To: Medicines and Healthcare products Regulatory Agency (MHRA)
Copy: EMA (all CHMP members)

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Janssen-Cilag and the off label prescription of the ADHD drug Concerta to adults in Sweden

The assessment of Janssen-Cilag's application to get Concerta approved for adults in Europe found that the drug could not be approved for adults.

The benefit/risk balance of Concerta for adults was found to be negative, serious harmful effects had been proven in the submitted material, the combined studies showed no significant positive effects, the drug was not to be given to adults.

Below I report about the exploding prescription of Concerta to adults in Sweden *after* the European disapproval of Janssen's application.

In May 2011 the European investigation was completed and a final agreement was presented in a Final Variation Assessment Report for Concerta. **[1]**

It can be summarized as follows:

- The combined studies showed that Concerta had no significant positive effects for adults and that the drug caused a number of serious adverse effects, Concerta had a "negative benefit/risk balance" for adults;

- The submitted studies gave clear evidence that Concerta could ***cause*** anxiety and agitated conditions in adults ("evidence for the risk of new-onset anxiety, tension and agitation");

- The submitted studies gave clear evidence of the abuse potential and of the risk of diversion of Concerta;

- A ***causal*** relationship was established for Concerta for aggression, tics, and depression;

- No warnings were to be issued about the fact that it had been proven that Concerta could cause anxiety, agitated conditions and aggression in adults, ***for the simple reason that Concerta should not be prescribed to adults*** ;

- Concerta could ***only*** be prescribed to adults who before the age of 18 had received methylphenidate (Concerta, Ritalin) and who were judged to have had an "adequate response and acceptable tolerance", ***and*** for which a withdrawal of the drug had

been tried without success. The pharmaceutical company Janssen-Cilag declared that it agreed to the following conditions: **"those patients with ADHD who would be considered for continuation of treatment into adulthood *must* have previously been treated with methylphenidate and continue to show adequate response and acceptable tolerability."** [Emphasis here.] No other adults could be considered.

It was decided (FVAR p. 9) the following for Concerta in Europe (for the period October 2010-October 2011): **("The usage [of Concerta] may not increase in this time period.") [1]**

But the opposite happened in Sweden.

In 2011 the prescription of Concerta to adults (19+) in Sweden increased with 25%, according to official data from Apotekens Service AB (Pharmacy Services Company). [2]

This means that Janssen-Cilag sold Concerta *to adults* for 113 million SEK in 2010, and increased the sales to adults up to 142 million SEK in 2011. The prescription in DDD to adults increased from 6 589 035 in 2010 to 8 290 329 in 2011. [2] 61% of all methylphenidate prescription (DDD) to adults was for Concerta. [2]

Instead of taking action to fulfill the requirements for the prescription of Concerta to adults (as agreed in FVAR 26 May 2011) the pharmaceutical company *increased* its sales volume of Concerta *to adults* with 25%.

Instead of informing doctors and patients that Concerta should NOT be used for adults, explaining what the European assessment of the studies showed, the pharmaceutical company announced the European decision about Concerta as a successful approval of the drug.

Janssen-Cilag is stating in its promotional material to health care personnel: "Concerta is now – as the only methylphenidate drug – approved for continued treatment in adult age!" [3]

The company is in other words turning the *disapproval* of the application for Concerta to adults into a unique *approval* of the drug for continued treatment in adult age.

In the latest RMP I have access to (version 2), Janssen- Cilag is stating: the vast majority (94.0%) of retail prescriptions of CONCERTA were prescribed to children and adolescents between the ages of 6 and 20 years", saying that off-label use was not a problem at all in Europe.

I don't have data about the off label prescription in other countries in Europe, but can for sure say that these figures are false and misleading as regards the off label prescription of Concerta in Sweden, the last couple of years.

As for 2011 we can, with access to the Prescription Drug Registry of the National Board of Health and Welfare, say: **57 % (!!) of the prescriptions for methylphenidate in Sweden 2011 were for off-label use, for adults 20+. (DDD for 0-19 was 9 570 246; DDD for 20+ was 12 808 417). [4]**

I want to know that this information is well received by the MHRA and made part of the investigation into the prescription of Concerta to adults.

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[1] MHRA, *Final Variation Assessment Report, FVAR*, Concerta, 26 May 2011,
[2] Apotekens Service AB, Prescription of ADHD-drugs in Sweden 2007-2011, http://jannel.se/ADHD.droger2007-2011.pdf
[3] Janssen-Cilag, Promotional letter, January 2012, http://www.janssen.se/content/backgrounders/janssen-cilag.se_swe/eNewsletters/concerta/ADHD_01_SE_01-2012.html
[4] The National Board of Health and Welfare, The Prescription Drug Registry http://192.137.163.49/sdb/lak/val.aspx