

FDA Patient Safety News: Show #69, November 2007

New Smallpox Vaccine Licensed

FDA recently licensed a new smallpox vaccine called ACAM2000 which is made by Acambis Inc. This new vaccine is not available for routine use, but will be stored in the country's Strategic National Stockpile. It could be used to inoculate people at high risk of smallpox exposure during a bioterrorist attack.

ACAM2000 is derived from the Dryvax smallpox vaccine, which is no longer made and in limited supply. The new vaccine is made with modern cell culture technology, which allows the vaccine to be produced on a large scale with more consistent quality.

The new vaccine was studied in two populations: those who'd never been vaccinated for smallpox and those who'd been vaccinated many years before. The percentage of unvaccinated people who had a successful immunization reaction was similar to that of the older vaccine. The new vaccine was also found to be acceptable as a booster for those previously vaccinated for smallpox.

Because the new vaccine contains live vaccinia virus, vaccinated people must be careful not to spread the virus from the inoculation site to other parts of their body or to other people. People who receive the vaccine must be given a Medication Guide that explains how to care for the vaccination site properly and lists the serious side effects that can occur.

Additional Information:

FDA Press Release. FDA Approves Second-Generation Smallpox Vaccine. September 1, 2007.

<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108976.htm>

Rare Side-Effect of Codeine in Nursing Mothers

FDA is alerting healthcare professionals about a very rare but serious side effect that can affect the babies of nursing mothers who are taking drugs that contain codeine. The problem affects mothers who are "ultra-rapid metabolizers" of codeine. Ultra-rapid metabolizers have a specific genotype that causes them to convert codeine to its active metabolite, morphine, more rapidly and completely than other people. This can result in the mother having unusually high morphine levels in her serum and breast milk, and this can put her nursing infant at risk of morphine overdose.

A recent report in the literature described a healthy, 13-day-old breast-feeding baby who died of a morphine overdose. His mother was taking codeine at less than the usual analgesic dose.

The prevalence of the ultra-rapid metabolizers of codeine varies for different populations. Among Caucasians, the figure is about 1 to 10 percent. Among African-Americans, about 3 percent are ultra-rapid metabolizers of codeine, and among Asians and Hispanics, about 1 percent. The highest prevalence is among some groups of North Africans, Ethiopians and Saudis, where it can be as high as 28 percent.

It is important to note that nursing mothers have used codeine safely for many years. Many women are sent home after having a baby with analgesics such as acetaminophen with codeine to relieve episiotomy pain or abdominal cramping and many of these women are also breast feeding. Despite this widespread use, FDA was able to find only the one case where the baby clearly died as a result of morphine overdose from breast milk. This means that many breast fed babies born to mothers who are ultra-rapid metabolizers and who are taking codeine will not have a problem, but some babies may.

FDA has cleared a genetic test that can determine whether someone is a rapid metabolizer of a number of drugs, but there's only limited information on using it for codeine. Which means at this point, the test result alone may not correctly predict whether the mother is an ultra-rapid metabolizer of codeine. In other words, the test is not a substitute for a doctor's judgment.

FDA recommends that clinicians who prescribe codeine for a nursing mother do so in the lowest dose for the shortest period of time in order to relieve pain. Clinicians should also educate nursing mothers who may be taking codeine about the signs of morphine overdose in themselves or their infants.

Mothers should understand that they don't need to go without pain relief if they're breast feeding, but they should know what to look for if there's a morphine overdose. For the mother herself, the signs include extreme sleepiness and constipation. The mother should also watch for increased sleepiness in her baby, keeping in mind that breastfed babies usually nurse every two to three hours and shouldn't sleep more than four hours at a time. She should also watch for trouble breast feeding, breathing difficulties and limpness. Mothers should also be aware that morphine may remain in the infant's body for up to several days after the last codeine dose.

Finally, in order to help the FDA understand and quantify this problem, it's important to report possible cases of morphine overdose in mothers and infants. To report an adverse event to the FDA please see the below link.

Additional Information:

FDA MedWatch Safety Alert. Codeine Products Used By Nursing Mothers. August 17, 2007.
<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm152107.htm>

Recall of Braun Normal Saline Flush Syringes

B. Braun Medical, Inc., is recalling over a million normal saline flush syringes because they may contain particles of medical grade silicone. Introducing these particles into the bloodstream could cause phlebitis and organ damage, and possibly pulmonary embolism. The risk is cumulative, and would increase with each additional exposure.

The recall affects normal saline 3 mL in 12 mL syringes, product code 513584, and normal saline 10mL in 12mL syringes, product code 513587. The lot numbers of the recalled syringes end in "SFR." These syringes are used in both healthcare facilities and in caring for patients at home.

Anyone with the recalled syringes should immediately discontinue using them and seek medical attention if they've experienced symptoms that may be related to the product. To arrange for replacement syringes, contact B. Braun at 800-227-2862.

Additional Information:

FDA MedWatch Safety Alert. B. Braun Medical Inc. Normal Saline Flush Syringes. September 14, 2007.
<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm152353.htm>

Heart Rhythm Problems with Haloperidol

A recent FDA alert, along with new labeling, warns health professionals about the possibility of QT prolongation and Torsades de Pointes (TdP) in patients treated with the antipsychotic drug Haldol (haloperidol).

The risk appears to be higher when the drug is administered intravenously or in higher doses than recommended. Injectable haloperidol is approved only for intramuscular administration, but it's sometimes used intravenously to treat severe agitation.

FDA is advising particular caution if the drug is used in patients who have other QT-prolonging conditions, including electrolyte imbalance. Caution should also be used in patients taking drugs known to prolong the QT interval, and in those who have underlying cardiac abnormalities, hypothyroidism or familial long QT syndrome. FDA also recommends ECG monitoring if haloperidol is given intravenously.

Additional Information:

FDA MedWatch Safety Alert. Haloperidol (marketed as Haldol, Haldol decanoate, and Haldol lactate). September 17, 2007.
<http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm174470.htm>

Caution on Abbott Blood Glucose Meters

Abbott Laboratories is warning that the display screens on some of the company's blood glucose meters can malfunction if the meter is dropped onto a hard surface which can interfere with proper glucose readings. The affected meters were manufactured after January 31, 2007 under these trade names:

- Precision
- Xtra
- Optium
- ReliOn Ultima
- Rite Aid
- Kroger

The company says practitioners should advise their patients to keep the meters in the wallet provided with the unit, which offers some protection. If the meter is dropped, the patient should perform a display check, which is described in the User's Guide.

During the display check, if the screen is functioning properly, it will show no missing or blank sections. If the screen is malfunctioning, either the entire screen or some sections of it will be blank. In this case, patients should stop using the device and call Abbott at 1-877-844-4404 to get a free new meter.

Additional Information:

FDA MedWatch Safety Alert. Abbott Blood Glucose Meters. September 11, 2007.

<http://www.fda.gov/medwatch/safety/2007/safety07.htm#Glucose>

Avoiding Dangerous Mixups between Amphotericin B Formulations

In the wake of two recent patient deaths in the UK, the Institute for Safe Medication Practices (ISMP) is again warning healthcare professionals about potentially fatal mixups between various formulations of amphotericin B, which is used intravenously to treat serious fungal infections. The problem occurs when the lipid-based or liposomal formulations of the drug are accidentally substituted for the conventional form, and vice versa.

Lipid-based and liposomal formulations of amphotericin B are prescribed at higher doses than conventional amphotericin B. If the conventional form is given at the dose used for the lipid-based or liposomal formulations, serious and possibly fatal overdosing can occur. Conversely, if the lipid-based or liposomal forms are given at dose appropriate for the conventional drug, underdosing and ineffective treatment can occur.

Here are some of ISMP's recommendations to avoid these errors:

- Ask prescribers to communicate orders using both the brand name and the full generic name. For example, "Ambisome, amphotericin B liposomal."
- With conventional amphotericin B deoxycholate, don't exceed a dose of 1.5 mg/kg daily. And consider establishing dose alerts in computer systems.
- Restrict the preparation and dispensing of amphotericin B products to the pharmacy.
- Store the different forms of the drugs separately, and use cautionary labels to highlight the difference.
- Include lipid-based and liposomal amphotericin B on your list of high-alert medications.
- Require an independent double-check before amphotericin B products are administered.

Additional Information:

ISMP Medication Safety Alert! Worth Repeating: Preventing Mix-ups Between Various Formulations of Amphotericin B. Volume 12, Issue 18. September 6, 2007.

http://www.ismp.org/Newsletters/acutecare/articles/20070906_1.asp

Caution on Baraclude Therapy for Certain HBV Patients

Bristol-Myers Squibb has notified healthcare professionals about a new boxed warning for the antiviral drug Baraclude (entecavir). Baraclude is approved to treat certain patients with chronic hepatitis B.

The boxed warning says that patients infected with both hepatitis B virus and HIV who are being treated with Baraclude for their hepatitis can develop resistance to certain HIV drugs unless the HIV infection is treated at the same time. Because of this, Baraclude is not recommended for HBV patients who also have HIV unless they're receiving highly active antiretroviral therapy.

The labeling also says that patients should be offered HIV antibody testing before starting Baraclude therapy. They should be told that if they have HIV and are not being treated for it, taking Baraclude could increase the chance of their becoming resistant to certain HIV medications.

Additional Information:

FDA MedWatch Safety Alert. Baraclude (entecavir) Tablets and Oral Solution. August 16, 2007.

<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm150836.htm>

Warnings for Rocephin

Roche Laboratories is warning about the danger of administering the antibiotic Rocephin (ceftriaxone sodium) along with IV products that contain calcium, such as parenteral nutrition, because harmful precipitates can occur.

The labeling describes cases of fatal reactions in neonates where precipitates were found in the infants' lungs or kidneys. In some of these cases, the Rocephin and the calcium-containing solutions were administered through different infusion lines or at different times. Even though there are no reported cases of these precipitates in patients other than neonates, there's a potential for this type of interaction in patients of any age.

Because particulates could form, the labeling now says:

- Don't reconstitute or mix Rocephin with products that contain calcium. These include Ringer's solution, Hartmann's solution and parenteral nutrition formulations with calcium.
- Don't administer Rocephin at the same time as calcium-containing solutions, even if they're delivered through different infusion lines.
- Don't administer Rocephin and solutions that contain calcium with within 48 hours of each other.

There are no data on whether Rocephin might interact with calcium-containing products that are given orally. It is also not clear whether intramuscular Rocephin might interact with calcium-containing products, either IV

or oral.

The labeling also reemphasizes that neonates with hyperbilirubinemia should not be treated with Rocephin, especially premature neonates. That's because in vitro studies have shown that Rocephin, like some other cephalosporins, can displace bilirubin from its binding to serum albumin, and that could result in bilirubin encephalopathy.

Additional Information:

FDA MedWatch Safety Alert. Rocephin (ceftriaxone sodium). September 11, 2007.
<http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm152863.htm>
