Danish Pharmacovigilance Update

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Sibutramine-containing medicines suspended due to increased risk of cardiovascular events

Due to an increased risk of cardiovascular events, the European Medicines Agency has recommended the suspension of all marketing authorisations for sibutramine-containing medicines.

The Danish Medicines Agency therefore advises

- doctors to stop prescribing sibutramine.

Patients can safely discontinue treatment without consulting their doctor.

Click this link to read the full sibutramine announcement: *European Medicines Agency recommends suspension of marketing authorisations for sibutramine due to increased risk of cardiovascular events*

Epoetins - important to record the trade name in patient files and ADR reports

It is important that doctors record the trade name for patients treated with epoetins in patient files and adverse drug reaction (ADR) reports. You can look up the information in the Medicine Profile. The trade names are important because the competent authorities of the EU Member States are currently assessing whether there is a difference between epoetin products when it comes to the risk of developing a very rare adverse reaction known as pure red cell aplasia.

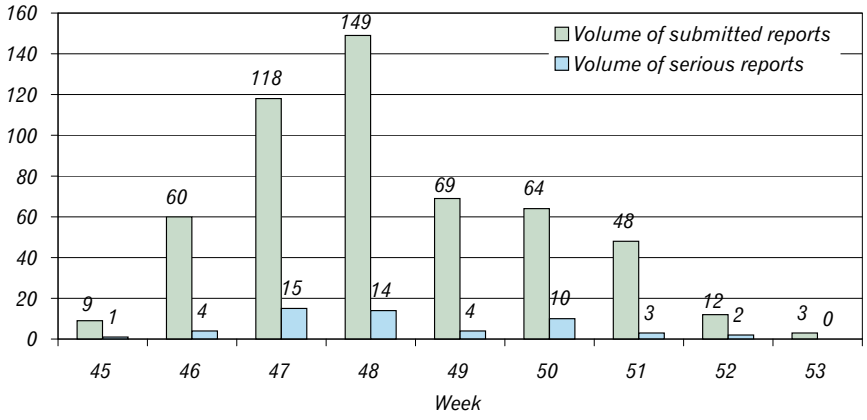
Click this link to read the recommendation: *CHMP Pharmacovigilance Working Party*

The H1N1 epidemic is over, but there is still influenza A virus in Denmark

The Danish National Board of Health still recommends vaccination for persons in an at-risk group, healthcare and nursing staff as well as persons in important functions in society. It is not unlikely that Denmark will see more people infected with influenza A later on. Find out more at the website of the Danish National Board of Health: *Influenza A (H1N1)*. The information is in Danish.

Pandemrix® update

The number of adverse reaction reports submitted since 4 November 2009 totals 547, covering altogether 1690 adverse reactions. The chart below shows you the weekly concentration of reports starting on 4 November 2009 when the first Pandemrix® vaccine was given in Denmark.



How many people have been vaccinated in Denmark?

The Danish State Serum Institute has dispensed approx. 1,050,000 vaccine doses. Currently, the number of vaccinees is registered at 420,000 persons. The actual number is expected to be far higher, but due to delays in the registrations the exact number is not available.
Read the latest Pandemrix® update at: *Side effects from Pandemrix® from 19 to 8 January 2010*

Who are behind the reports?

Since 4 November, 84 % of the adverse reaction reports have been submitted by doctors and other healthcare professionals, while 16 % have been submitted by the vaccinees.

Age distribution

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

Group	Age in years	Volume
Infants	0-1	7
Children	2-12	36
Adolescents	13-18	21
Adults	19-64	376
Elderly	65+	70

Gender distribution

Women	368
Men	178
Not specified	1

Current Eltroxin® status following change in excipients

New analyses of Eltroxin®

The Danish Medicines Agency has now finished laboratory tests of Eltroxin® 50 and 100 micrograms and has found no deviations from the approved specifications.

Based on the ADR data that we analysed, we conclude that there is no immediate cause for further analyses.

We are still keeping a close watch on the progression of adverse reactions reported for Eltroxin®.

Euthyrox® - new levothyroxine product on the market

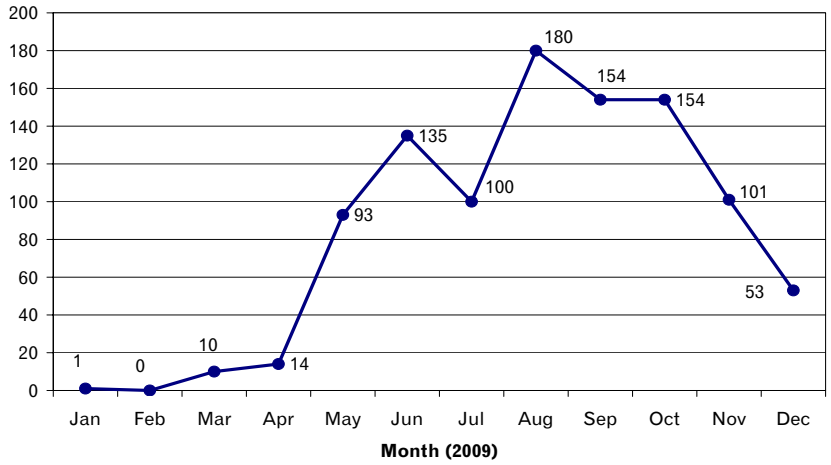
For years, Eltroxin® was the only levothyroxine-containing product sold in Denmark, but on 28 December 2009, Euthyrox® entered the market in the strengths of 25, 50 and 100 micrograms. You therefore no longer need a compassionate use permit for the dispensing of Euthyrox®.

Eltroxin® side effects reported in 2009

From 1 January to 31 October 2009, we received 995 reports describing 5481 suspected adverse reactions. Today, we primarily receive reports of adverse reactions that have been experienced before. The chart below shows how the ADR reports spread over the year.

It is not possible to distinguish between suspected adverse reactions from the new or old formulation of Eltroxin®, but most of the adverse reaction reports presumably concern the new formulation.

The 10 most common side effects reported in the past two years until 31 October 2009 appear in the table below. They are all symptoms suggestive of overmedication or undermedication with Eltroxin®.



Side effect	Volume
Sleepiness	386
Headache	329
Dizziness	231
Nausea	187
Weight increase	153
Disturbance in attention	152
Impaired memory	134
Aching muscles	133
Arthralgia	130
Stomach pain	105

Remember to monitor the level of thyroid stimulating hormone (TSH) when patients switch between levothyroxine products or formulations

When patients switch between different levothyroxine-containing products or formulations, it is very important that doctors monitor the level of thyroid stimulating hormone (TSH), in particular with respect to patients who experience side effects. However, due to the long half life of levothyroxine (approx. 7 days), the level of TSH should not be measured until approx. 5-6 weeks after the patient has started taking the new product/new formulation or the dose has been adjusted. If the patient's optimal TSH level is unknown, doctors should measure TSH level before the switch to a new levothyroxine product or formulation for comparison with the possibly changed TSH level.

Tablets with a scoreline

Euthyrox® tablets have a score-line so that they can be divided into two equal parts.

Click this link to read the latest status report:

Side effects from Eltroxin® - status January 2010

Please report any suspected drug abuse to the Danish Medicines Agency

If you suspect that a certain type of medicine is being abused, you can report it on a special Danish form: *Problems associated with the use of medicine, medical devices or suspicion of drug abuse*

You can also inform the Danish Medicines Agency using the custom form for reporting side effects, which you find at *www.dkma.dk > Pharmacovigilance > Report a side effect*. Remember to write that the report concerns drug abuse.

When is it a case of drug abuse?

Abuse of medicine refers to the persistent or sporadic, intentionally excessive use of a drug, accompanied by harmful physical or mental effects.

Medicine with a known abuse potential

Medicines like opioids, anxiolytics/hypnotics (benzodiazepines) and stimulants of the central nervous system are known for their addictive properties. But this is also the case for substances like anticholinergics, antihistamines and substances with other mechanisms of action.

In Denmark, medicines with a known potential for abuse appear on a special list of euphoriant substances (narcotic drugs and psychotropic substances). Find out what they are here: *Euphoriant substances (the list is in Danish)*

Apart from medicines with an already known potential for abuse, we also want to be advised of abuse problems involving a new medicine or medicine in general.

Focus on pregabaline, tramadol and methylphenidate

We are currently looking at pregabalin and tramadol, which are two substances that do not yet appear on the list of euphoriant substances. We are also looking at changes in consumption patterns for methylphenidate, which is already on the list.

Wider collaboration broadens knowledge and minimises risk

At the Danish Medicines Agency we cooperate nationally and internationally to broaden our knowledge and minimise the risk of drug abuse. We can add information to the concerned summaries of product characteristics and tighten provisions for drug dispensing. In cooperation with the Danish National Board of Health, we can also put drugs on the list of euphoriant substances, one of the effects being that the concerned substance is made subject to import/export and posession controls.

Correction regarding short-acting beta2 agonists brought in Danish Pharmacovigilance Update (17 December 2009)

In the last issue of Danish Pharmacovigilance Update, we wrote that the use of short-acting beta2 agonists to inhibit uterine contractions is contraindicated in women with pre-existing or with significant risk factors for ischaemic heart disease. This only applies when short-acting beta2 agonists are used to inhibit uterine contractions. Pregnant women with asthma can still be treated with short-acting beta2 agonists.

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Follow-up questions about ADR reports

Doctors who have filed an ADR report will not be contacted by the Industry

Any contact between doctors reporting side effects and the pharmaceutical company responsible for the products goes through the Danish Medicines Agency, with one exception. If a doctor chooses to contact the pharmaceutical company directly, the company may contact the doctor for further information about the adverse reaction.

When we receive a report from a doctor, the following chain of events occur:

1. The Danish Medicines Agency forwards all ADR reports to the responsible pharmaceutical companies - personal data are anonymised before dispatch.
2. The pharmaceutical company sends any follow-up questions directly to the Danish Medicines Agency.
3. The Danish Medicines Agency forwards these questions to the reporting doctor, who then returns with a reply to the Agency.
4. The Danish Medicines Agency forwards the answer to the company(ies) involved.

Doctors can actively reduce the volume of follow-up questions when they report ADRs to the Danish Medicines Agency

The side effect

When did the side effect start? Provide the start and end date of both the side effect and treatment with the medicine suspected to have caused the reaction.

List any disease that the patient has had or still suffers from that may have impacted the reaction. Other diseases may be crucial in assessing causality.

The medicine

Information about the medicine causing the adverse reaction Doctors are reminded that they have the option of providing the trade name of the medicine actually dispensed. The Medicine Profile gives easy access to information about the medicine dispensed by the pharmacy to the patient. If possible, provide the name of the manufacturing company(ies) as this will enable us to launch follow-up measures targeting the specific medicine suspected to have caused the adverse reactions experienced by the patients.

When the side effect began, did the patient take other medicines not directly linked to the reaction? Remember to list any other medicine that the patient is taking even if you do not suspect it to be directly linked to the side effect. This way, it is easier to assess possible interactions.

The patient

Patient data. If possible, give the patient's civil registration number and provide as many patient details you can. If you do not know the patient's civil registration number, please provide us with the patient's date of birth, initials, age and gender. Patient initials: write the first letter of the patient's first, middle, and last names (max five characters in total). Doing so makes it easier for us to identify the person having experienced the side effect, and double entries will be avoided.

Height (e.g. 180 cm - use numbers only) and weight (e.g. 75 kg - use numbers only) - always provide the patient's height and weight if known.

What is a suspected side effect?

Doctors must report side effects of medicines, even if it is only a suspicion. In other words, you do not need to be sure that there is a causal relationship between the observed adverse reaction and the medicine to report it to the Danish Medicines Agency.

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