PRODUCT UPDATE

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Public Health Advisory Issued Concerning Nonsteroidal Anti-Inflammatory Drugs

The U.S. Food and Drug Administration (FDA) issued a public health advisory summarizing the agency's current recommendations about nonsteroidal anti-inflammatory drugs (NSAIDs). A public health advisory is a temporary measure while the FDA continues to review the data. The FDA has made the following recommendations.

- "Physicians prescribing Celebrex® (celecoxib) [Pfizer Inc., New York, NY] or Bextra® (valdecoxib) [Pfizer Inc.] should consider this emerging information when weighing the benefits against risks for individual patients. Patients who are at high risk of gastrointestinal bleeding, have a history of intolerance to nonselective NSAIDs, or are not doing well on nonselective NSAIDs may be appropriate candidates for cyclooxygenase-2 selective agents.
- Individual patient risk for cardiovascular events and other risks commonly associated with NSAIDs should be taken into account for each prescribing situation.
- Consumers are advised that all over-the-counter (OTC) pain medications, including NSAIDs, should be used in strict accordance with the label directions. If use of an OTC NSAID is needed for longer than 10 days, a physician should be consulted."

Additional information can be found at www.fda.gov/cder/drug/analgesics/default.htm. The FDA encourages healthcare providers and patients to report adverse drug events to the FDA through the MedWatch program by phone (800-FDA-1088) or fax (800-FDA-0178) or online at www.fda.gov/medwatch/index.html.

Gefitinib Found Not to Improve Survival for Non-Small Cell Lung Cancer

Gefitinib (Iressa®, AstraZeneca Pharmaceuticals, Wilmington, DE) was approved by the FDA in March 2003 through an accelerated approval program. The approval was based on a surrogate end point, a 10% response rate in this case, that was considered reasonably likely to increase survival. The accelerated approval was conditional on continued research that would actually demonstrate increased survival. However, gefitinib failed to demonstrate a significant survival advantage over patients receiving a placebo in a large clinical trial that included more than 1,000 patients. The sponsoring company, AstraZeneca, has stopped marketing the drug but will continue to make it available to patients who appear to benefit from it. The company will continue to analyze the data. Physicians are reminded that docetaxel (Taxotere®, Aventis, Bridgewater, NJ) and erlotinib (Tarceva®, OSI Pharmaceuticals, Melville, NY) have received approval for this indication and that pemetrexed (Alimta®, Eli Lilly and Company, Indianapolis, IN) has received accelerated approval. After further review of the study results, the FDA will determine whether gefitinib should be withdrawn from the market or if other regulatory actions are appropriate.

Erlotinib Approved for Advanced Non-Small Cell Lung Cancer

The FDA has announced approval of erlotinib (Tarceva) for the treatment of patients with locally advanced or metastatic non-small cell lung cancer and who have failed at least one other prior chemotherapy regimen. Erlotinib inhibits epidermal growth factor receptor tyrosine kinase. It is an oral medication taken once daily until disease progression or unacceptable side effects occur. The most common side effects are rash and diarrhea. Reports of interstitial lung disease have been rare but occasionally fatal.

Results of a randomized, placebo-controlled, double-blind study were that patients in the erlotinib arm had a median survival of 6.7 months compared to 4.7 months in the placebo arm; at one year, 31.2% of patients in the erlotinib arm were alive compared to 21.5% in the placebo arm. For more information, visit www.gene.com or call 877-TARCEVA.

Palifermin Approved for Prevention and Treatment of Mucositis

Mucositis can be a painful and debilitating side effect of chemotherapy. Amgen Inc. announced that the FDA has approved palifermin (Kepivance™, Amgen Inc., Thousand Oaks, CA) for the prevention and treatment of mucositis in patients with hematologic cancers undergoing high-dose-rate chemotherapy with or without radiation therapy followed by bone marrow transplantation.

Palifermin is a recombinant human keratinocyte growth factor. It stimulates the growth and development of new epithelial cells to build up the mucosa. Palifermin is administered via IV for three consecutive days immediately before chemotherapy or radiation therapy and again for three consecutive days after bone marrow transplantation. The most common side effects were rash, pruritus, erythema, paresthesia, mouth or tongue disorders, and taste alterations. These side effects were transient and mild to moderate in severity. The most common serious adverse effect was skin rash. Currently, palifermin is not approved for use in solid tumors or in treatments that do not include bone marrow transplantantation. For more information, visit www.amgen.com or www.fda.gov/cder/drug/infopage/palifermin/paliferminQA.htm. To receive the full prescribing information via fax, call 800-772-6436.

Caspofungin Acetate Receives Expanded Indication

Merck & Co., Inc., in Whitehouse Station, NJ, has announced that the FDA has approved expanded indications for caspofungin acetate (Cancidas®). Caspofungin now may be used empirically to treat presumed fungal infections in patients with febrile neutropenia. The mechanism of action of caspofungin is to inhibit fungal cell wall synthesis of β (1,3)-D-glucan, an essential component of fungal cell walls. Caspofungin is administered via IV. The most commonly occurring side effects of caspofungin are fever, chills, rash, headache, hypokalemia, vomiting, and nausea. Hepatic abnormalities have been seen in healthy volunteers as well as patients receiving caspofungin. Full prescribing information should be reviewed prior to administering this drug. Several drug interactions are possible. For more information, visit www.merck.com.

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Bortezomib Granted Priority Review by FDA

The FDA has accepted a supplemental new drug application and granted priority review for bortezomib (Velcade®, Millennium Pharmaceuticals, Cambridge, MA). The supplemental application asks that bortezomib be approved as a second-line treatment for multiple myeloma. Bortezomib currently is approved as a third-line treatment. According to Millennium Pharmaceuticals, bortezomib has shown a significant delay in disease progression and increased survival compared to standard treatment. The priority review status means that the FDA will expedite the approval process by decreasing the review time from 10 months to 6 months. For more information, call 866-VELCADE or visit www.millennium.com.

BAY 43-9006 and Phenoxodiol Are Granted Fast-Track Status

Bay 43-9006 (Onyx Pharmaceuticals, Emeryville, CA) is a novel rapamycin analog drug kinase and vascular endothelial growth factor inhibitor that is being tested for its efficacy in treating metastatic renal cell carcinoma. Fast-track status, granted from the FDA, is designed to expedite review of a drug for serious or life-threatening diseases where a medical need is unmet. Phenoxodiol (Marshall Edwards Inc., New South Wales, Australia) also has been granted fast track status for the treatment of recurrent ovarian cancer. Phenoxodiol may restore chemosensitivity in resistant or refractory ovarian cancer. Phenoxodiol is being investigated for its use in other cancers as well. For more information about Bay 43-9006, visit www.onyx-pharm.com. For more information about phenoxodiol, visit www.marshalledwardsinc.com.

FDA Approves Oxaliplatin for Adjuvant Treatment

Sanofi-Aventis has announced that the FDA has approved oxaliplatin used in combination with infusional 5-fluorouracil/leucovorin (5-FU/LV) for adjuvant treatment of stage III colon cancer. Oxaliplatin previously had been approved in combination with 5-FU/LV for the treatment of advanced colorectal cancer. In a large, randomized trial of more than 2,000 patients, oxaliplatin with 5-FU/LV demonstrated significantly longer disease-free survival compared to 5-FU/LV alone. The most commonly seen side effects of oxaliplatin are granulocytopenia, paresthesia, diarrhea, vomiting, and nausea. For more information and full prescribing information, visit www.ELOXATIN.com or call 877-4ELOXATIN.

New Pediatric Treatment Approved for Leukemia

The FDA has approved clofarabine (Clolar™, Genzyme Oncology, Cambridge, MA) for the treatment of refractory or relapsed acute lymphoblastic leukemia (ALL) in children after at least two prior regimens. It is the first drug that has been approved for leukemia in children in more than a decade. The new drug was approved under the FDA's accelerated approval process and previously had been granted orphan drug status.

Clofarabine interferes with DNA synthesis and repair. It is given via IV over two hours for five consecutive days and is dosed based on body surface area. Common side effects include nausea, vomiting, diarrhea, anemia, neutropenia, thrombocytopenia, febrile neutropenia, and infection. Less common but more severe side effects also have been seen, including cardiac toxicity, hepatic toxicity, renal toxicity, sepsis, tumor lysis syndrome, and systemic inflammatory response syndrome or capillary leak syndrome. For more information, call 800-RX-CLOLAR or visit www.clolar.com.

New Nonopioid Pain Medication Approved for Severe Chronic Pain

Ziconotide (Prialt®, Elan Pharmaceuticals, Dublin, Ireland) is a new, non-narcotic pain medication approved for chronic severe pain administered via intrathecal infusion. Ziconotide is the first in a new class of drugs called N-type calcium channel blockers. Ziconotide is synthetically produced but was modeled after a naturally occurring conopeptide found in a marine snail known as *Conus magus.* Because this is not a narcotic drug, it has no associated risk of addiction or withdrawal.

Severe psychiatric symptoms and neurologic impairment may occur with ziconotide. Patients with a history of psychosis should not be treated with ziconotide. Patients also may experience cognitive and neuropsychiatric events, reduced consciousness, elevation of serum creatine kinase, and, possibly, meningitis (from the route of administration). For more information, visit www.prialt.com or call 888-PRIALT-1.

NEW PRODUCTS

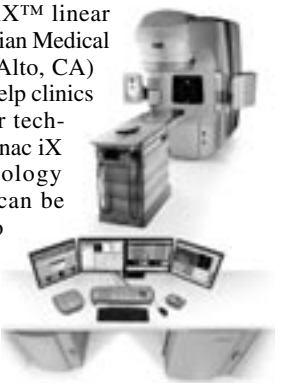
Premier Genetic Laboratory Test Is Approved

This new genetic test uses a microarray or "DNA chip" to selectively identify particular gene sequences. A small amount of DNA is needed for the analysis. The AmpliChip Cytochrome P450 Genotyping Test (Roche Diagnostics, Basel, Switzerland), used with the GeneChip® Microarray Instrumentation System (Affymetrix®, Santa Clara, CA), tests for common mutations in two specific genes. These genes are from the cytochrome P450 gene family. Variations in these genes cause variations in how people process or metabolize drugs. This test can determine whether a person is a "poor metabolizer" and therefore has trouble inactivating or eliminating certain drugs. This might make the person at increased risk for adverse drug reactions and toxicities. Someone who tests as a "ultrarapid metabolizer" may inactivate or eliminate drugs before the drug can have a therapeutic effect.

In a practical example of how this test might be used, Roche Diagnostics cited that 10% of the general population carries only a single copy of a key catalytic enzyme crucial to metabolism of certain drugs. About one in 250 people carry two defective copies of this gene. If one of these people was prescribed warfarin, he or she would be at high risk for bleeding if prescribed the standard dose. If the physician knew in advance who was at risk for slowly metabolizing the drug, the physician could start patients on a lower dose or even prescribe a different drug.

These kinds of tests will help to tailor drug therapy, including chemotherapy, to each individual in the future. For more information, visit www.roche-diagnostics.com.

Varian Medical Systems Introduces Clinac iX



The Clinac iX™ linear accelerator (Varian Medical Systems, Palo Alto, CA) is designed to help clinics maximize their technology. The Clinac iX offers a technology platform that can be customized to support every type of radiotherapy treatment. It will support everything from two-dimensional treatments to intensity-modulated radiation therapy and image-guided radiation therapy. The Clinac iX also has an ergonomic command center to control every aspect of treatment. For more information, visit www.varian.com.