PRODUCT UPDATE

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Totect™ Approved for Extravasation Treatment

The U.S. Food and Drug Administration's Division of Drug Oncology Products in the Office of Oncology Drug Products approved dexrazoxane hydrochloride for injection (Totect™, TopoTarget) for the treatment of extravasation resulting from IV anthracycline chemotherapy.

Totect is the only FDA-approved drug to treat the often horrific effects of extravasation (accidental leakage into the surrounding tissues) resulting from IV anthracycline chemotherapy doses.

In two studies, patients who received single-agent anthracycline via IV (usually as part of combination chemotherapy) and developed extravasation symptoms of pain, burning, swelling, or redness near the infusion site received Totect to reduce surgical interventions for tissue injury following anthracycline extravasation. Extravasation was confirmed by the presence of fluorescence in tissue biopsies.

The first Totect dose is given as soon as possible, within six hours of extravasation. Treatment is repeated 24 and 48 hours later for a total of three doses. Totect is administered via IV infusion over one to two hours at various venous access locations. The first two doses are 1,000 mg/m^2, with a third dose of 500 mg/m^2. Maximum daily dose on days 1 and 2 is 2,000 mg, dropping to 1,000 mg on day 3.

Extravasation was confirmed in 57 patients. The most common anthracyclines were epirubicin (56%) and doxorubicin (41%). Peripheral sites of extravasation included the forearm (63%), hand (21%), and antecubital area (11%); four patients received anthracycline via a central venous access device. Most presented with swelling (83%), redness (78%), or pain (43%).

Only one of the patients required surgery after Totect treatment. Thirteen had late sequelae at the event site, such as pain, fibrosis, atrophy, and local sensory disturbance; all were considered mild except in the one patient who required surgery. None of the four patients with central venous access devices required surgery.

Totect is a cytotoxic drug. When administered to patients receiving anthracycline-containing cytotoxic therapy, additive cytotoxicity may occur. Totect treatment is associated with leukopenia, neutropenia, and thrombocytopenia. Reversible elevations of liver enzymes may occur. Renal excretion is the primary metabolic pathway. Dimethylsulfoxide should not be used in patients who are receiving dexrazoxane to treat anthracycline-induced extravasation.

Full prescribing information, including clinical trial data, safety and dosing recommendations, drug interactions, and contraindications, is available at www.fda.gov/cder/foi/label/2007/022025lbl.pdf. Additional information is at www.totect.com/totect.htm.

FDA Issues New Box Warnings for Several Erythropoiesis-Stimulating Agents

The FDA approved new box warnings and other safety-related product-labeling changes for the erythropoiesis-stimulating agents (ESAs) Epogen® (epoetin alfa, Amgen Inc.), Procrit® (epoetin alfa, Ortho Biotech Products), and Aranesp® (darbepoetin alfa, Amgen Inc.).

The revised labeling incorporates advice from an FDA advisory committee and expands on labeling changes made in March 2007.

Clinical trials conducted in patients with cancer have shown decreased overall survival or an increased rate of tumor progression when ESAs are used in advanced breast, head and neck, lymphoid, and non-small cell lung malignancies. Trials were conducted to achieve hemoglobin levels of 12 g/dl or more. The new labeling emphasizes that clinical studies have not been conducted to exclude ESA-associated tumor progression or shortened survival when ESAs are dosed to achieve lower hemoglobin levels.

Prescribers should consider the risks of tumor progression and decreased survival in prescribing ESAs, particularly because the risks have not been excluded with lower hemoglobin levels. Risks should be weighed against the potential need for red cell blood transfusions and their associated risks. The FDA strongly recommends that prescribers discuss risks of ESA-associated tumor progression and shortened survival with patients prior to initiating or continuing ESA therapy.

ESAs should be used in patients with cancer only when treating anemia specifically caused by chemotherapy. ESAs should be discontinued when the patient's planned chemotherapy course has been completed.

New labeling also emphasizes that ESAs have not improved symptoms of anemia, poor quality of life, fatigue, or patient well-being in controlled clinical trials of patients with cancer.

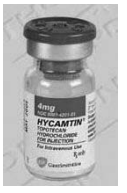
For an FDA healthcare professional sheet and other documents regarding evolving safety issues with ESAs, visit www.fda.gov/cder/drug/infopage/RHE/default.htm.

Prescribing information for Aranesp is available at www.fda.gov/cder/foi/label/2007/103951s5164lbl.pdf, and for Epogen and Procrit at www.fda.gov/cder/foi/label/2007/103234s5158lbl.pdf.

The content of the labels for Epogen and Procrit are the same except for proprietary name.

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine or device to the FDA's MedWatch Reporting Program, online at www.fda.gov/medwatch/report.htm; by faxing (+1-800-FDA-0178); by mailing postage-paid Form 3500, available at www.fda.gov/medwatch; or by calling (+1-800-FDA-1088).

Topotecan Approved for Small Cell Lung Cancer



The FDA has approved topotecan (Hycamtin®, GlaxoSmithKline) capsules for the treatment of relapsed small cell lung cancer (SCLC), specifically for patients who demonstrated complete or partial response to first-line chemotherapy and who are at least 45 days from the end of that treatment.

Approval was based on a phase III study comparing topotecan capsules and best supportive care to best supportive care alone in patients with relapsed SCLC who were not suitable candidates for IV therapy.

Approval of an oral agent to treat SCLC provides physicians with an alternative to IV therapy and may allow patients to self-administer chemotherapy.

Common side effects are neutropenia, anemia, and thrombocytopenia, as well as nausea, diarrhea, vomiting, fatigue, and alopecia.

Topotecan belongs to a class of drugs known as topoisomerase I (topo-I) inhibitors.

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Topo-I is a naturally produced protein essential for cell division in normal and cancer cells. Interaction between topo-I and topotecan causes permanent damage to the cancer cell's genetic material and prevents continued growth.

For more information, visit http://us.gsk.com/products/assets/us_hycamtin_capsules.pdf.

New Dosing Regimen Receives Accelerated Approval

The FDA granted accelerated approval of a new dosing regimen of dasatinib (Sprycel™, Bristol-Myers Squibb) for the treatment of adults with chronic phase chronic myeloid leukemia with resistance or intolerance to prior therapy, including imatinib mesylate. The new dosing regimen consists of 100 mg taken orally once daily. The FDA previously granted accelerated approval to dasatinib in June 2006 for the treatment of adults with chronic, accelerated phase, or myeloid or lymphoid blast phases of chronic myeloid leukemia with resistance or intolerance to prior therapy, including imatinib mesylate. In June 2006, the FDA also granted regular approval for the treatment of patients with Philadelphia-positive acute lymphoblastic leukemia. The recommended dosing regimen in the 2006 approval was 70 mg twice daily.

A randomized, open-label study evaluated the safety and efficacy of four dosing regimens of dasatinib in 670 patients with chronic phase chronic myeloid leukemia. Dasatinib was administered at a dose of 100 mg once daily, 140 mg once daily, 50 mg twice daily, or 70 mg twice daily. Significant cardiac disease excluded patients from the study. The primary end point was major cytogenetic response (MCyR), defined as elimination or substantial diminution (by at least 65%) of Philadelphia-positive hematopoietic cells. The primary analysis showed comparable efficacy for the 100 mg once-daily schedule (MCyR = 53%, 95% confidence interval: 44%–62%) and the 70 mg twice-daily schedule (MCyR = 51%, 95% confidence interval: 42%–60%).

Safety analyses revealed a reduction in adverse reactions with the 100 mg once-daily dose regimen compared with the previously approved 70 mg twice-daily regimen. The adverse events included fluid retention all grades (24% versus 32%), pleural effusion all grades (10% versus 18%), and grade 3–4 hematologic toxicities, including neutropenia (34% versus 43%), thrombocytopenia (22% versus 38%), and anemia (10% versus 17%).

Follow-up data from further studies will convert accelerated approval to regular approval. Full prescribing information, including clinical trial data, safety and dosing recommendations, drug interactions, and contraindications, is available at www.fda.gov/cder/foi/label/2007/021986s001lbl.pdf.

NEW PRODUCTS

Computed Tomography Scanner Unveiled

Philips's new Brilliance Computed Tomography (CT)–Big Bore Oncology configuration, designed specifically for radiation oncology, provides improved image quality, accuracy, and workflow efficiency, while offering shorter examination times for patients. Brilliance CT–Big Bore Oncology allows breast positioning, prostate treatment, respiratory gating studies, integrated absolute marking, and functional CT examinations, options previously unavailable in one location. Philips's exclusive CT localization application is on the console, allowing clinicians to localize the tumor and mark the patient without leaving the console.

Philips's scanners and software combine to provide the following dimensions of tumor analysis: physical position of the tumor, temporal measurement of organ motion in real time, and tumor metabolic processes of chemistry and biology. Data management systems allow for more decision support, storage of larger volumes of patient information, and remote collaboration with colleagues. CT scans are used in oncology for radiation treatment planning. The Brilliance CT–Big Bore system is designed to address the need for precise position information for the application of external beam radiation. For more information, visit www.medical.philips.com/main/clinicalsegments/oncology/portfolio/pet.

Product Adds Comfort to Wig Use

Headline It!, a thin, easy-to-use, disposable headliner, brings comfort to patients wearing wigs after cancer treatment and acts as a barrier between the sweat and oil secreted from the head, improving hygiene and reducing frequent wig washings.

Headline It! is available in two models, active and medical. The medical model was developed with a neutral tan-colored underside (which is placed directly against the wig netting) and a blue top (which comes in contact with the wearer's head). The coloring closely resembles the natural skin color, and the product has a nonslip element for enhanced wig stability. Headline It! comes with an adhesive backing that directly applies to the wig. The backing absorbs perspiration and prevents salt stains and cosmetics from reaching the wig. The biodegradable product can be thrown away after becoming saturated.

For more information, visit www.headlineitstore.com.

RECALLS AND ALERTS

Alert Issued for Provigil®

The FDA and Cephalon have notified healthcare professionals of warnings added to the prescribing information for Provigil® (modafinil). Provigil improves wakefulness in adult patients who experience excessive sleepiness associated with narcolepsy, obstructive sleep apnea or hypopnea syndrome, or shift-work sleep disorder. The revised prescribing information updates safety content to include warnings regarding serious rashes, including Stevens-Johnson Syndrome and hypersensitivity reactions, and psychiatric symptoms. Rare cases of a serious or life-threatening rash, including toxic epidermal necrolysis and drug rash with eosinophilia and systemic symptoms, have been reported. Angioedema and multiorgan hypersensitivity reactions also have been reported. Patients should discontinue use and contact a physician if a rash or other hypersensitivity reaction occurs. Provigil is not approved for use in pediatric patients for any indication. In addition, adverse psychiatric events, including anxiety, mania, hallucinations, and suicidal ideation, have been reported. Healthcare providers should exercise caution when prescribing Provigil to patients with a history of psychosis, depression, or mania. Additional labeling revisions have been made to the clinical pharmacology precautions and patient package insert sections. Read the complete MedWatch 2007 Safety Summary, which includes a link to the manufacturer's healthcare letter and revised prescribing information, at www.fda.gov/medwatch/safety/2007/safety07.htm#Provigil.

Exubera® Marketing Shelved

Pfizer Inc. has decided to end the marketing of Exubera®, its inhaled insulin for type 1 diabetes, phasing it out over a three-month period. Exubera failed to gain patient and physician acceptance; therefore, Pfizer will end investment in the product.

Although clinical trials demonstrated Exubera to have efficacy similar to that of short-acting insulins, without the needle stick, a host of concerns arose, including worries about pulmonary toxicities and questions about Exubera's ability to reduce glycosylated hemoglobin levels below 7%, the accepted standard.

NOTEWORTHY

Guide Created for Cancer Journey

An experimental program was described to the American Society of Therapeutic Radiation and Oncology that creates a guide for patients' cancer journey. The primary focus

of the program is to assist poor and minority patients with cancer.

With support from the National Cancer Institute, 68 volunteers were trained as patient navigators to lead the 297 patients enrolled in the program. Main barriers to care were transportation, psychosocial issues, financial issues, fear of cancer, childcare needs, and difficulty with English.

When the program began, an average of 42 days was needed to work through the barriers facing each patient. Four years later, the mean time is one day.

The navigator program also increases the likelihood that patients will enroll in clinical trials. Fear and uncertainty often come with a cancer diagnosis, so patient support is crucial.

The National Cancer Institute addresses unequal access to standard care by sponsoring the Patient Navigation Research Program at multiple sites. The National Cancer Institute's Center to Reduce Cancer Health Disparities has conducted several pilot patient navigator projects. For more information, visit http://crchd.cancer.gov/attachments/equal_access_volume1_issue4.pdf or visit the patient navigator fact sheet at www.cancer.gov/cancertopics/factsheet/PatientNavigator.

Web Site May Revolutionize Chemotherapy Use

ChemoOrders.com offers physicians and nurses an innovative way to prescribe chemotherapy to patients by creating patient-specific chemotherapy orders and supporting documents based on physician- or nurse-entered vital signs and disease parameters. ChemoOrders.com uses established, peer-reviewed clinical guidelines to ensure that the most current disease protocols are outlined. Protocol selection and scientific content oversight are performed by a group of physicians, oncology-certified nurses and nurse practitioners, and pharmacists. All listed protocols are FDA approved, compendia listed, or both. ChemoOrders.com is free to medical professionals and the public. The site is modeled after a disease management system developed by Georgia Cancer Specialists and used in patient care for several years. ChemoOrders.com can enhance patient care by

- Providing the latest treatment protocols to oncology professionals, with strict adherence to published dose, schedule, and administration guidelines
- Dramatically increasing the efficiency of chemotherapy orders and related documents
- Reducing prescribing mistakes, administration errors, patient risk, and physician liability.

The site offers chemotherapy order forms, print-ready chemotherapy flow sheets, informed consent sheets, and patient education materials. For more information, visit www.ChemoOrders.com.