the use of Lariam by NATO allies and others¹²⁷:

Country	Use of Lariam
Denmark	Mefloquine offered but Malarone and doxycycline preferred.
Germany	Mefloquine offered but Malarone and doxycycline preferred.
Netherlands	Mefloquine offered but Malarone preferred.
France	Mefloquine offered but doxycycline preferred.
Czech Rep	Mefloquine offered. (Supplies are imported as an exception).
Slovakia	Mefloquine offered.
Sweden	Mefloquine offered. No general restrictions on its use.
Belgium	Mefloquine offered but Malarone and doxycycline preferred.

88. While this provides a headline account of the use of Lariam, our witnesses painted a picture of UK policy becoming increasingly divergent from its allies. Dr Nevin argued that the MoD was “increasingly isolated among Western militaries in its continued preferential use of Lariam” and that that “many of our Western allies have all but abandoned the use of the drug”.¹²⁸

89. In a recent interview in the Independent, Dr Croft, claimed that Defence Ministries in Germany, the Netherlands, Denmark and Canada had either banned the use of Lariam completely, or restricted its use to a drug of last resort. In the article he highlighted the fact that:

The French military, although with a large presence in the tropics, has deliberately and sensibly never used the drug, for malaria prophylaxis.¹²⁹

90. In supplementary evidence, Dr Nevin stated that, while the US and Australian militaries continued to prescribe Lariam to military personnel, it was now only used as a drug of last resort, employed “exclusively by those rare service members who cannot tolerate these two safer and equally effective alternatives”.¹³⁰

91. Dr Nevin also highlighted the fact that the US placed restrictions on the use of Lariam in 2009¹³¹ and that in 2013 the US Army Special Operations Command had become the first U.S. military command to prohibit the drug outright.¹³² He declared that it was of “some note” that the US military had declared Lariam a drug of last resort and

127 Ministry of Defence ([LAR0013](#))

128 [Q138](#)

129 '[Lariam: Hundreds of British soldiers suffering from mental illness after being given anti-malarial drug](#)' The Independent, 15 April 2015

130 Dr Nevin ([LAR0007](#))

131 Dr Nevin ([LAR0007](#))

132 Dr Nevin ([LAR0007](#))

that the US Army Special Operations Command had taken the “very wise step of banning it altogether”.¹³³ He concluded by telling us that the reason for the decision was based on “the totality of evidence” presented to the US military”.¹³⁴

92. However, the MoD did not believe that these changes could be considered as “sufficient evidence” to justify a change to its policy.¹³⁵ Brigadier Hodgetts accepted that US Special Forces had now stopped using Lariam, but argued that the change was for administrative rather than clinical reasons.¹³⁶ In addition, he highlighted what he described as another “confounding factor” in that all US service personnel were issued with an antibiotic—moxifloxacin—which “directly interacted with Mefloquine, and could cause abnormal heart rhythms”.¹³⁷

93. In written evidence, Dr Nevin disputed the reasons given by the MoD for the U.S. Army Special Operations Command (USASOC) decision to discontinue its use of Lariam. He said the decision was made “primarily on clinical grounds” and was specifically intended to “decrease the risk of negative drug-related side-effects”. Furthermore, Dr Nevin argued that the policy was informed by “a clinical statement in a publication of the US Centers for Disease Control and Prevention (CDC) that the symptoms caused by [Lariam] may confound the diagnosis of post-traumatic stress disorder and traumatic brain injury, and by the addition of the boxed warning to the approved U.S. drug label advising that side-effects from the drug could be “permanent” or last “years after [Lariam] use”.¹³⁸

94. In respect of France, Surgeon Vice Admiral Walker told us initially that while the French Armed Forces did not use Lariam “routinely” it did have the drug within its “armamentarium”.¹³⁹ He went on to say that this was also the case in Canada and the Republic of Ireland.¹⁴⁰ However, he was unable to provide any details on whether France had actually used Lariam.¹⁴¹

95. In similar vein, Dr Nevin argued that the Australian Defence Force had long “de-prioritised” the use of Lariam on the clinical basis of its known adverse neurological effects and had declared it a “third-line” drug.¹⁴² He acknowledged that both the US and Australian Armed Forces continued to prescribe Lariam but highlighted the fact that it was retained only as ‘drug of last resort’, for use “exclusively by those rare service members who cannot tolerate these two safer and equally effective alternatives”.¹⁴³

96. 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

133 [Q116](#)

134 [Q116](#)

135 [Response from the Secretary of State to the Chairman, 21 September 2015](#)

136 [Q221](#)

137 [Q222](#)

138 Dr Nevin ([LAR0027](#))

139 [Q224](#)

140 [Q226](#)

141 [Q227](#)

142 Dr Nevin ([LAR0027](#))

143 Dr Nevin ([LAR0027](#))

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.

7 Conclusion

97. 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.

98. 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.

99. 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.

100. 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.

Conclusions and recommendations

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)*

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 Centers for Disease Control and Protection's Yellow Book. (Paragraph 23)*
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)*
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)*

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)*
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)

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)*
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)*
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)*
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)*
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 side-effects of Lariam

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)*
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 through 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)

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)

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)

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)

Formal Minutes

Tuesday 10 May 2016

Members present:

Rt Hon Dr Julian Lewis, in the Chair

James Gray

Ruth Smeeth

Johnny Mercer

Rt Hon John Spellar

Mrs Madeleine Moon

Phil Wilson

Jim Shannon

Draft Report (*An acceptable risk? The use of Lariam for military personnel*), proposed by the Chair, brought up and read.

Ordered, That the draft Report be read a second time, paragraph by paragraph.

Paragraphs 1 to 100 read and agreed to.

Summary agreed to.

Resolved, That the Report be the Fourth Report of the Committee to the House.

Ordered, That the Chair make the Report to the House.

Ordered, That embargoed copies of the Report be made available, in accordance with the provisions of Standing Order No. 134.

[Adjourned till Thursday 24 May 2016 at 10.15am

Witnesses

The following witnesses gave evidence. Transcripts can be viewed on the [inquiry publications page](#) of the Committee's website.

Tuesday 10 November 2015

Question number

Dr Frances Nichol, Head of Drug Safety Quality, and **Mike Kindell**, Lead, Established Products, Roche Products Limited

[Q1–91](#)

Tuesday 8 December 2015

Dr Ashley Croft, **Mrs Trixie Foster**, Lieutenant Colonel (Retired) **A G Marriott MBE**, and **Dr Remington Nevin**

[Q92–144](#)

Tuesday 12 January 2016

Mark Lancaster TD MP, Minister for Defence Personnel, Welfare and Veterans, **Surgeon Vice Admiral Alasdair Walker OBE**, Surgeon General, **Brigadier Timothy Hodgetts CBE**, Medical Director, Defence Medical Services, and **Surgeon Captain John Sharpley**, Defence Consultant in Psychiatry

[Q145–235](#)

Published written evidence

The following written evidence was received and can be viewed on the [inquiry publications page](#) of the Committee's website.

LAR numbers are generated by the evidence processing system and so may not be complete.

- 1 Colin Swift ([LAR0012](#))
- 2 Dr Ashley Croft and Dr Remington Nevin ([LAR0027](#))
- 3 Dr Jane Quinn ([LAR0010](#))
- 4 Dr Jane Quinn ([LAR0025](#))
- 5 Dr Remington Nevin ([LAR0007](#))
- 6 Dr Remington Nevin ([LAR0022](#))
- 7 Dr Remington Nevin ([LAR0026](#))
- 8 Lieutenant Colonel (Retired) Andrew Marriott ([LAR0006](#))
- 9 Lieutenant Colonel (Retired) Andrew Marriott ([LAR0023](#))
- 10 Mark Iles ([LAR0002](#))
- 11 Ministry of Defence ([LAR0013](#))
- 12 Mr John Paul Aisbitt ([LAR0017](#))
- 13 Mr Lance Cole ([LAR0019](#))
- 14 Mr Simon Harvey ([LAR0005](#))
- 15 Mrs Ellen Duncan ([LAR0014](#))
- 16 Mrs Trixie Foster ([LAR0011](#))
- 17 Mrs Trixie Foster ([LAR0028](#))
- 18 Ms Philippa Tuckman ([LAR0021](#))
- 19 Paul Shephard ([LAR0009](#))
- 20 Roche Products Limited ([LAR0001](#))

List of Reports from the Committee during the current Parliament

All publications from the Committee are available on the [publications page](#) of the Committee's website.

The reference number of the Government's response to each Report is printed in brackets after the HC printing number.

Session 2015–16

First Report	Flexible response? An SDSR checklist of potential threats and vulnerabilities	HC 493 (HC 794)
Second Report	Shifting the goalposts? Defence expenditure and the 2% pledge	HC 494
Third Report	Beyond endurance? Military exercises and the duty of care	HC 598
First Special Report	Ministry of Defence Annual Report and Accounts 2013–14: Government response to the Committee's Eight Report of Session 2014–15	HC 365
Second Special Report	Re-thinking defence to meet new threats: Government response to the Committee's Tenth Report of Session 2014–15	HC 366
Third Special Report	Decision-making in Defence Policy: Government response to the Committee's Eleventh Report of Session 2014–15	HC 367