June 29, 2010 — The US Food and Drug Administration (FDA) has unveiled a new plan designed to curb the misuse of prescription opioids. The long-awaited and controversial Risk Evaluation and Mitigation Strategy (REMS) for long-acting and extended-release opioids includes mandatory prescriber and patient education.

"The misuse and abuse of long-acting and extended-release opioid drug products have resulted in a widespread and serious public health crisis of addiction, overdose, and death," Bob Rappaport, MD, from the FDA’s office of drug evaluation, said in a recent letter to advisory committee members. In addition to the clear human costs, an estimated 60% of hospital costs related to opioid overdoses are paid for with public funds.

"It is critical we find ways to intervene," Dr. Rappaport noted, "while maintaining the necessary balance to assure continued access to these important analgesic drug products for people with chronic pain."

Regulators have released their new plan in advance of an advisory committee meeting scheduled for July 22 and 23. They are seeking input from stakeholders and the public.

The new proposal is advocating more oversight but FDA has dropped a number of earlier ideas such as prescriber accreditation and patient registration programs.

Prescriber education is in the plan, but the burden will be on drug manufacturers to offer training and demonstrate improvements in prescribing through surveys.

Regulators say they will not require any formal prescriber enrolment or real-time verification of training.

Regulations Dropped

FDA officials say that in the long term, linking education to the existing Drug Enforcement Administration registration system "would more efficiently ensure appropriate education of physicians, but would require legislation."

More than 1 million prescribers are registered with the Drug Enforcement Administration to prescribe opioids. Approximately 700,000 of these prescribe long-acting and extended-release opioids.

**Interruptions and Medication Administration Errors**

Efforts to improve patient safety and reduce medical errors are receiving renewed attention. In this observational study, conducted at two Australian teaching hospitals, researchers assessed the association between interruptions during medication administration and medication administration errors. Ninety-eight nurses were observed directly as they prepared and administered medications; the nurses were aware of the study aim.

Interruptions occurred during 53% of more than 4000 observed drug administrations for 720 patients. At least one procedural error (e.g., failure to check patient's identification, record medication administration, use aseptic technique) occurred in 74%, and at least one clinical error (e.g., wrong drug, dose, route) occurred in 25% of administrations.

Each interruption was associated with a 12% mean increase in procedural errors and a 13% mean increase in clinical errors. Most errors were rated as clinically insignificant; 2.7% were considered to be major errors (i.e., likely to lead to longer hospital stay or to permanent loss of function). Risk for a major error rose from 2.3% with no interruptions to 4.7% with four interruptions.


**Ups and Downs in Development of New Drugs for Lung Cancer**

June 30, 2010 — Two new experimental agents hold promise in the treatment of lung cancer, according to data presented here during the American Society of Clinical Oncology 2010 Annual Meeting.

The results of a phase 2 trial show that the epidermal growth-factor receptor (EGFR) tyrosine kinase inhibitor PF299804 (Pfizer) appears to be more effective than erlotinib (Tarceva) in improving progression-free survival in patients with nonsmall-cell lung cancer (NSCLC) who have failed chemotherapy.

A second phase 2 study found that when ARQ197 (ArQule), a selective non-ATP-competitive inhibitor of c-MET, was combined with erlotinib, progression-free survival was prolonged in patients with advanced NSCLC, compared with those who received erlotinib alone.

However, 2 other investigational agents failed to improve outcomes. In a phase 3 trial, the addition of figitumumab (Pfizer) to paclitaxel and carboplatin did not increase overall survival in patients with advanced nonadenocarcinoma NSCLC.
In addition, the trial was halted early because of serious adverse effects and increased mortality associated with the experimental agent.

In a phase 2 trial, combining mapatumumab (Genome Sciences) with carboplatin and paclitaxel as first-line therapy in advanced NSCLC did not improve response rate or progression-free survival.

In the first study, 188 patients with advanced NSCLC who had failed at least 1 chemotherapy regimen were randomized to receive either oral PF299804 45 mg or erlotinib 150 mg once daily until disease progression or toxicity.

Progression-free survival was 12.4 weeks (range, 8.3 to 16.1) for patients receiving PF299804 and 8.3 weeks (range, 8.0 to 11.4) for patients receiving erlotinib (hazard ratio [HR], 0.681; P = .019). The benefit was also consistent across several subgroups, including EGFR wild-type.

Overall survival data are being collected, but are not yet mature," lead author Michael Boyer, MBBS, PhD, clinical professor of medicine at the University of Sydney in Australia, told Medscape Oncology. "Further follow-up will be required before we have this information."

The objective response rate also favored PF299804 over erlotinib (17% vs 4.3%; 2-sided P = .009).

Neither group has reached the median duration of response. One patient who received PF299804 achieved a complete response of 48-plus weeks, as of April 15, 2010, explained Dr. Boyer.

The number of patients achieving clinical benefit (complete response, partial response, or stable disease for 24 or more weeks) was significantly higher for those who received PF299804 than for those who received erlotinib (27.7% vs 13.8%; P = .03).

The results of this study lend support to phase 3 trials of PF299804. "A phase 3 trial of PF299804 is currently active the CAN-NCIC-BR26 study and is being carried out in Canada and Australia," said Dr. Boyer. "It compares single-agent PF299804 with placebo in patients who have failed erlotinib."

"The design of other potential phase 3 trials is currently under discussion," he added.

The majority of treatment-related adverse events were grade 1 or 2, although 9 patients discontinued therapy because of them: 6 in the PF299804 group and 3 in the erlotinib group. Four treatment-related grade 5 adverse events were reported: 2 in the PF299804 group (1 pneumonia and 1 pneumonitis) and 2 in the erlotinib group (1 pneumonia and 1 pulmonary embolism).

The adverse events were easily manageable and not problematic," said Dr. Boyer, "and 94% of patients were able to continue with planned treatment, with the discontinuation rate being only 6%."

Figitumumab The insulin-like growth-factor type 1 receptor (IGF-IR) plays an important role in normal cellular growth and development, and is implicated in the regulation of tumor growth. Figitumumab is a monoclonal antibody that targets the IGF-IR. In this study, a planned enrollment of 820 patients were to be randomized in a 1:1 manner to receive paclitaxel (200 mg/m2), carboplatin (area under the curve [AUC] 6), and fitigumumab (20 mg/kg), or paclitaxel and carboplatin alone.

**Source:** www.medscape.com.
Vitamin E and Allergic Contact Dermatitis

Reports of vitamin E–induced allergic contact dermatitis (ACD) and frequent use of vitamin-E derivatives (tocopherol, tocopheryl linoleate, tocopherol acetate, etc) in skin care products deserves further investigation into tolerability and suitability of vitamin E in skin care preparations. A PubMed search was conducted to review the prevalence of vitamin E–induced ACD. It revealed 931 cases of vitamin E–induced ACD mainly from one large study. There were no reported deaths and only three patients required hospitalization for treatment. It appears that vitamin E–induced ACD is an uncommon phenomenon; incidence is low despite its widespread use in skin care products. Given its antioxidant and photoprotective properties, vitamin E should remain an ingredient in skin care products. Vitamin E protects skin by absorbing the ultraviolet (UV) wavelengths that are most damaging to skin and by forming stable nonradical intermediates in the presence of oxidative stress. Although there are no conclusive data on its efficacy, vitamin E is postulated to minimize photoaging, decrease UV-induced damage, increase stratum corneum hydration and help accelerate wound healing.

Source: www.medscape.com

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