Danish Pharmacovigilance Update

Volume, 1 # 7
20 May 2010

Pandemrix® update

Since 4 November 2009, the Danish Medicines Agency has received 611 adverse drug reaction reports (ADR reports), covering altogether 1850 suspected adverse reactions. Most of the reports describe non-serious and already known adverse reactions. The Danish Medicines Agency concludes that the nature and seriousness of the adverse reactions seen so far after vaccination with Pandemrix® correspond to expectations, which is also in line with observations made by the European Medicines Agency, which receives all ADR reports from the European countries.

How many people have been vaccinated in Denmark?

The Danish Serum Institute has dispensed approx. 1,050,000 vaccine doses, and an estimated 340,000 persons have been vaccinated, of which 100,000 have been vaccinated twice.

Who are behind the reports?

Since 4 November, 85 % of the ADR reports have been submitted by doctors and other healthcare professionals, while 15 % have been submitted by the vaccinees.

Age distribution of persons experiencing side effects after vaccination with Pandemrix ®

The age distribution is as follows (based only on reports where age was disclosed):

Group	Age	Volume
Infants	0-1	7
Children	2-12	36
Adolescents	13-18	21
Adults	19-64	416
Elderly	65+	86

Gender distribution	
Women	403
Men	206
Not specified	2

The table below shows the ten most frequently reported side effects from Pandemrix®. They are all recognised side effects of the vaccination.

Side effect	Volume
Fever	137
Headache	106
Sleepiness	74
Discomfort	72
Nausea	70
Aching muscles	70
Dizziness	65
Pain at injection site	61
Arm pain	50
Joint pain	41

The Danish Medicines Agency will continue to closely monitor the development in the reported side effects from Pandemrix®.

Read the latest status report here: *Side effects from Pandemrix® from 23 January to 18 April 2010*

Focus on the safety of treating ADHD with methylphenidate (Ritalin, etc.)

The Danish Medicines Agency reports a steady upward trend in the use of medicines for the treatment of ADHD (Attention Deficit Hyperactivity Disorder) measured over the last 10 years. Read the report here: *More than a 10-fold increase in the number of people treated with ADHD drugs in the last 10 years in Denmark*

Especially methylphenidate-containing drugs (Ritalin, etc.) have been the preferred choice of drug. This has led the Danish Medicines Agency to put greater focus on the safety of methylphenidate-containing drugs.

New recommendations for the use of methylphenidate-containing drugs in ADHD treatment

The European Medicines Agency (EMA) has updated the recommendations for the use of methylphenidate-containing medicines after an in-depth review of data from ADR reports, clinical trials and published literature. The updated recommendations appear from the summary of product characteristics for methylphenidate-containing drugs.

Prescribers should pay special attention to:

Indications:

- Methylphenidate is indicated as part of a comprehensive treatment programme for attention-deficit / hyperactivity disorder (ADHD) in children aged 6 years of age and over when remedial measures alone prove insufficient.
- Treatment must be under the supervision of a specialist in childhood behavioural disorders.
- The decision to use the drug must be based on a thorough assessment of the severity and chronicity of the child's symptoms in relation to the child's age.

Contraindications:

- Diagnosis or history of severe depression, anorexia nervosa/ anorexic disorders, suicidal tendencies, psychotic symptoms, severe mood disorders, mania, schizophrenia, psychopathic/ borderline personality disorder.
- Diagnosis or history of severe and episodic (Type I) Bipolar (affective) Disorder (that is not well-controlled).
- Cardiovascular or cerebrovascular disorders.

Pre-treatment screening:

- A comprehensive history must be obtained including a family history of any sudden cardiac death, unexplained death or malignant arrhythmia and of past or present comorbid psychiatric disorders.

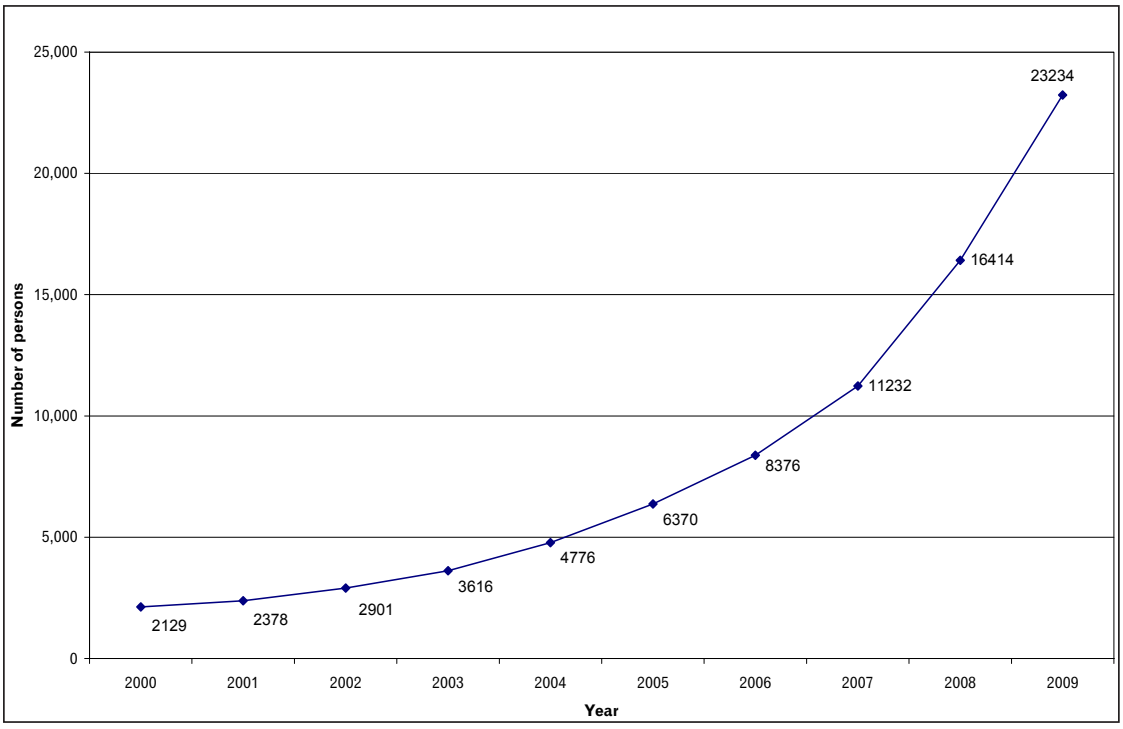


Figure 1. Number of persons in methylphenidate-treatment from 2000 to 2009.

- It is necessary to conduct an objective evaluation to assess the presence of cardiac disease and to evaluate the patient's general cardiovascular status – including blood pressure and heart rate.

Monitoring of treatment (at each dose adjustment or at least every 6 months):

- Blood pressure and heart rate must be monitored.
- Patients who develop symptoms of heart disease such as palpitations, chest pain, fainting or similar symptoms should promptly be examined by a specialist.
- Weight, height and appetite should be measured regularly.
- Signs of development or worsening of psychiatric disorders such as depression, suicidal ideation, aggression, anxiety, psychosis and mania should be monitored.
- Prescribers and relatives should pay attention to signs of abuse, excessive use and the possibility that the medicine is passed on to others.

Special precautions associated with long-term use of methylphenidate

The safety and efficacy of long-term use of methylphenidate have not been systematically evaluated in controlled trials. If long-term treatment (over 12 months) is necessary, it is advised to discontinue treatment at least once a year to assess the patient's functioning without pharmacotherapy.

Danish ADR reports concerning methylphenidate-containing medicine

The Danish Medicines Agency has received a total of 183 ADR reports, describing altogether 427 suspected adverse reactions from the use of methylphenidate-containing drugs. The vast majority of the reports (95 %) came from physicians and other healthcare professionals, while the rest were reported by patients themselves or their relatives. Overall, the number and type of adverse reactions reported are in proportion with the quantity of methylphenidate consumed and correspond to the established risk profile of methylphenidate-containing medicines.

The majority of the reports concern boys or young men who have been/are treated with methylphenidate. About half of the reports (43 %) are classified as serious. The ten most frequently reported adverse reactions appear in the table below.

Side effect	Number of reports
Headache	13
Dizziness	11
Anxiety	9
Sleepiness	9
Reduced appetite	8
Chest pain	7
Nausea	7
Depressed mood	6
Depression	6
Palpitations	6

Table 1. The ten most frequently reported adverse reactions to methylphenidate medicines.

In addition, the Danish Medicines Agency has received 19 and 18 reports, respectively, describing lack of effect or decreased effect of methylphenidate.

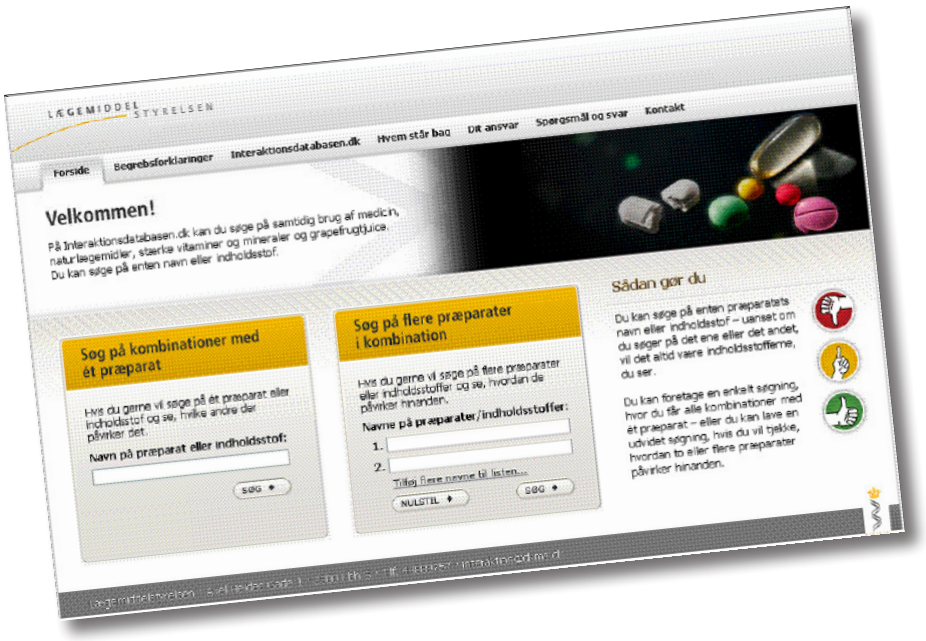
During the summer 2010, the Danish Medicines Agency will publish a more detailed report about adverse reactions and the safety of treatment with methylphenidate.

Isotretinoin (Roaccutan®, etc.) and rare risk of serious skin reactions

The EU Pharmacovigilance Working Party is presently investigating the possible relation between the use of isotretinoin for the treatment of severe acne and the development of serious skin reactions such as erythema multiforme, toxic epidermal necrolysis and Stevens Johnson syndrome.

Doctors should discontinue treatment with isotretinoin in patients who develop any such serious skin reactions.

The Danish Medicines Agency is following the case.



Quality assurance of the Danish Drug Interaction Database

Clinical pharmacologists from Denmark's three pharmacological departments at Bispebjerg Hospital, Odense University Hospital and Aarhus University Hospital are presently validating the quality of the Drug Interaction Database.

The project is to help maintain and preserve the quality of the database's content so that medical recommendations can still be made on the basis of validated data.

Integrated in the Medicine Profile

The Drug Interaction Database is an integrated element of the Medicine Profile, which means that the Medicine Profile automatically checks for interactions between the products that are registered in the patient's medical profile.

The Medicine Profile is accessed via www.sundhed.dk.

The Drug Interaction Database in brief

Since 2003, doctors have been able to look up information about drug interactions in the Danish Medicines Agency's Drug Interaction Database. Worded in Danish, the database describes approx. 2,500 interactions between a variety of drugs. It also contains interactions with some herbal medicines and strong vitamin and mineral products as well as grapefruit juice.

Each interaction contains a brief description and a recommendation instructing doctors on how to handle the interaction, which, for example, could be to adjust the dose.

It is also possible to see detailed information about each interaction, available in the form of short reviews of relevant literature including reference lists.
www.interaktionsdatabasen.dk

Danish Pharmacovigilance Update is published by:
Danish Medicines Agency
www.dkma.dk
Editor-in-Chief:
Henrik G. Jensen (HGJ)
Editor:
Nina Vucina Pedersen (NVP)
ISSN 1904-2086