NEW DRUGS

Efloornithine for Excess Facial Hair in Women

Barrier Therapeutics has launched efloornithine HCl cream 13.9% (Vaniqua®) in Canada. The company acquired the exclusive right to distribute this product from Shire in June 2005. This is the only topical prescription product approved by Health Canada for slowing the growth of unwanted facial hair in women.

When used together with traditional hair-removal methods, the nonhormonal cream reduced the growth rate of facial hair by blocking an enzyme necessary for hair growth. This agent may offer both emotional and functional benefits.

(Source: Barrier Therapeutics, Inc., November 3, 2005.)

Nelarabine for Leukemia and Lymphoma

GlaxoSmithKline has announced the accelerated approval of nelarabine (Arran- non®) Injection by the FDA. This chemotherapy agent is indicated for the treatment of patients with T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma whose disease has not responded to, or has relapsed following treatment with, at least two chemotherapy regimens.

This use is based on the induction of complete responses. Randomized trials demonstrating increased survival or other clinical benefits have not been conducted. Postmarketing evaluation will be pursued though a randomized, multicenter, phase 3 trial.

In December 2003, nelarabine received a “fast track” designation and was later granted orphan drug status. In September 2005, the FDA’s advisory committee voted to recommend that the FDA grant accelerated approval of nelarabine for both children and adults.

(Source: GlaxoSmithKline, October 28, 2005.)

NEW INDICATIONS

Ertapenem for Foot Infections in Diabetes without Osteomyelitis

The U.S. Food and Drug Administration (FDA) has approved ertapenem (Invanz®, Merck), a once-daily injectable antibiotic, for the treatment of moderate-to-severe complicated foot infections caused by pathogens in diabetic patients without osteomyelitis.

This medication was approved in 2001 for adults with moderate-to-severe infections caused by common gram-positive and gram-negative aerobic and anaerobic bacteria.

Ertapenem is a carbapenem related to the class of antibiotics known as beta-lactams. The adult dose is generally 1 g once daily by intravenous (IV) infusion or intramuscular injection. The cream should be used only to treat or prevent infections that are thought to be caused by susceptible bacteria.

(Source: Merck & Co., November 14, 2005.)

Venlafaxine for Panic Disorder

Extended-release venlafaxine HCl (Effexor® XR) has been approved for the treatment of adults with panic disorder. This marks the first antidepressant approved for the disorder since 2002.

In two double-blind, 12-week, placebo-controlled studies, venlafaxine was significantly more effective than placebo.

Panic disorder may be associated with depression and other anxiety disorders. As a serotonin norepinephrine reuptake inhibitor, venlafaxine is also indicated for the treatment of major depressive disorder, generalized anxiety disorder, and social anxiety disorder.

(Source: Wyeth, November 21, 2005.)

Long-Acting Insulin for Diabetes in Children

Novo Nordisk Inc. has announced the FDA’s approval of insulin detemir injection of rDNA origin (Levemir®) for use in children. This basal (long-acting) form of insulin lasts for up to 24 hours and causes little weight change in adults.

It is indicated for once-daily or twice-daily subcutaneous administration for adults and children with type-1 diabetes mellitus or adults with type-2 diabetes mellitus who require long-acting insulin to control hyperglycemia.

This product was approved for use in adults in June 2005.

(Sources: FDA, October 20, 2005; JAMA 2003;290:1884–1890.)

Hyaluronan for Arthritic Knee Pain

Ferring Pharmaceuticals has launched highly purified hyaluronan (Euflexxa™) for the treatment of pain caused by knee osteoarthritis (OA). This product was approved in 2004 and was acquired by Ferring in 2005 from Savient Pharmaceuticals.

This is the first non-avian derived hyaluronic acid indicated for a three-injection treatment regimen for patients who have not responded adequately to conservative nonpharmacological therapy and simple analgesics. After 12 weeks, more patients treated with this product were symptom-free than those treated with a leading product in its class.

Hyaluronic acid is a viscous, elastic liquid that is naturally found in many tissues of the body and in high concentrations in joint cartilage and synovial fluid.

In a prospective, multicenter, randomized, double-blind controlled trial, 321 patients with confirmed knee osteoarthritis received either Euflexxa™ or Synvisc® (Genzyme). Both products were administered as a course of three weekly injections, with follow-up evaluations at weeks three, six, and 12.

Both treatment groups experienced statistically significant improvements...
from baseline. At the endpoint, 63% of the Euflexxa™ patients were symptom-free compared with 52% of the Synvisc® patients.

Because Euflexxa™ is not derived from chicken or rooster combs and is free of chemical cross-linking, the risk of related reactions is minimized.

(Source: Ferring, November 14, 2005.)

**NEW FORMULATION**

**IV Pegaspargase for Children**

The FDA has changed the label for its pediatric oncology drug, pegaspargase (Oncaspar®, Enzon Pharmaceuticals), which can now be given by the intravenous (IV) route. IV administration offers a new option that will potentially reduce the number of injections for children with cancer. Previously, the drug had to be injected directly into the muscle, a technique that was often painful for patients.

This medication is a PEG-enhanced version of the naturally occurring enzyme L-asparaginase, which depletes the amino acid asparagine, needed by some leukemic cells for survival.

The product was granted a marketing license in 1994.

(Source: Enzon, November 10, 2005.)

**Oral, Liquid Tamoxifen Available**

The FDA has approved the marketing of tamoxifen oral solution (Soltamox™, Savient) for the treatment and prevention of breast cancer. This is the first liquid form of tamoxifen to be available in the U.S.

This product has caused uterine cancer, strokes, and blood clots, but the benefits may outweigh the risks in women who already have breast cancer. It should not be used in women who need a coumarin-type anticoagulant. Cataracts may also be more common with the use of this drug. Adverse reactions include hot flashes and vaginal discharge.

(Source: Savient Pharmaceuticals, October 31, 2005.)

**DRUG NEWS**

**Higher Initial Levothyroxine Doses in Thyroid Disorders?**

Even though the mantra for treating hypothyroidism is usually “start low and go slow”—irrespective of a patient’s age or health status—that may be unnecessary, say researchers from Rotterdam.

The practice stems from concerns that hypothyroidism is associated with ischemic heart disease. After finding no prospective studies on various starting doses, the researchers conducted their own trial and found, in fact, that a full starting dose of levothyroxine (Synthroid®, Abbott) was safe and effective. They compared a full dose of 1.6 mcg/kg with a low starting dose of 25 mcg/kg in 50 patients with newly diagnosed cardiac asymptomatic hypothyroidism.

The study results apply only to patients without suspected silent ischemia, the researchers caution. Because it isn’t known what the initial dose should be in patients with hypothyroidism and cardiac disease, starting low is still the prudent choice in this situation.

(Source: Arch Intern Med 2005;165:1714–1720.)

**Extended-Release Carbamazepine for Epilepsy**

Switching patients with epilepsy from immediate-release to extended-release carbamazepine (e.g., Tegretol®, Novartis) enhances seizure control, reduces adverse drug events (ADEs), and improves quality of life (QoL).

Researchers conducted a three-month study of 458 patients. The number of adults with toxic nervous system side effects dropped by half, from 101 to 54. The researchers say that probably because the ADEs lessened, overall QoL scores improved in all measures. “Epilepsy impact” and “health perception” showed significant improvement. At the third month, switching to the extended-release formulation led to a mean reduction of 0.36 in the monthly seizure count.

Drawbacks with the immediate-release form included daily fluctuations in blood levels when the medication was not taken on a strict regimen of three or four times daily. Peak blood levels of carbamazepine have been correlated with increased rates of ADEs. Low trough levels can also increase the risk of breakthrough seizures.

The researchers suggest that the extended-release formulation helped to reduce serum fluctuations, thereby leading to fewer breakthrough seizures.

(Source: Neurology 2005;65:593–595.)

**Magnesium Alleviates Myoclonic Movements and Pain**

Myoclonic movements and pain on injection are common problems during induction of anesthesia with etomidate (Amidate®, Bedford Labs). Researchers from Turkey, investigating ways to pre-treat the pain, randomly assigned 100 patients to four groups: ketamine 0.2 mg/kg, ketamine 0.5 mg/kg, magnesium sulfate 2.48 mmol, and normal saline.

Pre-treatment with magnesium sulfate reduced the incidence and intensity of myoclonic movements; 19 patients (76%) had none. By contrast, 18 patients (72%) in the 0.5-mg ketamine group, 16 (64%) in the 0.2-mg ketamine group, and 18 (72%) in the control group had myoclonic movements.

After magnesium treatment, 64% of patients experienced mild-to-moderate pain associated with the etomidate injection. However, both doses of ketamine provided better pain relief; at the lower dose, 44% of the patients experi-
ence, followed by the NSABP. Since 1998, BCPT participants have been followed by the NSABP.

The researchers say that this is the first reported clinical study showing that pre-treatment with magnesium reduces myoclonic muscle movements without any adverse effects.


**Tamoxifen Reduces Risk of Invasive Breast Cancer In Older and Younger Women**

Researchers from the National Surgical Adjuvant Breast and Bowel Project (NSABP) who conducted the landmark Breast Cancer Prevention Trial (BCPT) have reported a final update of the trial. They found that reductions in breast cancer incidence among participants taking tamoxifen (Nolvadex®, AstraZeneca) were similar to those reported in 1998, when the initial findings from the BCPT were released. The incidence of breast cancer was relatively constant through seven years of follow-up among women who received tamoxifen; this rate stayed stable for at least two years beyond the time that women stopped taking the drug. The risks of stroke, deep-vein thrombosis, and cataracts—possible side effects of tamoxifen treatment—were also similar to those reported previously.

The BCPT was designed to see whether tamoxifen could prevent breast cancer in women who were at an increased risk of developing the disease. Women in the study were randomly assigned to receive tamoxifen or a placebo, and neither the participants nor their physicians were aware of the treatment assignment. Since 1998, BCPT participants have been followed by the NSABP.

When the initial results of the BCPT were first announced, researchers found a 49% reduction in invasive breast cancer in the tamoxifen participants at increased risk for the disease. The initial study results also showed a 4% reduction in the incidence of noninvasive breast cancer.

By 2005, after seven years of follow-up, the healthy women assigned to take tamoxifen developed 145 cases of invasive breast cancer compared with 250 cases in the women taking placebo.

In summary, tamoxifen reduced the occurrence of invasive breast cancer in both premenopausal and postmenopausal women at increased risk for the disease. The risk of pulmonary embolism was 11% lower than initially reported, and the risk of endometrial cancer was about 29% higher, but neither of these differences was statistically significant.

(Source: J Natl Cancer Institute, November 16, 2005.)

**Lifestyle Changes Plus Meds Improve Weight Loss Better Than Meds Alone**

A study from the University of Pennsylvania shows that a lifestyle modification program of diet, exercise, and behavioral therapy, when combined with the weight-loss medication sibutramine (Meridia®, Abbott) resulted in significantly greater weight loss than treatment with the medication alone.

A total of 224 obese adults, aged 18 to 65 years, participated in the one-year study. Participants were randomly assigned to a weight-loss drug alone, a lifestyle modification alone, a weight-loss drug plus lifestyle modification, or a weight-loss drug plus brief physician-mediated therapy, including counseling.

After one year, patients in the weight-loss medication/lifestyle group lost an average of more than 26 pounds, more than double the weight loss seen with medication alone (11 pounds).

Seventy-three percent of participants in the combined therapy group lost 5% or more of their initial body weight, compared with 56% of those in the brief therapy/weight-loss medication group, 53% of participants in the lifestyle modification-alone group, and 42% of participants in the weight-loss medication alone therapy group.

More than half (52%) of those in the combined therapy group lost 10% or more of their initial body weight, compared with 29% of participants in the lifestyle modification-alone group, 26% of participants in the brief therapy/weight-loss medication group, and 26% of participants in the weight-loss medication-alone group.

The participants using combined therapy who were the most successful were those who frequently recorded their food intake. Subjects with high adherence to food intake record-keeping lost more than twice as much weight (41.5 pounds) as those with low adherence (17 pounds).

A limitation of the study was that it only included obese patients who were otherwise healthy.

The National Institutes of Health’s guidelines recommend that weight-loss drugs be used in a supportive role in a program of behavioral treatment, diet therapy, and increased physical activity and that physicians prescribe lifestyle adjustments for at least six months before prescribing a weight-loss medication.

(Source: N Engl J Med, November 17, 2005; National Cancer Institute.)

**Labeling Warning for Contraceptive Patch**

The FDA has approved updated labeling for Ortho-McNeil’s contraceptive patch, Ortho Evra®, to warn health care providers and patients that this product exposes women to higher levels of estrogen.
With Ortho Evra® than with the tablets. Women are exposed is about 25% lower maximum amount of estrogen to which ing 35 mcg of estrogen. However, the ing a typical birth control tablet contain-

60% more estrogen than if they were tak-

The patch releases the estrogen hor-
mone ethinyl estradiol and the progestin hormone norelgestromin through the skin into the bloodstream.

Women taking this product should consult their health care providers to balance the potential risks related to increased estrogen exposure against the risk of pregnancy if they do not follow the daily regimen associated with typical birth control pills. Because the patch is changed once a week, it decreases the chance that one or more daily doses might be missed, as may occur with birth control pills.

The new bolded warning states that users of the product are exposed to about 60% more estrogen than if they were taking a typical birth control tablet containing 35 mcg of estrogen. However, the maximum amount of estrogen to which women are exposed is about 25% lower with Ortho Evra® than with the tablets.

The FDA is continuing to monitor safety reports for problems with the patch.

(Source: FDA, November 11, 2005.)

**Alefacept Label Warning**

Biogen Idec and the FDA have notified health care professionals of revisions to the contraindications section of the prescribing information for alefacept (Amevive®), indicated for the treatment of adults with moderate-to-severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy.

This product should not be adminis-
tered to patients with HIV infection. The drug reduces CD4+ T-lymphocyte counts, which might accelerate disease progression or increase complications of disease in these patients. Other sections of the product labeling are being revised to reflect additional safety information.

(Source: FDA, November 10, 2005.)

**Even Stricter Warnings For Three Asthma Drugs**

GlaxoSmithKline has been asked to add stricter risk warnings to its top-sell-
ing asthma drug fluticasone propionate (Advair®). The FDA’s Safety Information and Adverse Event Reporting Program said that the use of Advair® and sal-

temol xinafoate (Serevent®) might increase the chance of severe asthma episodes, which can be fatal.

The FDA also singled out formoterol fumarate inhalation powder (Foradil® Aerolizer®, Novartis AG). This product and others contain long-acting beta2-
adrenergic agonists, which decrease the number of asthma episodes but at the same time can exacerbate episodes when they occur.

The asthma drugs already carry the FDA’s black-box warnings. The FDA says that these drugs should be used only after other medications have failed to control the asthma.

GlaxoSmithKline disagreed with the label changes and is challenging the FDA’s request.

(Source: Market Watch, November 18, 2005; The Philadelphia Inquirer, November 19, 2005.)

**Pregabalin: A Fast-Working Antianxiety Agent**

Pregabalin (Lyrica®, Pfizer), an anti-

covulsant medication, is one of a poten-
tially new class of drugs for treating generali-
dized anxiety disorder, a common psychiatric diagnosis. In a four-week, study of 454 patients, pregabalin was comparable to alprazolam (Xanax®, Pfizer), another anxiolytic drug.

Pregabalin offers several benefits, including a mechanism of action that differs from that of the selective serotonin reuptake inhibitors and serotonin nor-

epinephrine reuptake inhibitors, according to researchers from the University of Pennsylvania and Massachusetts Gen-
eral Hospital.

Pregabalin was notable for its early onset, with statistically significant improvement by week one, more than was seen with alprazolam.

Pregabalin does not bind with proteins or act at cytochrome P450 enzymes, which suggests a favorable drug–drug interaction profile. It is absorbed rapidly, with the maximum drug concentration reached at one hour. All doses were well tolerated, although more patients dis-

continued taking the medication at the higher doses. However, the 300-mg/day dose was fully effective; augmenting the dose did not increase its effectiveness.

The researchers say pregabalin’s profile is in marked contrast to that of benzodiazepines, which are abruptly dis-

continued after four weeks. They observed no rebound anxiety during dis-

continuation of pregabalin, also in con-

trast to benzodiazepine therapy.

(Source: Arch Gen Psychiatry 2005;62: 1022–1030.)

**Quiet, Please! Hospital Noise Harms Patients and Staff**

Telephones; hallway conversations; announcements; heavy rolling equip-

dment and carts; waking patients up for meals, medications, and checks for vital signs; intercoms; pagers; televisions; and medical monitoring equipment may make it impossible for patients to rest in a hospital.

Johns Hopkins University acoustical engineers have found that hospital noise levels have grown steadily over the past five decades, disturbing patients and staff members, raising the risk of medical errors, and hindering efforts to mod-

erize hospitals with speech-recognition systems. Some studies even show that excessive noise can slow healing and contribute to stress and “burnout” among hospital workers.

During a two-year research project,
acoustics experts learned that noise is among the top complaints of patients and hospital staff members, but little is being done to address the problem.

The researchers presented their conclusions at the annual meeting of the Acoustical Society of America in Minneapolis.

Since 1960, average daytime hospital sound levels have risen from 57 to 72 decibels (dB); nighttime levels have jumped from 42 to 60 dB. The World Health Organization’s 1995 guidelines suggest that sound levels in patients’ rooms should not exceed 35 dB.

Much hospital noise falls in the human speech frequency range, making oral communication more difficult. This can force doctors and nurses to speak even more loudly to be heard.

Sound congestion can lead to a misunderstanding of spoken orders for tests and medications. Many hospitals are moving to more automated systems, but amid the cacophony of competing sounds, voice recognition software does not work well.

Noise levels often remain high at all hours, partly because of ventilation systems and alarm-laden electronic devices.

The researchers obtained modest noise reductions by making two changes. In the pediatric intensive care unit, personnel were given small hands-free personal communicators, worn on a lanyard. The communicators operate like cell phones. This system cut the frequency of overhead pages, and staff members were so pleased that the hospital purchased the system for that unit.

Acoustical ceiling tiles, which can absorb sound, might be absent from patient areas because they can provide a hiding place for infectious organisms. The researchers wrapped fiberglass insulation inside an antibacterial fabric, then attached these sound-absorbers to the ceiling and walls of a cancer unit.

Noise raises blood pressure, increases stomach acid, and boosts stress and anxiety. A well-rested person’s immune system is stronger than a sleep-deprived person’s.

(Sources: Johns Hopkins University, November 21, 2005; www.jhu.edu; Los Angeles Times, November 28, 2005.)

NEW MEDICAL DEVICES

Marvin M. Goldenberg, PhD, RPh, MS
Name: AcrySof® Toric Intraocular Lens
Manufacturer: Alcon, Inc., Fort Worth, TX
Approval Date: September 28, 2005
Use Classification: Toric intraocular lenses (IOLs) are designed to correct astigmatism after cataract surgery.

Description: The IOL is based on a single-piece lens design and an acrylic material platform. The lens incorporates an optical design that corrects for pre-existing astigmatism in cataract patients.

Purpose: This device is used in cataract patients with pre-existing corneal astigmatism. Artificial IOLs replace the eye’s natural lens, which is removed during cataract surgery.

Benefit: The toric IOL significantly improves distance vision. It can also correct lenticular astigmatism, caused by an irregularity in the shape of the natural lens capsule.

Sources: www.pharmacyonesource.com; www.fda.gov

Name: Green Hills Platform for Medical Devices
Manufacturer: Green Hills Software, Inc., Santa Barbara, CA
Approval Date: November 15, 2005
Use Classification: The software is used for medical devices requiring either the premarket notification process—FDA 510(k)—or the more stringent Premarket Approval process.

Description: The platform includes the INTEGRITY real-time operating system (RTOS); the multi-development environment; a full set of life cycle documentation for INTEGRITY; the INTEGRITY satisfaction matrix for FDA guidelines and regulations; optional middleware, INTEGRITY source code, and quality system audit services; and optional Rhapsody environment.

INTEGRITY provides complete support for the guaranteed separation of high-risk and low-risk tasks running concurrently on a single microprocessor. INTEGRITY and its associated life cycle documentation will be available for a broad range of target microprocessors.

Purpose: The platform helps to lower

continued on page 750
the cost of medical approval of the product and its risk because of its faster time to market.

**Benefit:** The device offers absolute information security, reduces hardware costs, and decreases power and heat dissipation requirements. It delivers advantages to the developers of such medical devices as implantable pacemaker pulse generators, automated heparin analyzers, and infant radiant warmers.

**Source:** www.pharmacyonesource.com; www.ghs.com

---

**Medical Device Alerts**

**Faulty Blood Glucose Meters.** The FDA has notified health care providers and patients worldwide of a problem with blood glucose meters made by Abbott Diabetes Care in Alameda, California.

The meters are designed to report blood glucose levels in two different measurements: the U.S. standard, milligrams per deciliter (mg/dl) and the foreign standard, millimoles per liter (mmol/L). The meters can be accidentally switched from one measurement to the other when a user is setting the time and date for the meter or if a meter is dropped or a battery is replaced.

Users in the U.S. should make sure that their meter reading is displayed as “mg/dl” because an inaccurate reading can result in taking the wrong dose of insulin or in making an incorrect dietary change, thereby causing higher levels of blood glucose. Abbott is not instructing users to return their blood glucose meters.

**Sources:** www.drkoop.com; www.consumerreports.org

**Electromagnetic Interference with Medical Telemetry Systems.** The FDA issued a Public Health Notification regarding an increased risk of electromagnetic interference in medical telemetry systems operating in the 460–470 megahertz (MHz) frequency bands after December 31, 2005. This interference has the potential to compromise patient safety.

In January 2006, the Federal Communications Commission will begin issuing new licenses for mobile radio transmitters to operate in the 460–470 MHz band. According to the FDA, the transmitters operating under new licenses in this frequency band may lead to lapses in patient monitoring and missed alarm events, thereby putting patients at risk. The anticipated interference will not be limited to urban areas. All medical facilities in the vicinity of a mobile radio could be affected.

**Source:** www.fda.gov/medwatch/safety/2005/safety05.htm#glucose