

FDA Patient Safety News: Show #80, October 2008

Warning on Tendon Injuries with Fluoroquinolone Antibiotics

FDA has asked that a boxed warning be added to the prescribing information for fluoroquinolone antibiotics. The warning will remind healthcare professionals that patients taking these drugs may experience an increased risk of tendinitis and tendon rupture. Fluoroquinolones include Cipro (ciprofloxacin), Factive (gemifloxacin), Levaquin (levofloxacin), Avelox (moxifloxacin), Noroxin (norfloxacin), Floxin (ofloxacin) and Proquin (ciprofloxacin hydrochloride).

FDA is concerned that large numbers of tendon problems were continuing to be reported, despite a warning that already appears in the labeling for these drugs. The boxed warning is being added to draw the practitioner's attention to this information. This can also affect the benefit-risk decisions that are made when these drugs are prescribed.

Certain patients are at greater risk for these injuries, including those over 60, those taking corticosteroids, and patients who have had heart, lung or kidney transplants. Certain tendons are also more likely to be affected. The Achilles is the most commonly affected, but other tendons can also be involved, including those in the rotator cuff, the biceps, the hand and the thumb.

It is important to remember that the risk for injury is not necessarily gone when the drug is stopped. Cases have been reported in which tendon problems occurred up to several months after the drug was discontinued. Also, this increased risk of tendon problems applies only to patients who are getting fluoroquinolones systemically; patients taking eye drops or ear drops are not affected.

Fluoroquinolones may be associated with serious risks other than tendinitis and tendon rupture. These risks are rare but may include convulsions, hallucinations, depression, heart rhythm changes, and serious allergic reactions.

Since fluoroquinolones are vital drugs in treating certain bacterial infections, the practitioner may decide that the benefits of the drug outweigh the risk for a given patient. In these cases, the practitioner should caution patients to watch out for pain, swelling or inflammation in a tendon area, because that could signal tendinitis, and to know the signs and symptoms of a tendon rupture.

If patients experience any of these things, they should avoid using or exercising that area of the body, stop the drug, and see their doctor about the possibility of switching to another type of antibiotic. It is important that patients understand what to look for and what to do, so FDA has asked the manufacturers of fluoroquinolones to develop a Medication Guide containing this information, which will be given to the patient with each prescription.

Additional Information:

FDA MedWatch Safety Alert. Fluoroquinolone Antimicrobial Drugs. July 8, 2008.

<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm089652.htm>

CT Scanning May Cause Malfunction of Electronic Medical Devices

FDA is alerting healthcare professionals that the x-rays emitted during CT exams may cause some electronic medical devices to malfunction. These malfunctions are different from those related to MRI scanning, which

are caused by strong electrical and magnetic fields.

Most patients with electronic medical devices do not experience problems with CT scans, but FDA has received a small number of reports in which the scans may have caused unintended shocks from neurostimulators, malfunctions of insulin pumps, and transient changes in pacemaker output. Theoretically, defibrillators, cochlear implants and retinal implants could also be affected.

Here is what FDA recommends to help reduce any possible risk:

- Before beginning a CT scan, use scout views to check whether the patient has an electronic medical device and where it is. If the device is in or very near the area to be scanned, there are several steps to take.
- Determine the device type. If it is an externally worn device, try to move it out of the scan range, if possible. If it is a neurostimulator, ask the patient to temporarily shut it off.
- During the scan, minimize x-ray exposure to the device by using the lowest x-ray tube current that will allow you to get the required image, and by making sure that the x-ray beam does not dwell over the device for more than a few seconds. If the procedure requires continuous scanning over the device for longer than that, as with CT perfusion or interventional exams, be ready to take emergency measures to treat adverse reactions if they occur.
- After the scan, remind the patient to turn the device back on if it was turned off beforehand. Even if the device was turned off during the scan, ask the patient to be sure that it is working properly. If not, tell the patient to contact their healthcare provider as soon as possible.

Additional Information:

FDA MedWatch Safety Alert. Electronic Medical Devices. July 14, 2008.

<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm078709.htm>

Update on Cardiopulmonary Reactions with Ultrasound Micro-bubble Contrast Agents

FDA is alerting healthcare professionals about labeling changes for ultrasound micro-bubble contrast agents, which are sold as Definity (Perflutren Lipid Microsphere) Injectable Suspension and Optison (Perflutren Protein-Type A Microspheres for Injection). These products are used during echocardiography to enhance a cardiac image.

The revised labeling continues to highlight the risk of serious cardiopulmonary reactions, either while the contrast agent is being administered or within 30 minutes afterwards, especially in patients with pulmonary hypertension or unstable cardiopulmonary conditions.

However, based on a review of published reports and information from physicians, FDA has now determined that the benefits of the diagnostic information provided by Definity or Optison may outweigh the risk of cardiopulmonary reactions, even among some high-risk patients. As a result, these products are no longer contraindicated for patients with unstable cardiopulmonary status, including those with unstable angina, acute myocardial infarction, respiratory failure, or congestive heart failure that has recently worsened.

The boxed warning points out that in these high risk patients, it is important to monitor vital signs, electrocardiography and cutaneous oxygen saturation while administering the contrast agents and for at least

30 minutes afterwards.

Additional Information:

FDA MedWatch Safety Alert. Micro-bubble Contrast Agents (marketed as Definity (Perflutren Lipid Microsphere) Injectable Suspension and Optison (Perflutren Protein-Type A Microspheres for Injection). July 17, 2008.

<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm092270.htm>

Avoiding Cardiotoxicity with Mitoxantrone

FDA is reemphasizing the importance of monitoring cardiac function in patients treated with mitoxantrone, sold as Novantrone and also as a generic. Mitoxantrone is used to treat certain patients with prostate cancer, leukemia and multiple sclerosis (MS).

Congestive heart failure can occur while a patient is being treated with mitoxantrone, or even months or years after therapy is stopped. The risk of cardiotoxicity increases as the cumulative dose increases.

In 2005, the product labeling was updated to recommend that MS patients have their left ventricular ejection fraction (LVEF) checked before each dose of mitoxantrone, in addition to having a baseline measurement before starting treatment. Since that time, a postmarketing safety study has shown that quantitative LVEF monitoring was not being performed in a majority of MS patients treated with the drug.

Given the possibility of severe cardiotoxicity, FDA is reminding healthcare professionals about the importance of cardiac monitoring of MS patients during treatment with mitoxantrone. Also, FDA is now advising that all MS patients who have finished mitoxantrone receive yearly quantitative LVEF evaluation to detect late-occurring cardiac toxicity.

Additional Information:

FDA MedWatch Safety Alert. Mitoxantrone Hydrochloride (marketed as Novantrone and generics). July 29, 2008

<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm092708.htm>

Serious Complications from Using Recombinant Bone Morphogenetic Protein in the Cervical Spine

FDA is alerting healthcare professionals about reports of life-threatening complications from the use of recombinant human Bone Morphogenetic Protein (rhBMP) in cervical spine fusion. Although FDA has approved two rhBMP products for very specific medical conditions, the safety and effectiveness of rhBMP in the cervical spine have not been demonstrated, and FDA has not approved it for this use.

Over the past four years, FDA has received about 40 reports of complications associated with using rhBMP in the cervical spine. They involved swelling of neck and throat tissue, which resulted in compression of the airway or neurological structures in the neck. Some reports describe difficulty swallowing, breathing or speaking.

Most of the complications occurred between 2 and 14 days following surgery. When airway complications occurred, emergency medical intervention was frequently necessary.

FDA recommends that practitioners either use approved alternative treatments for cervical spine fusion, or consider enrolling as investigators in approved clinical studies. Patients treated with rhBMP in the cervical spine should seek medical attention immediately if they have symptoms of an airway complication, such as difficulty breathing or swallowing, or swelling of the neck, tongue, mouth, throat, shoulders or upper chest. Patients should be especially watchful 2 to 14 days following the procedure, when airway complications are more likely to occur.

Additional Information:

FDA MedWatch Safety Alert. Recombinant Human Bone Morphogenetic Protein in Cervical Spine Fusion. July 2, 2008.

<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm079019.htm>

Potentially Fatal Glucose Monitoring Errors with Icodextrin

The Institute for Safe Medication Practices (ISMP) is warning again about the possibility of potentially fatal glucose monitoring errors in patients receiving products that contain other sugars. These include oral xylose, parenterals that contain maltose or galactose, and peritoneal dialysis solutions that contain icodextrin. This issue was also reported in an earlier edition of FDA Patient Safety News.

The problem is that some point-of-care glucose meters use a type of test strip that cannot distinguish between glucose and other sugars. So in these cases, the meter's reading of the test strip will reflect both the patient's actual blood glucose and the other sugar the patient has received. This falsely elevated reading can lead to aggressive insulin treatment, which can result in hypoglycemic shock and death.

The latest ISMP report concentrates on Extraneal, a peritoneal dialysis solution containing icodextrin, which is metabolized in the body to maltose. The ISMP report notes that FDA has received 18 reports of hypoglycemic adverse events associated with Extraneal since it was first marketed in 2002. In three cases, the patient or a family member told the hospital staff about the potential problem, but the staff still relied on erroneous readings from portable monitors.

In one of the reported cases, a 62 year-old hospitalized dialysis patient on Extraneal therapy died from severe hypoglycemia because his treatment was based on falsely elevated glucose readings from an inappropriate meter. This occurred despite glucose readings from the hospital lab that were strikingly lower than those produced by the meter.

Test strips that cannot distinguish between glucose and other sugars contain reagents called GDH-PQQ or GDO. Other types of meters use reagents that are capable of distinguishing glucose from the other sugars. These reagents are called GDH-NAD, GDH-FAD, glucose oxidase and glucose hexokinase. It is important to check the package insert that comes with the test strips to determine which type of reagent they contain.

Here is what ISMP recommends to prevent these glucose monitoring errors in hospitals. Consider using only glucose meters that use test strips that can distinguish between glucose and other sugars. If you use meters and strips that cannot distinguish between the sugars, take these additional precautions:

- On admission and periodically during the hospital stay, find out whether the patient is receiving medications containing other sugars. If so, monitor glucose using only hospital laboratory methods.
- Periodically verify point-of-care blood glucose readings with laboratory results. This can detect errors in

glucose meter readings early enough to prevent harm. This is especially important in patients who are unconscious or unable to communicate, since it may be difficult to ascertain the symptoms of hypoglycemia or the medication history.

- Educate the staff about this potentially fatal problem, and consider safeguards such as drug interaction alerts in computer order entry systems, patient profiles and charts.

Additional Information:

ISMP Medication Safety Alert! FDA Advise-ERR: Prevent dangerous drug-device interaction causing falsely elevated glucose levels. June 19, 2008.

<http://www.ismp.org/Newsletters/acutecare/articles/20080619.asp>
