Select List of New Drugs Approved in 2005

Listed below is a select list of new drugs that were recently approved by the FDA. Note, this list does not include all new drug approvals. For a complete list of all newly approved drugs, please visit the FDA website at:

**Drug:** mometasone furoate (Asmanex® Twisthaler®)  
**Manufacturer:** Schering-Plough  
**Route:** Inhaler  
**Approval Date:** 3/30/2005  

**Indication:** For first-line maintenance treatment of asthma as prophylactic (preventative) therapy in patients 12 years of age and older, and treatment of asthma patients who require oral corticosteroid therapy where adding Asmanex Twisthaler may reduce the need for oral corticosteroids.

**Therapeutic Considerations:** Asmanex® Twisthaler® 220 mcg (mometasone furoate) is a once-daily inhaled corticosteroid for initiation and maintenance of asthma in patients previously treated with bronchodilators alone or inhaled corticosteroids. In clinical studies, Asmanex improved lung function, decreased use of rescue medication (albuterol), decreased the number of nighttime awakenings, and improved daytime symptoms such as coughing or wheezing. This is similar to results seen with other corticosteroid inhalers.

Dosing: The recommended doses are based on prior asthma therapy. Patients previously being treated with bronchodilators alone or inhaled corticosteroids should initiate Asmanex therapy with 220 mcg once-daily in the evening. The highest recommended daily dose for these patients is 440 mcg, either administered once daily in the evening or as 220 mcg twice daily. Patients previously receiving oral corticosteroids should initiate Asmanex therapy with 440 mcg twice daily; the highest recommended daily dose for that population is 880 mcg.

How supplied:  
· The Asmanex Twisthaler inhaler is an inhalation driven device that does not use a propellant, which eliminates the need for hand-breath coordination. It also provides patients with a numeric dose counter that indicates how many doses are remaining.  
· The device contains 14 inhalations (institutional use only), 60 inhalations or 120 inhalations. Each actuation delivers 220 mcg of active drug. The inhaler should be discarded 45 days after opening the foil pouch or when the dose counter reads 00, whichever comes first.
Launch date: Fall 2005

Affected Population: Asthma affects approximately 20 million people in the US.

Peak Sales Estimate: $500 million.

Cost (AWP): Not available.
Drug: entecavir (Baraclude™)
Manufacturer: Bristol-Myers Squibb
Route: Oral
Approval Date: 3/29/2005; Priority Review (IP)

Indication:
For the treatment of chronic hepatitis B infection in adults with evidence of active viral replication and either evidence of persistent elevations in serum aminotransferases (ALT or AST) or histologically active disease.

Therapeutic Considerations:
Baraclude™ is a once-daily oral antiviral drug for the treatment of chronic hepatitis B.

Other oral antivirals for hepatitis B are lamivudine (Epivir-HBV®) and adefovir (Hepsera®). One of the major problems with Epivir-HBV is that many patients become resistant to the drug. So far, the development of resistance does not seem to be a problem with Baraclude. Baraclude was shown to be more effective than Epivir-HBV in clinical trials for patients who have not been previously treated with Epivir-HBV. It is also effective in for patients who have demonstrated resistance to Epivir-HBV. Hepsera has also shown to be effective in patients that have become resistant to Epivir-HBV, but it lacks data showing that it is more effective than Epivir-HBV in patients who have not been previously treated. There are currently no trials comparing Baraclude and Hepsera.

Interferon alfa (Intron A® or Roferon®), which is given via subcutaneous injection, is also indicated for the treatment of hepatitis B. The recommended duration of treatment with interferon alfa is limited, whereas the oral antivirals are used chronically until the patient relapses or until the presence of intolerable side effects.

Adverse effects and safety:
· The overall safety and tolerability of Baraclude is similar to Epivir-HBV. The most common side effects of Baraclude were headache, tiredness, dizziness, and nausea.
· Baraclude was associated with development of cancerous tumors in rodent studies which used very high doses of the drug. It is currently not known if this cancer risk applies to humans. The company plans to conduct an additional long-term study to determine if there is any carcinogenic potential in humans.
· Similar to Epivir-HBV and Hepsera, Baraclude contains a black box warning about the risk of lactic acidosis and severe hepatomegaly (enlargement of the liver) with steatosis (fat in the liver), including fatal cases, that have been reported with the use of nucleoside analogues alone or in combination with
antiretrovirals. Acute exacerbations of hepatitis B have been reported in patients who have discontinued anti-hepatitis B therapy.

Dose:
· Nucleoside treatment naïve adults and adolescents (≥16 years of age): 0.5 mg once daily.
· Epivir-HBV-resistant patients: 1 mg once daily.

How supplied: 0.5 mg and 1 mg tablets; 0.05 mg/mL oral solution

Launch date: April 8, 2005

**Affected Population:** In the US, more than 1 million people have developed chronic hepatitis B infection and more than 5,000 Americans die from hepatitis B and hepatitis B-related liver complications each year.

**Peak Sales Estimate:** $400 million.

**Cost (AWP):** 0.5 mg and 1 mg tablet = $24.67
**Drug:** ibandronate (Boniva®)  
**Manufacturer:** Roche, GlaxoSmithKline  
**Route:** Oral  
**Approval Date:** 5/16/2003 (once-daily formulation); 3/24/2005 (once-monthly formulation)  

**Indication:** For treatment and prevention of postmenopausal osteoporosis

**Therapeutic Considerations:**

Boniva® is a once-monthly oral bisphosphonate for the treatment and prevention of postmenopausal osteoporosis. Once-daily Boniva was approved in May 2003, but the companies did not launch at that time until approval of a less frequent dosing regimen. Other bisphosphonates on the market are Fosamax® (alendronate) and Actonel® (risendronate). Both are available in once-daily and once-weekly dosage forms.

The monthly dosing regimen is expected to minimize frequency of taking bisphosphonates and their associated side effects. Bisphosphonates are associated with upper gastrointestinal disorders such as difficulty swallowing, inflammation of the esophagus, and esophageal or gastric ulcers. To minimize risk of irritation to the esophagus, patients are instructed to take Boniva with plain water on an empty stomach upon arising in the morning. They should also remain upright and avoid food, drink, and other medications for at least 60 minutes. Other bisphosphonates (Fosamax and Actonel) have similar patient instructions, but require that the patient wait 30 minutes before eating, drinking or lying down.

A supplemental NDA was also submitted in December 2004 for an IV formulation of Boniva, which would be given every 3 months.

**Efficacy:**

Monthly Boniva was approved based on the results of MOBILE (Monthly Oral iBandronate In LadiEs) study, which compared the once-monthly dose (150 mg) with the once daily dose (2.5 mg) in 1602 postmenopausal women for the treatment of osteoporosis. The once-monthly dose was at least as effective as the daily dose in increasing bone mineral density (BMD) at the lumbar spine and other skeletal sites. With the once-monthly dose, the mean increase from baseline in lumbar spine BMD was 4.9% compared to 3.9% for the daily dose (p=0.002). Patients taking the once-monthly dose had higher BMD increases at other skeletal sites compared to those taking the daily dose.

**Dosing:** 2.5 mg once-daily or 150 mg once-monthly taken on the same date of each month. This dosage regimen is approved for both the treatment and prevention of osteoporosis.
How supplied: 2.5 mg tablets (once-daily dosing); 150 mg tablets (once-monthly dosing) are packaged in boxes of 3 blister packs containing 1 tablet each. The blister packs can be separated so that monthly quantities can be dispensed.

Launch date: April 2005 (both monthly and daily tablets)

**Affected Population:** Approximately 10 million people in the US, 8 million of whom are women, have osteoporosis. Almost 34 million more are estimated to have osteopenia, placing them at increased risk for osteoporosis.

**Peak Sales Estimate:** $500 million.

**Cost (AWP):** 150 mg tablet given once a month = $80.25.
**Drug:** pramlintide acetate (Symlin®)  
**Manufacturer:** Amylin  
**Route:** Subcutaneous injection  
**Approval Date:** 3/16/2005

**Indication:** For type 1 diabetes, as an adjunct treatment in patients who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy.  
For type 2 diabetes, as an adjunct treatment in patients who use mealtime insulin therapy and have failed to achieve desired glucose control despite optimal insulin therapy, with or without a concurrent sulfonylurea agent and/or metformin.

**Therapeutic Considerations:** Symlin is a new anti-diabetic drug that is administered by subcutaneous injection to patients who use mealtime insulin therapy but continue to fail to achieve glucose control. It is indicated for both type 1 and type 2 diabetes patients.

Symlin is the synthetic analog of human amylin, a hormone synthesized by the beta cells of the pancreas which produce insulin. In patients with type 1 diabetes, and patients with type 2 diabetes who use insulin, the beta cells malfunction, resulting in reduced secretion of both insulin and amylin after meals. The use of Symlin contributes to glucose control after meals. Symlin also causes satiety which leads to decreased caloric intake and potential weight loss.

Symlin was studied in over 5300 patients in clinical trials. The studies showed that Symlin, injected prior to meals helps patients achieve lower blood glucose after meals, leading to less fluctuations during the day, and better long-term glucose control (hemoglobin A1c, HBA1c) compared to patients taking insulin alone. Of note, however, Symlin cannot be mixed with insulin. Fluctuations in blood glucose levels have been shown to increase the risk of long-term diabetes complications such as kidney failure, nerve damage, blindness, amputation and cardiovascular disease. Patients taking Symlin also used less insulin during meals and lost weight compared to those taking insulin alone, who either gained weight or remained the same.

The product label for Symlin carries a black box warning about the risk of severe insulin-induced hypoglycemia, which is usually seen within 3 hours following Symlin injection. Severe hypoglycemia is more common in patients with type 1 diabetes. Careful patient selection is critical in order to minimize the risk of severe hypoglycemia.
The most common adverse event reported with the use of Symlin was nausea. This reaction was higher at the beginning of treatment and decreased over time in most patients. The incidence and severity of nausea are reduced when Symlin is titrated slowly to recommended doses.

The company will provide educational programs for physicians, diabetes care teams, and patients to help ensure appropriate administration and patient selection. Additionally, a Patient Medication Guide will be distributed to patients by pharmacists when dispensing the drug.

Dosing: The dose of Symlin differs depending if the patient has type 2 or type 1 diabetes. The target dose is 120 mcg for type 2 and 30 or 60 mcg for type 1. To minimize the risk of hypoglycemia, the dose of Symlin and insulin must be carefully titrated, and the glucose levels monitored often when initiating therapy. Slow upward titration of Symlin may also lessen incidence of nausea. Specific dosing recommendations are described in the product label.

Symlin is injected immediately prior to meals. It cannot be mixed with insulin.

How supplied: 5 ml vial containing 0.6 mg/ml. Each vial has a 28 day expiration date after opening.

Launch date: June 2005

Affected Population: There are approximately 18 million Americans who have diabetes. Among these, approximately 4.5 million use insulin.

Peak Sales Estimate: $200-$300 million.

Cost (AWP): Not available.
**Drug:** levalbuterol HFA inhalation aerosol (Xopenex HFA™ metered dose inhaler)

**Manufacturer:** Sepracor

**Route:** Inhaler

**Approval Date:** 3/11/2005

**Indication:** For the treatment or prevention of bronchospasm in adults, adolescents and children 4 years of age and older with reversible obstructive airway disease, such as asthma and chronic obstructive pulmonary disease (COPD)

**Therapeutic Considerations:**
This is a new formulation of Xopenex (levalbuterol), which is the single isomer version of the short-acting beta agonist bronchodilator albuterol (Proventil/Ventolin). This new formulation is a CFC-free, hydrofluoroalkane (HFA) metered-dose inhaler (MDI) for the treatment asthma and COPD.

Xopenex has been available as an inhalation solution for use with a nebulizer since 1999.

**Affected Population:** Approximately 20 million people in the US have asthma.

**Peak Sales Estimate:** Not available.

**Cost (AWP):** Not available.
**Drug:** doxazosin extended-release (Cardura XL®)  
**Manufacturer:** Pfizer  
**Route:** Oral  
**Approval Date:** 2/22/2005  
**Indication:** For the treatment of benign prostatic hypertrophy (BPH)

**Therapeutic Considerations:**
This is an extended-release formulation of the selective alpha-1 blocker Cardura® (doxazosin), which is available generically. Cardura XL has a more limited indication than immediate-release doxazosin, which is approved for both hypertension and BPH. Both formulations are dosed once a day, but the XL version requires less frequent dose titration steps. The efficacy of the 2 formulations appears to be comparable, based on head-to-head studies. In general, the side effect profiles of the 2 formulations are similar, although certain side effects were more frequent with the immediate-release formulation compared to the XL (postural hypotension: 2.2% vs. 1.2%; dizziness: 9.1% vs. 5.3%, vertigo: 4.1% vs. 1.5%, nausea: 2.3% vs. 1.2%, asthenia: 6.9% vs. 3.9%).

**Dosing:** With Cardura XL, the initial dose is 4 mg once daily. The dose may be increased to a maximum of 8 mg depending on patient response and tolerability. The recommended titration interval is 3-4 weeks.

With immediate-release doxazosin, the initial dose is 1 mg. The dose can be increased to 2 mg, then 4 mg, up to a maximum of 8 mg once daily. The recommended titration interval is 1-2 weeks.

**How supplied:** 4 mg and 8 mg tablets.

**Affected Population:** BPH symptoms affect more than half of men in their 60’s and close to 90% of men by age 80.

**Peak Sales Estimate:** Not available.

**Cost (AWP):** Not available.