Danish Pharmacovigilance Update

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Unintended pregnancies with Implanon®

The lack of efficacy of the contraceptive implant Implanon® has recently been discussed subsequent to receiving reports of a large number of unintended pregnancies among women in England who had Implanon® inserted under the skin.

Problems with inserting Implanon® subdermally

Most reports from Britain are due to incorrect insertion and removal of the Implanon® implant. In some cases, the implant had not been inserted just under the skin as directed in the summary of product characteristics.

Danish reports

Since 1999, when Implanon® was marketed in Denmark, the Danish Medicines Agency has received 28 reports about women who fell pregnant despite using the Implanon® implant. Some of these reports are also about incorrect insertion of the Implanon® implant under the skin.

Doctors should therefore:

- Closely follow the instructions in the summary of product characteristics on how to correctly insert and remove the Implanon® implant. Please find the Danish summary of product characteristics for Implanon here:
  Implanon® NXT, implantat til anvendelse under huden.doc

- Inform their patients how they themselves can locate the Implanon® implant when it has been inserted under the skin.

New version of Implanon®

At the end of December 2010, a new version of Implanon® was marketed, Implanon® NXT, which differs from Implanon® in two ways:

1. Implanon® NXT has a new applicator which is easier to use and increases correct insertion of the implant.
2. Implanon® NXT contains barium sulphate which makes it possible to locate the implant using X-rays or CT scans.

The manufacturer offers doctors an electronic training module followed up with a training session using placebo applicators on artificial arms before inserting Implanon® NXT in patients.

Implanon® is a long-acting contraceptive implant containing third generation progestins for use under the skin.

From January to November 2010, 2546 persons in Denmark had an Implanon® implant inserted (the number has only been calculated for the primary sector, so the total amount is a little higher).

Thelin® withdrawn from market worldwide

On 10 December 2010, Pfizer announced its decision on withdrawing Thelin® from the market worldwide further to reports on serious liver damage.

Indication

Thelin® (sitaxentan) is in the group of angiotensin II antagonists, and is indicated for treatment of pulmonary arterial hypertension (PAH) to improve exercise capacity.

Why Thelin® has been withdrawn

Thelin® has been withdrawn due to a review of three deaths related to liver damage; a post-marketing case from 2009 in Britain and two cases from clinical trials in India and Ukraine. An idiosyncratic pattern of Thelin®-related liver damage, identified recently, cannot be ruled out. The Thelin®-related liver damage does not appear to be related to identifiable risk factors or be detectable at monthly monitoring, and in some cases, the liver damage is irreversible after Thelin® is discontinued. Therefore, it does not appear possible to minimise the risk of liver damage in treatment with Thelin®.

Based on the available information and given alternate treatments, it was concluded that the benefits of Thelin® no longer outweigh the risk in the population of PAH patients.

The company has notified the relevant healthcare professionals about its decision to withdraw Thelin® from the market.

Thelin® has rarely been used in Denmark. The Danish Medicines Agency has not received any reports concerning Thelin®.

Fluoroquinolones and risk of QT prolongation

The European Council for Adverse Drug Reactions has completed a study of a number of substances from the fluoroquinolone class of antibiotics with regard to risk of QT prolongation.

The Council concluded that, with respect to the potential for inducing QT prolongation, fluoroquinolones can be divided into three groups based on a review of adverse reaction reports and studies covering the period from 1999 to 2008:

1. Fluoroquinolones **with a potential risk** of inducing QT interval prolongation: Gemifloxacin and moxifloxacin.

2. Fluoroquinolones **with a low potential risk** of inducing QT interval prolongation: Norfloxacin, levofloxacin and ofloxacin.

3. Fluoroquinolones **with a very low potential risk** of inducing QT interval prolongation **or for which there are insufficient data available to assess the risk**: Enoxacin, perfloxacin, prulifloxacin and rufloxacin.

The Council found that the fluoroquinolones, especially those in group 1, have the potential risk of inducing life-threatening torsades de pointes, especially under conditions favouring the development of QT prolongation, e.g. hypokalaemia, hypomagnesaemia or bradycardia.

The risk of QT prolongation is already described in some summaries of product characteristics for fluoroquinolones. However, in regard to the study, the Council has recommended updating the summaries of product characteristics identically for each of the three risk groups.

For further information on the recommended updates, please read (pp 4-5):
http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/01/WC500100459.pdf

The substances included in the study were: enoxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin, pefloxacin, prulifloxacin and rufloxacin.

Only three of these substances are licensed in Denmark: moxifloxacin, levofloxacin and ofloxacin.

Medicines with special precautions for use

- Isotretinoin-containing medicine
- Aclasta®
- Benefix®
- Cimzia®
- Daxas®
- Efient®
- Exwjade®
- Gliolan®
- Ilaris®
- Increlex®
- Instanyl®
- Kaletra®
- Lucentis®
- MabCampath®
- Macugen®
- Mircera®
- Mycamine®
- Multaq®
- Nplate®
- Qutenza®
- Renvela®
- Retacrit®
- Revlimid®
- Revolade®
- Simponi®
- Soliris®
- Stelara®
- Tasigna®
- Thalidomide Pharmion®
- Thelin®
- Tracleer®
- Tysabri®
- Valdoxan®
- Volibris®
- Zypadhera®

Medicines with special precautions for use

The list to the left contains the names of medicines that doctors must pay special attention to before prescribing them to patients.

For example:
- Prescription may require additional training for doctors.
- Patients must be given important information before use.

Click the name of a medicine to read its special precautions for use and see who is responsible for them. The names link to the summaries of product characteristics in Danish. English versions are available (for centrally authorised products only) at the website of the European Medicines Agency: *www.ema.europa.eu*

The list is updated regularly.

Find out more about medicines with special precautions for use:

Medicines linked to a risk management plan (in Danish only)

Medicines with stricter reporting requirements

Prescribers are reminded to report all suspected adverse reactions observed within the first two years following placement on the market.

Click on the list below to see what medicines are subject to stricter reporting requirements.

List of medicines with stricter requirements for doctors, dentists and veterinarians to report side effects (Excel file, only in Danish)

At the Danish website *www.medicin.dk*, you can also see if a medicine is subject to stricter reporting requirements. If this is the case, it will be stated under the description of adverse reactions.

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