Open Letter to BfArM-Präsident Prof. Dr. Walter Schwerdtfeger
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10 June 2013

Will BfArM handle the Concerta and Medikinet scandal by approving Ritalin for adults?

In the beginning of 2011 secret internal documents from the British regulator MHRA 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.

At the same time, 14 April 2011, Das Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) announced via its President that Germany had approved the first methylphenidate drug, Medikinet, for adults in Germany. In the Press Release it was said that "the efficacy and safety of use in adults has been well documented" ("die Wirksamkeit und Sicherheit einer Anwendung bei Erwachsenen hinreichend belegt werden") http://www.bfarm.de/DE/BfArM/Presse/mitteil2011/pm02-2011.html?nn=1009632

In other words, while European countries *disapproved* the methylphenidate drug Concerta, and found it to be harmful and without any significant positive effects for adults, BfArM approved an almost *identical* drug for adults, saying it was effective and safe.

Big Pharma recently applauded the decision to approve Medikinet: "In Germany, the private company Medice recently received approval for its methylphenidate drug, Medikinet, in adult ADHD. Germany is the only region to successfully approve a drug for adult ADHD." http://www.ft.com/intl/cms/s/2/8b721a20-b8e9-11e2-a6ae-00144feabdc0.html#axzz2VqbiOOH8

And now BfArM has taken on the "responsibility" to lead the investigation supposed to result in the approval of Novartis' Ritalin in some friendly countries in Europe – countries which the pharmaceutical industry in the article above say are "on board with adult ADHD".

Let's take a look on a very interesting table from the Concerta papers, showing the real harmful effects of methylphenidate on adults – revealed after a medical assessor (UK) asked sharp questions to the manufacturer, Janssen.

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 had requested the following from Janssen: "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."

But in this situation Janssen had to back down and said: **"**The Company no longer seeks an extension of the indication to include adults with ADHD." In other words, Janssen avoided the disastrous situation of having to issue warnings to adults about the harm caused by Concerta.

Concerta is almost identical to Medikinet, both being methylphenidate drugs. The harmful effects of Medikinet are of course the same as for Concerta (see table above).

The only reasons Medikinet could be found to be "safe" would be that manufacturer had designed smarter studies where these effects were hidden – or that the BfArM did not ask the same sharp questions as the UK assessor.

It is a big medical scandal that the German medical agency could approve Medikinet knowing the real effects of methylphenidate on adults, as shown in the Concerta investigation.

While countries like France and Holland were very active in the Concerta investigation, seeking the actual effects and recommending disapproval, Germany was quiet.

And the manufacturer of Ritalin, Novartis, knew which countries and medical agencies in Europe are "on board with adult ADHD" and has chosen to apply for approval of Ritalin only in these countries (to begin with).

And now we know that BfArM is *leading* the work-sharing procedure supposed to result in the approval of Ritalin in these "friendly" countries.

I am sure Novartis has learned from the failed Concerta submission and that there is a big interest from German officials to push through the approval of Ritalin for adults. We can expect that the submitted studies will get a positive assessment exactly as in the Medikinet case – no embarrassing questions – and suddenly the concealed and alarming Concerta results can be expected to no longer exist!

But it's hard to see how the above can fit with the BfArM declaration: "Protection of human health is our highest goal. We therefore strive together towards guaranteeing the best possible provision of medicinal products and medical devices to the general public as well as towards preventing the abuse of narcotic drugs."

Finally I want to put your attention on the astonishing new research data about methylphenidate to adults, presented by some of most known researchers in the field some weeks ago. These research data ***must*** be taken into consideration when handling applications for the approval of methylphenidate to adults. It is very clear from this unique research project ***that methylphenidate is the cause of harmful changes in brain chemistry after long-term (one year) use.***

Please see the article **"Long-Term Stimulant Treatment Affects Brain Dopamine Transporter Level in Patients with Attention Deficit Hyperactive Disorder"**, in PLOS ONE, 15 May 2013**,**
http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0063023

So, Mr. Schwerdtfeger, will the BfArM really take part in this dirty game of approving Ritalin, so that we can forget about the Concerta and Medikinet scandal?

Yours sincerely,

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