DANBURY HOSPITAL
Department of Pharmacy Services
Physician's Newsletter

Volume # 39 **November, 2007** **Number 11**

P&T Actions - Insulin Therapeutic Substitution Protocol Approved:

The Institute for Safe Medication Practices (ISMP) has identified insulin as a high alert medication. High-alert medications are drugs that bear a heightened risk of causing significant patient harm when they are used in error. One of the ways to address this issue is to reduce the number of insulins available in the hospital in order to decrease the potential for adverse drug events. In conjunction with the Section of Endocrinology, the Pharmacy and Therapeutics Committee has approved an insulin substitution protocol. Orders for insulin are to be reviewed by pharmacists prior to administration (except in an emergency). Pharmacists shall evaluate insulin regimens with respect to appropriate formulary product, dose regimens, and timing in relation to meals. When a non-formulary insulin product is ordered, the pharmacist is to provide formulary therapeutic substitution. The available rapid acting insulin analogue will be lispro insulin (Humalog). This substitution will be on a unit-for-unit basis if another brand of rapid acting insulin (such as aspart or glulisine) is ordered. In a similar manner, Humulin NPH will be the intermediate acting insulin and Humulin regular will be the short acting insulin available on the hospital formulary. All mixed human insulins (such as Humulin 70/30) will be substituted for with the appropriate combination of NPH and Regular insulin. The mixed analogue insulins (such as Humalog Mix 75/25) will be substituted for using the appropriate combination of NPH insulin and lispro insulin. The long acting insulin available on the formulary will be glargine (Lantus). If a patient is taking insulin detemir (Levemir) as an outpatient, the total daily dose of insulin detemir will be reduced by 20% and converted to lantus insulin and administered once daily. This is because insulin detemir has a lower unit to unit bioavailability compared to human insulins or glargine. In the initial phase of this program, pharmacists will contact the physician to get authorization for the conversion of insulin detemir to glargine.

John Morehouse, R.Ph.

Risk of Warfarin-Related Bleeding Events and Supratherapeutic INR Associated with Complementary and Alternative Medicine: A Longitudinal Analysis:

Objective: To determine the risk of bleeding and supratherapeutic international normalized ratios (INRs) associated with use of complementary and alternative medicine (CAM) in patients receiving warfarin.

Design: Prospective, longitudinal study.

Setting: An acute care, academic and research hospital in Canada.

Patients: A total of 171 adults who were prescribed warfarin anticoagulation therapy for an expected duration of at least 4 months after enrollment.

Intervention: Patients were asked to complete a 16-week diary by recording bleeding events and exposure to factors previously reported to increase the risk of bleeding and supratherapeutic INRs, including CAM consumption.

Measurements and Main Results: Prescription, medical, and laboratory records were reviewed. Risk factors for bleeding events and supratherapeutic INR (at least 0.5 units above the target range) were evaluated longitudinally by using generalized estimating equation (GEE) modeling. Of the 171 patients completing a diary, 87 (51%) reported at least one bleeding event and 36 (21%) had a supratherapeutic INR. Seventy-three patients (43%) indicated they had used at least one CAM product previously reported to interact with warfarin. Warfarin use of less than 3 months' duration was the only statistically significant risk factor identified for supratherapeutic INR. The CAM therapies associated with an increased risk of self-reported bleeding included cayenne, ginger, willow bark, St. John's wort, and coenzyme Q10. Use of more than one CAM while receiving warfarin was also a significant risk factor. Two CAMs were independently associated with an increased risk of self-reported bleeding: coenzyme Q10 (odds ratio [OR] 3.69, 95% confidence interval [CI] 1.88–7.24) and ginger (OR 3.20, 95% CI 2.42–4.24). Other risk factors significantly associated with increased bleeding included high target INR (2.5–3.5), diarrhea, acetaminophen use, increased alcohol consumption, and increased age.

Conclusions: The use of CAM by patients receiving warfarin is common, and consumption of coenzyme Q10 or ginger appears to increase the risk of bleeding in this population.

Reference: Shalansky, S, Lynd, L, Richardson, K, Ingaszewski,A , Kerr,C; Risk of Warfarin-Related Bleeding Events and Supratherapeutic International Normalized Ratios Associated with Complementary and Alternative Medicine: A Longitudinal Analysis; Pharmacotherapy. 2007;27(9):1237-1247.

FDA MedWatch: Byetta® (exenatide) and postmarketing reports of acute pancreatitis:

The FDA has reviewed 30 postmarketing reports of acute pancreatitis in patients taking Byetta (exenatide), a drug used to treat adults with type 2 diabetes. An association between Byetta and acute pancreatitis is suspected in some of these cases. Amylin Pharmaceuticals, Inc. has agreed to include information about acute pancreatitis in the PRECAUTIONS section of the product label.

Healthcare professionals should be alert to the signs and symptoms of acute pancreatitis and instruct patients taking Byetta to seek prompt medical care if they experience unexplained, persistent, severe abdominal pain which may or may not be accompanied by vomiting. If pancreatitis is suspected, Byetta should be discontinued. If pancreatitis is confirmed, Byetta should not be restarted unless an alternative etiology is identified.

FDA - MedWatch – Provigil® (modafinil) Tablets- WARNINGS Added To Prescribing Information Regarding Serious Rash And Hypersensitivity Reactions, And Psychiatric Symptoms:

The FDA and Cephalon notified healthcare professionals of Warnings added to prescribing information for Provigil (modafinil). Provigil is indicated to improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome, and shift work sleep disorder. The revised prescribing information updates safety information to include warnings regarding serious rash, including Stevens-Johnson Syndrome (SJS) and hypersensitivity reactions, and psychiatric symptoms. Rare cases of serious or life-threatening rash, including Toxic Epidermal Necrolysis, and Drug Rash with Eosinophilia and Systemic Symptoms have been reported in adults and children in worldwide postmarketing experience. Angioedema and multi-organ hypersensitivity reactions have also been reported in postmarketing experience.

Physicians should instruct their patients to immediately discontinue the use of Provigil and contact them if a rash or other hypersensitivity reaction occurs. Healthcare professionals and consumers should also be aware that Provigil is not approved for use in pediatric patients for any indication. In addition, psychiatric adverse experiences (including anxiety, mania, hallucinations, and suicidal ideation) have been reported in patients treated with Provigil. Caution should be exercised when Provigil is given to patients with a history of psychosis, depression, or mania.

FDA MedWatch: Use of CellCept® (mycophenolate mofetil) associated with increased pregnancy loss and congenital malformations:

Roche and the FDA notified healthcare providers that use of CellCept (mycophenolate mofetil) is associated with increased risk of first trimester pregnancy loss and increased risk of congenital malformations, especially external ear and facial abnormalities including cleft lip and palate, and anomalies of the distal limbs, heart, esophagus, and kidney. Based on postmarketing data from the United States National Transplantation Pregnancy Registry and additional postmarketing data collected in women exposed to systemic mycophenolate mofetil during pregnancy, the pregnancy category for CellCept has been changed from Category C (risk of fetal harm cannot be ruled out) to Category D (positive evidence of fetal risk). Labeling changes include the following sections: BOXED WARNING, WARNINGS/Pregnancy and Pregnancy Exposure Prevention, PRECAUTIONS/Information for Patients, and ADVERSE REACTIONS/Postmarketing Experience.

Within one week of beginning CellCept therapy, women of childbearing potential should have a negative serum or urine pregnancy test. In addition, women of childbearing potential (including pubertal girls and peri-menopausal woman) taking CellCept must receive contraceptive counseling and use effective contraception. Healthcare professionals and patients should be aware that CellCept reduces blood levels of the hormones in the oral contraceptive pill and could theoretically reduce its effectiveness.

FDA MedWatch: Trasylol® (aprotinin injection) - FDA requests marketing suspension and Bayer Pharmaceutical has agreed, pending a review of preliminary results from a Canadian study that suggested an increased risk for death:

The FDA announced that, at the agency's request, Bayer Pharmaceuticals Corp. has agreed to a marketing suspension of Trasylol (aprotinin injection), a drug used to control bleeding during heart surgery, pending detailed review of preliminary results from a Canadian study that suggested an increased risk for death. FDA requested the suspension in the interest of patient safety based on the serious nature of the outcomes suggested in the preliminary data. FDA has not yet received full study data but expects to act quickly with Bayer, the study's researchers at the Ottawa Health Research Institute, and other regulatory agencies to undertake a thorough analysis of data to better understand the risks and benefits of Trasylol.

Until the FDA can review the data from the terminated study it is not possible to determine and identify a population of patients undergoing cardiac surgery for which the benefits of Trasylol outweigh the risks. However, understanding that individual doctors may identify specific cases where benefit outweighs risk, FDA is committed to exploring ways for those doctors to have continued, limited access to Trasylol. There are not many treatment options for patients at risk for excessive bleeding during cardiac surgery. Thus, FDA is working with Bayer to phase Trasylol out of the marketplace in a way that does not cause shortages of other drugs used for this purpose.

Mark B. Zonenshine, MBA, R.Ph.
Editor

The Department of Pharmacy Services provides Pharmacokinetic and Pain Management Consultation services. Consults may be requested formally, with an order, or informally by contacting Arthur Gruber, R.Ph. at extension 3253