



David G Perahia /EMA/LLY
10/19/2006 09:52 AM

To James M Russell/AM/LLY@Lilly, Michael
Detke/AM/LLY@Lilly
cc David G Perahia/EMA/LLY@Lilly

bcc

Subject Re: Duloxetine/Cymbalta Withdrawal Question

Guys,

Quick process question.

I got an e-mail from an unknown person who had read my discontinuation manuscript and wanted answers to a number of questions.

While I don't have the time to come up with lengthy and detailed responses to his questions, I at least wanted to reply to him and provide some brief answers (below).

I then wondered whether there's in fact a process I should be going through when I get these kind of questions, and/or whether my responses needs to go through an approval process.

Any info welcome.

Cheers,

D.

Hi Nathaniel,

Thanks for your message.

Brief responses to your questions as follows:

1. what is the method of which duloxetine initiates DEAE's

I think it's fair to say that nobody knows for sure how any of the antidepressants cause DEAEs, although we briefly discuss some of the hypotheses on page 6 of the manuscript. There are a number of published manuscripts which examine the different hypotheses in much more detail, and some relevant references are included in the text.

2. how quick is the onset (mean) ?

I believe that the earliest timepoint following discontinuation that symptoms were enquired about was 1 week. Onset of many of the DEAEs was within one week of duloxetine discontinuation, but because there were no study visits prior to the 1 week timepoint, time of onset can't easily be pinpointed more accurately than this.

3. was there a demarcation (if noted in the study) of abrupt discontinuation versus a "taper" method ?

9 of the 10 studies included in the report featured abrupt discontinuation. Only Study 10 (relapse prevention study) featured a taper, and because the taper in this study was only 3 days in duration, I don't

think it really provides an adequate basis to compare the DEAEs associated with tapered versus abrupt discontinuation.

4. was intervention taken into minimizing DEAE's and what pharmacological intervention was used with noticeable failure or success ?

Most centrally-acting drugs were excluded by the study protocols, although a limited quantity of benzodiazepines were permitted in some of the trials. We did not however evaluate the effect of concomitant medication on DEAEs.

5. of the 35% of DEAE's that did not resolve in 7 days, was follow up done, what was the mean resolvment for these patients, and shortest and longest resolvment after 7 days ?

Data were not systematically collected beyond the end of the lead-out phases of the studies (detailed in Table 1 in the paper), so we have no way of knowing when these symptoms subsided.

Hope the above clarifications are helpful.

Best wishes,

David.

Nathaniel Ziering <nziering@gmail.com>



Nathaniel Ziering
<nziering@gmail.com>
14/10/2006 22:56

To d.perahia@lilly.com
cc

Subject Duloxetine/Cymbalta Withdrawal Queston

Dear Sir or Madam,

I am write you today as admirer of your work with duloxetine/cymbalta research. I know you are quite but I was hoping you may find the time and sympathy to anser my query. It would be graciously appreciated.

I am a student who is working on a project researching the effects of duloxetine (and other SSRI and SNRI's) in a epidemiology class. I am working on a theoretical model for recognition by the clinician for patients suffering from SSRI/SNRI withdrawal and subsequently drawing up a treatment guideline.

I don't want to take up to much of your time so I will do my best to be exigient as possible with my questions.

RE: "Symptoms following abrupt discontinuation of duloxetine treatment in patients with major depressive disorder".

J Affect Disord. 2005 Dec;89(1-3):207-12. Epub 2005 Nov 2.

- what is the method of which duloxetine initiates DEAE's
- how quick is the onset (mean)
- was there a demarcation (if noted in the study) of abrupt discontinuation versus a "taper" method
- was intervention taken into minimizing DEAE's and what pharmacological intervention was used with noticeable failure or success
- of the 35% of DEAE's that did not resolve in 7 days, was follow up done, what was the mean resolvment for these patients, and shortest and longest resolvment after 7 days.

Any other information you have that you think would be relevant from your vast experience with duloxetine would be great. I hope you haven't seen this letter as imprudent or unbecoming.

Thank you for your time.

Sincerely,
Nathaniel Ziering

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Please be advised of my new email address for your records.