To: European Commission
Copy: WHO Collaborating Centre Uppsala
Copy: Swedish Ministry of Health and Social Affairs
Copy: Director General Swedish Medical Products Agency

17 January 2009

The Swedish Medical Products Agency and serious deficiencies in the Pharmacovigilance Activities – in violation of Volume 9A: The Rules Governing Medicinal Products in the European Union

According to the EC Directive Volume 9A: The Rules Governing Medicinal Products in the European Union, the Competent Authorities "should have in place systems for receipt and evaluation of all pharmacovigilance data and to ensure that appropriate regulatory action may be taken" (Establishment of a Pharmacovigilance System, page 109) **[1]**. In their pharmacovigilance activities the Competent Authorities "should also interact regularly and as required with relevant national and international bodies (e.g. national haemovigilance centres, centres for disease control, poison centres), regarding exchange of appropriate and timely information" (page 117).

The data presented below should be compared to these requirements.

An investigation has been done into all suicides reported to the Swedish National Board of Health and Welfare in 2007 and what psychopharmacological treatment, if any, preceded these suicides. The data gathered has then been compared with the serious adverse drug reaction reports, with outcome death in form of suicide, submitted to the Medical Products Agency (MPA) for that year.

Methods and results of investigation

All suicides in Sweden committed *in health care and within four weeks after last health care visit* should be reported (Lex Maria) to the National Board of Health and Welfare. The first full year of reporting per the new law was 2007. It is estimated that this subgroup of suicides is about one third of all suicides committed in the country for this year.

For this study, data about the cases reported to the six regional offices of the National Board of Health and Welfare for 2007 was requested using the Freedom of Information Act (FOIA). *Focus was on the psychiatric drug treatment that the persons received within one year of their suicides.* (Note that the information in this part is taken from actual copies of patient journals where sensitive information has been excluded by the regional offices, *but* with full data about prescribed drugs included.

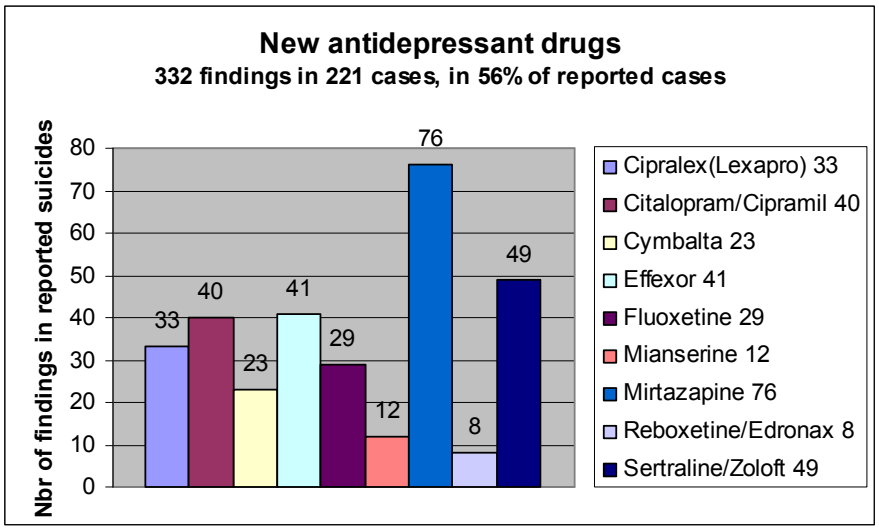
In total, according to the data received, **393 cases** were reported to the six regional offices for 2007.

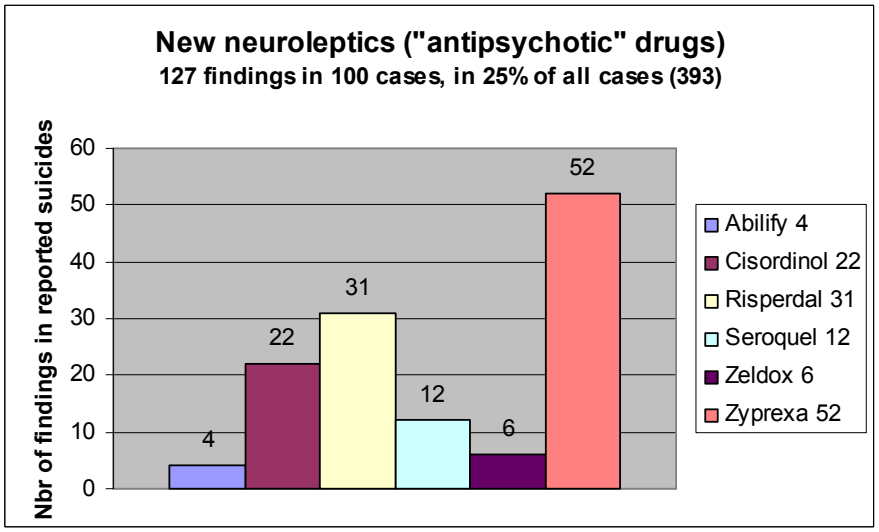
The information in these cases has been analysed with regard to *what* psychiatric drug treatment preceded the tragic suicide in each of the cases. Data has been compiled about the *classes* of psychiatric drugs used (neuroleptics, antidepressants, benzodiazepines etc.) and about the *individual* drugs used.

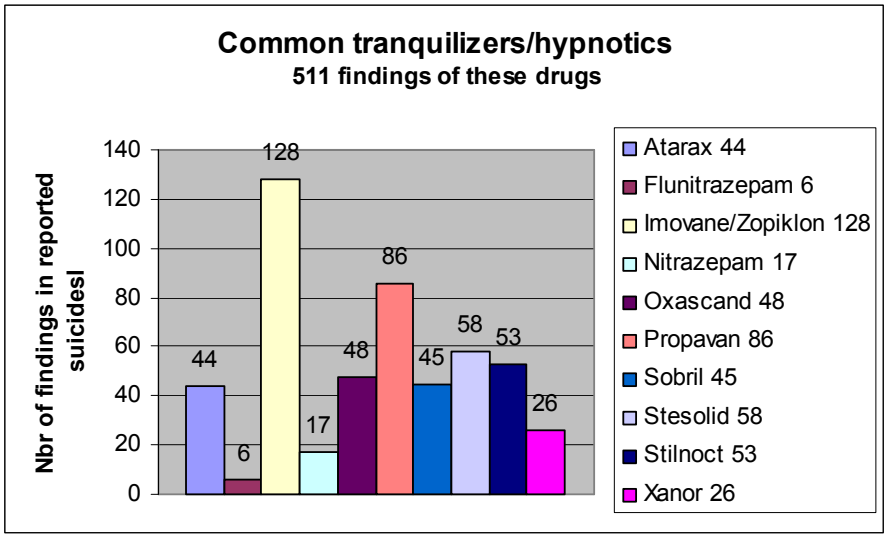
The analysis of the treatment given shows that in 338 of the 393 cases – **in 86% of the cases** – the persons were treated with psychiatric drugs ***within one year of their suicide***. In 304 cases – **in 77% of the cases** – the persons were treated with antidepressant drugs *and/or* neuroleptics.

The persons described got (as an example):
the new antidepressant drugs (Cymbalta 23 persons, Effexor 41, Zoloft/Sertralin 49, Cipralex 33);
the new forms of neuroleptics (Risperdal 31, Zyprexa 52,);
the new hypnotics, similar to benzodiazepines (Zopiclone/Imovane 128, Stilnoct [Ambien] 53);
the new "mood stabilizers" (Lamictal 21, Lyrica 19).

See diagram below for details:





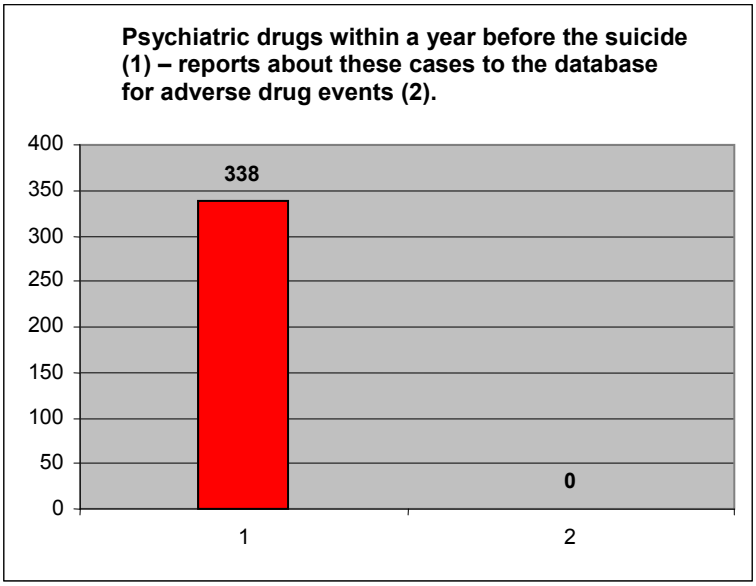


From the research material many serious adverse drug reactions, having a direct or indirect relation to the following suicide, can be observed.

The reporting of the serious adverse drug reactions to the Medical Products Agency

Upon questioning the Medical Products Agency about reported adverse drug reactions in relation to these 338 cases with outcome death (in form of suicide), the following was revealed:

Not a single adverse event report was submitted about the 338 persons who committed suicide 2007 after having been prescribed psychiatric drugs!



This means that the *only place* where this wealth of data is available *in a compiled* form is in the shelves of a lay person (the undersigned) – and that *none of it* is available for risk analysis by the Competent Authority, the Medical Products Agency!

In the research material different phenomena having to do with psychiatric drugs can be seen. It can be seen that the psychiatric drugs prescribed induced suicidality or increased suicidality (especially in the beginning, when doses were increased/lowered, when other drugs were added, or during the withdrawal phase). Examples of the harmful drug effect *akathisia* as an underlying cause in cases of suicide can be found. As the persons who committed suicide got on the average four different psychiatric drugs the preceding year, quite some examples of harmful interactions can be seen.

In short, and as said, this is an extremely important material for the Competent Authority to analyse – yet no information about this exists in the data base of the Medical Products Agency.

What should be done to follow the rules established in the EC Directive

I have notified the MPA about the wealth of vital data described above and about the complete breakdown of the reporting system. However the interest in rectifying the deficiencies in the pharmacovigilance activities has been low. In an answer (18 November 2008) the Acting Director General (note, not the current Director General) just explained: "Only the circumstance that somebody commits suicide with the help of medical drugs does not motivate that this is registered as an adverse event from the medical drug in question." As seen in the material above the outcome suicide was not just for *somebody*, it was for 338 persons, and of course the situations differed very much, it was not at all only suicides "with the help of medical drugs" (meaning overdose). Further the Acting Director General explains in his letter that persons with a psychiatric disease "have a considerable increased death rate" and that this depends upon "the psychiatric disease they are suffering from". He says: "Treatment with psychiatric drugs decreases to a high degree the risk for early death through for example suicide, but unfortunately it cannot be eliminated completely."

I find these comments very inapproriate considering that the MPA has not got and has not evaluated the data I have described above.

One of the requirements for the Competent Authorities is to "encourage reporting of suspected adverse reactions by Healthcare Professionals" (Undertaking of Pharmacovigilance Activities by Competent Authorities in Member States, page 108). The fact that *none* of these adverse drug reactions with outcome suicide was reported to the MPA shows that the agency *has failed completely on this point*. The comments from the Acting Director General – if seen as representative for the message sent out by the MPA – further says that the Competent Authority does not only *not encourage* reporting but also *invalidates* the reporting of adverse events. This should of course be rectified as soon as possible.

As the MPA does not, per the Directive, "have in place systems for receipt and evaluation of all pharmacovigilance data" – as evidenced by the fact that not one single of the above described serious adverse events is reported – the data submitted to the EC and WHO Collaborating Centre is flawed – to say the least. This means that the appropriate regulatory actions cannot be taken, and that patients are put in serious risk.

The Competent Authorities "should also interact regularly and as required with relevant national and international bodies (e.g. national haemovigilance centres, centres for disease control, poison centres), regarding exchange of appropriate and timely information".

The MPA has also on this point failed to follow the established rules. *All* data about adverse drug reactions described above (the 338 cases) are available at the six regional departments of the National Board of Health and Welfare. The MPA has not cooperated with this very relevant national body in order to get the safety data sent to the MPA. This should of course be done as the first step of rectifying this serious situation.

Yours sincerely,

Janne Larsson
Reporter
Snöbollsgränd 22
129 45 Hägersten
Sweden
janne.olov.larsson@telia.com

References:

[1] European Commission, *Volume 9A of The Rules Governing Medicinal Products in the European Union (Guidelines on Pharmacovigilance for Medicinal Products for Human Use)* September 2008, http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-9/pdf/vol9a_09-2008.pdf