David G Perahia /EMA/LLY
07/02/2003 11:36 AM

To Madelaine M Wohlreich/AM/LLY@Lilly
cc John M Plewes/AM/LLY@Lilly, Melissa J Joliat/AM/LLY@Lilly, Michael Detke/AM/LLY@Lilly, Nancy Jean Trapp/AM/LLY@Lilly
bcc David G Perahia/EMA/LLY
Subject Re: An obscure question

Cheers, Madelaine - you've hit the nail squarely on the head !

It's not that the discontinuation issue will necessarily be something we can proactively use to sell duloxetine (I believe not, at least from a historical perspective), more that it's something that the media and regulatory authorities might well latch on to unless we are proactive about it. I sense we are being a bit complacent around this, and it could hurt us (e.g. no diffs from parox on abrupt discontinuation in our trials, short t1/2 etc. etc.)

As an opening gambit, I would define proactive as :

(1) Write up our data and get it published as a priority rather than dragging our heels
(2) Consider running a trial which might add to the evidence base on how best to manage stopping the drug, e.g. over how long should drug be tapered ? (open label treatment, then perhaps 3 arms looking at abrupt discontinuation vs. 2 week taper vs. 4 week taper in a double blind fashion, with frequent visits). Good PR due to being open and pushing the science, with an evidence-based recommendation at the end to boot. I'm sure Matt would blanch at this suggestion, but we can't just stick our head into the sand.

Paroxetine is being torn to pieces by the media (and in fact regulators too) over in Europe, and much of the criticism is stemming from the perception that GSK have been, to put it politely, less than transparent about discontinuation with paroxetine and how best to manage it. I would rather we didn't fall into the same trap.

Re : writing resource, I can look into this. I'm certainly willing to offer my services as an author on a manuscript discussing discontinuation with duloxetine, however, and there is the perfect thought leader in the UK (Peter Haddad, who has published pretty widely on the topic in general) to work on it with us.

D.

Madelaine M Wohlreich

Madelaine M Wohlreich
02/07/2003 16:01

To: Michael Detke/AM/LLY@Lilly
cc: David G Perahia/EMA/LLY@Lilly, John M Plewes/AM/LLY@Lilly, Melissa J Joliat/AM/LLY@Lilly, Nancy Jean Trapp/AM/LLY@Lilly
Subject: Re: An obscure question

The feeling here has been that since it will be in our FDA label that tapering is recommended, that there is not a lot more that needs to be done proactively.
When we have said at consulting conferences that discontinuation type side effects could be seen on abrupt taper, clinicians have not appeared to be terribly concerned.

Madelaine
Michael Detke

Michael Detke
07/02/2003 09:47 AM

To: David G Perahia/EMA/LLY@Lilly
cc: Melissa J Joliat/AM/LLY@Lilly, John M Plewes/AM/LLY@Lilly, Nancy Jean Trapp/AM/LLY@Lilly, Madelaine M Wohlreich/AM/LLY@Lilly

Subject: Re: An obscure question

David:

I think it is somewhat geography-specific, but I'm not entirely sure how much. I was told by someone who was then a Prozac sales rep in the US that they tried to increase the importance of DESS and half-life in prescribing decisions, as it was rated as the 30th most important on a list of 30 issues by prescribers, and after concerted education about the issue, it moved all the way up to about 28th. But that was a while ago. I'll let Madelaine or John comment further.

Is there any possibility of writing resources in the region/country?

-Mike

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David G Perahia

David G Perahia
07/02/2003 02:46 AM

To: Michael Detke/AM/LLY@Lilly
cc:
Subject: Re: An obscure question

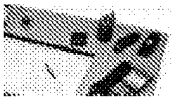
OK Miguel.

I must confess to being a little unconfortable about the whole discontinuation thing. Maybe it's more of a UK specific issue, but paroxetine is taking a fearsome battering in the media over here at the moment, and a significant part of that is discontinuation-related stuff. It's clear that duloxetine has a significant DESS liability (on abrupt discontinuation, admittedly, but how much taper data do we have yet ?), and the perception will be further reinforced by our short t1/2 which is seen by many as being directly linked (partly due to the work Lilly did around Prozac's long t1/2.....).

I've already asked Melissa to look into what publications we have on our "to do" list in this area. If we're not careful, the environment is set for this to blow up in our faces unless we're proactive about it.

Diego.

Michael Detke



Michael Detke
01/07/2003 19:43

To: David G Perahia/EMA/LLY@Lilly
cc:
Subject: Re: An obscure question

David, I think most of the studies checked at one week, and we probably don't have the data broken out in finer temporal intervals than that.

Sorry amigo,

-Miguel

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David G Perahia

David G Perahia
06/30/2003 11:13 AM

To: Michael Detke/AM/LLY@Lilly
cc:
Subject: An obscure question

Hi hombre,

Quick question : I was recently asked whether we have any discontinuation data at around 3 days post-discontinuation, this being the time when you might expect maximal symtomatology (approx. 5 half-lives after the final dose). I didn't think we did, but thought I'd check.

Cheers,

David.