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FDA approves Orlistat for OTC use by Gina Bartos

The Food and Drug Administration (FDA) has approved orlistat for over-the-counter (OTC) use in adults. Orlistat is manufactured by GlaxoSmithKline under the name Alli, and was originally approved as prescription only (Xenical) in 1999 at a higher dose (double strength of the OTC version).^{1,2}

Used as a weight loss aid for overweight adults, orlistat, is a non-systemically acting lipase inhibitor that ultimately decreases the intestinal absorption of fat. This product is indicated for overweight adults ages 18 years and older, along with a reduced-calorie, low-fat diet, and exercise program. It should not be used for patients with absorption problems, those who are NOT overweight, or patients who have received organ transplants, due to possible drug interactions. The dosing regimen is a 60mg capsule that can be taken up to three times a day with each fat-containing meal. Taking a multivitamin at bedtime is recommended due to a possible loss of certain nutrients¹: fat soluble (A,D,E, and K) vitamins and beta carotene.² Also, anyone taking blood thinning medicines or being treated for diabetes or thyroid disease should consult a physician.¹

The most common side effect is a change in bowel habits which may include: oily spotting, gas with discharge, fecal urgency, fatty/oily stools, or frequent bowel movements.² Eating a low fat diet will reduce the likelihood of these side effects.¹

Using the drug alone is unlikely to be beneficial; however, an additional 2-3 pounds may be lost for every 5 pounds lost through diet and exercise. The product cost is expected to be about \$1-\$2/day. It may also be important to note that studies have associated the prescription version of the drug with precancerous lesions of the colon.³

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Label and indication changes for the antibiotic Ketek® Two of the three previously approved indications, acute bacterial sinusitis and acute bacterial exacerbations of chronic bronchitis, have been removed from the labeling of Ketek . It will retain an indication for the treatment of mild-moderate community acquired pneumonia. A boxed warning was also added stating a contraindication with myasthenia gravis. In 2006, warnings regarding the potential for liver toxicity were added to the label. More information is available at: <http://www.fda.gov/cder/drug/infopage/telithromycin/default.htm>

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FDA approves new medication for hypertension. The FDA has approved Tekturna® for the treatment of high blood pressure. Tekturna is the first high blood pressure medication of its kind. It works by inhibiting kidney enzymes associated with regulation of blood pressure. Tekturna may be used alone, or in combination with a diuretic medication. The most common adverse effect noted in clinical trials was diarrhea. Rarely, patients may develop allergic reactions with swelling of the face, lips or tongue, or difficulty breathing. Tekturna is manufactured by Novartis Pharmaceuticals.

Proton Pump Inhibitor use and fracture risk by Michael Rea

Patients 50 years of age and older have been shown to have lower calcium absorption and higher urinary calcium excretion. It has been suggested that proton pump inhibitors may further inhibit calcium absorption and reduce bone resorption. This combination of factors led to retrospective study to determine if a correlation exists between Proton Pump Inhibitor (PPI) use and an increased risk for hip fracture.

In December 2006, the Journal of the American Medical Association published a case-control study performed by the Center for Clinical Epidemiology and Biostatistics at the University of Pennsylvania Medical School¹. The patient group was identified from the Group Practice Research Database (GPRD), which contains preexisting information on more than 9 million patients in the United Kingdom. Patients from the years of 1987-2003 were reviewed.

Patients were selected for the study based on age of 50 years or older, use/non-use of acid suppression drugs, and incidence of hip fracture. 13,556 patients fit the criteria for the hip fracture group, and 135,386 patients fit the criteria for the control group. The findings of the study show that the risk of hip fracture was significantly higher among patients who had been taking long-term (defined as more than one year) PPI therapy (adjusted OR=1.44; 95% CI, 1.30-1.59, P<0.01), as compared to those who have not. The patients included in the PPI group were considered to be long term users, which was quantified as one year or more. Results indicated those subjects taking higher doses (which was defined as 1.75 times the "normal" dose in the study), for longer periods of time had a higher incidence of hip fracture than the those taking a lower dose for a shorter duration of time.

For comparison purposes, a separate

nested case-control analysis for Histamine-2 Receptor Antagonist (H2RA) therapy was conducted in a similar fashion. H2RA users for more than one year showed a significant increase of 23% in hip fractures; however, the risk of fracture was found to be greater with long-term PPI use.

As this data was based on a retrospective analysis, further research in the form of a prospective, randomized, double-blind trial is needed to confirm these findings.

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Cancer rates drop for second straight year by Janice Frueh

In the most recent report from the American Cancer Society (ACS), the decrease in the total number of cancer-related deaths surmounted the decline seen in the previous year. For 2004 (the most current year for actual data available) there was an estimated 3,014 fewer deaths from the previous year compared to the reported 369 fewer deaths for 2003^{1,2}. Similar reductions in cancer-related deaths were found for men and women, and were reported to be 1,160 and 1,854, respectively. Colorectal cancer had the largest drop in total number of deaths when evaluating specific cancer sites for both men and women¹. Although this current trend is very encouraging in battling the cancer epidemic, cancer is still the second leading cause of death in the U.S., and is in the top five leading causes of death across all

ages which were also found in the 2006 ACS report^{1,2}.

This most current report also included long-term trends in cancer incidence and mortality. Incidence rates have begun to stabilize for men, but are still slightly increasing for women. These long-term trends also show that for both men and women cancer-related death rates have been steadily declining from 1992/93¹.

When evaluating the death rates of specific cancer sites from 1990/91-2003, it was found that declines in lung, prostate, and colorectal cancer death rates accounted for 80% of the decrease in cancer rates for men whereas over 60% of the decrease for women occurred from lower death rates from breast and colorectal cancer¹. Dr. Elizabeth Ward from the American Cancer Society

summarized the reports findings to be attributed to years of effort and investment in tobacco control, early detection and screening, and research.³

One of the areas in need of improvement was the poorer survival rates of minorities once they are diagnosed with cancer. The 2007 ACS report found that African Americans were more likely to be diagnosed with cancer at a regional or distant stage and had a lower five-year relative survival rate compared to whites. Survival rates for other ethnic populations were unavailable due to incomplete data for these groups¹. Proposed factors that may individually or jointly attribute to these inequalities were access to health care, quality of health care, and/or differences in tumor characteristics within a stage at diagnosis.

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Aranesp ineffective in non-chemo patients by Shane Stowe

In January of 2007, Amgen and the Food and Drug Administration (FDA) issued a letter to health care professionals regarding the lack of effectiveness of Aranesp® (darbepoetin alfa) for the treatment of cancer induced anemia in patients.¹ The current FDA labeled indications for Aranesp (darbepoetin alfa) are:²

- Anemia due to chemotherapy (non-myeloid malignancy)
- Anemia of chronic renal failure

Amgen recently conducted a study with the main goal of establishing Aranesp (darbepoetin alfa) as being effective for anemia due to active malignant disease. The study was done to investigate the potential for this as a new indication for Aranesp.¹

This study was a large, multi-center, randomized, double blind, placebo-controlled, phase 3 trial comparing Aranesp (darbepoetin alfa) to placebo in patients with active malignant disease not receiving or expected to receive myelosuppressive chemotherapy or radiation therapy, and having a hemoglobin ≤ 11 g/dl. The target hemoglobin for the Aranesp treatment group was 12 g/dl. Nine hundred eighty nine patients met the inclusion criteria and were enrolled. The initial treatment period was 16 weeks followed by a 16

week treatment extension to further assess the safety and effectiveness.

All patients have completed the extension study but the results are yet to be reported. However, the results of the initial 16 weeks of treatment have been reviewed. The primary endpoint was the incidence of red blood cell (RBC) transfusions; in Aranesp 18% versus placebo 24%, which was not found to be statistically significant. (Hazard ratio 0.89; 95% CI: 0.65,1.22, p=0.15). More deaths were also seen in the Aranesp group (26% (136/515)) than in the placebo group (20% (94/470)), during the initial treatment period. Furthermore, a median survival follow up of 4.3 months continued to show a significant increase in deaths in the Aranesp group over the placebo group. More details of this study will be available once it is peer-reviewed and published.¹

According to the American Society of Hematology clinical guidelines about the use of epoetin alfa, anemia resulting from malignancy or chemotherapy is an important clinical problem that is being treated more and more with recombinant hematopoietic growth factor erythropoietin.³ Epoetin alfa (Epogen®, Procrit®) and darbepoetin alfa (Aranesp) are both erythropoiesis-

stimulating agents, and the FDA recently warned that the results of Amgen's Aranesp study may also be applicable to epoetin alfa.⁴ In summary, Aranesp treated patients had a higher mortality rate and no reduction in the need for transfusions. These results may also be applicable to epoetin alfa products. Aranesp should only be used for its approved indications and not for the treatment of anemia that is due to a malignancy itself. The FDA is currently evaluating the safety of this entire class of medications.

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Cancer rates decline cont.

Although the findings of this report hold a potential positive outlook for the future, cancer has been the second leading cause of death in the United States for the past two years^{1,2}. Across all age groups for both males and females, cancer-related deaths are in the top five causes of death. Increased awareness of risk factors, screening tools, and prevention measures will help to attain even greater reductions in incidence and mortality rates seen in this report.

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