In clinical trials, Iprivask was found to be superior to both heparin and enoxaparin (Lovenox, Sanofi-Aventis) for preventing proximal DVT and major venous thromboembolic embolism (VTE) after elective hip replacement surgery. VTE is a common postsurgical complication and is associated with increased hospital costs, length of stay, morbidity, and mortality.

Administered as a fixed subcutaneous (SQ) dose, Iprivask is considered easier to use than intravenous (IV) agents and may be a safer alternative for DVT prophylaxis.

Iprivask does not pose a risk for thrombocytopenia or heparin-induced thrombocytopenia; it is relatively short-acting and is easy to monitor. It is modeled after hirudin, an anticoagulant found in the saliva of medicinal leeches. However, it must be used with caution in patients with renal impairment.


VPRIV for Gaucher Disease

Shire’s velaglucerase alfa for injection (VPRIV) has been approved to treat children and adults with type-1 Gaucher disease. This rare genetic disorder affects people who do not produce enough of an enzyme called glucocerebrosidase. The new product is an alternative to imiglucerase (Cerezyme, Genzyme), which has been in short supply.

Type-1 is the most common form of the disease and is more prevalent among Jews of Eastern European descent. In patients lacking the enzyme, harmful amounts of a certain lipid can build up in the liver, spleen, bones, bone marrow, and nervous system, resulting in the inability of cells and organs to function properly.

The FDA’s approval of velaglucerase replacement therapy was based on a priority review of data from 3 clinical studies of 82 patients four years of age and older, some of whom had previously received imiglucerase.

The recommended velaglucerase regimen is 60 IU/kg every other week as a one-hour IV infusion.

Adverse events have been infusion-related and have included headache, dizziness, hypotension, hypertension, nausea, fatigue, asthenia, and pyrexia. Infusion reactions were generally mild and occurred most frequently during the first six months of therapy in treatment-naive patients. Children were more likely than adults to experience rash, upper respiratory tract infection, prolonged partial thromboplastin time, and pyrexia.

Sources: FDA, March 2, 2010; Medscape, March 1, 2010

Exalgo ER Tablets For Pain Relief

The FDA has approved Covidien’s New Drug Application for hydromorphone HCl (Exalgo) extended-release tablets. A boxed warning mentions the potential for abuse.

This once-daily Schedule II agent is indicated for the management of moderate-to-severe pain in opioid-tolerant patients requiring continuous, around-the-clock opioid analgesia for an extended period of time.

Patients considered opioid-tolerant are those who are taking at least 60 mg/day of oral morphine, 25 mcg/hour of transdermal fentanyl, 30 mg/day of oral oxycodone, 8 mg/day of oral hydromorphone, 25 mg/day of oral oxymorphone, or an equianalgesic dose of another opioid for a week or longer.

Hydromorphone HCl has been used in treating chronic pain for more than 80 years, but the extended-release formulation is new. Alza’s osmotic delivery system is designed to release the opioid at a controlled rate and to help minimize the peaks and troughs that are sometimes
Orphan Drug Designations

AP24534 for Leukemia

AP24534, an investigational pan-bcr-abl inhibitor made by Ariad Pharmaceuticals, has been granted orphan drug designation by the FDA and the European Medicines Agency. In the U.S., the drug is indicated for patients with chronic myeloid leukemia (CML) and Philadelphia chromosome–positive acute lymphoblastic leukemia (Ph+ ALL). In the U.S. and European Union, its orphan designation is for CML and ALL.

In preclinical studies, AP24534 demonstrated inhibition of kinase targets associated with acute myeloid leukemia (AML) as well as proliferation and angiogenesis in multiple solid tumors.

Source: Ariad, March 1, 2010

IMGN901 for Merkel Cell Carcinoma

ImmunoGen’s IMGN901 compound has received an orphan drug designation when used to treat patients with Merkel cell carcinoma (MCC). The European Union also granted an orphan medicinal product designation for the treatment of MCC.

IMGN901 is designed to kill cancer cells that express CD56, a protein. MCC is an aggressive neuroendocrine cancer of the skin that typically occurs on the head and neck, most often in individuals of European ancestry.

Approximately 2,000 new cases of MCC are diagnosed in the U.S. each year, and the incidence is increasing. The company plans to begin pivotal testing in 2011.

Source: ImmunoGen, March 8, 2010

Ciprofloxacin Inhaler

In Cystic Fibrosis

Bayer HealthCare Pharmaceuticals has announced the approval of an orphan drug designation for ciprofloxacin dry powder inhaler to manage pulmonary infection caused by Pseudomonas aeruginosa in patients with cystic fibrosis. A similar designation has already been granted by the European Medicines Agency.

This investigational agent combines the powder (formulated by Novartis) with a delivery inhaler. The product is in phase 2 development.

Patients with cystic fibrosis have thickened respiratory secretions that are difficult to clear, thus increasing the risk of infection and inflammation.

Source: Bayer, March 11, 2010

Carbaglu for Elevated Ammonia Levels

The FDA has approved carglumic acid tablets (Carbaglu, Orphan Europe) to treat excessive levels of ammonia in the blood. N-acetylglutamate synthase (NAGS) deficiency is a rare genetic disorder that can manifest soon after birth. The deficiency and the resulting hyperammonemia can be fatal if they are not detected and treated rapidly. DNA testing can confirm the diagnosis.

The drug’s safety was evaluated in 23 patients who were treated for periods ranging from six months to 21 years. Carbaglu reduced blood ammonia levels within 24 hours and normalized levels within three days. Most patients appeared to maintain normal plasma ammonia levels with long-term treatment.

Carbaglu should be administered only by physicians with experience in treating metabolic disorders. The recommended initial dose for acute hyperammonemia is 100 to 250 mg/kg per day. Other ammonia-lowering therapies with Carbaglu during episodes of acute hyperammonemia are recommended. Dose adjustments may be needed according to the patient’s ammonia levels and symptoms.

Source: FDA, March 18, 2010

Benicar for Children With Hypertension

Olmesartan medoxomil tablets (Benicar, Daiichi Sankyo) are now approved for the treatment of hypertension in children and adolescents 6 to 16 years of age. The approval was based on study data from a phase 3 clinical trial involving pediatric patients.

This angiotensin II receptor blocker is already indicated for adults with elevated BP. For more information on the pediatric indication, please see this month’s Pharmaceutical Approval Update feature, page 218.


Botox for Spastic Upper-Limb Muscles

The FDA has approved botulinum toxin type A (Botox, Allergan) to treat spasticity in the flexor muscles of the elbow, wrist, and fingers in adults. Spasticity is common after stroke, traumatic brain injury, or the progression of multiple sclerosis.
**NEW DRUGS**

**Botox**

Botox temporarily blocks connections between nerves and muscles, resulting in a temporary paralysis of the spastic muscle. The tightness and stiffness of the muscles can lead to pain, difficulty in performing activities of daily living, and changes in physical appearance.

A boxed warning notes that the effects of the toxin may spread from the area of injection to other areas of the body, causing symptoms similar to those of botulism, such as swallowing and breathing difficulties that can be life-threatening.

Botox has not been shown to be safe or effective for other upper-limb muscles; spasticity in the legs; or fixed contractures, which affect range of motion.

Source: FDA, March 9, 2010

**NEW FORMULATIONS**

**Trelstar 22.5 mg**

Triptorelin pamoate 22.5 mg for injectable suspension has been approved. This twice-yearly version of Trelstar (Watson Pharmaceuticals) is a palliative therapy for advanced prostate cancer.

A gonadotropin-releasing hormone (GnRH) agonist, the drug suppresses testosterone production for six months. Developed by the Debiopharm Group and first approved in the U.S. in 2000, Trelstar is also available in one-month (3.75-mg) and three-month (11.25-mg) forms. The new, longer-acting formulation can be stored at room temperature.

The product is administered with a thin needle and is associated with little injection-site pain.

Source: Watson, March 11, 2010

**PREVNAR 13 VACCINE FOR PNEUMOCOCCAL INFECTIONS**

A new version of Wyeth’s Pneumococcal 7-valent conjugate vaccine (diphtheria CRM197 Protein) (Prevnar 7) has been approved. Prevnar 13 is indicated for the prevention of pneumococcal illnesses, such as ear infections, sepsis, and meningitis, in infants and young children.

The vaccine is the first product to win FDA approval since Pfizer acquired Wyeth last year. Prevnar 13 is designed to reduce the risk of infection by 13 strains of pneumococcal disease in children five years old and younger. Prevnar 13 adds protection against six additional strains of bacterial infection compared with Prevnar 7. In the U.S., children receive four injections. Children who have not been fully vaccinated with the original Prevnar can finish their schedule with the new vaccine.

Infections from pneumococcal disease dropped dramatically after Prevnar 7 was released in 2000, but infections began rising again in 2005 with the development of new variants of the disease.

Prevnar 13 costs about $100 per dose, or 30% over the previous vaccine. Pfizer plans to file an indication for adults in countries where Prevnar 7 has not yet been sold.

The vaccine is discussed in the Pharmaceutical Approval Update feature on page 217.


**DEVICE BRIEFS**

**New approval.** The FDA has approved Boston Scientific’s Express LD Iliac Pre-mounted Stent System for use in iliac arteries. In patients with atherosclerotic iliac disease, plaque has built up within the arteries that supply blood to the legs, resulting in poor blood flow and leg pain. The disease can be treated with medication, surgery or angioplasty. The stent design offers physicians a less invasive alternative to surgery. This balloon-expandable stent has received CE Mark approval and is approved for iliac use in international markets.

Source: Boston Scientific, March 11, 2010

**Charges against Guidant.** Guidant LLC, a subsidiary of Boston Scientific Corp., has been charged with criminal violations of the Federal Food, Drug, and Cosmetic Act related to safety problems with some of its implantable defibrillators. Because the device delivers an elec-
for patients needing a ventral, incisional, or inguinal hernia repair and may avoid the long-term complications associated with permanent synthetic meshes.

The mesh is designed to retain its mechanical strength for at least six months, yielding better compliance because of its dual fiber construction. The matrix gradually degrades; like other natural by-products, it is absorbed and excreted. As the world’s first long-term resorbable matrix, it represents a significant breakthrough.

Source: www.novusscientific.com/novus/index.asp?finsigmaCollectionId=341

Name: Dyna-Link Spinal System/Presidio Spinal Plating System
Approval Date: January 28, 2010
Purpose: This stand-alone device is indicated for use in spinal surgery.
Description: The spinal system accommodates two types of screws, and the thoracolumbar plating system features multiple types of low-profile implants. The device combines a surgical-grade titanium component and an Invibio Peek Optima interbody cage. Either fixed or variable angle screws can be used to control compression on the interbody device. The two systems incorporate an innovative, zero-step locking mechanism and use comprehensive instrumentation. Up to four screws can be accommodated for optimal torsional resistance.
Benefit: The instrumentation is designed to reduce the number of surgical steps and intraoperative complexity.
Sources: www.lifespine.com; www.beckersorthopedicandspine.com

Name: ProGel Pleural Air Leak Sealant
Manufacturer: NeoMend, Inc., Irvine, Calif.
Approval Date: January 14, 2010
Purpose: Surgeons performing open resection of lung tissue use ProGel to seal air leaks on pulmonary tissue after sutures or staples are used to close the incision. After a lung tumor is removed, air leaks can develop around the sutures or staples that were used. The surgeon usually closes an air leak by suturing and stapling tissue or applying a surgical mesh over the leak. In some patients, lung tissue is so fragile that the surgeon might not try to use these usual closure methods.

In addition to the standard surgical closure methods, the sealant can be used to close lung tissue.

Description: ProGel sealant is composed of human serum albumin and a polyethylene glycol cross-linker that forms a clear flexible gel on mixing.
Benefit: The sealant is sprayed or painted on the lung tissue. In clinical studies, 35% of patients treated with ProGel and standard surgical closure were free of any air leaks upon hospital discharge, in contrast to 14% of patients treated with standard techniques alone. ProGel also reduced the number of air leaks occurring during surgery. The incidence and severity of side effects for both treatment groups were similar; however, the total number of kidney-related adverse events was higher in the ProGel patients (9.5%) than in the controls (3.8%).

Precautions: ProGel should not be used in patients who are allergic to human blood proteins or who have renal impairment. It should not be used after surgery for open or closed defects of the branches of the airway that lead to the lung because of a possible increased incidence of undesired air passageways between the lung and the tissue surrounding the lung.

Source: www.accessdata.fda.gov/cdrh_docs/pdf/P010047a.pdf