

[REDACTED]

From: Woolley, Dr Jane
Sent: 23 August 2019 10:05
To: Ord, Kathryn
Subject: RE: Finasteride and the potential risk of sexual dysfunction and psychiatric disorders

Hehe – thanks Kathryn! :-)

I agree, on re-reading the DSU it really doesn't have many teeth left, does it! Such a watered down version of what [REDACTED] and I really wanted to say!!

Yes, let's keep this one in the back of our minds and in the meantime see what [REDACTED] has to say in terms of what there is that's new since 2017 (other than anxiety).

Thanks for offering to respond to [REDACTED] – would you mind copying me into the e-mail?

Jane

From: Ord, Kathryn <Kathryn.Ord@mhra.gov.uk>
Sent: 23 August 2019 09:17
To: Woolley, Dr Jane <Jane.Woolley@mhra.gov.uk>
Subject: RE: Finasteride and the potential risk of sexual dysfunction and psychiatric disorders

Hi Jane
I joked to [REDACTED] that I should ask for a deerstalker hat and magnifying glass for my birthday!

Thanks for this and for sending the attachments. I found some of the correspondence on SharePoint yesterday and can see the pressure we had from patient groups at the time. It's interesting that [REDACTED] draft DSU (even with [REDACTED] comments) and the final version bear very little resemblance to each other, so there must have been some serious editorial changes made after this. Unfortunately, this is to the point where the messages seem to have been slightly lost and have put us in a situation where our communications are not quite in line with those from other regulators. As you say though, there's not much of a driver for another DSU article right now – the only thing that's new it's that 'anxiety' has recently been added as an ADR – but we wouldn't usually communicate on updates to 4.8.

Perhaps this is one to keep at the back of our minds as an issue that we may need to return to. I think your suggestion for going back to the [REDACTED] is a good one – I'm happy to reply on this.

Best regards,

Kathryn

From: Woolley, Dr Jane <Jane.Woolley@mhra.gov.uk>
Sent: 23 August 2019 08:35
To: Ord, Kathryn <Kathryn.Ord@mhra.gov.uk>
Subject: RE: Finasteride and the potential risk of sexual dysfunction and psychiatric disorders

Hi Kathryn,

Thanks very much for digging around further – you'd make such a good investigative journalist!!

It's a tricky one. As you say, it would seem Germany and France published due to media and patient pressure. However, the only reason any action took place at all in 2017 was because we had patient pressure, reviewed everything the PFS had produced and thought something needed to be done. [REDACTED] felt very strongly about this. So in a way the others are catching up a bit.

Thinking back to the DSU article we initially drafted, [REDACTED] and I wanted to link persistent sexual dysfunction with depression/suicide (attachment 1) but [REDACTED] wasn't happy about it and so it ended up getting taken out (attachment 2).

Unfortunately I imagine the same thing would happen if we tried to do it again. And the SmPC/PIL does list persistent sexual dysfunction, so it's not as if we have a regulatory need to issue an update article.

I know DSU is pretty busy over the coming months and so, unless you feel very strongly, I don't know if there is sufficient justification to have a reminder article, despite the new cases (some of which I imagine are likely to be stimulated). Btw, as well as DSU, [REDACTED] also wrote to the private hair loss clinics (attachment 3).

It's a shame, as I would personally like to do something more, as I'm sure would [REDACTED], and the MAHs have come to us but I'm not sure there would be much appetite to do anything more right now. Perhaps we should get back to [REDACTED] saying we have already communicated on this and ask them whether they are aware of any important new data that would justify communicating again?

Thanks
Jane

From: Ord, Kathryn <Kathryn.Ord@mhra.gov.uk>
Sent: 22 August 2019 18:02
To: Woolley, Dr Jane <Jane.Woolley@mhra.gov.uk>
Subject: RE: Finasteride and the potential risk of sexual dysfunction and psychiatric disorders

Hi Jane
Sorry, this got a bit long.

I did a bit more digging and it seems that DE communicated on this due to media pressure. I found the article below from Jul 2018, which mentions that in Feb 2018 Die Zeit ran a 4,500-word report on "post-finasteride syndrome", which stated that that BfArM "*should be the one to take action and request that doctors in Germany today better educate their patients*". The article then reports that BfArM had acted on this by sending the DHPC. The article goes on to say that 7 other MS had already communicated on the risk of suicide and permanent sexual dysfunction (including BE, CR, DK, FR, NL, PL and the UK, almost all with links to comms from 2017 included in the article).

<https://www.pfsfoundation.org/news/germanys-fda-equivalent-issues-red-hand-letter-on-finasteride-adrs-3/>

Interestingly, it seems that France also sent a DHPC on this (from multiple MAHs) in Feb 2019 and issued a reminder on their website – even more recently than Germany. A separate article mentions that the ANSM "*is preparing to make available to the general public an additional information document, drawn up in partnership with patient representatives concerned*". I haven't been able to find this document, but the ANSM website says it will be made available at some point.

https://www.santemagazine.fr/actualites/chute-de-cheveux-nouvel-appel-a-la-prudence-avec-le-finasteride-336203?fbclid=IwAR2vwAApA8JnzQqhZu5GFnwnLMXeHwc8VJDResHZpR9MClyF1-b_DExZu8

As for why it was sent in Feb 2019, the PFS foundation published an article which mentions that "*Prompted by an increasing number of adverse drug-reaction reports to finasteride, France's FDA-equivalent agency yesterday issued a letter to 100,000 health professionals reminding them that patients treated with the drug are at risk for developing psychiatric disorders and persistent sexual disorders*":

<https://www.pfsfoundation.org/news/le-monde-finasteride-users-beware-2-2/>

The drivers for issuing communications in Germany and France therefore differ to each other. I am not up to speed on finasteride yet so I am not aware of any recent media attention or a surge of ADR reporting. I had a look on Empirica to see what's been reported since we published the DSU article.

- There are 2 new cases of completed suicide (of 7 in total). Both are from the same Daily Mail article published on 22 July 2019 (although 1 of the 2 cases is actually about "59 suicides associated with the drug globally"; the second case originates from a quote from David Healy, who said "People kill themselves after taking this drug," he says. 'I had a colleague who took his own life 15 years ago, so I know it happens "): <https://www.dailymail.co.uk/health/article-7274057/How-baldness-drug-ruin-mans-love-life-Finasteride-devastating-effects.html>
- There are 8 new cases of suicidal ideation (of 26 in total), though 2 involved historical use of finasteride – some of these cases related to sexual dysfunction.
- There are 5 cases of depression suicidal (of 8 in total), 1 of which also reported suicidal ideation – some of these cases related to sexual dysfunction.

Having thought about this a bit more, I'm not sure a DHPC or info leaflet is warranted, but a reminder DSU article might be worth considering, given that the messages conveyed in the May 2017 article are not entirely aligned with the final wording agreed in the variation, and we did not emphasise that sexual dysfunction can persist after treatment is stopped.

What do you think?

Best regards

Kathryn

From: Woolley, Dr Jane <Jane.Woolley@mhra.gov.uk>
Sent: 18 August 2019 09:39
To: Ord, Kathryn <Kathryn.Ord@mhra.gov.uk>
Subject: RE: Finasteride and the potential risk of sexual dysfunction and psychiatric disorders

Hi Kathryn,

Thanks for looking into this a bit more – much appreciated.

I think the persistence of sexual dysfunction was something that was discussed at the time of drafting the DSU, however as the thrust of the article was depression and we didn't want to falsely create a link between the persistence of sexual dysfunction and depression/suicide (on the basis of weak evidence) it was felt inappropriate to do so.

However, I'm not quite sure why we didn't refer to the need for monitoring, seeing as the wording had been agreed by then (I think).

This is an issue we feel quite strongly about and so if there is a specific reason for Germany sending this now it may be worth trying to find out.

Would you mind seeing what you can dig up? It may be that they agreed something for the brandleader at the time and have made the generics follow suit at approval.

Thanks
Jane

From: Ord, Kathryn <Kathryn.Ord@mhra.gov.uk>
Sent: 16 August 2019 18:54
To: Woolley, Dr Jane <Jane.Woolley@mhra.gov.uk>
Subject: RE: Finasteride and the potential risk of sexual dysfunction and psychiatric disorders

Hi Jane

It looks like Germany went it alone with a DHPC on this issue (I found it online, and as an Annex to a published Aurobindo RMP, approved through a procedure with DE as RMS). As you say, the UK SmPC for Propecia was updated in June 2017 after a review of depression, however, the DSU article predates this (May 2017) and does not contain the same level of information as the DHPC or SmPC wording, i.e.

- patients should be monitored for psychiatric symptoms; if patient develops psychiatric disorders treatment should be stopped [the DSU article refers only to stopping treatment if depression occurs, and doesn't suggest patients should be monitored]
- Symptoms of sexual dysfunction can persist even after discontinuation of treatment [the DSU article reminds HCPs only that sexual dysfunction can occur, not that it can persist after treatment has stopped]

The final SmPC and PIL wording refers to both the issues above. PRAC advice was sought on the variation in 2017, and they said:

The PRAC did not find it necessary to implement further EU- level communication activities beyond updating the product information; however need for health-care communications may be considered further at a national level.

I'm not really sure why the DSU article wasn't quite in line with the final SmPC wording, but this seems to have been our opportunity to communicate on this update to PI. Therefore, I'd agree that it would be difficult to argue that anything additional is needed now.

We could contact DE and ask why they sent the DHPC at that particular time (i.e. about a year after the wording was approved), to see if this sheds more light on the issue?

Best regards

Kathryn

From: Woolley, Dr Jane <Jane.Woolley@mhra.gov.uk>

Sent: 16 August 2019 16:20

To: Ord, Kathryn <Kathryn.Ord@mhra.gov.uk>

Subject: FW: Finasteride and the potential risk of sexual dysfunction and psychiatric disorders

Hi Kathryn,

Please see e-mail from [REDACTED] forwarded by Leigh.

I'm assuming the DHPC referred to relates to the regulatory updates wrt depression/suicidal ideation that followed a PRAC review in 2017. [REDACTED] reviewed the issue for PEAG and was instrumental in pushing the RMS to take action.

We did a DSU in 2017 (<https://www.gov.uk/drug-safety-update/finasteride-rare-reports-of-depression-and-suicidal-thoughts>) and requested PI updates but as far as I recall there was no decision at EU level for aRMMs. I'm not quite sure why Germany is communicating now and whether they have had national pressure but it might be worth requesting a copy of the DHPC.

Even though it would be nice to do, I think we would need some reason to justify requiring aRMMs at this stage. I'm also not sure how this would be achieved if it wasn't a PRAC recommendation.

Happy to discuss

Thanks
Jane

From: Henderson, Leigh <Leigh.Henderson@mhra.gov.uk>

Sent: 16 August 2019 16:03

To: Woolley, Dr Jane <Jane.Woolley@mhra.gov.uk>

Subject: FW: Finasteride and the potential risk of sexual dysfunction and psychiatric disorders

Hi Jane

Not sure if this has already come your way – as the new Group Manager.

I think [REDACTED] copied me in as my team have been dealing with various communications that [REDACTED] have been co-ordinating.

However, finasteride is not one of my team's products and I am not sure if communications are planned.

Kind regards

Leigh

