SAFETY CONCERNS

Ceftriaxone and Calcium Gluconate Contraindication Revised

After additional review, the U.S. Food and Drug Administration (FDA) has revised the contraindication associated with concomitant ceftriaxone and calcium gluconate administration to apply only to patients 28 days or younger. The contraindication previously applied to all age groups based on deaths attributed to calcium precipitation in the lungs of three infants following the administration of ceftriaxone and calcium gluconate.

Regardless of age, ceftriaxone and IV calcium gluconate should not be administered simultaneously via the same IV line (y-site or secondary line) because of precipitation risk. If administered sequentially via the same line, thorough flushing should occur.

For more information, visit www.fda.gov/cder/drug/InfoSheets/HCP/ceftriaxone042009HCP.htm.

Boxed Warning Added for Metoclopramide Use

The FDA has required the addition of a boxed warning for formulations of metoclopramide secondary to risks of tardive dyskinesia associated with chronic use and high dosages. No longer a first-line agent in the prevention of chemotherapy-induced nausea and vomiting, metoclopramide still has some use as a second-line agent. Tardive dyskinesia frequently is irreversible and patients should be informed of the risk to ensure informed consent in treatment decisions.

For more information, visit www.fda.gov/bbs/topics/NEWS/2009/NEW01963.html.

PHARMACY CORNER

Everolimus Approved for Use in Patients With Advanced Renal Cell Carcinoma

Everolimus (Afinitor™, Novartis Pharmaceuticals) has received FDA approval in the treatment of advanced renal cell carcinoma after treatment failure with sunitinib or sorafenib. Everolimus is an inhibitor of mTOR (mammalian target of rapamycin), and it inhibits cellular proliferation, angiogenesis, and glucose reuptake.

Dosing for most patients is 10 mg daily by mouth with or without food. The drug should be avoided in the presence of severe hepatic failure, and dosage should be reduced to 5 mg in the presence of moderate hepatic impairment. Tablets should not be crushed and should be taken at the same time each day.

In a study of patients on therapy (N = 274), noninfectious pneumonitis occurred in 14% of patients. For asymptomatic patients, therapy may be continued. However, if symptoms occur, corticosteroids and treatment interruption followed by reinitiating therapy at a reduced dose may be indicated.

Other common side effects observed on treatment included stomatitis (44%), infection (37%), diarrhea (30%), rash (29%), nausea (26%), and vomiting (20%).

Concomitant use of strong or moderate inhibitors of CYP3A4 and PgP inhibitors should be avoided as they result in dramatically increased serum concentrations of everolimus. Examples of these inhibitors include ketoconazole, erythromycin, and verapamil.

For more information, visit www.fda.gov/cder/foi/label/2009/022334lbl.pdf or www.ons.org/fda/documents/FDA033009.pdf.

NOTEWORTHY

Pancreatic Cancer Linked to Certain Blood Types

As reported by Wolpin et al. (2009), research has confirmed the increased risk of pancreatic cancer in people with blood types A, B, and AB compared to those with blood type O. About 17% of pancreatic cancer cases were attributable to having a non-O blood type. The mechanism by which the inheritance of specific blood types affects pancreatic cancer risk remains unknown. Pancreatic cancer remains a relatively rare cancer with an 1.3% lifetime risk for development of the disease.

Wolpin, B.M., Chan, A.T., Harge, P., Chanock, S.J., Kraft, P., Hunter, D.J., et al. (2009). ABO blood group and the risk of pancreatic cancer. *Journal of the National Cancer Institute, 101*(6), 424–431.

Prostate-Specific Antigen Screening Shows No Significant Benefit Toward Mortality

The hope in screening for any cancer is to catch disease in its early stages and, ideally, improve the chances of cure. With prostate cancer, screening via prostate-specific antigen testing has been a common approach since the late 1980s, along with digital rectal examinations. Unfortunately, as reported by Andriole et al. (2009), a review of data from 76,693 men randomly assigned to annual screening versus usual care from 1993–2001 showed no significant benefit with annual screening in terms of mortality from prostate cancer. It should be noted, however, that the actual rate of death from prostate cancer in both groups was low. Although 2,820 cancers were detected in the screening group and 2,322 in the control group, only 50 deaths occurred in the screening group and 44 in the control group.

Andriole, G.L., Crawford, E.D., Grubb, R.L., Buys, S.S., Chia, D., Church, T.R., et al. (2009). Mortality results from a randomized prostate cancer screening trial. *New England Journal of Medicine, 360*(13), 1310–1319.

Hepatocellular Carcinoma Rates Tripled in 30-Year Span

Highlighting the need for better treatment options and additional research, hepatocellular carcinoma (HCC) incidence rates tripled from 1975–2005 and, despite improvements related to screening and treatment over time, the overall one-year survival rate remains less than 50%. HCC remains the third leading cause of cancer mortality worldwide (Altekruse, McGlynn, & Reichmann, 2009).

Altekruse, S.F., McGlynn, K.A., & Reichmann, M.E. (2009). Hepatocellular carcinoma incidence, mortality, and survival trends in the United States from 1975–2005. *Journal of Clinical Oncology, 27*(9), 1485–1491.