

[REDACTED]

From: [REDACTED]
Sent: 13 January 2015 14:54
To: [REDACTED]
Cc: [REDACTED]
Subject: Finasteride penis disorder
Attachments: Finasteride penis disorder APN 12.01.2015.xls

Follow Up Flag: Follow up
Flag Status: Flagged

Hi [REDACTED]

Apologies for sending being later than expected. Had problems validating the numbers with [REDACTED] and finally got everything to match on Friday.

Please find attached line listings for finasteride and penis disorder. Currently, we have 177 cases: 46 UK cases and 131 foreign cases.

Please find the excel first page: UK cases with the outcome "not recovered" highlighted in purple. All data/countries can be found on the excel second page.

Out of the UK cases, 18 are associated with Proscar, 17 with Propecia and 11 reported as Finasteride. In terms of reaction outcomes:

27 - not recovered
6 – recovered
3 – recovering
10 – unknown

I have left comments on the side, a few cases with temporal relationships within the highlighted rows – good/strong comment left. As there were many [REDACTED] advised not to go into depth but please let me know if you need any further information or looking into the cases.

Kindest regards,
[REDACTED]

From: [REDACTED]
Sent: 24 December 2014 11:24
To: [REDACTED]
Cc: [REDACTED]
Subject: FW: Finasteride syndrome

Hi All,

Please can I ask each of you to help [REDACTED] with some assessment work for finasteride.

[REDACTED] your drug event combinations relate to signals you found and [REDACTED] yours have been looked at previously by another assessor.

[REDACTED] needs the data by 13th January. Please can you provide line listings of the current cases (data can be anonymised if needed afterwards) looking through each report for the points [REDACTED] mentions in [REDACTED] email below including whether the effects are persistent (using a highlighting colour code maybe).

█ is looking for some strong HCP reports.

Any questions please ask me or one of the other co-ords

Thanks,

█

From: █
Sent: 23 December 2014 15:03
To: █
Subject: FW: Finasteride syndrome

Here you go

From: █
Sent: 23 December 2014 10:26
To: █
Subject: RE: Finasteride syndrome

Hi █

In terms of the signals below is a list of all the current issues for finasteride. Most of the case folders have documents in 'records' which provide case details of the UK case we had at the time along with the qualification of the reporter, if you need this info. Otherwise someone from █ will be in touch with current YC data.

I hope you find this useful.

Thanks,

█

SA █ Finasteride & penis disorder: █

█

█

PC is currently being updated following completion of the work sharing assessment (P-RMS is Sweden), however, no further penile reactions have been added. SPC currently lists impotence, ejaculation disorder and testicular pain. Action: Signal meeting suggested checking the dosage data for cases where finasteride was indicated for alopecia and to check the frequency of the PSUR.

08/07/2010 - letter sent to MAH requesting review

20/08/2010 - MAH provided review, presented as Alert meeint 09/09/2010

24/09/2010 - letter sent to MAH agreeing with MAH conclusions. not updates to UK product information at this time. Issue to be monitored and kept under review.

SA █ Finasteride & memory impairment: █

█

█

SPC lists: depressed mood. A SACF had been previously created in 2006 (█) and subsequently closed on the basis that the spontaneous data was inconclusive, no plausible mechanism for memory impairment was identified and a PubMed search revealed no

papers suggesting an association between memory impairment and finasteride. The MAH (MSD) commented the cases were confounded due to depression and age, however agreed to keep signal under review. The MHRA have received 16 new UK cases since 2006 (all patient reports). In total the MHRA have received 29 UK cases within the memory loss and mental impairment HLTs. Impact Analysis result - D. From looking at the last PSUR it doesn't appear that the MAH have made any comments concerning memory impairment (appears in 08-09 PSUR). Next PSUR DLP August 2012. It was suggested that this would be an appropriate regulatory procedure to raise concerns. Action: Create a SACF and raise within the next WS PSUR (P-RMS Sweden).

SA [redacted] **Finasteride & Peyronie's Disease:** [redacted]

[redacted]

In total, the MHRA have received 13 UK cases, 3 of which are described above and concerning the 1mg product, 9 report either the indication of BPH or the 5mg product Proscar as suspect drug and 1 case is unknown. The cases concerning the 5mg product and unknown finasteride product are old cases, received from 1993 to 2000; 2 reported as resolved, 1 as resolving and 7 not recovered. 2 cases report a medical history of Dupuytren's contracture, confounding the cases as this is a risk factor for Peyronie's disease. [redacted]

We have information on the onset times for 4 of these 5mg product cases, ranging from 92 to 265 days. The SPC for Proscar (5mg) and Propecia (1mg) list various reactions in 4.8 within the reproductive SOC; however none similar in terms to penile tissue change. No relevant comments available in the PSUR (only 1 report of Peyronie's Disease is mentioned cumulatively in the PSUR for reporting period 19/08/2010 to 18/08/2011). 8 reports available on Eudravigilance database, with a PRR of 26.45 (reaching threshold for a signal in respect to eRMR's in EVDAS i.e. established products the criterion is met when the number of spontaneous cases is > 5 and PRR lower confidence interval > 1).

The PSUR is on a yearly cycle and the assessment is expected to be received in the near future (WS-PSUR Sweden). Action: Review this in the next PSUR, and there will also be a spotlight review conducted for finasteride. Updated action 08/11/2013: The UK have received a total of 14 UK cases (1 further case since signal initially raised). Confirmation from assessor [redacted] - Peyronie's disease has been picked up in PSUR and will review in next PSUR.

SA [redacted] **Finasteride & Sexual Dysfunction: To be closed**

SPC alignment issue. [redacted] to update SPC section 4.8 in line with brand leader Proscar: sexual dysfunction (erectile dysfunction and ejaculation disorder) which may continue after discontinuation of treatment; male infertility and/or poor seminal quality. Normalization or improvement of seminal quality has been reported after discontinuation of finasteride.

July 2013: Wrote to company, proposed wording currently being agreed. [redacted] confirmed the alignment will be made during the renewal application. [redacted] submitted variation and has been granted. [redacted]

June 2014: [redacted] (MR) SPC still waiting alignment with brand leader

[redacted] **Finasteride & suicidal ideation:** [redacted]

[redacted]

[REDACTED]

6/23 Non-UK cases were indicated for alopecia, many seem to be litigation cases from the US and 19/23 also report depression along with other problems such as loss of libido and erectile dysfunction (listed) which could also contribute towards suicidal ideation. 9/10 UK cases were indicated for alopecia, 7/10 also report reactions of sexual dysfunction or penile disorders. 2 cases are confounded by other drugs (antidepressants) or PMH of depression. SPCs: Proscar 5mg indicated for BPH lists depression, Propecia 1mg indicated for alopecia lists depressed mood. Cognitive impairment and memory loss have been raised via the PSUR.

Depressive disorders including suicidal ideation are identified as a key risk factor and this is undergoing monitoring in the PSUR.

Action: The meeting requested more information on how many cases under the Suicide SMQ along with the EBGM. It was noted that these reactions should be monitored in PSURs generally therefore was decided just to inform Steph to keep an eye out for when the PSUR is in house.

SA [REDACTED] Finasteride & cognitive disorder: [REDACTED]

[REDACTED]

[REDACTED]

Currently there are 5 UK cases on Sentinel; Onset time 1-18days all on 1mg dosage.

[REDACTED]

SPC: only covers decreased libido and depressed mood.

PIL: depressed mood.

BNF: impotence and decreased libido.

PSUR [REDACTED]; 19TH Aug 2012- 18th Aug 2013. Propecia 1mg [REDACTED] Cognitive disorder was not reviewed as a signal.

Previous signals: Finasteride & Memory impairment [REDACTED]: 6 UK E- 2.03: Raise within the next WS PSUR (P-RMS Sweden).

Action: There are currently 2 other pending SACFs in association with finasteride

Memory impairment [REDACTED]

Suicidal ideation [REDACTED]

Action: Raise all psychiatric and cognitive concerns which have been identified reactions with the p-RMS Sweden. Further information is required such as sales, usage, background rates and disproportionality for both the 1mg and 5mg products. This should be added as a signal on EPITT.

[REDACTED] Finasteride & Skin atrophy: [REDACTED]

[REDACTED]

[REDACTED]

[Redacted]

Action: Raise as comment during PSUR procedure (DLP 31st October) [Redacted] to review PSUR determine if combined for 1mg and 5mg strengths. [Redacted] to perform literature review for further evidence.

From: [Redacted]
Sent: 22 December 2014 16:06
To: [Redacted]
Subject: Finasteride syndrome

Dear [Redacted]

Sorry to hear this on you before Christmas but I have just received a PSUR in finasteride which has not reviewed any of the signals I asked them to. Would someone be able to pull out the latest data on all signals with case folders so that I can get back to the MAH with what we have.
There is the cognitive disorders memory loss; depression one; muscle and skin atrophy; 'finasteride syndrome'- persistent sexual effects.. These are the comments I sent:

[Redacted]	[Redacted]	[Redacted]
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There may be a couple of additional Case folders since these comments were sent.
I am particularly keen to TTO, Outcome- how long effects lasted. If there are some good HCP reports that I could draw on, that would be really helpful
I really appreciate your help with this

Many thanks

