



Blue Cross and Blue Shield
of New Mexico

U.S. Food and Drug Administration (FDA) Updates Summer 2010 Generic drug approvals

- **Venlafaxine extended-release (EFFEXOR XR[®]):** Indicated for the treatment of major depressive disorders, Teva will have 180 days of market exclusivity.
- **Anastrozole (ARMIDEX[®]):** Indicated for the treatment of breast cancer, multiple manufacturers have generic versions of ARMIDEX.
- **Enoxaparin (LOVENOX[®]):** Indicated for the treatment and/or prophylaxis of venous thrombotic events. Sanofi-Aventis, the manufacturer of LOVENOX, has requested a temporary restraining order to halt the release of the generic versions and a decision is not expected until mid-August.
- **Naratriptan (AMERGE[®]):** Indicated for the treatment of migraine headaches, multiple generic versions will be available, and naratriptan will be the second triptan available as a generic following the launch of sumatriptan (IMITREX[®]).
- **Omeprazole/sodium bicarbonate (ZEGERID[®]):** Indicated for the short term treatment of gastric and duodenal ulcers, Par launched its generic version of ZEGERID in two strengths (20 mg/1,100 mg, 40 mg/1,100 mg) and will hold 180 days of market exclusivity. The 20 mg/1,100-mg strength is also available over-the-counter (OTC) without a prescription.
- **Rivastigmine (EXELON[®]):** Indicated for treatment of mild to moderate dementia of Alzheimer's disease or secondary to Parkinson's disease, several manufacturers have launched their generic products in the 1.5 mg, 3 mg, 4.5 mg, and 6 mg strengths and share 180-day market exclusivity.
- **Pantoprazole (PROTONIX[®]):** As of July 19, 2010, manufacturers Sun Pharmaceutical and Teva, with effective FDA approvals, can continue to distribute pantoprazole without risk of further financial penalties. There are now three proton pump inhibitors (PPIs)—omeprazole, pantoprazole, and lansoprazole—available as generic equivalents.
- **Drospirenone/ethenyl estradiol (YAZ[®]):** Indicated for the prevention of pregnancy, Teva's generic version (GIANVI[™]) was launched prematurely and is being challenged in court for patent infringement.
- **Adapalene gel 0.1% (DIFFERIN[®]):** Indicated for the topical treatment of acne vulgaris, DIFFERIN cream (0.1%) and DIFFERIN gel (0.3%) are available as brand products only.
- **Metaxalone (SKELAXIN[®]):** Indicated for the relief of discomforts associated with acute, painful muscle conditions, Sandoz will hold 180-day marketing exclusivity on this product.

New drug information:

- **PROLIA[™] (denosumab):** Indicated for the treatment of postmenopausal women with osteoporosis who are at high risk for fracture, who have a history of osteoporotic fracture, or who have multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapies. The usual dosage is 60 mg subcutaneously every six months. The medication appears as effective as other agents (e.g., bisphosphonates)

currently on the market. Safety concerns include exacerbation of hypocalcemia, increased risk of serious infections, dermatological adverse reactions, and osteonecrosis of the jaw. The estimated annual cost of therapy is roughly \$1,600 vs. \$400 for generic alendronate. (1)

- **DULERA® (mometasone/formoterol):** This combination inhalation product is indicated for the treatment of asthma in patients 12 years of age and older. DULERA is similar to ADVAIR® (fluticasone/salmeterol) and SYMBICORT® (budesonide/formoterol) except that ADVAIR DISKUS® has the indication to treat children as young as 4 years. The recommended dosing is two inhalations of either strength (100 mcg/5 mcg, 200 mcg/5 mcg) twice daily. Each inhaler provides a one-month supply (i.e., 120 inhalations). DULERA contains the same black box warning (i.e., long-acting beta agonists) as the other two agents. (2)
- **PROVENGE® (sipuleucel-T):** Indicated for the treatment of asymptomatic or minimally symptomatic metastatic castrate-resistant (hormone-refractory) prostate cancer. Patients receive three injections over a one-month period. Data from a pivotal clinical trial showed that study patients lived an average of 4.1 months longer (25.8 vs. 21.7 months) than those treated with a placebo. The total cost of therapy an estimated \$93,000. (3)

Market withdrawal:

- **MYLOTARG® (gemtuzumab ozogamicin):** On June 21, 2010 Pfizer announced the voluntary withdrawal from the U.S. market of MYLOTARG, which was indicated for the treatment of acute myeloid leukemia (AML). The company took the action at the request of the FDA after results from a recent clinical trial raised new concerns about the product's safety as well as the fact that the drug failed to demonstrate clinical benefit over the placebo alternative. The drug was originally approved in May 2000 under the FDA's accelerated approval program, but the company was required to conduct additional studies to confirm the drug's clinical safety and efficacy. (4)

FDA news releases:

- **Proton pump inhibitors—new labeling changes:** On May 25, 2010, the FDA notified health care professionals of revisions to both prescription and OTC labels for PPIs to include safety information about a possible increased risk of fractures of the hip, wrist, and spine. The new safety information is based on FDA's review of several epidemiological studies that found that those who were at greatest risk for these fractures received high doses of PPIs for one year or more and were 50 years of age or older. The FDA recommended that health care providers prescribing PPIs to consider whether a lower dose or a shorter duration of therapy would adequately treat their patients' conditions. (5)
- **QUALAQUIN® (quinine sulfate) for leg cramps:** On July 8, 2010, the FDA warned that the unapproved use of the malaria drug QUALAQUIN to treat nighttime leg cramps had resulted in serious side effects. Between April 2005 and September 2008, a total of 38 side effects were sent to the FDA through its Adverse Event Reporting System, 24 of which were serious or life-threatening (e.g., thrombotic thrombocytopenia purpura, permanent kidney impairment). As a result, the manufacturer will be developing a risk management plan to educate health care providers and patients. (6)
- **ARAVA® (leflunomide)—risk of severe liver injury:** In July, the FDA decided to add information about the risk of severe liver injury to the boxed warning of ARAVA, based on

the FDA's review of adverse event reports, which included 49 cases of severe liver injury, 14 of which resulted in fatal liver failure, between April 2002 and May 2009. The highest risk appears to be with patients taking concomitant therapies known to cause liver injury and patients with pre-existing liver disease. (7)

- **FDA safety warnings on supplements:** More than half the American population takes supplements. In 2009, Americans spent \$26.7 billion on supplements. Consumers and some medical professionals might not realize that supplement manufacturers routinely and legally sell their products without first demonstrating that they are both safe and effective. In 2008 and 2009, the FDA received 1,359 reports of serious adverse effects from supplement manufacturers and 602 and from consumers and health professionals. The FDA routinely reports on recalls of supplements for a variety of safety reasons. Two examples of recent FDA recalls of supplement products due to "undeclared" medications include: a) RevivexxX[®] Extra Strength and b) Solo Slim[®] and Solo Slim Extra Strength. In the case of RevivexxX Extra Strength the product was found to contain tadalafil, which is the generic name for CIALIS[®], and was therefore considered an unapproved drug. Solo Slim was found to contain sibutramine, which is the generic name for the weight-loss prescription drug MERIDIA[®]. (8)

For more information about these and many other drug-related topics (e.g., drug safety, the MedWatch adverse drug reaction reporting system, market recalls, regulations, and educational programs) visit the FDA's [website](#) and click on *Drugs*. You may also receive FDA drug updates; select one of the links under the *Get Updates* heading on the FDA home page.

References:

1. Wan-Chih T. New Drug: Prolia (Denosumab). Pharmacist letter. 2010; 26 (8):260803. Accessed on 8.9.10 @ <http://www.pharmacistsletter.com>.
2. Highlights of Prescribing Information (DULERA): Accessed on 8.9.10 at <http://www.spfiles.com/pidulera.pdf>.
3. Timmerman L. Dendreon Sets Provenge Price at \$93,000, Says Only 2,000 People Will Get it in First Year. Xconomy. 4.29.10. Accessed online on 8.9.10 at <http://www.xconomy.com/seattle/2010/04/29/dendreon-sets-provenge-price-at-93000-says-only-2000-people-will-get-it-in-first-year/>.
4. FDA: Pfizer Voluntarily Withdraws Cancer Treatment MYLOTARG from U.S. Market. 6.21.10. Accessed online on 8.9.20 at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm216448.htm>.
5. FDA: Proton Pump Inhibitors (PPIs): Class Labeling Changes. 5.25.10. Accessed online on 8.9.10 at <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm213321.htm>.
6. FDA Warns of Risks with Unapproved use of Malaria Drug Qualaquin. 7.8.10. Accessed online on 8.9.10 at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm218383.htm>.
7. FDA: ARAVA (leflunomide): Boxed Warning: Risk of severe Liver Injury. 7.13.10. Accessed online on 8.9.10 at <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm218912.htm>.
8. Anon. Dietary Supplements can be risky; Consumer Reports recommends avoiding some. The Washington Post. 8.3.10. Accessed on 8.9.10 online at: <http://www.washingtonpost.com/wp-dyn/content/article/2010/08/02/AR2010080203870.html>.