Family Medicine Clinical Pharmacy Forum

Vol. 1, Issue 6 (Nov/Dec 2005)

Family Medicine Clinical Pharmacy Forum is a brief bi-monthly publication from the Family Medicine clinical pharmacists distributed to faculty and residents of the Department of Family Medicine. Our intent is to provide timely information on broad-based issues of pharmacotherapy, as well as regulatory and practiced-based issues affecting you as a prescriber. If you have suggestions for things you would like to see, please contact us.

Pharmacotherapy Issues.

New Drug: Rozerem® (Ramelteon) is a highly selective, potent MT1 and MT2 melatonin receptor agonist approved for the treatment of insomnia due to prolonged sleep onset, and is the first FDA approved hypnotic that is not classified as a controlled substance. Recommended dose for the treatment of chronic or transient insomnia characterized by difficulty with sleep onset is 8 mg PO taken within 30 minutes of going to bed. Ramelteon should not be taken with or immediately after a high-fat meal due to slower absorption, which is expected to reduce the effect on sleep latency. Common side effects include somnolence, headache, fatigue, nausea, and dizziness. Rozerem® is avaliable as an 8mg tablet; cost per tablet is approximately $2.50, or about $75 for a 30 day supply. This is less expensive than other brand name prescription medications for sleep such as Lunesta® and Ambien® which are approximately $100 for 30 tablets.

New Indication: Lyrica® (pregabalin) was approved by the FDA in December 2004 for the treatment of diabetic neuropathic pain and post herpetic neuralgia. In June 2005, it gained approval as an adjunctive therapy in the treatment of seizure disorders. Pregabalin is structurally similar to gabapentin but has shown 3-10 times the potency of gabapentin for pain and seizure disorders in animal models. Pregabalin is a structural analog of GABA but does not bind GABA receptors. For neuropathic pain 50 mg TID can be initiated followed by an effective dosage of 100mg TID. Dosages up to 600mg/d have been studied but not shown to increase efficacy. Manufacturer reported adverse events included dizziness, somnolence, dry mouth, peripheral edema, blurred vision, weight gain, and difficulty with concentration and attention. Somnolence was frequently reported but appears to be dose-dependent. As with gabapentin, pregabalin dosages need to be limited when creatinine clearance is less than 60ml/min. Pregabalin is a controlled substance in DEA category C-V.

Practice-Based Issues.

Authored and edited by:
Cindy Buys, Pharm.D.; BCPS with contributions by Jennifer Jepsen, Pharm.D. student and Corey Teska, Pharm.D. student
Siouxland Medical Education Foundation
Sioux City, Iowa

Paroxetine in Pregnancy: GlaxoSmithKline in conjunction with the FDA have recently announced revisions to the Pregnancy section of the package labeling for paroxetine and paroxetine CR. Paroxetine is a Pregnancy Category C medication and will continue in this category but GSK is informing health care professionals about additional information regarding its use in pregnancy. A recent retrospective epidemiologic study of 3581 pregnant women exposed to paroxetine or other antidepressants during the first trimester suggested and increased risk of overall major congenital malformations for paroxetine compared to other antidepressants (OR 2.20;95% CI 1.34-3.63). There was also an increased risk of cardiovascular malformations for paroxetine compared to other antidepressants. The majority of cardiovascular malformations were ventricular septal defects.

A separate Swiss study reviewed 4291 infants exposed to SSRI's in early pregnancy and reported no increased risk of overall major malformations in 708 infants born to women with paroxetine exposure in early pregnancy.

Previous epidemiological studies of pregnancy outcomes following early exposure to SSRI's (including paroxetine) has not provided evidence for an increased risk of major malformations. It is important to note that all current epidemiologic information is relative to the use of other antidepressants without a group representing no drug treatment. This is typical for information about drug use in pregnancy because of the inherent difficulties in performing randomized controlled trials in pregnancy. Additional information can be obtained at http://ctr.gsk.co.uk/welcome.asp.

Amantadine Resistance in Influenza A (H3N2): A recent study in Lancet (October 2005) details an alarming increase in the number of amantadine resistant strains of influenza A. The sample of viral isolates (6524) was obtained over the past 10 years from countries throughout the world. Over the past 10 years, the number of resistant isolates has increased from 0.4% to 12.3%. There is wide variability between countries/continents related to the overall incidence of resistant strains, with Asia having the highest levels of resistance, with Hong Kong and China having the highest levels at approximately 70% resistance. The US had significant 1 year (2004-2005) change in susceptibility, with 15% of all US isolates having amantadine resistance. The drug resistant mutations yielded resistance to amantadine as well as rimantidine.

Opticlik Device: is a reusable insulin delivery device (insulin pen) for use with a 3-mL Lantus® (insulin glargine [rDNA origin] injection) Cartridge (U-100) System. Pharmacies stock the Lantus® cartridges; however the Opticlik device is currently only distributed through physicians and diabetic educators. Information on the device can be found at www.opticlik.com.

Authored and edited by:
Cindy Buys, Pharm.D.; BCPS with contributions by Jennifer Jepsen, Pharm.D. student and Corey Teska, Pharm.D. student
Siouxland Medical Education Foundation
Sioux City, Iowa

Ortho-evra/ Clotting controversy – The FDA has recently (November 2005) approved updated labeling to warn healthcare providers and patients that Ortho-Evra® contraceptive patch exposes women to higher levels of estrogen than most birth control pills. The estrogen AUC (area under the concentration time curve) is 60% higher for patch users than birth control pill (35 mcg estrogen) users. The peak estrogen concentration is 25% less in patch users than birth control pill users. In general, increased estrogen exposure may increase the risk of blood clots. It is not yet known if women using Ortho Evra® are at a greater risk of experiencing serious adverse events. Ortho-McNeil Pharmaceuticals is conducting additional studies to compare the risk of developing serious blood clots in users of Ortho-Evra® versus users of a birth control pill containing 35micrograms of estrogen.

Regulatory Issues.

Meningococcal vaccine Menactra® safety update: Menactra® immunization is a meningococcal polysaccharide (Serogroups A, C, Y and W-135) diphtheria toxoid conjugate vaccine. Menactra® is approved for use in persons aged 11-55 to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y and W-135. Meningococcal infection affects 1 person in 100,000 annually and has a fatality rate of 10-14%. FDA posted an announcement on September 30, 2005 that five case reports of Guillain-Barre syndrome have been linked to the Menactra® vaccine. All five individuals affected were either 17 or 18 years of age and had been immunized from June 10- July 25, 2005. Two males and three females were affected and all have recovered with appropriate treatment. Onset of symptoms ranged from 14-31 days following vaccination. All individuals presented with tingling and/or bilateral weaknesses of either upper or lower extremities. ACIP recommendations for immunization remain unchanged at this time but healthcare professionals are encouraged to report any adverse events related to Menactra® to the Vaccine Adverse Event Reporting System (VAERS).

Pseudoephedrine availability during cold and flu season: This will be the first cold and flu season since the implementation of restricted pseudoephedrine availability in May of 2005. This may produce additional patient requests for prescriptions for pseudoephedrine containing products to avoid problems with late night or weekend access to decongestants.

Pemoline (Cylert®) a treatment for ADHD has recently been removed from the market. Remaining ADHD treatments include traditional CNS stimulants (methylphenidate, etc.) and atomoxetine (Strattera®).

Authored and edited by:
Cindy Buys, Pharm.D.; BCPS with contributions by Jennifer Jepsen, Pharm.D. student and Corey Teska, Pharm.D. student
Siouxland Medical Education Foundation
Sioux City, Iowa