

Five Minutes with Professor Jane Quinn **Interview Transcript**

We've been talking a lot about Mefloquine recently. The drug, sold under the brand name Lariam, has been known to cause several neurological side effects. Could you talk me through what side effects someone taking Lariam may experience?

I certainly can. There's quite a range. So people can experience anxiety, depression, paranoia, some people suffer seizures, some people exhibit balance disorders so problems with maintaining upright positions, nausea, the feelings of dizziness and seasickness and an aggregation of that. So some people can be extremely severely affected and have quite marked cognitive dysfunction and cognitive decline. But it can be more mildly affected, but in general it's a range of neurological effects that span a lot of areas in the brain. And in addition to that there were some systemic effects on the gut, some neuromuscular effects people get muscle weakness and loss of feeling. So it's a really broad spectrum of clinical signs and that's really quite well documented in the literature.

And what do you say to people who say that actually this has nothing to do with Mefloquine, it's do to with being in the military, it's to do with PTSD?

Look there are quite clear way of establishing causality from a medical perspective. So there are a number of key criteria that need to apply. One of which is that you didn't experience those symptoms before you took the drug. You take the drug and do experience the symptoms and there is a relationship between taking that drug and experiencing those symptoms and then when you discontinue the drugs, so you stop taking it, some or all of those symptoms go away. Those are the things that prove that there's a direct relationship between taking a drug and suffering an adverse reaction, and in the case of Mefloquine, it's very clear that a significant majority of the people who have experienced side effects from it did not have those symptoms before they took the drugs. Certainly had those symptoms while they were taking the drug and in some cases that onset can be delayed. And that's why they're accepted so they can appear sometime after you start taking it. And in many cases those symptoms disappear but there are a significant proportion where those symptoms continue. And that's a clear causality relationship between being exposed to a particular substance in this case it's a pharmaceutical drug and suffering an adverse side effect from the drug.

And you have personal experience with Mefloquine, your husband was given the drug whilst serving in the army. Could you tell us how he reacted to the drug?

Yes he was. He was given Mefloquine for a live firing exercise in Kenya and that was a common training deployment for the British Army and still is. He experienced severe nightmares while he was taking Mefloquine while he was in the Kenyan exercise and an acute depression. He'd never experienced depression before in his life, he had no concept of what that was actually like prior to taking Mefloquine and that was something that really was extremely powerful. He was a very profound depression and he became suicidal. That subsided when he stopped taking the drug, but the longevity of feeling of deep unrest, anxiety and paranoia remains and the dream continued. So right up until the point of his death he was still experiencing what we called 'Lariam dreams' and that was really so much because of how that impacts his life.

And do you believe that given the side effects, Mefloquine should be banned altogether with the FDA revoking its endorsement?

I think it utterly unsuitable for use in military sections. I think the circumstances around military deployment make it an extremely unsafe drug to be used, not least due to its ability to induce severe outbursts to anger, changes of mood, sleeplessness and other really significant impacts on that person's health and wellbeing while they are utilising heavy machinery, using live firing weapons and other other parts of military equipment. I think that's an extremely dangerous position to face those individuals who and their colleagues and peers. It also is extremely difficult to withdraw people in treatment easily or to monitor their side effects. So for me, that makes it absolutely unsuitable for using any military population during deployment at any time. And I think that is not becoming widely accepted universally to be the case. There is there is always some requirement for a drug with a high side effect profile to be available in those extreme cases where there is a life and death requirement. So do I think the drugs should be withdrawn completely? No. Do I think it should be used under the most stringent conditions and only as an inpatient under clinical supervision 24/7? Yes absolutely I do.

There's some debate as to whether Mefloquine and Tafenoquine are similar and will cause similar side effects, are they similar drugs?

They come from the same chemical family. Both Mefloquine and Tafenoquine are synthetic compounds, so they were discovered as part of a drug discovery process. They are not identical in their chemical structure and they're not identical in their mode of action. However, there are enough similarities between the two that the side effect

profile of them is extremely similar. So, regardless of the drugs works at a biochemical level, the chemical similarity is enough that the tissues in the body that are highly reactive and responsive in Mefloquine and also highly active and responsive to Tafenoquine. Therefore it's very clear that the two drugs, regardless of how they look biochemically, are actually exerting a very similar effect when we look at the negative impacts of them.

So what do you say to people who say that Tafenoquine is a very safe and effective drug?

I would say that the evidence is not there to prove that. And in fact we've seen a significant amount of evidence presented to the FDA in the last two weeks. One dossier came from GlaxoSmithKline where they were clearly stating a side effect profile related to use of Tafenoquine in some of their clinical trials and having to explain that side effect profile that the FDA. The dossier that was produced by 60 Degrees Pharmaceuticals actually presented a very significant side effect profile and the safety of that drug in the context of prophylaxis was considered to be marginal by the committee in that there was not a unanimous vote for safety 4 members out of 13 suggested that the safety profile was inadequate for that particular job to proceed. So there is clear evidence both in the scientific literature and in these documents that have been presented to the FDA that Tafenoquine has a problematic safety profile and that's what the future is for.

With that being said, do you believe the FDA made the right decision in approving the drug?

I think what we need to do is wait and see what caveat places around its registration. So the FDA has the ability to put things with requirements in place around use and supervision around pretesting to ensure safety and the patient who'll be given the drug. And I think those stringent measures need to be absolutely required particularly for the use of Tafenoquine for prophylaxis.

We've heard a lot about the financial potential of drugs like Tafenoquine. GSK said at it's Q2 Results that Tafenoquine was the fourth highest factor driving growth over the two years. Given the financial incentive, are companies like GSK and 60P putting money before ethics?

Well this is a really interesting question isn't it. So the philanthropic reasons given behind the development of antimalarial drugs and the amount of money that is presented to companies who are developing drugs for third world use is that these are

absolutely required for containing the disease which is catastrophic to countries that are emerging or second or third world nature. Now that's absolutely true. We do have to contain malaria. We have to be able to treat it. We have to be able to protect people from it. However, currently the testing requirements that pre-screening requirements that would be needed to be employed in order for Tafenoquine specifically to be both safe and effective, can only be done in third world countries. So, this is for me a significant issue in the way that these drugs are pushed to market, which is that first scaled market is always a first world country, whereas their rationale for development are those third world countries which have enormous issues with endemic malaria. How this drug can be developed and delivered safely in that environment, I'm not clear and neither are GSK or 60P have come out and told us how that is exactly going to happen.

Dr Jane Quinn thank you so much.

You're very welcome.