Danish Pharmacovigilance Update

Volume, 1 # 9
19 August 2010

New safety information on the use of medicine with ketoprofen for local inflammatory disorders (Fastum Gel®, Orudis Gel® and Ketospray®)

After several adverse reaction reports on serious skin reactions from use of medicine with ketoprofen for topical use, the Committee for Medicinal Products for Human Use (CHMP) has performed a scientific study of medicine containing ketoprofen for topical use.

The study showed that the vast majority of serious skin reactions have occurred in connection with sunlight or by concurrent use of octocrylene – a UV filter present in several lotions and especially in sunscreens. Some skin reactions even led to hospitalisations.

Medicine containing ketoprofen for topical use is made prescription-only, and prescribers should therefore inform their patients of the following recommendations:

1. Wash your hands thoroughly after each application of the gel.
2. During treatment and for two weeks after stopping treatment, the skin must be protected from sunlight and UVA rays.
3. Use clothing to protect treated skin areas from sunlight.
4. Don't use medicine with ketoprofen for topical use under a bandage.
5. Stop the treatment immediately if you develop a skin reaction after application of spray/gel and consult your GP.

The Committee has concluded that the benefits of medicine containing ketoprofen for topical use still outweigh the risks.

In all EU countries, harmonised guidelines will be implemented for healthcare professionals, and a pictogram will be added to the outer packaging. Summaries of product characteristics and package leaflets will be updated on an ongoing basis.

Read more here:

Press release

Q&A

Updated summary of product characteristics for oral contraceptives with drospirenone (Yasmin®)

Two new epidemiological studies of the risk of venous thromboembolism (venous blood clots) in users of contraceptive pills have caused updates of the summaries of product characteristics of contraceptive pills with drospirenone (Yasmin®).

The risk of venous thromboembolism from use of oral contraceptive pills containing drospirenone is slightly higher than previously assumed.
The new studies suggest that the risk of venous blood clots from use of contraceptive pills with drospirenone is slightly higher than previously estimated. The risk falls between the risks of second and third generation oral contraceptives, whereas the risk was previously assumed to be at the same level as contraceptive pills with levonorgestrel (i.e. second generation pills).

Among women using combined oral contraceptives with a low oestrogen content (<50 g ethinylestradiol), the prevalence of blood clots is 20 in 100,000 for contraceptives with levonorgestrel (second generation pills) and 40 in 100,000 for contraceptives with desogestrel/gestodene (third generation contraceptives).

The new findings have been added to the summary of product characteristics:

Yasmin, film-coated tablets (in Danish)

Low general risk of blood clots from use of oral contraceptives
The risk of venous blood clots from use of contraceptive pills remains very low. The risk should be considered against the benefits of contraceptives. In women not using hormonal contraception, the prevalence of blood clots is 5-10 in 100,000 women. In pregnant women, the prevalence of blood clots is 60 in 100,000 pregnancies.

These are the two new epidemiological studies:

- Lidegaard Ø, Løkkegaard E, Svendsen A, Agger C. Hormonal contraception and risk of venous thromboembolism: a national follow-up study. Br Med J. 2009; 339: b2890.

- Van Hylckama Vlieg A, Helmerhorst FM, Vandenbroucke JP, Doggen CJ, Rosendaal FR. The venous thrombotic risk of oral contraceptives, effects of oestrogen dose and progestagen type: results of the MEGA case-control study. Br Med J. 2009; 339: b2921.

Read more here:

Monthly report from the Pharmacovigilance Working Party

Status on Eltroxin®

In 2009, the Danish Medicines Agency experienced a large increase in the number of adverse reaction reports on Eltroxin®, following the manufacturer's change in excipients. A little over a year after this increase, we still monitor the number of reports closely. Here is the latest status.

Number of adverse reaction reports submitted from January 2009 to June 2010

From 1 January 2009 to 31 June 2010, the Danish Medicines Agency received 1,125 side effect reports concerning Eltroxin®. See the chart below.

Who are behind the reports?

80 % of the adverse reaction reports were submitted by patients and/or their relatives, while 20 % were submitted by doctors and other healthcare professionals.

Type of adverse reaction reports submitted from January 2010 to June 2010

The reports submitted now mainly describe side effects that patients have experienced before. About 15 % of the adverse reactions reported from January 2010 to June 2010 occurred in 2010.

The 10 most common side effects from Eltroxin® reported in the period January 2010 to June 2010 appear in the table below.

Side effect	Volume
Sleepiness	526
Headache	425
Dizziness	299
Nausea	228
Disturbance in attention	214
Weight increase	211
Impaired memory	186
Joint pain	177
Aching muscles	178
Hair loss	134

These side effects are all symptoms which may indicate overdosage or underdosage of Eltroxin®.

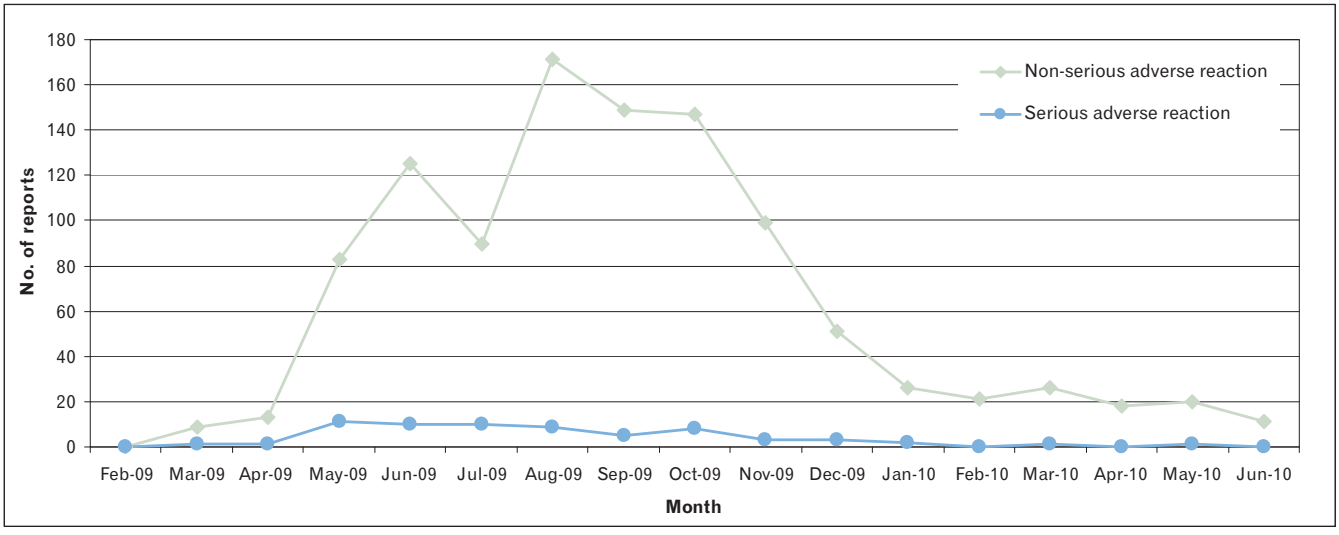
Current status

We expect that the majority of the adverse reactions reported to the Danish Medicines Agency occurred in response to the reformulation of Eltroxin®, which can cause symptoms suggestive of overmedication or undermedication. We therefore estimate that the number of reports containing new adverse reactions will continue to decline. But we will continue to monitor the development of the number of reported side effects.

Precautionary measures to be taken by doctors

When patients switch between different levothyroxine-containing products or formulations, it is very important that a doctor monitors 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 after dose adjustment.

Previously, Eltroxin® was the only levothyroxine-containing product sold in Denmark, but on 28 December 2009, Euthyrox® entered the market in the strengths 25, 50 and 100 micrograms. Euthyrox® tablets have a scoreline so that they can be divided into two equal parts.



See the latest status on Eltroxin® on the Danish Medicines Agency's website: *Side effects from Eltroxin® - status July 2010*

Report side effects from food supplements to the Danish Veterinary and Food Administration

Lately, several doctors have submitted adverse reaction reports to the Danish Medicines Agency that concern side effects from food supplements. Food supplements fall under the Danish food legislation, and any suspected side effects from food supplements should therefore be reported to the Danish Veterinary and Food Administration (DVFA).

If doctors suspect that a food supplement has caused a side effect, they can report it to the DVFA by e-mail *fvst@fvst.dk*. As topic, please write "Fødevarestyrelsens 7. kontor".

If possible, the report should include:

- A brief description of the suspected side effect – (possibly with a suggestion of the ingredient suspected to have caused the adverse reaction).
- Information about the food supplement suspected to have caused the side effect (name, type, declared content, place of purchase, period of use and dose).
- Information about concurrent use of other food supplements and/or medicines.
- The patient's gender and age.
- Reporter details.

Side effect report led to withdrawal of food supplement

Last year, the Danish Veterinary and Food Administration received a side effect report from a doctor concerning a woman hospitalised with severe hepatitis and incipient hepatic failure after having used a food supplement with bark from the plant Rhamnus purshiana DC.

Based on these serious adverse reactions, the Danish National Food Institute made a new risk assessment of this plant ingredient. This caused five food supplements to be withdrawn from the Danish market. Subsequently, the DVFA issued a warning to consumers about using food supplements with a high content of bark from Rhamnus purshiana DC.

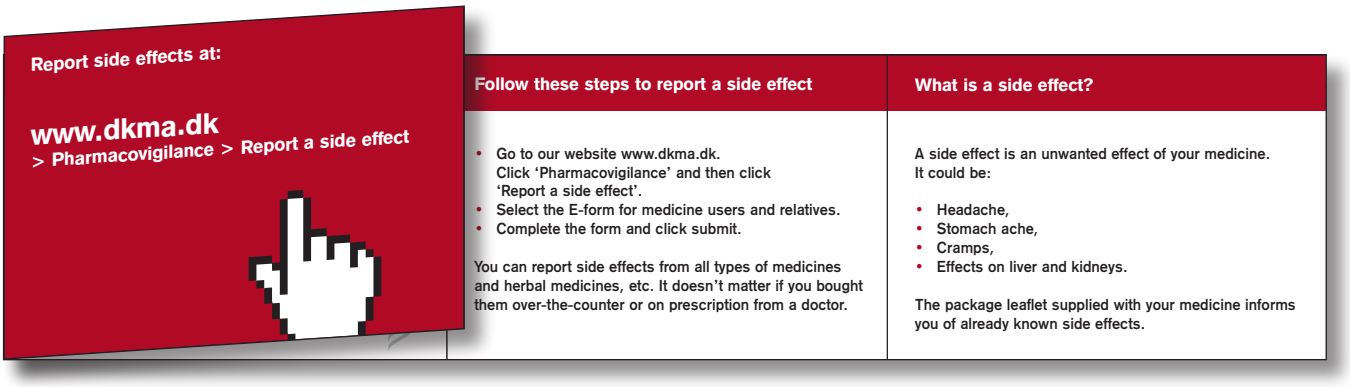
Read more about food supplements on the Danish Veterinary and Food Administration's website: *www.dvfa.dk*

Order side effect leaflets for patients and relatives

"If you have side effects from your medicine" is the title of a small leaflet, which briefly and concisely informs medicine users and relatives of what a side effect is, what to do if you experience side effects, how to report side effects to the Danish Medicines Agency, and what happens to the side effects that are reported.

The leaflet is available in Danish, Turkish and Arabic, and you can order it for your waiting room via the Danish Medicines Agency's website:

Leaflet on reporting side effects from medicine



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