Open Letter to Dr. Ian Hudson, Chief Executive of the MHRA

2 February 2014

ADHD drugs - Will MHRA handle the Concerta scandal by approving Ritalin for adults?

In the beginning of 2011 secret internal MHRA documents revealed: The application to get the ADHD drug Concerta approved for adults was **refused**; Concerta was found to have "negative benefit/risk balance" for adults.

The disapproval of the drug for adults has been a well-kept secret: NO information whatsoever has been issued by the MHRA or the other European medical agencies about the disastrous results.

Let's look on what was hidden for doctors and the public.

This is the not published table over the Adverse Events of Concerta in clinical trials. It is part of the manufacturer Janssen's "Response Document" (page 84) to the MHRA, from 11 January 2011.

Table 59. Number (%) of Subjects With an Important Adverse Event by Adverse Event Category of Special Interest and by Treatment Group
(CONCERTA EU SCS: All Treated Subjects Analysis Set)

Adverse Event Categories of Special Interest	Placebo (N=309) n (%)	DB CONCERTA (N=596) n (%)	Total CONCERTA (N=1369) n (%)
Total no. subjects with Adverse Events	87 (28.2)	307 (51.5)	815 (59.5)
Hypertension	12 (3.9)	32 (5.4)	136 (9.9)
Tachycardia	0	36 (6.0)	81 (5.9)
Raynaud's phenomenon	2 (0.6)	3 (0.5)	6 (0.4)
Psychosis/mania	3 (1.0)	17 (2.9)	45 (3.3)
Anorexia	23 (7.4)	174 (29.2)	394 (28.8)
Migraine	6 (1.9)	7 (1.2)	25 (1.8)
Repetitive behaviours	0	1 (0.2)	1 (0.1)
QT prolongation	1 (0.3)	0	4 (0.3)
Arrhythmias	11 (3.6)	80 (13.4)	240 (17.5)
Cerebrovascular disorders	0	1 (0.2)	1 (0.1)
Aggression	17 (5.5)	71 (11.9)	202 (14.8)
Hostility	0	3 (0.5)	11 (0.8)
Depression	32 (10.4)	100 (16.8)	270 (19.7)
Suicidality	0	1 (0.2)	3 (0.2)
Tics/tourette's syndrome/dystonias	4 (1.3)	25 (4.2)	72 (5.3)
Carcinogenicity	0	0	5 (0.4)
Withdrawal syndrome	0	1 (0.2)	1 (0.1)

In the Company's **three best (!)** studies of Concerta on adults, the ones **chosen** for Janssen's application, the following harmful events emerged in the short-term studies (up to 13 weeks), where Concerta was compared to placebo:

- The persons who received Concerta had a **270% increased risk for heart disorders in form of Arrhythmias**;
- The persons who received Concerta had a **116% increased risk for Aggression**;
- The persons who received Concerta had a **62% increased risk for Depression**;
- The persons who received Concerta had a **225% increased risk for neurological disorders in form of Tics/Dystonias**;
- The persons who received Concerta had a **190% increased risk for Psychosis/Mania**;
- The persons who received Concerta had a **295% increased risk for Anorexia**;

The combined studies showed that Concerta had no significant positive effects for adults and that the drug caused a number of serious adverse event – the most important ones

described in the table above. Some countries like Holland and France were very negative to the presented evidence from Janssen, while others, like Sweden, wanted to *in some way* get the application through anyway (despite the disastrous results in the trials).

The assessor at the MHRA requested the following in July 2010: "The risks of anxiety/anxiety disorders, depression, aggression, agitation restlessness, suicide related events, psychosis, mania/delusions, decreased appetite, clinically important decreased weight, cardiac arrhythmias, tics/worsening of tics or tourette's syndrome should be added to the Safety Specification as Important Identified Risks."

Janssen had to back down and said: "**The Company no longer seeks an extension of the indication to include adults with ADHD."** Janssen repeats this statement 29 times (!) in the "Response Document" to the MHRA. And so, no new warnings were issued to other authorities, doctors or patients.

The disapproval was a shock to the ADHD industry and to some medical agencies in Europe. In Sweden the Medical Products Agency (MPA) had for years allowed an explosion in the "off label" prescription of Concerta to adults, with the assumption that the drug was soon to be approved.

And the agency had been assisted by the current Chairman of the Committee for Medicinal Products for Human Use (CHMP) at the European Medical Agency (EMA), Tomas Salmonson, in his position at the MPA.

However Concerta was disapproved, found to be harmful and without any significant positive effects for adults. This did not stop the marketing in Sweden.

The prescription of Concerta to adults in Sweden increased with 60% (!!) from 2010 to 2013. Janssen sold the ***disapproved*** drug Concerta to adults in Sweden for 488 million SEK (45 million GBP) in these three years. (See updated figures from Apotekens Service AB **http://jannel.se/N06BA.pdf**)
The highest sales figures for 2013 for methylphenidate in Sweden are for the disapproved drug Concerta to adults.

But now a fantastic "solution" to handle the problem has been presented, having the potential to save the drug manufacturer and all the officials involved in this medical scandal.

And the help for MHRA, MPA and Janssen to handle the scandal comes from an unexpected player – the pharmaceutical company Novartis. The manufacturer of **Ritalin – basically the same drug as Concerta** – has announced its application to get Ritalin approved for adults in Europe. (Swedish press release from 30 January 2013, **http://www.cisionwire.se/novartis/r/novartis-ansoker-om-godkannande-for-ritalin-for-behandling-av-vuxna-patienter-med-adhd,c9362988**)

Novartis has sought "scientific advice" from some of the more positive countries in Europe, about how to get the drug approved. The company has also chosen to only submit this application for Ritalin approval in *some* countries – the more positive ones. Meaning that the company can avoid the negative statements from the same assessors handling the Concerta application.

A spokesperson from the Swedish Medical Products Agency, Bengt Andrée, announced (!) that Novartis´ application about Ritalin for adults will soon be approved. Andrée said in

media: “Everything indicates that treatment for adults will be approved” and that “a statement [about Ritalin] is expected in early summer” (2013).

I am sure Novartis has learned from the failed Concerta submission and that there is a big interest from the officials mentioned above to push through the approval of Ritalin for adults. We can expect that the submitted studies will get a positive assessment this time – no embarrassing questions – and suddenly the concealed and alarming Concerta results can be expected to no longer exist! Janssen will also be saved; no criminal actions will be taken.

But it’s hard to see how the above can fit with the MHRA declaration: “We protect and improve the health of millions of people every day through the effective regulation of medicines and medical devices, underpinned by science and research.”

So Mr Hudson, will the MHRA take part in this dirty game of approving Ritalin, so that we can forget about the Concerta scandal?

Yours sincerely,

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