NEW DRUGS

Temsirolimus (Torisel) For Advanced Kidney Cancer

The Food and Drug Administration (FDA) has approved temsirolimus (Torisel, Wyeth) for the treatment of advanced kidney cancer.

In a clinical trial of 626 patients, one group received the study drug alone, another received a comparator agent (interferon alfa), and the third group received a combination of the two. The temsirolimus-alone group showed a significant improvement in overall survival.

Temsirolimus blocks a key protein that regulates cell proliferation. It also blocks angiogenesis, which creates a blood supply to tumors to maintain their growth.

For more details on temsirolimus, please see this month’s Pharmaceutical Approval Update column, page 377.

(Source: FDA, May 30, 2007.)

Estradiol (Divigel) For Hot Flashes

Upsher-Smith Laboratories has received the FDA’s approval to market estradiol gel 0.1% (Divigel). The gel offers the lowest approved dose of estradiol available for women with moderate-to-severe hot flashes associated with menopause.

Estrogen hormone therapy should be used at the lowest effective dose for the shortest amount of time.

The estrogen in Divigel is derived from plant sources and is identical to the primary estrogen produced by the ovaries before menopause. The quick-drying gel is available in individual-use packets. One packet of gel is applied daily to an area approximately 5 x 7 inches on the thigh, where it is absorbed directly into the bloodstream without having to pass through the liver.

Divigel is available in doses of 0.25 mg, 0.5 mg, and 1 mg of estradiol per day. More information is presented in the Pharmaceutical Approval Update column, page 377.

(Source: Upsher-Smith, June 5, 2007.)

Levocetirizine (Xyzal) Relieves Allergies and Hives

The FDA has approved once-daily levocetirizine dihydrochloride (Xyzal, UCB/Sanofi-Aventis), an antihistamine for the relief of symptoms associated with seasonal and perennial allergic rhinitis and uncomplicated skin manifestations of chronic idiopathic urticaria. The medication is indicated for adults and children six years of age and older.

The approval was based primarily on the results of eight randomized, placebo-controlled clinical trials involving more than 2,000 patients. Levocetirizine significantly reduced the severity of itching and the number and size of wheals.

Xyzal was first launched in Europe in 2001. The tablets are expected to be available in the U.S. during the 2007 fall allergy season.

(Sources: FDA; Sanofi-Aventis, May 29, 2007, www.ucb-group.com; http://products.sanofi-aventis.us.)

Valsartan/Amlodipine (Exforge) for Hypertension

A tablet made by Novartis combines two agents used to treat hypertension: valsartan (Diovan), an angiotensin-receptor blocker (ARB), and amlodipine (Norvasc), a calcium-channel blocker (CCB). Both drugs allow blood vessels to relax so that blood can flow more easily.

The FDA’s approval was supported by a clinical program involving more than 5,000 patients. Exforge was approved in January 2007.

Exforge is not indicated for the initial treatment of high blood pressure. It is intended for use when other ARBs or CCBs do not control blood pressure and when patients have experienced dose-limiting side effects from either valsartan or amlodipine.

(Source: June 21, 2007; www.novartis.com.)

Armodafinil (Nuvigil) For Sleepiness with Apnea

A non-amphetamine, wake-promoting agent, armodafinil (Nuvigil C-IV, Cephalon), a Schedule IV product, has been approved to treat excessive sleepiness associated with obstructive sleep apnea or hypopnea syndrome, narcolepsy, and shift-work sleep disorder.

Armodafinil is a single-isomer formulation of modafinil, the active ingredient in Provigil, which was approved in 1998 to improve Wakefulness. Armodafinil has a longer duration of action than modafinil.

The FDA has included a bolded warning about the potential occurrence of skin rash and hypersensitivity and plans to request similar labeling for modafinil.

(Source: Cephalon, June 18, 2007, www.cephalon.com.)

Ambrisentan (Letairis) For Pulmonary Arterial Hypertension

The FDA has approved an orphan drug, ambrisentan (Letairis, Gilead), for patients with pulmonary arterial hypertension. This rare, life-threatening condition is characterized by continuous high blood pressure within the arteries of the lungs.

Ambrisentan was granted a priority review. The drug’s safety and effectiveness were demonstrated in two international clinical trials. Ambrisentan significantly improved physical activity capacity, compared with a placebo, in a six-minute walk, and it delayed the worsening of pulmonary hypertension.

This drug should not be used by pregnant women or by women who might become pregnant. Monthly blood tests...
are required to check for potential liver injury.

Ambrisentan will be available as 5-mg and 10-mg once-daily tablets. Gilead holds the U.S. rights to this agent; GlaxoSmithKline holds rights outside the U.S. (Source: FDA, June 15, 2007.)

NEW INDICATIONS
Evicel Fibrin Sealant In Vascular Surgery
A topical liquid, Evicel Fibrin Sealant (Omrix/Ethicon), has been approved for use in vascular surgery. Evicel helps control oozing from small blood vessels. Derived from pooled human plasma, the sealant consists of a fibrinogen concentrate and thrombin, both of which promote clotting and help reduce the risk of viral transmission in manufacturing.

Crosseal, the predecessor of Evicel, was originally licensed for use during liver surgery. With Evicel, no stabilizing agent is required to slow the natural dissolution of clots.


Growth Hormone (Somatropin [Norditropin]) For Short Stature in Children with Noonan Syndrome
Somatropin (rDNA origin) injection (Norditropin, Novo Nordisk) is approved for the treatment of short stature in children with Noonan syndrome.

This autosomal dominant genetic syndrome is commonly characterized by short stature, congenital heart defects, and unusual facial features.

Somatropin is also indicated for children with growth failure resulting from inadequate secretion of endogenous growth hormone (GH) and for replacement of endogenous GH in adults with GH deficiency of either adult or childhood onset. The agent is featured in this month’s Pharmaceutical Approval Update column, page 377.

(Source: Novo Nordisk, June 1, 2007.)

Pregabalin (Lyrica) For Fibromyalgia
After a priority review, the FDA has approved pregabalin (Lyrica, Pfizer) capsules CV (Schedule V) for the management of fibromyalgia. Characterized by chronic widespread pain that can be relentless, fibromyalgia is usually accompanied by poor sleep, stiffness, and fatigue; patients also experience deep tenderness, soreness, and flu-like aches.

Pregabalin binds to a specific protein within overexcited nerve cells and helps to calm damaged nerves. This is thought to reduce the level of pain.

Pregabalin is also approved for the management of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia and for the adjunctive therapy for adults with partial-onset seizures.

(Sources: FDA, June 21, 2007; www.lyrica.com.)

NEW FORMULATIONS
Extended-Release Zileuton (Zyflo) for Asthma
Dey LP has announced the FDA’s approval of its New Drug Application (NDA) of its marketing partner, Critical Therapeutics, Inc., for twice-daily extended-release zileuton tablets (Zyflo CR).

Zyflo CR and Zyflo are approved for the prophylaxis and chronic treatment of asthma in adults and children 12 years of age and older. Zyflo was first approved in 1996 for the treatment of asthma.

The recommended dose of Zyflo CR is two extended-release 600-mg tablets twice daily within one hour after morning and evening meals (for a total daily dose of 2,400 mg).

The recommended Zyflo dose is one 600-mg immediate-release tablet four times a day (for a total daily dose of 2,400 mg).

(Sources: Dey, May 31, 2007; www.zyflo.com.)

IV Insulin (Apidra) For Quick Glycemic Control
The FDA has approved rapid-acting insulin glulisine (rDNA origin) injection (Apidra, Sanoﬁ-Aventis) for intravenous (IV) administration in adults with type-1 and type-2 diabetes.

Apidra was approved in April 2004 for treating diabetes mellitus and controlling hyperglycemia. It can also be given subcutaneously in vial form, by insulin pen, or by an external insulin infusion pump.

Apidra can be taken within 15 minutes before or within 20 minutes after starting a meal. In clinical studies, the drug maintained its rapid onset of action and absorption in both lean and obese patients.

(Source: Sanofi-Aventis, June 15, 2007.)

Higher-Dose Adapalene (Differin) for Acne
A higher concentration of the topical retinoid adapalene 0.1% (Differin, Galderma) is now approved for patients with acne. The new formulation of 0.3% is efficacious enough to treat moderate to moderately severe acne and provides a favorable side-effect profile.

In a randomized, double-blind, parallel-group study, the higher dose resulted in better success rates and demonstrated a fast onset of action.

This prescription medication is odorless and free of oil and alcohol. The gel normalizes the improper accumulation of skin cells that plug the pores and keeps them clear.

(Sources: FDA, June 20, 2007; www.differin.com.)
**NEW DRUGS**

**DRUG NEWS**

**FluMist Vaccine Favored For Younger Children**

An FDA advisory committee has voted to include children younger than five years of age to be eligible to receive MedImmune’s live intranasal influenza virus vaccine (FluMist). FluMist is approved for healthy children and adolescents 5 to 17 years of age and for healthy adults 18 to 49 years of age.

The data demonstrated the efficacy of FluMist nasal spray in children 6 to 59 months of age. The committee also voted in favor of the risk–benefit profile of FluMist for children 12 to 59 months of age without a history of wheezing and for children 24 to 59 months of age with or without a history of wheezing.

On January 5, 2007, the FDA approved a refrigerated version of FluMist.

(Source: FDA, www.fda.gov/MedImmune, May 16, 2007.)

**Once-Yearly Zoledronic Acid (Reclast) Reduces Fractures**

A once-a-year infusion of zoledronic acid (Reclast, Novartis) may be as effective as monthly or weekly regimens in reducing the incidence of bone fractures, according to researchers at the University of California, San Francisco.

In a three-year study (HORIZON), the risk of spinal fractures was reduced by 70% and the risk of hip fractures was reduced by 40% with zoledronic acid. The effect was sustained over three years.

An investigational bisphosphonate, Reclast is approved for treating Paget’s disease of bone. (See also this month’s feature article on osteoporosis, p. 392.)


**FDA Creates Panel For Consumers**

A new FDA panel has been formed to educate consumers about the risks of taking medications.

The Risk Communication Advisory Committee will comprise 15 experts and patient advocates who will communicate safety information on drugs, medical devices, and other regulated products. The panel’s initial charter will last two years.

(Source: The Philadelphia Inquirer; Associated Press, June 5, 2007.)

**Update: Taxus Stent Registry**

Boston Scientific Corp. has completed enrollment of more than 23,000 patients in the European and Intercontinental phases (2 and 3) of its Taxus Olympia registry. The registry is designed to evaluate the safety and performance of its second-generation drug-eluting coronary stent, Taxus Liberté, in a real-world setting. Olympia is the world’s largest drug-eluting stent registry. Plans are to enroll at least 27,000 patients treated for complex coronary lesions at more than 400 centers worldwide.

(Source: Boston Scientific, May 14, 2007.)

**Recall: Contact Lens Solution**

Advanced Medical Optics has recalled its Complete MoisturePlus Multi Purpose Solution because of an association with Acanthamoeba keratitis (AK). The CDC described two analyses showing an elevated risk of AK among users of the solution.

Caused by a common water-borne amoeba, AK can result in vision loss or blindness if the infection is not treated.

Symptoms can be similar to those of other ocular infections (eye pain or redness, blurred vision, light sensitivity, sensation of a foreign body in the eye, or excessive tearing), but AK is more difficult to treat.

Patients who have used the solution should discard it along with their current lenses and storage containers.

(Source: FDA, May 26, 2007.)