Danish Pharmacovigilance Update

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Increased risk of adverse incidents by use of transdermal patches for treatment of severe pain

Transdermal patches that release morphine analgesic are to an increasing extent used for treating chronic pain conditions. Transdermal patches are a relatively new and advanced treatment form that may come with an increased risk of adverse incidents.

Presently, the Danish market only has transdermal patches with one of the two active substances: fentanyl and buprenorphine. The transdermal patches Matrifen® and Durogesic® contain fentanyl, whereas the transdermal patches Norspan® and Transtec® contain buprenorphine.

Several adverse incidents have occurred in relation to prescription and administration of the pain-relief patches.

Therefore, prescribers should pay special attention to:

- Dosing interval of the pain-relief patches.
- Whether the patient receives treatment with a pain-relief patch before prescribing any other morphine analgesics.

In addition, you should thoroughly inform the patient about how the patch works, where to place it, and how often it need to be changed.

Find out more about treatment with transdermal patches at:
Focus on safe handling and use of pain-relief patches

Updated product information for the OTC medicine Alli®

Alli® was introduced in May 2009 as an over-the-counter (OTC) medicine containing the active substance orlistat (60 mg). Orlistat is also known from the prescription-only medicine Xenical® (120 mg). After a recent review of adverse reaction data on products containing orlistat, several potential side effects described for Xenical® have been added to Alli®'s summary of product characteristics.

Doctors enquired about Alli® bought over-the-counter should pay special attention to the following three groups of patients:

- **Patients with renal disease** – Orlistat can in rare cases cause hyperoxaluria and oxalate nephropathy.
- **Patients treated with a levothyroxine medicine** – If levothyroxine and orlistat are taken simultaneously, they can interact to an extent that makes it difficult to control patients' hypothyroidism. It may be necessary to take orlistat and levothyroxine at different times of the day, and the levothyroxine dose may need adjustment.
- **Patients treated with antiepileptics** – Seizures have been reported in connection with concomitant use of orlistat and antiepileptics (e.g. valproate and lamotrigine)

In addition, instances of pancreatitis have occurred after use of orlistat. Pancreatitis is therefore added to the list of potential side effects in the product information of Alli®.

Most common side effects from use of Alli®

- Loose or oily stools.
- Flatulence.
- Urgent need to defecate.

Please find the entire summary of product characteristics for Alli® here:
alli

Be observant of patients who have used Alscreme 'Creme nr. 2' for eczema and wounds

Alscreme 'Creme nr. 2' has been sold in Denmark via the website www.eminescu.dk, and the cream contains the active substance clobetasol (a group IV glucocorticoid). Apart from the active substance clobetasol, the cream also contains aristolochic acid. This is a toxic extract of the plant Aristolochia clematitis, which can cause hepatic impairment and in the worst case scenario kidney cancer.

The cream is **not** licensed as medicine.

If doctors suspect that a patient may have used Alscreme 'Creme nr. 2' for a long-term period, they should control the patient's renal function because of the aristolochic acid content.

Furthermore, patients who have used Alscreme for treatment of inflammatory skin disease can experience a severe rebound if the treatment is suddenly discontinued. Therefore it may be necessary to treat the skin disease with another corticosteroid-containing cream for a short period.

Find the Danish Medicines Agency's warnings against Alscreme 'Creme nr. 2' at: *Strengthened warning against Alscreme 'Creme nr. 2' from www.eminescu.dk*

New updated product information for Aclasta® (zoledronic acid)

Aclasta® is used for treatment of osteoporosis in men and in postmenopausal women and for treatment of osteoporosis in connection with long-term systemic glucocorticoid treatment.

In addition, Aclasta® is used for treatment of Paget's disease of bone.

In some instances, patients have experienced renal impairment and kidney failure after administration of Aclasta® – especially patients already suffering from renal dysfunction, older patients, patients with concomitant use of nephrotoxic medications, patients with concomitant use of diuretic treatment and patients who were dehydrated when they were administered Aclasta®.

Therefore, the following has been added to Aclasta®'s summary of product characteristics and package leaflet:

- Patients with subjacent renal impairment can have a higher risk of a temporary increase of serum creatinine – patients with a creatinine clearance < 35 ml/min should not be given Aclasta®.
- The serum creatinine level should be monitored in risk patients.
- Aclasta® should be used with due caution when used simultaneously with other medicine that can affect the renal function.

Please find a detailed summary of the conclusion for Aclasta® here: *Monthly Report*

New annual report on monitoring of adverse reactions 2009

At the end of March 2010, the Danish Medicines Agency publishes an annual report taking stock of the 2009 ADR monitoring.

Apart from the chart below (figure A), the annual report gives an account of the ten active substances and vaccines which yielded the most adverse reaction reports in 2009. Also, it contains a joint status of Pandemrix®, Gardasil® and Eltroxin® – the three cases we particularly focused on last year. Finally, we present a selection of cases from the European Pharmacovigilance Working Party to which we have contributed, and take a look at the coming work with side effects in 2010.

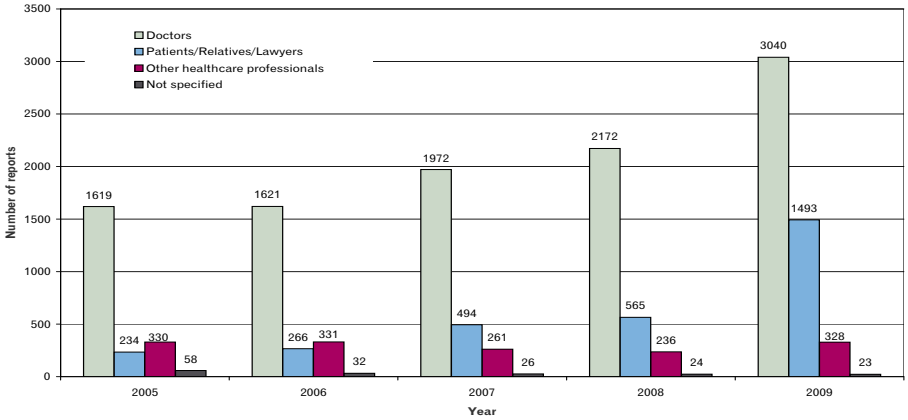

Figure A. Development of the number of adverse reaction reports from 2005 to 2009 according to the function of the person who submitted the report.

Since 2005, the overall number of reported side effects increased markedly. In fact, the number of reports more than doubled from 2005 to 2009. Several factors may explain this development, but one significant cause of the increased reporting is the past years' enhanced focus on reporting of side effects.

The next issue of the Danish Pharmacovigilance Update will link directly to the annual report. However, you may also read the annual report online. The Danish version will be posted on the Danish Medicines Agency's website at the end of March, and the English version will be posted at the end of April.

Danish Pharmacovigilance Update

Status report on Pandemrix®

Now, the Danish Medicines Agency receives a very small number of adverse reaction reports concerning Pandemrix®, but we maintain our strong focus on reported side effects concerning the vaccine. In April, we will therefore issue a status on adverse reaction reports concerning Pandemrix®.

You may find out more by reading the European overview of side effects from the influenza A vaccine at: *Updates on pandemic safety monitoring*

New member of the Pharmacovigilance Working Party

The Danish Medicines Agency's work with side effects is characterised by a great degree of cooperation with other EU countries. Concretely, the cooperation takes place in the European Medicines Agency's (EMA) Pharmacovigilance Working Party (PhVWP). So far, Denmark has been represented by one member, Chief Medical Officer Doris I. Stenver from the Danish Medicines Agency's Consumer Safety Division. Now yet another member of staff from the Danish Medicines Agency's Consumer Safety Division has been appointed by the EMA to participate in the Working Party's tasks, as Chief Medical Officer Torbjörn Callréus has become member of the Working party due to his specialist knowledge within pharmacoepidemiology.

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