



## NEW DRUGS

### Synribo for Chronic Myelogenous Leukemia

The FDA has approved omacetaxine mepesuccinate injection (Synribo, Teva) for adults with chronic myelogenous leukemia (CML) that has progressed after treatment with at least two tyrosine kinase inhibitors (TKIs).

Omacetaxine blocks certain proteins that promote the development of cancerous cells. It is injected subcutaneously twice daily for 14 consecutive days over a 28-day cycle until the white blood cell counts normalize. It is then given twice daily for 7 consecutive days over a 28-day cycle as long as clinical benefits are seen.

The drug was granted an accelerated approval and an orphan product designation. Its effectiveness was demonstrated by a reduction in the percentage of cells expressing the Philadelphia chromosome genetic mutation, found in most CML patients (i.e., 14 of 76 patients, or 18.4%).

This is the second drug recently approved to treat CML. In September, Pfizer's bosutinib (Bosulif) was approved to treat chronic, accelerated, or blast phase Philadelphia chromosome-positive CML.

Source: FDA, October 26, 2012

### Xeljanz for Rheumatoid Arthritis

Tofacitinib citrate (Xeljanz, Pfizer) 5-mg tablets are now approved for the treatment of moderately to severely active rheumatoid arthritis (RA) in adults who have had an inadequate response to, or who are intolerant of, methotrexate. Taken twice daily, the drug blocks molecules (Janus kinases) that are associated with joint inflammation.

However, the approval was granted with the caveat that the potentially harmful effects be clearly expressed on the package insert. A boxed warning mentions an increased risk of serious infections. Tofacitinib is also associated with elevated cholesterol levels, elevated liver enzymes, and decreased blood counts.

Tofacitinib was approved with a Risk Evaluation and Mitigation Strategy (REMS), including a medication guide, ahead of the product's prescription drug user fee goal date of November 21, 2012.

Patients may prefer tofacitinib because of its needle-free delivery and relatively low cost in comparison to other biologics, but fears regarding increased risks of infections, cancer, and tuberculosis threaten to dampen its entrance into the market, according to GlobalData.

Some physicians may consider tofacitinib as a third-line therapy until it is shown to be as safe and efficacious as the current selection of biologics.

Sources: FDA, November 6, 2012; GlobalData, November 8, 2012

### A Flu Vaccine Made From Cultured Animal Cells

Flucelvax is the first seasonal influenza vaccine to be licensed in the U.S. that is produced with the use of cultured animal cells instead of fertilized chicken eggs. The vaccine is intended for individuals 18 years of age and older.

The manufacturing process is similar to the egg-based method; however, the virus strains in the vaccine are grown in animal cells of mammalian origin. Cell culture technology has already been used for several decades to produce other vaccines. The new technique provides for the ability to maintain an adequate supply of previously tested cells and the potential for a faster startup of the vaccine-manufacturing process in the event of a pandemic.

In a study conducted in the U.S. and Europe, about 7,700 people 18 to 49 years of age received either Flucelvax or placebo. The vaccine was 83.8% effective in preventing influenza compared with placebo. The use of Flucelvax in people older than age 49 is supported by antibody responses in approximately 1,700 adults; the new vaccine was found to be comparable to Agriflu, an egg-based,

FDA-approved seasonal flu vaccine for people 18 years of age and older.

Source: FDA, November 20, 2012

## NEW INDICATION

### Xarelto for Pulmonary Embolism And DVT Recurrence

Rivaroxaban (Xarelto, Janssen) can now be used to treat acute deep vein thrombosis (DVT) and pulmonary embolism (PE) and to prevent recurrences. The drug was previously approved for preventing thromboembolism and stroke in patients with nonvalvular atrial fibrillation and for DVT prevention in patients undergoing joint surgery.

Rivaroxaban is the first oral anticlotting drug indicated for treating and reducing the recurrence of blood clots since the approval of warfarin nearly 60 years ago. The approval was based mainly on results from three randomized trials.

Close monitoring of coagulation activity is not required with rivaroxaban as it is with heparin and its analogues. However, as with other anticoagulants, there may be an increased risk of bleeding.

Source: FDA, November 2, 2012

## NEW FORMULATION

### Cystaran 0.44% Eyedrops

Sigma-Tau Pharmaceuticals, Inc., has introduced cysteamine (Cystaran) 0.44% as a topical ophthalmic solution to lower the cystine content of cells in patients with cystinosis, a genetic lysosomal storage disease. The product was developed in partnership with the National Institutes of Health to treat corneal cystine crystal accumulation resulting from cystinosis.

Cystinosis causes accumulations of the amino acid cystine in various organs. A buildup of the crystals in the kidneys, eyes, liver, muscles, pancreas, brain, and white blood cells slowly devastates the organs, eventually causing kidney failure or end-stage renal disease. Corneal cystine accumulation can cause ocular squinting, foreign-body sensations, visual changes,



corneal haziness, and photophobia. Other complications may include muscle weakness, diabetes, hypothyroidism, difficulty swallowing, and rickets.

Oral cysteamine is used for children and adults with nephropathic cystinosis, but that formulation has no effect on crystal formation in the eyes. Ocular adverse drug reactions have included photophobia, redness, eye pain, eye irritation, headache, and visual field defects.

Cystaran received an orphan drug designation with 7 years of market exclusivity and will be sold through specialty pharmacy distribution channels.

Sources [www.sigmatau.com](http://www.sigmatau.com); [www.drugs.com](http://www.drugs.com), October 4, 2012

## DRUG NEWS

### Ameridose Products Recalled

In October, Ameridose, LLC, based in Westborough, Mass., voluntarily recalled all of its unexpired products in circulation. A preliminary FDA inspection raised concerns about sterility, and the company agreed to cease pharmacy and manufacturing operations as a precaution.

This recall was not based on reports of infections linked to any Ameridose products. Practitioners were instructed to stop using the products and return them to the firm, but they did not have to follow up with patients who had already received company products.

Along with the state of Massachusetts, the FDA initiated the inspection of the Ameridose facility as part of its ongoing fungal meningitis outbreak investigation. Ameridose shares common management by the same parties as New England Compounding Center in Framingham, Mass., the firm associated with compounded drugs linked to the outbreak.

Some Ameridose products currently appear on the critical drug shortage list. These products were in short supply before this recall and might become even more scarce as a result of the recall.

Source: FDA, October 31, 2012

### Orphan Status For Leukemia Drug

Oxigene's product candidate—combretastatin A1 diphosphate/CA1P (OXi4503)—has been granted an orphan designation by the FDA for the treatment of acute myelogenous leukemia (AML). OXi4503 is a second-generation anticancer agent that combines vascular-disrupting activity with direct cytotoxicity, thereby collapsing blood vessels in tumors and starving them from within. In a preclinical study, OXi4503 produced remissions in AML models, including those with activating mutations in the high-risk subtype FLT3.

A phase 1 study of OXi4503 in patients with AML or myelodysplastic syndrome (MDS) is under way. Initial results are expected from the study by the year's end.

Sources: *The Wall Street Journal* (online); [www.clinicaltrials.gov](http://www.clinicaltrials.gov); [www.rttnews.com](http://www.rttnews.com), November 21, 2012

### Extended-Release Byetta Safe With TZDs

It is recognized that exenatide (Byetta, Amaryl) is safe to use with thiazolidinediones (TZDs). Researchers from San Francisco and Ontario, Canada now say that the extended-release (ER) formulation is also safe in exenatide-naïve patients and in those switching from twice-daily exenatide.

In an open-label study of treatment for up to 104 or 117 weeks, patients received exenatide 2 mg once weekly, continuing their stable dosage with a TZD—either rosiglitazone (Avandia, GlaxoSmithKline) or pioglitazone (Actos, Takeda/Eli Lilly) and metformin (Glucophage, Bristol-Myers Squibb) if applicable. Of 134 patients in the intent-to-treat group, 44 were exenatide-naïve and 90 patients were switched from twice-daily exenatide.

At 52 weeks, the intent-to-treat patients experienced significant reductions in glycosylated hemoglobin (HbA<sub>1c</sub>) values. Overall, 80% of patients reported at least

one adverse event.

TZDs have been linked to weight gain in diabetic patients, whereas glucagon-like peptide-1 receptor agonists such as exenatide have been associated with weight loss. In this study, exenatide-naïve patients lost 2.7 kg, and those who switched lost 0.8 kg. Exenatide-naïve patients continued to lose weight, and those who switched to once-weekly therapy maintained their weight similar to that at baseline.

Type-2 diabetes is discussed further on pages 687 and 699.

Source: *Clin Ther* 2012;34:2082–2090

### Patent Protection for Vascepa

The U.S. Patent and Trademark Office has issued a patent covering Amarin Corp.'s icosapent ethyl (Vascepa). This prescription-grade, ultra-pure omega-3 fatty acid (fish-oil) product is indicated as an adjunct to diet in adults with severe hypertriglyceridemia who are at risk for a heart attack or stroke. The FDA approved Vascepa in July based on the company's MARINE clinical trial results. On September 4, 2012, Amarin announced the issuance of a Notice of Allowance for claims under this application.

The term of the newly issued patent (No. 8,318,715) expires no earlier than in 2030. Amarin plans to list the patent in the FDA's "Orange Book."

Sources: [www.globenewswire.com](http://www.globenewswire.com) and <http://investor.amarincorp.com>, November 27, 2012; [www.vascepa.com](http://www.vascepa.com); [www.amarincorp.com](http://www.amarincorp.com)

## DEVICE NEWS

### Zilver Stent For Peripheral Artery Disease

The FDA has approved Cook's Zilver PTX drug-eluting, self-expanding stent for patients with peripheral artery disease. The stent is implanted in the femoropopliteal artery and releases paclitaxel (Taxol, Bristol-Myers Squibb) to prevent restenosis.

Source: FDA, November 15, 2012

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## NEW MEDICAL DEVICES

Marvin M. Goldenberg PhD, RPh, MS

**Name:** Relay Thoracic Stent-Graft with Plus Delivery System

**Manufacturer:** Bolton Medical, Sunrise, Fla.

**Approval Date:** September 21, 2012

**Purpose:** The Relay endovascular stent-graft is used to repair fusiform and saccular aneurysms as well as penetrating ulcers of the aorta in the chest.

**Description:** Each stent-graft is compressed into the end of a long, thin, tube-like delivery catheter, which is inserted into an artery in the groin through a small incision in the skin. It is carefully guided within the artery into the chest to bridge the site of the aneurysm or the ulcer in the aorta. The stent-graft is then released in the aorta, where it expands to the diameter of the aorta to seal off the aneurysm or ulcer, relining the artery wall.

**Benefit:** The system helps to prevent further growth and rupture of aneurysms and penetrating ulcers. The device is also less invasive than other methods.

**Sources:** [www.fda.gov](http://www.fda.gov), [www.fierce-medicaldevices.com](http://www.fierce-medicaldevices.com), October 12, 2012; [www.boltonmedical.com](http://www.boltonmedical.com), September 24, 2012

### *Class I Recall*

Accutron, Inc., has voluntarily recalled its Ultra PC% Cabinet Mount Flowmeter. The product is used during some dental procedures to control the flow of gases used in nitrous oxide/oxygen sedation systems. The flowmeter was recalled because of the possibility that it might continue to release nitrous oxide gas when the oxygen is turned off. When nitrous oxide is not mixed with oxygen, inhaling nitrous oxide can lead to temporary and permanent brain damage and death.

**Sources:** FDA, [www.fda.gov](http://www.fda.gov), October 16, 2012; American Association of Oral and Maxillofacial Surgeons, [www.aaoms.org](http://www.aaoms.org), October 25, 2012 ■