To: MHRA, RMS for Concerta in Europe
Copy: Barbara van Zwieten-Boot (Chair, Efficacy Working Party, EMA)
Copy: Martin Terberger, European Commission, Directorate General for Health & Consumers
Copy: Other relevant medical authorities

29 October 2011

Regarding the Final Variation Asessment Report for Concerta 26/5-11 and the off-label prescription and abuse of Concerta in Sweden

The Benefit/Risk in the prescription of Concerta to adults has been found to be negative. There is a lack of efficacy coupled with serious safety issues, as cardiovascular risks, abuse potential and psychiatric (aggression, anxiety) adverse events.

Concerta is therefore NOT to be prescribed to adults (except in specified cases noted in the SPC).

This report gives additional vital information for the RMS about the off-label prescription of Concerta to adults in Sweden and about the abuse of the drug. Information that is *not* submitted by the pharmaceutical company or by IMS Health (in the Drug Utilisation Study).

In the Risk Management Plan (RMP) for Concerta, from 23 November 2009, Johnson & Johnson states (p. 118) under the heading *Potential for off label-use*:

> "According to IMS covering CONCERTA retail prescriptions in the 4 major European countries where CONCERTA is available (Germany, France, Spain, and United Kingdom), from January 2003 to June 2009, **the vast majority (94.0%) of retail prescriptions of CONCERTA were prescribed to children and adolescents between the ages of 6 and 20 years."** (Emphasis added.)

This is the ***only*** information about off-label prescriptions to adults in this 319 pages long document.

In the updated *Methylphenidate Drug Utilisation Study (DUS) in Europe*, from IMS Health, 3 November 2010 **[2]**, it is stated (p. 19): **"According to 2008 data, in most countries the percentage of prescriptions given to patients between 6 and 18 years old was above 80% … The same was seen in data from 2009."** For Sweden no reliable national data is presented in the report, and no data at all for 2009.

However national data for Sweden is quite easy to find, and this data contradicts what is stated in the RMP and in the report from IMS Health.

In the Swedish Prescribed Drug Register **[3]** it can be found that for 2009, the number of prescriptions of methylphenidate for adults (20+) was 110 064 and for children (5-19) 95 283. ***The number of prescriptions to adults was 53 % of the total number of prescriptions.*** The number of DDD for adults, 6 586 891, were 52% of the total number (12 592 651). The number of adults being prescribed methylphenidate was 12 903, and was 41% of the total number (31 257).

For 2010 the number of adults being prescribed methylphenidate in Sweden has increased 39% (!) to 17 919. **[3]**

The negative Benefit/Risk for Concerta was communicated already in the Preliminary Variation Assessment Report for Concerta in July 2010, and was confirmed in the FVAR from 26 May 2011. In the FVAR the responsibility for the MAH to follow the decision was made clear. It was also clearly stated about the period 11 October 2010 to 10 October 2011: **"The usage [of Concerta] may not increase in this time period."**

Nevertheless, no actions have been taken by the MAH or the relevant authorities in Sweden to communicate the negative B/R for Concerta to adults and so the prescription of the drug has just continued to increase. This according to the latest information issued by the National Board of Health and Welfare. **[4]** (For example: DDD for October 2010 was 542 455 and for September 2011 it was 692 832 for 20+.)

The off-label prescription in Sweden is also exploding due to the fact that Sweden is not adhering to the prescriber rules in the SPC. The European Commission has earlier made it clear that these rules were "legally binding", but the Swedish Medical Products Agency did not agree. And so we see an explosion in the prescriptions of methylphenidate to adults.

The abuse potential of Concerta has been confirmed by the data submitted by Johnson & Johnson in application for adult indication for Concerta. In two of the studies submitted (12-007, 12-005) it became clear that the "Liking element" for Concerta in the DRQS (Drug Rating Questionaire, Subject) was of high value, meaning that the answer on the question "Do you like the drug effect you are feeling now?" was positive for the so called therapeutic doses (54 mg, 108 mg).

This did even raise the question in the assessment of how much of the effects seen in RCTs was due to this euphoric effect of Concerta.

Johnson & Johnson has also, in the submitted study Concerta Crushed 12-004, proven the high abuse potential for crushed Concerta (see further below about the stories from users). It should be noted that the abuse potential studies above were done with Concerta in an intact form.

This information is confirming the "anecdotal data" from users in Sweden. Anyone looking for information about *diversion and abuse* of prescribed methylphenidate in Sweden will easily find an abundance of data. Via this link it is possible to read **103 pages** (from Swedish web sites) where the Swedish "users" tell about diversion and abuse of Concerta and Ritalin.

The stories are in Swedish **http://jannel.se/concrit.Apr2010.pdf** **, *excerpts are presented in English in Appendix 1 below*.**

The stories about diversion and abuse tell about a scene already out of control.

It would be easy to further investigate this scene but neither the MAH nor the relevant authorities have done anything in this area.

The data above should also be compared to the misleading data given by the MAH in the RMP (p. 128-129) under the heading *Drug Abuse and Drug Dependence,* where it is stated:

> "CONCERTA has a unique pharmaceutical design that prohibits the dosage form from being crushed, opened, or emptied **making it virtually impossible to abuse it through injection, snorting, or inhalation means.** In addition, it is a long-acting prolonged-release product and **high, spiking blood levels that individuals may perceive as euphoric effects cannot be achieved with an intact dosage form.** Due to these characteristics the CONCERTA formulation would probably not be the preferred choice for methylphenidate abuse." (Emphasis added.)
> …
> "The limited number of paediatric reports in the postmarketing database supports that CONCERTA treatment confers a low risk of drug dependence. **The formulation makes it difficult, if not impossible to effectively abuse; therefore, is not expected to have an impact with respect to overall public health."** (Emphasis added.)

On page 127 in RMP it is said that the total number of postmarketing reports about drug abuse events for Concerta *worldwide* is 16 (!).

I hope this information is of value and I look forward to an acknowledgement that it is well received.

Janne Larsson
Reporter

(Snöbollsgränd 22
129 45 Hägersten, Sweden)
janne.olov.larsson@telia.com

References:

[1] Johnson & Johnson, *Risk Management Plan Concerta*, 23 November 2009, http://jannel.se/RMP-ConcertaNov2009.pdf
[2] IMS Health, *Methylphenidate Drug Utilisation Study (DUS) in Europe*, 3 November 2010.
[3] The National Board of Health and Welfare, *Läkemedelsregistret*, http://www.socialstyrelsen.se/statistik/statistikdatabas
[4] The National Board of Health and Welfare, Concerta, 20+, October 2010-September 2011, http://jannel.se/ConcertaAdultsSwedenOct10-Sept11.pdf

APPENDIX 1

Swedish user reports about Concerta and Ritalin

On getting high/getting a buzz on the doses doctors prescribe:

”I think Concerta 36 was excellent to chew ... feel somewhat high on 2”;
”Ritalin 40mg is not so strong, you need 2 such to experience a fairly drunk [state], like Concerta 54mg is much better ...”;
”... Has Ritalin prescribed for my possible ADD and take a total of 40mg in the morning for it ... I am very easily influenced by the Ritalin, I feel very alert and I am almost in a euphoric state the next few hours after I took it. I can sit in trance ... ';
”54-100 mg do I need if I should be high on it”;
”2 40mg now. Damn it is actually power in these. Thought in the beginning that there would be some shit, but they may be called ”good enough”;
”Have a friend who becomes truly stoned at 20mg (and yes, he has taken much drugs too), myself, who need about 40-60”;
”From my own experience you can be stoned if you chew a few 10 mg”;
”Takes conserta 18 mg to concentrate pretty good, I take 18mg 2, then I am just speeded as a parrot”.
”I absolutely become high on Concerta ... 60-100 mg will be good enough ”;
”took 3x36 MG [Concerta] and got a fucking buzz”;
”yes one can get speeded on a 36mg's Concerta, but more is desirable ”;
”I am using conserta 54 mg daily. Well, I can get high on it sometimes. Could be badly speeded”;
”I have at least one friend who I have seen to become *very* speeded on 1 ½ tablet 36mg Concerta ...”;
”Buy Ritalin myself and it's only 10mg, but I'll be right nice on them! but the high will not be for very long ”;
”Is it just 18mg [Concerta] you have to eat 4-6x to get a buzz that works..”;
”You can become sick high by Methylphenidate, I become ”socially high” on a 37mg-tab ”;
”What is a normal dose of ADHD drug (beginners and experienced)?”
[Answer:] ”Something between 40-60mg I would say, more is needed after an hour or so to keep the buzz alive ...”

“…euphoric effects cannot be achieved with an intact dosage form”.
Johnson & Johnson, RMP, 23 November 2009

“ritalin 40 mg are not so strong you need 2 to experience a pretty good buzz, think Concerta 54mg is much better ...The buzz: SPEED, generally happy, want to talk about feelings…”
“54-100 mg do I need to get stoned on. works very well…almost like taking amphetamine but a bit worse because it is shorter and doesn’t give such an intensive high….”
“You don’t fucking need 100 tablets, it was 40mg's capsules. People felt eating 2-3.
Then if you injected Ritalin you didn’t even need 40mg, and it was a damn strong shot. So do not talk about stuff you do not have a clue about.”
“I'm no expert on Concerta, but I've taken 90 mg at the most ... On it, and even on a little smaller doses, I got a high that clearly has been in the same class as amphetamine (enormous energy, outward direction, commitment, euphoria…”
“My God .. That's because amphetamines are the drug of choice, in order to feel harmony and euphoria. It is not because you have ADHD that you feel comfortable on amphetamines .. That's because it is a drug that makes you feel like you want to feel. People seem to have incorrect expectations of amphetamine that you should be "nervous" and "running around" - and that it is "unique" that you become concentrated and creative on amphetamine .. Haha. It's a classic effect.”
“From my own experience you can get stoned on nibbling a few 10mg [Ritalin]! The capsules I have never been prescribed so have not actually tested them ..”
“Another thing I noticed is that with Concerta [54 mg] about 20 minutes after I took the pill, I get an extremely pleasant "buzz" feeling. A sort of euphoria. It does not last as long, 1 hour maybe,

but it's so fucking beautiful in that first hour! I will be happy, social, energetic, feel good simply! Is that how it feels with “normal” amphetamines too, or?
“I can chew two pieces of 36mg and feel a little speeded. but it always ends with anxiety and shit, hate Concerta.”
“I have eaten Ritalin 30mg for 3 days and has not had the desired effect yet, but feel more merry about 2 hours after eating a tablet. Then go over to where I get my heart rate sky-high and trembling all day and finally a "withdrawal" consisting of nervous twitches and I get tired. Do hope that it will improve over time ...(Diagnosed with ADD and autism, faint traces of Asperger's.)”

On increasing the dose to get a better buzz:

”I have strong ADHD and Ritalin, 80 mg per day, have never taken it as I should, just abused but if I crush and snort 40mg I get a little power, and I continue then I get greatly speeded ”;
”I do not know what Concerta costs on the black market because I have been diagnosed with ADD and get the shit basically free ... This is my speed, can catch balls and count faster than a calculator at doses of 108mg or more ”;
”I have concerta prescribed fr 72mg (2 * 36mg daily, to get ”high” I take at least 10 54mg chewing of course because it is prolonged”;
”I started taking a bit more than I should because I did not know the impact I had at the beginning, and it became just more and more each time. Now I sit here, a monthly ration finished in 3 days”;
”Have just managed to get my psychiatrist to prescribe Ritalin to me (rimmed up that I have ADHD etc.), But…capsules tablets of 10 mg. My question to you experts is how many of those should be taken to have a bit fun? ”;
”Take Concerta (same as Ritalin) right now, have it prescribed. 1.begins within ten minutes, going up in 30 minutes to. Important: crushed orally if you eat something extra to, a fruit or banana maybe. The increase is VERY nice, I must say, especially if you listen to music. ”;
”but I am prescribed 3x 54mg Concerta ... since 2 months back but sometimes it takes 4-5 (not crushed) so you feel good for many hours ”;

“The formulation makes it difficult, if not impossible to effectively abuse; therefore, is not expected to have an impact with respect to overall public health.”
Johnson & Johnson, RMP, 23 November 2009

”I've had both Concerta and Ritalin prescription since some week even though I have a long addiction behind me with cs. This my psychiatrist knows about. I made the ADHD test and had clear ADHD. The worst thing is that I can not help but chew the capsules in concerta to get a kick effect.. ”.
“I ate 8 pieces Concerta 36 mg total, shared and swallowed them last Thursday. Was super sick speeded so I would not even touch one of those pills again ha ha .. it was super sick. Felt so bad on withdrawal 10 times worse than on the ordinary amphetamine cannot even describe the low and tormented myself night until morning without being able to sleep more than maybe 10 minutes all night and just stare at the ceiling and felt bad .. am still not normal after those .. but you know well but never feel normal anyway I really do prefer real amphetamine!”
“yes it is good to have more than two 54mg, but be prepared for a tough withdrawal. Everyone do not get an annoying withdrawal but can imagine that most people get it. I think it is far worse than usual withdrawal from amphetamine.”
“Of course to get a good buzz so I need to take 2 and a half Concerta 54mg”
“162 mg of Concerta is sufficient enough to get decently speeded!”
“I have a neuropsychiatric disorder (ADHD) and treated with Ritalin tablets 10 mg orally (active substance: methylphenidate). The dose I really need is about. 2 times less than what I have been prescribed per month (managed to fool my doctor that I need more). The rest I have some fun with after I solve the tablets, filters, etc. so I can shoot it. When I shoot, I am almost always home.”

On experimenting with different ways to take the amphetamine preparations to get a better buzz (chew, crush, snort, inject):

”Ritalin is so fucking nice, I love them. Smash balls or snort alternative mix with water the drink kicks in like hell between 20-80mg is usually enough for me one evening ”;
”Ritalin is taken up in an excellent way orally and gives effect almost immediately. Ritalin is possible to shoot, and it provides a similarity to cocaine ”;
”yes, Ritalin gives a buzz. similar to amphetamine I would say. I am using my medication nasally when I am partying, works fine. but can imagine to crush it and bomb it works very fine ”;
”Concerta ... Add tab between 2 spoons, then take a hammer and hit so you get them apart, is also possible to inject this, but sticky, so best to swallow!”;
”You can take it both orally and nasally, of course, different dosing then”.
“Use to be on 40mg tabs [Ritalin] that I crush and take the best way!”
“If it should turn, I usually take between four and eight 36es [Concerta] .. If you do not want to chew them so it's a simple thing to take a knife and split them lengthwise … However the withdrawal is not play with ..”
“I took 80mg and felt a little speeded. Snorted 40mg and felt at least 4-5 times more speeded.”
“It is possible to be stoned and the easiest is to nibble. Personally, I have to take at least 100 mg. [Ritalin] to be speeded, but *the more, the merrier*.”
“I tested my sister's Concerta a few months ago, I think I began with 4*36mg crushed. I got a nice feeling in the body that reminded a bit of tramadol, but less euphoria (though I do not have much to compare with)”
“Agree Concerta works great shit to snort. Do snort half 54 mg and take the other half orally (crushed) then I feel damn good for 2-3 hours.”
“I have Concerta prescribed, most people think it is a pretty fun thing, but withdrawal is bloody boring, and sometimes even more annoying than on true A[mphetamine. By the way I peel them and usually run at 2-3, it makes me a little bit happy…”
“Sitting at the moment and a bit fuzzy on Concerta I came across. Took 3 pieces, because I'm pretty inexperienced. Crunching them btw, tasted shit. Anyway, I got me a decent kick None überrus [big buzz] exactly but will do.”

“…it is virtually impossible to abuse it through injection, snorting, or inhalation means.”
Johnson & Johnson, RMP, 23 November 2009

“Enough to snort about 50mg [Concerta] for me, and then I get totally comfortable "speeded".”
“Well, I know a guy who shoots Ritalin instead of amphetamine and now he also said that he thinks it beats better for him than what amphetamines do.”
“I've always got a really nice buzz from them, and one can only hope that the effect would be there longer. The short half-life similar to that of coffeine makes you have to snort in more every two hours to keep the high. The high, however, is very nice. A completely clean feeling of energy and focus.”
“Concerta is of course true nice to take. Nice buzz, talkative, speeded, emotional (but not so good if you have too many secrets)
The first time I took 2, 36R, crunching them. Felt gold, but was not prepared for withdrawal, so of course it sucked hard. Now I have to take around 100-120mg to get the desired effect.”
“have eaten 5 peeled today and this is a horrible withdrawal.”

On selling or giving away the preparations to others and in that way spreading the abuse:

”Ritalin **…**mates with ADD do not take and I'll get 'them. 2 cans of 30mg 30 buttons in each ie 60 tablets. What are they worth? ”;
”A buddy've fixed up some maps Ritalin that he thought to “feast” on. Is it easy to mix with alcohol, how cautious should you be? ”;
”My buddies poked in the 3 tab of these ADHD medication when he was really drunk because of alchohol. Resulting in that he could [not] breathe, type slobbered all the time, impossible to contact every now and then and lost his breath when he was trying to sleep ”;
”My friend (who…has DAMP) does not like to take his medication, and usually give it to me I do not have huge experience of drugs, just think

“A total of 3 adverse events with…Drug diversion have been received in the postmarketing database cumulative 01 August 2000 to 10 August 2009.”
Johnson & Johnson, RMP, 23 November 2009

that it can be fun sometimes. So, if I want to get the maximum effect of Concerta, how should I proceed? ”;

”hey, one buddy has ADHD and is eating Concerta, so I wonder. How many 18mg tablets we need chew / swallow to get us drunk? ”;

”I did try ADHD pills from a friend, Concerta, and yes, I started taking type - 4 pieces, chewed and swallowed, then I took some booze and beer”;

”Have a buddy who had ADHD before. And he kept a jar with Concerta. But not so strong, he says (?). 30 tablets of 200 SEK. Good price? ”;

”A friend has Concerta 18 mg and now, I wonder how the hell I'm going to abuse them (the capsules) like an instruction manual step by step”.

“Remember when I took 300mg of my then girlfriend's Ritalin. There we can we talk about the worst I have experienced in form of withdrawal! Maximum anxiety and quite impossible to sleep even though I was exhausted, succeeded to go to sleep after 18 hours.”

“The girlfriend has ADHD and Concerta 36mg has been prescribed. have tried a few times, even earlier today. There is nothing like pulling a rope in my opinion. Concerta lasts longer. With alcohol, it is actually quite nice. 'll have a great pleasure in the body, with a little shudder very often. Then I chewed the tablet before…Do not get speeded, or something like that, but calmer, and release of some concern. However, I have only taken 38mg at most.”
