

2007 LCD UPDATES

May 2007

APRIL 2007

J2505: Pegfilgrastim (Neulasta)

The “Indications and Limitations of Coverage and/or Medical Necessity” section of the LCD was revised to correct wording related to the administration of Neulasta. The following sentence, “The administration should not occur within 14 days before or 24 hours after, administration of cytotoxic chemotherapy,” was revised to read per the product label. The revised sentence reads as follows: “The administration should not occur within 14 days before, and 24 hours after, administration of cytotoxic chemotherapy.” Effective Date: April 30, 2007.

MARCH 2007

NESP: Darbepoetin alfa (Aranesp[®]) (novel erythropoiesis stimulating protein [NESP])—LCD Revision

The local coverage determination (LCD) for darbepoetin alfa (Aranesp) (novel erythropoiesis stimulating protein [NESP]) was last updated February 26, 2007. Since that time, the FDA (U.S. Food and Drug Administration) notified health care professionals of new safety information for erythropoiesis-stimulating agents (ESAs) Aranesp (darbepoetin alfa), Epogen[®] (epoetin alfa), and Procrit[®] (epoetin alfa), drugs used to treat certain causes of anemia.

Four new studies in patients with cancer found a higher chance of serious and life-threatening side effects or death with the use of ESAs. These research studies were evaluating an unapproved dosing regimen, a patient population for which ESAs are not approved, or a new unapproved ESA. In another study, patients scheduled for orthopedic surgery had a higher rate of deep venous thrombosis when treated with ESA at the approved dose. This new information is consistent with risks found in two clinical studies in patients with chronic renal failure treated with an unapproved regimen of an ESA that were reported in November 2006.

The Agency will present this new information to the Oncologic Drugs Advisory Committee on May 10, 2007. The FDA will seek advice on the need for additional labeling changes and/or additional studies to further assess safety.

Medicare covers all labeled (FDA-approved) indications for the drugs, though issues of dose and endpoints have been raised by the recent studies. Also, First Coast Service Options, Inc. (FCSO), as well as other Medicare contractors, allows off-label (non FDA-approved) drug coverage based on the local coverage determination process that includes review of the evidence based medical literature and input from practicing physicians. ESAs currently have coverage for off-label indications such as the anemia of cancer not due to concurrent chemotherapy for Medicare patients in Connecticut and Florida. Given the preliminary data and warning released by the manufacturer to health care

professionals and now the FDA notification, **FCSO has evaluated all off-label coverage of darbepoetin alfa (Aranesp) and will be removing coverage for anemia of malignancy not due to concurrent chemotherapy for Medicare patients in Connecticut and Florida. With this decision, the LCD for Aranesp (darbepoetin alfa), will be revised in several ways:**

- Under the “Indications and Limitations of Coverage and/or Medical Necessity” section of the LCD:
- Removed the indication for anemia of malignancy not due to concurrent chemotherapy.
- Revised the FDA-approved covered indications to read exactly per the FDA-approved label.
- Under general indications and limitations, removed recommended dosing for anemia associated with malignancy not due to concurrent chemotherapy.
- Under the “Utilization Guidelines” section of the LCD:
- Added a statement about endpoints for administering Aranesp for anemia associated with concurrent chemotherapy and added language from the FDA-approved label regarding the safety and effectiveness of Aranesp.
- Under the “ICD-9 Codes that Support Medical Necessity” section of the LCD for HCPCS code J0881:
- Removed ICD-9-CM codes 205.00-205.91, 206.00-206.91 and 207.00-208.91 as these ICD-9-CM codes are no longer supported as medically necessary.
- Added a dual diagnosis requirement for the following ICD-9-CM codes:

140.0-149.9	150.0-159.9	160.0-165.9	170.0-176.9	179-189.9	190.0-199.1
200.00-	201.00-	202.00-	203.00-	204.00-	230.0-234.9
200.88	201.98	202.98	203.81	204.91	
235.0-235.9	236.0-236.99	237.0-237.9	238.0	238.1	238.2
238.3	238.4	238.5	238.6	238.8	238.9
239.0-239.9	995.20	995.29	V58.11		

One of the malignancy ICD-9-CM codes in the table above and one of the following ICD-9-CM: 995.20, 995.29 and V58.11 must be billed when Aranesp is given for anemia of malignancy related to concomitantly administered chemotherapy. ICD-9-CM V58.11 would be billed with a malignancy code if the patient is currently receiving chemotherapy treatment. ICD-9-CM 995.20 or 995.29 would be billed with one of the malignancy codes if the patient has received chemotherapy treatment and it has been no more than 120 days since the last chemotherapy treatment.

FCSO is making these revisions in accordance with the Program Integrity Manual, Pub 100-08, Chapter 13, Section 13.7.3, “being issued for compelling reasons.”

CMS announced on March 14, 2007, the opening of a national coverage analysis (NCA) on the use of ESAs for the conditions other than end-stage renal disease (ESRD). This is the first step toward issuing a national coverage determination (NCD). Information on this national coverage analysis may be found at

<http://www.cms.hhs.gov/mcd/viewtrackingsheet.asp?id=203>.

FCSO is continuing to evaluate all off-label coverage of darbepoetin alfa (Aranesp) and epoetin alfa (Epogen, Procrit). FCSO will communicate to physicians and allied providers if and when such off-label indications are removed from the local coverage determinations.

Effective Date

These revisions to the LCD are effective for services rendered on or after April 19, 2007. The full text for this LCD is available through the provider education website at <http://www.floridamedicare.com> on or after this effective date.

JANUARY 2007

J9000: Antineoplastic Drugs—LCD Revision

The local coverage determination (LCD) for antineoplastic drugs was last updated on October 30, 2006. Since that time, revisions were made to add additional ICD-9-CM codes and indications, as well as update verbiage based on the Food and Drug Administration (FDA) label where applicable for the following drugs:

Docetaxel (J9170)

Under the “Indications and Limitations of Coverage and/or Medical Necessity” section, the following FDA-approved indication was added:

- Docetaxel in combination with cisplatin and fluorouracil is indicated for the induction treatment of patients with inoperable locally advanced squamous cell carcinoma of the head and neck.

Under the “ICD-9 Codes that Support Medical Necessity” section, the following diagnoses were added:

- 173.0 Other malignant neoplasm of skin of lip
- 173.1 Other malignant neoplasm of skin, eyelid, including canthus
- 173.2 Other malignant neoplasm of skin of ear and external auditory canal
- 173.3 Other malignant neoplasm of skin of other and unspecified parts of face
- 173.4 Other malignant neoplasm of skin, scalp and skin of neck

This revision is effective for claims processed on or after December 19, 2006, for services rendered on or after October 17, 2006.

Rituximab (J9310)

Under the “Indications and Limitations of Coverage and/or Medical Necessity” section, the following off-label indication was added:

- For the treatment of refractory thrombotic thrombocytopenic purpura (TTP) for patients who do not respond to plasmapheresis.

Under the “ICD-9 Codes that Support Medical Necessity” section, the following diagnosis was added:

- 446.6 Thrombotic microangiopathy [use this code for refractory thrombotic thrombocytopenic purpura (TTP)]

This revision is effective for services rendered on or after December 19, 2006.

Trastuzumab (J9355)

Under the “Indications and Limitations of Coverage and/or Medical Necessity” section, the following FDA approved indication was added:

- Trastuzumab, as part of a treatment regimen containing doxorubicin, cyclophosphamide, and paclitaxel, is indicated for the adjuvant treatment of patients with HER2-overexpressing, node-positive breast cancer.

This revision is effective for services rendered on or after November 16, 2006. The full text of this LCD is available through our provider education website at <http://www.floridamedicare.com> on or after these effective dates.

2007 CODING UPDATES

NOVEMBER 2007 New J Codes effective January 1, 2008

New information from CMS around the new J codes recently issued to IGIV (non-lyophilized) or liquid products. A chart appears below. CMS had issued Q codes that will now be converted to permanent J codes. Until 12/31/2007, the current Q codes remain in effect. Gamunex(Q-4092), Octagam (Q-4087), Gammagard (Q-4088), Flebogamma (Q-4091)

HCPCS Code Minimum Unadjusted Copayment	Short Descriptor	CI	SI	APC	Relative Weight	Payment Rate
J1561 6.41	Gamunex Injection	NI	K	0948		32.06
J1562 1.40	Vivaglobin Injection		K	0804		7.01
J1568 6.64	Octagam injection	NI	K	0943		33.19
J1569 6.21	Gammagard liquid injection	NI	K	0944		31.06
J1572 6.45	Flebogamma injection	NI	K	0947		32.27

MARCH 2007

FEBRUARY 2007

Coding Issue: Monitoring Anticoagulation with Coumadin

Code 99363 is a new 2007 code for coagulation management for the first 90 days. It is assigned 2.10 RVUs in the facility (hospital) setting and 3.01 in the office setting. For each additional 90 days of coagulation management, the physician can bill Code 99364. For the hospital setting, 0.82 RVUs are assigned and for the office setting 1.05 RVUs are assigned. Medicare has decided not to pay for these codes as CMS considers these services to be "bundled" into the E/M services provided.

JANUARY 2007

2007 ICD-9-CM Coding Changes—Correction (CMS)

The local coverage determinations (LCDs) impacted by the Annual 2007 ICD-9-CM Update (effective October 1, 2006), were published in the October 2006 Medicare B Update! (pages 45-47). The procedure code listed in the article for the Epoetin alfa (EPO) LCD was incorrect. The article indicated, "Add diagnoses 238.72, 238.73, 238.74, and 238.75 or procedure code J0585". The procedure code should reflect J0885.

Dacogen:

Reminder - Dacogen (decitabine) for injection has been assigned a permanent HCPCS code which went into effect on January 1, 2007. **The new code is J0894.** Please note that the billing unit is **1 mg**.

2007 USP DI & DRUG POINTS UPDATES

NOTE: *The term off-label refers to indications other than those reviewed by the Food and Drug Administration (FDA) and referenced on the FDA approved label. Off-label uses for drugs used in anticancer chemotherapeutic regimens must be covered by Medicare if they are accepted by the USP-DI.

Note: Bracked [] information refers to uses that are not included in U.S. product labeling:

OCTOBER 2007

Revlimid:

DrugPoints, the successor publication to the *USP DI* compendia, has updated its monograph for Revlimid (lenalidomide) (Celgene Corporation, Summit, N.J.) to include: multiple myeloma, in

combination with dexamethasone, first-line therapy. Evidence favors efficacy, Class IIa recommendation

JULY 2007

Accepted

Caelyx; Doxil.

[Carcinoma, breast (treatment)]¹—Liposomal doxorubicin is indicated for first-line treatment or treatment at some point in the management of locally advanced and metastatic breast carcinoma.

[Multiple myeloma, in combination with vincristine and dexamethasone {35} {36} {37} {38}]¹—Data from published trials indicate that substitution of doxorubicin HCl with liposomal doxorubicin in combination with vincristine and dexamethasone for patients with multiple myeloma is active and well tolerated. {35} {36} {37} {38} Because the need for a 96-hour continuous infusion or daily injections for four days are eliminated, outpatient administration and patient convenience are achieved. Also, since liposomal doxorubicin is not a vesicant it can be administered via a peripheral line, eliminating the potential complications of central venous access.

Usual adult dose

[Carcinoma, breast (treatment)]¹ Patients have benefited from intravenous doses of 30 to 50 mg per square meter of body surface area, repeated every 2 to 4 weeks.{18}

Hycamtin.

[Carcinoma, lung, non–small cell (NSCLC) (treatment)]¹—Topotecan is indicated for the treatment of NSCLC {18}{19} {20} {21} {22} {23} (Evidence rating: IIIA). Topotecan is not recommended as first-line therapy, but may be considered for use at a later point in the management of patients with this disease. {18} {24}

[Myelodysplastic syndrome (treatment)]¹—Topotecan is indicated, alone {32} or as part of a combination regimen containing cytarabine {33} {81} {83} and/or amifostine, {81} {82} {83} for the treatment of myelodysplastic syndromes (MDS). There was not a clear consensus by the USP medical experts, regarding combination use with amifostine. Some of the experts are hesitant about the use of amifostine and suggest reserving amifostine combination regimens for salvage treatment. Individual case factors (e.g., International Prognostic Scoring System [IPSS] risk group, patient characteristics, etc.) be considered when choosing an appropriate treatment {83} (Evidence rating: II/IIID). Preliminary evidence indicates that topotecan may correct genetic abnormalities and prolong survival in patients with these diseases, {33} for whom treatment options are limited.

[Chronic myelomonocytic leukemia (CMML) (treatment)]¹—Topotecan is indicated, alone or in combination with cytarabine for the treatment of CMML {32} {33}(Evidence rating: IIID). Preliminary evidence indicates that topotecan may correct genetic abnormalities and prolong survival in patients with this disease, {33} for whom treatment options are limited.

Nexavar - Accepted - [Advanced hepatocellular carcinoma]

Other Updates:

Herceptin:

Thompson Micromedex recently designated Herceptin in neoadjuvant breast cancer therapy as “Acceptance Not Established.”

Tarceva:

The Tarceva USP DI monograph was updated with information based on a new product package insert (PI) that was approved by the FDA in May 2007. No changes in the indications sections of the monograph.

Relevant changes to the Tarceva USP DI monograph can be found in the following sections:

- Patient Monitoring – regarding renal function and serum electrolytes
- Side/Adverse Effects – regarding renal insufficiency and acute renal failure.
- General Dosing Information – regarding dosage reduction; avoiding grapefruit juice; and management of dehydration
- Oral Dosage Form – regarding interaction with strong CYP3A4 inhibitors and inducers.

JUNE, 2007

Avastin (June 21, 2007)

[Metastatic breast carcinoma, HER2-negative disease, first line therapy in combination with paclitaxel]—Bevacizumab-containing regimens have demonstrated anti-tumor activity in patients with metastatic breast cancer.{13}{14}{15}{16} Interim analysis of the Eastern Oncology Cooperative Group (E2100) phase III trial assessing the addition of paclitaxel to bevacizumab as first-line therapy in mostly HER2-negative metastatic breast cancer patients yielded improvements in response rates, progression-free survival, and a trend toward improved survival.{17}

Revised Monographs for Epoetin

[Anemia associated with frequent blood donation (prophylaxis)] {32} {40}— Epoetin is indicated to prevent anemia in patients who donate blood and to increase the capacity for donation (for future autologous transfusion) prior to elective surgery. The medication has been found to be effective in females, patients with low packed-cell volumes due to anemia or small body size, and patients requiring donation of 4 units or more of blood {33}.

[Anemia associated with the management of hepatitis C (treatment)]¹— Epoetin is indicated for the treatment of anemia in patients with hepatitis C virus infection who are being treated with the combination of ribavirin and interferon alfa or ribavirin and peginterferon alfa.{52}{53}{54}{55}{56}{57}{58}{59}{60}{61}

[Anemia, in critically ill patients (treatment)]¹—Epoetin is indicated for the treatment of anemia in critically ill patients in hospital intensive care units. Epoetin therapy has been shown to increase hematocrit values and hemoglobin concentrations and to reduce the need for red blood cell transfusions in this patient population.{62}{63}{64}{65}{66}{67} {68}

APRIL, 2007

New Indication for Capecitabine (Xeloda)

The USP-DI monograph for this drug has been revised to include the following off-label* use:

Accepted: Gastric cancer, advanced/metastatic, as first-line therapy . Capecitabine, as monotherapy or in combination with various other chemotherapy agents, is an acceptable option for the first-line treatment of patients with advanced gastric Cancer. (Published 4/19/07)

MARCH 2007

Inatinib (Systemic) – Gleevec –Revised to include Acute lymphoblastic leukemia, Philadelphia chromosome-positive, newly diagnosed, as art of combination chemotherapy.

JANUARY/FEBRUARY 2007

January/February 2007 Revised Monographs

Irinotecan (Camptosar) –

[Carcinoma, lung,non-small cell treatment]

[Extensive-state small-cell lung cancer, first-line treatment, in combination with cisplatin]

[Ovarian cancer, platinum-refractory or platinum-resistant]

Mercaptopurine (Purinethol)– (6-MP)

[Leukemia, chronic myelocytic (treatment)]

[Lymphomas, non-Hodgkins' (treatment)]

[Bowel disease, inflammatory (treatment)]

Topotecan (Hycamtin)

[Carcinoma, lung, non-small cell (NSCLC) (treatment)]

[Myelodysplastic syndrome (treatment)]

[Chronic myelomonocytic leukemia (CMML) (treatment)]

Darbepoetin Alfa

Unaccepted: Anemia associated with malignancy

Abraxane® (paclitaxel protein-bound particles for injectable suspension) to include metastatic breast cancer as a monotherapy for first-line treatment. (Abraxis Oncology)

Trisenox™ (arsenic trioxide) to include myelodysplastic syndrome, monotherapy in transfusion-dependent patients. (Cephalon Oncology)

Evista® (raloxifene) to include breast cancer prophylaxis in high-risk, postmenopausal women. (Eli Lilly and Company)

Campath. – Revised to include B-cell chronic lymphocytic leukemia, first-line monotherapy for progressive disease. (Mfg. Genzyme, Berlex Distributor)

FDA UPDATES

November 2007

Tasigna® (nilotinib) – (Novartis)

The United States Food and Drug Administration (FDA) has approved the targeted agent Tasigna® (nilotinib) for the treatment of chronic and accelerated-phase chronic myeloid leukemia (CML) for patients who are not able to tolerate or who have stopped responding to Gleevec® (imatinib).

SPRYCEL (Dasatinib) -(Bristol-Myers Squibb)

On November 8, 2007, the U. S. Food and Drug Administration (FDA) granted accelerated approval of a new dosing regimen of dasatinib (SPRYCEL, Bristol-Myers Squibb) for the treatment of adults with chronic phase (CP) chronic myeloid leukemia (CML) with resistance or intolerance to prior therapy, including imatinib mesylate. The new dosing regimen is 100 mg taken orally once daily.

Submission of further follow-up data from ongoing studies will convert this accelerated approval to regular approval. Full prescribing information, including clinical trial information, safety, dosing, drug-drug interactions and contraindications is available at [_www.fda.gov/cder/foi/label/2007/021986s001lbl.pdf_](http://www.fda.gov/cder/foi/label/2007/021986s001lbl.pdf).

Velcade – (Millennium)

The FDA recently approved Millennium's supplemental new drug application, supporting the use of VELCADE® (bortezomib) for Injection in patients with renal insufficiency, including those on dialysis.

The VELCADE full Prescribing Information (PI) has been updated to reflect this important change. The new information can be found in the "Use in Special Populations" section of the new PI, as follows:

8.6 Patients with Renal Impairment

The pharmacokinetics of VELCADE are not influenced by the degree of renal impairment. Therefore, dosing adjustments are not necessary for patients with renal insufficiency. Since dialysis may reduce VELCADE concentrations, the drug should be administered after the dialysis procedure.

October 2007

Taxotere:

Sanofi-aventis announced October 1 that the U.S. Food and Drug Administration (FDA) has approved Taxotere® (docetaxel) Injection Concentrate in combination with cisplatin and 5-fluorouracil for induction therapy of locally advanced squamous cell carcinoma of the head and neck before patients undergo chemoradiotherapy and surgery. The FDA based its approval on the results of the phase III randomized, open-label, international trial, TAX 324, which established the efficacy and safety of the Taxotere-based regimen in significantly improving survival\\

Evista:

The U.S. FDA has approved Eli Lilly and Company's (Indianapolis, Ind.) osteoporosis drug Evista® (raloxifene HCl) for a new use to reduce the risk of invasive breast cancer in two populations: postmenopausal women with osteoporosis and postmenopausal women at high risk for invasive breast cancer. Evista, a selective estrogen receptor modulator or SERM (recently classified by the FDA as an estrogen agonist/antagonist), is already approved for the prevention and treatment of osteoporosis in postmenopausal women

Campath:

Genzyme Corp. and Bayer HealthCare Pharmaceuticals Inc. (Cambridge, Mass. and Wayne, N.J.) announced that the U.S. FDA has approved a supplemental biologics license application (sBLA) for Campath® (alemtuzumab) and granted regular approval for single-agent Campath for the treatment of B-cell chronic lymphocytic leukemia (B-CLL). Campath was initially approved in 2001 under accelerated approval regulations and the FDA has determined that the study results submitted in the sBLA fulfill the post-marketing commitment to verify clinical benefit. Campath is the first and only monoclonal antibody approved by the FDA for the treatment of B-CLL.

Aloxi:

MGI Pharma, Inc., (Minneapolis, Minn.) and its partner Helsinn Healthcare SA, announced approval of a supplemental new drug application (sNDA) for Aloxi® (palonosetron hydrochloride) Injection by the U.S. FDA allowing for repeated dosing for cancer patients receiving multiple day chemotherapy regimens. This sNDA includes the removal of a dosing recommendation, which limited Aloxi use to once per seven day interval, from the product's label. Data from several safety and efficacy trials that evaluated multiple day dosing of Aloxi were included in the sNDA. Aloxi is approved by the FDA for the prevention of acute nausea and vomiting associated with initial and repeat courses of moderately and highly emetogenic cancer chemotherapy and for the prevention of delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy

IPI-504:

Infinity Pharmaceuticals, Inc., and MedImmune, Inc., (Cambridge, Mass. and Gaithersburg, Md.) announced that the FDA has granted orphan drug designation to IPI-504 for the treatment of gastrointestinal stromal tumors (GIST). IPI-504, the companies' heat shock protein 90 (Hsp90) inhibitor, is currently being evaluated in two separate multi-center clinical trials in patients with GIST and other soft tissue sarcomas, and in patients with non-small cell lung cancer.

ALS-357:

Advanced Life Sciences Holdings, Inc. (Woodridge, Ill.) announced that the U.S. FDA has granted orphan drug designation to the company's oncology product, ALS-357, for the topical treatment of metastatic melanoma. ALS-357 is a novel drug entering phase I/II clinical development that has demonstrated potent anti-tumor activity against malignant melanoma. ALS-357 operates by inducing apoptosis in tumor cells.

Treanda:

Cephalon Inc. (Frazer, Pa.) has submitted a new drug application (NDA) to the U.S. FDA requesting approval of Treanda® (bendamustine HCl) for the treatment of patients with chronic lymphocytic leukemia (CLL). In August 2007, the FDA granted orphan drug designation to Treanda for this indication. The NDA is based on a large, international multi-center Phase III clinical trial that evaluated the safety and efficacy of bendamustine HCl, the active ingredient in Treanda, compared to chlorambucil in patients who were not previously treated for their disease. In the pivotal trial, bendamustine HCl met both primary endpoints, overall response and progression-free survival and demonstrated an acceptable tolerability profile. The company is also studying Treanda for treatment of patients with indolent non-Hodgkin's lymphoma (NHL), who are refractory to the monoclonal antibody rituximab.

IXEMPRA™

Bristol-Myers Squibb Company has announced today that the U.S. Food and Drug Administration (FDA) has granted approval of IXEMPRA™ (ixabepilone) as monotherapy for the treatment of patients with metastatic or locally advanced breast cancer in patients whose tumors are resistant or refractory to anthracyclines, taxanes, and capecitabine. The FDA has also granted approval of IXEMPRA in combination with capecitabine for the treatment of patients with metastatic or locally advanced breast cancer resistant to treatment with an anthracycline, and a taxane, or whose cancer is taxane resistant and for whom further anthracycline therapy is contraindicated. IXEMPRA is a microtubule inhibitor belonging to a class of antineoplastic agents, the epothilones. Bristol-Myers Squibb anticipates that IXEMPRA will be available within days.

Erbix for tx of pts with EGFR-expressing metastatic colorectal cancer

On October 2, 2007, FDA expanded labeling and granted regular approval for single-agent Cetuximab (Erbix®, ImClone Systems, Inc.) for the treatment of patients with EGFR-expressing Metastatic Colorectal Cancer (mCRC) after failure of both Irinotecan- and Oxaliplatin-based chemotherapy regimens. Erbix® was initially approved in 2004 under accelerated approval regulations.

APP Receives Tentative FDA Approval for Irinotecan Hydrochloride Injection, 20 mg/mL Packaged in 2 mL and 5 mL Single-Use Vials

Abraxis Pharmaceutical Products (APP), the hospital-based business of Abraxis BioScience, Inc. (NASDAQ:ABBI), announced the tentative approval from U.S. Food and Drug Administration (FDA) to market Irinotecan Hydrochloride Injection, 20 mg/mL, 2 mL, and 5 mL, the generic equivalent of Camptosar(R) Injection manufactured by Pfizer Inc. APP will package this product in 40 mg/2mL and 100 mg/5mL single-use vials.

As one of the only companies to receive a tentative approval, APP is in the process of securing contracts and expects to commence marketing of this product upon patent expiry in February 2008.

Hycamtin – GlaxoSmithKline

GlaxoSmithKline announced today approval by the U.S. Food and Drug Administration (FDA) for oral Hycamtin® (topotecan) capsules for the treatment of relapsed small cell lung cancer

(SCLC). Specifically, Hycamtin capsules are indicated for patients who had a complete or partial response to first-line chemotherapy and who are at least 45 days from the end of that treatment. Hycamtin capsules are the only oral single-agent chemotherapy approved for the treatment of SCLC after failure of first-line therapy. The product will be available in 2008.

This approval was based on positive results from a Phase III study comparing Hycamtin capsules plus best supportive care (BSC) to BSC alone in patients with relapsed SCLC, in addition to Phase II and Phase III supporting studies. Best supportive care refers to treatments intended to control, prevent and relieve disease complications to improve comfort and quality of life for the patient, but are not intended to have any anti-tumor effects. In the pivotal Phase III clinical trial, Hycamtin capsules added to BSC were associated with prolonged survival in patients with relapsed SCLC. This was the first randomized study ever to demonstrate that patients with relapsed SCLC live longer when they are treated with BSC and chemotherapy compared to BSC alone. Study results were published in the December 1, 2006, issue of the *Journal of Clinical Oncology*.

JUNE 2007

Erbix (Cetuximab)

The FDA has approved a new 200 mg vial of Erbitux (cetuximab). The new 200 mg vial will offer a reduction in preparation time and effort, requiring the use of only three vials where previously five vials would have been required. Additionally, the 200 mg vial will require less storage space than that required for the equivalent mgs. quantity of the 100 mg vial. The 100 mg vial will continue to be available to provide convenience and minimization of waste. The new Erbitux vial will be priced on an equivalent basis to the 100 mg vial price. The price remains unchanged from the product launch price in 2004.

MAY 2007

APRIL 2007

Fragmin® -(Pfizer, Inc.) FDA Approves Fragmin® for Extended Treatment to Reduce the Recurrence of Blood Clots in Patients with Cancer

The U.S. Food and Drug Administration (FDA) has approved a new indication for Fragmin® (dalteparin sodium injection), for the extended treatment of symptomatic venous thromboembolism (VTE) [proximal deep vein thrombosis (DVT) and/or pulmonary embolism (PE)] to reduce the recurrence of VTE in patients with cancer. Fragmin is the first low-molecular-weight heparin (LMWH) approved in the U.S. for the extended treatment of recurrent VTE in patients with cancer. Patients with cancer have an increased risk of VTE compared to those without cancer. Additionally, patients with cancer may be immobilized, which predisposes the patient to this condition.

Full prescribing information, including clinical trial information, safety, dosing, drug-drug interactions and contraindications, is available at www.fda.gov/cder/foi/label/2007/020287s0351bl.pdf.

MARCH 2007

FDA approves GlaxoSmithKline's Tykerb

The Food and Drug Administration (FDA) approved Tykerb® (lapatinib) in combination with Xeloda® (capecitabine) for the treatment of patients with advanced or metastatic breast cancer whose tumors overexpress HER2 and who have received prior therapy including an anthracycline, a taxane, and trastuzumab. It is the first targeted, once-daily oral treatment option for this patient population. Tykerb is a small molecule that inhibits the tyrosine kinase components of the EGFR (ErbB1) and HER2 (ErbB2) receptors.

Tykerb is available in tablets of 250 mg. The dosing for Tykerb is continuous, while the dosing of capecitabine is based on a 21-day cycle. Therefore, a months' supply of 5 tabs daily for Tykerb should be written as 150 tabs for a 30-day supply. Additionally, Tykerb is to be given continuously until progression or unmanageable toxicity occurs

FEBRUARY 2007

Pharmion Corporation (Vidaza)

Pharmion Corporation announced that it has received approval from the U.S. Food and Drug Administration (FDA) for its new drug application (NDA) supplement to add intravenous (IV) use as a new route of administration to the instructions in the approved prescribing information for its DNA demethylating agent Vidaza® (azacitidine for injection). With this approval, Vidaza may now be administered intravenously over a period of 10 to 40 minutes in a clinic or hospital setting.

Millenium Pharmaceuticals, Inc., (Velcade)

Millennium Pharmaceuticals, Inc. announced the U.S. FDA has granted full approval of Velcade® (bortezomib) for Injection for the treatment of patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. The approval is based on

data from the PINNACLE trial, the largest study to date in patients with MCL. PINNACLE was a prospective, multi-center, single-arm, open-label study in patients with MCL whose disease progressed following at least one prior therapy.

Wyeth Pharmaceuticals (Torisel)

The U.S. FDA has granted priority review status to Wyeth Pharmaceutical's (Madison, N.J.) new drug application for the investigational drug Torisel™ (temsirolimus). The company is seeking an indication for Torisel for the treatment of advanced renal cell carcinoma (RCC). The FDA previously granted fast track designation and orphan drug status for investigational temsirolimus for the treatment of advanced RCC. Torisel is the first mTOR (mammalian target of rapamycin) inhibitor to be filed for approval the treatment of cancer. It is an investigational drug that specifically inhibits the mTOR kinase, a protein that regulates cell proliferation, cell growth, and cell survival.

Medarex, Inc. (MDX-010)

Medarex, Inc., has received FDA fast track designation for MDX-010 (Ipilimumab) used in combination therapy with chemotherapy (dacarbazine) in previously untreated (first-line) metastatic melanoma patients. The FDA also granted fast track designation for ipilimumab used as monotherapy in previously treated (second-line) metastatic melanoma patients. Ipilimumab is an investigational fully human antibody against human CTLA-4, a molecule on T cells that is believed to be responsible for suppressing the immune response.

Pfizer's Sutent receives US approval to update label for kidney cancer

Pfizer received FDA approval to update the label for Sutent (sunitinib), to include the first-line treatment of advanced renal cell carcinoma (RCC).

JANUARY 2007

Ranpirnase (Onconase®)

On January 30 the FDA approved orphan drug status for ranpirnase (Onconase®) (Alfacell Corp, Bloomfield, N.J.) in the treatment of malignant mesothelioma. According to a company news release, ranpirnase has demonstrated the ability to target tumor cells while sparing normal cells in both in vivo and in vitro studies. Incorporated into the cytosol of malignant cells by endocytosis, the agent selectively degrades cytosol transfer RNA (tRNA), thereby inhibiting protein synthesis, stopping cell proliferation, and inducing apoptosis. Ranpirnase therapy for malignant mesothelioma is currently being evaluated in a confirmatory phase 3b study involving more than 50 sites in the United States, Canada, Europe, New Zealand, and Australia. Other potential indications under investigation include non-small cell lung cancer and other solid tumors.

OTHER ISSUES & UPDATES

SEPTEMBER 2007

Campath

Genzyme Corp. and Bayer HealthCare Pharmaceuticals Inc. announced that the U.S. Food and Drug Administration (FDA) has approved a supplemental biologics license application (sBLA) for Campath® (alemtuzumab) and granted regular approval for single-agent Campath for the treatment of B-cell chronic lymphocytic leukemia. Campath was initially approved in 2001 under accelerated approval regulations, and the FDA has determined that the study results submitted in the sBLA fulfill the post-marketing commitment to verify clinical benefit.

Aloxi's once weekly dosing limitation has been lifted.

The FDA has granted approval of a supplemental New Drug Application (sNDA) for Aloxi (palonosetron hydrochloride) Injection. This sNDA includes the removal of a dosing recommendation, which limited aloxi use to once per seven day interval, from the product's label. Aloxi is approved by the FDA for the prevention of acute nausea and vomiting associated with initial and repeat courses of moderately and highly emetogenic cancer chemotherapy and for the prevention of delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.

Evista Now Approved to Reduce Breast Cancer Risk in Postmenopausal Women (Eli Lilly)

FDA has approved Evista (raloxifene hydrochloride) for reducing the risk of invasive breast cancer in postmenopausal women with osteoporosis or at a high risk of invasive breast cancer. Evista was approved in 1997 for osteoporosis prevention in postmenopausal women and in 1999 for treating postmenopausal women who have osteoporosis. <http://www.fda.gov/bbs/topics/NEWS/2007/NEW01698.html>

AUGUST 2007

DRUG UPDATES:

TREANDA® (bendamustine HCl)

Cephalon, Inc., has announced that the U.S. Food and Drug Administration Office of Orphan Products Development granted orphan drug designation for the company's investigational therapy, TREANDA® (bendamustine HCl), for the treatment of chronic lymphocytic leukemia (CLL).

Eloxatin® (oxaliplatin injection)

Sanofi-aventis U.S. has launched a new 200 mg single-use vial of its chemotherapy treatment Eloxatin® (oxaliplatin injection) for patients who have adjuvant stage III colon cancer and advanced colorectal cancer. The new vial is expected to offer more convenience, efficiency, and safety in the preparation of the injectable cancer drug. Previously, Eloxatin® had been available in 50 mg and 100 mg single-use vials. The 200 mg vial was expected to be available for order by cancer treatment clinics and hospitals nationwide starting the last week of August 2007 (NDC number: NDC 0024-0592-40).

MARCH 2007

Radioactive Tracer Fluorodeoxyglucose F-18 (FDG)

Effective for services processed on or after March 16, 2007, First Coast Service Options (FCSO) will allow separate payment of \$220.80 per study dose for FDG. An article regarding FDG, Nitrogen N-13 ammonia and Rubidium Rb-82 has been posted to the Medicare website at www.floridamedicare.com under Part B special release articles and will also be published in the April Part B provider update. Providers who have received denials may refile claims on or after March 16, 2007.