New MS Drug Approved
The first oral, first-line treatment for relapsing forms of MS, Gilenya (fingolimod, Novartis) 0.5mg daily, received FDA approval.

Data submitted to the FDA showed Gilenya 0.5mg reduced relapses by 52 percent (P<0.001) at one year compared with interferon beta-1a IM. Gilenya also reduced disease activity as measured by the number of new and newly enlarged T2 lesions on MRI scans compared to interferon beta-1a IM (1.6 vs 2.6, respectively, P=0.002) at one year. Data from a two-year placebo-controlled study showed a reduction in relapse rate (54 percent reduction, P<0.001, compared with placebo) and risk of disability progression among Gilenya patients (30 percent reduction confirmed at three-month follow-up visit, P=0.02, compared with placebo).

Gilenya is the first in a new class of drugs called sphingosine 1-phosphate receptor (S1PR) modulators. The mechanism is unknown, but researchers believe it works by reducing the immune system's attack on the CNS by retaining lymphocytes in the lymph nodes.

Meanwhile, Merck KGaA's caldribine pill for MS was rejected by the European Medicine's Agency, which found that benefits do not outweigh risks—including four cases of cancer observed during clinical trials.

Lacosamide Oral Solution Now Available
Vimpat (lacosamide 10mg/mL, UCB) Oral Solution is now available for add-on treatment of partial-onset seizures in people with epilepsy age 17 or older. The oral solution joins the already-available oral tablets and IV injection—and all three have equivalent dosing, with no need for titration.

The Swear Jar Test
You can't charge them a quarter, but if a patient yells “a$$,” “sh*t,” or “f@*k” during letter fluency testing, you may be able to rule out Alzheimer's disease and support a diagnosis of frontotemporal dementia. In research published in the September issue of Cognitive & Behavioral Neurology, study authors found that 6/32 (18.8 percent) patients with FTD used the “F-word” during the “F” trial as opposed to zero of 38 patients with AD. Patients who cursed had diagnoses of either behavioral variant FTD (3/15), progressive nonfluent aphasia (2/8), or semantic dementia (1/3). The authors conclude: “Though the specific neuropathy in these cases is uncertain, generation of ‘f*ck’ during letter fluency testing seems to have use in differentiating FTD from AD.”

Oxymorphone Gets Reformed
Endo Pharmaceuticals has filed a New Drug Application with the FDA for a new extended-release formulation of oxymorphone for the treatment of moderate to severe pain in patients requiring around-the-clock treatment for an extended period of time. The NDA submission is based on a non-clinical and clinical development program designed to demonstrate that the crush-resistant formulation addresses attempts to break, crush, extract, powder, and pulverize the pill. One of the ideas behind the redesign is to reduce accidental misuse and deter methods of intended abuse.

Study Links Gene to PD
A genetic mutation in an immune system gene may play a role in the development of Parkinson's disease, according to a study published in the September issue of Nature Genetics. Researchers confirmed three genetic mutations and found evidence of a fourth—located in the human leukocyte antigen—during a genome-wide association study of 2,000 individuals with PD and 1,986 unaffected controls from the NeuroGenetics Research Consortium (NGRC).

In addition to confirming associations with SNCA and MAPT and replicating an association with GAK, the researchers uncovered a new association with the HLA region. The authors note, “HLA association was uniform across all genetic and environmental risk strata and was strong in sporadic and late-onset disease.”

Levadex Update
Researchers found no statistically significant difference in pulmonary artery pressure among patients taking the experimental inhalable migraine therapy Levadex
(dihydroergotamine mesylate) or those receiving placebo two hours after administration. For the study, 24 healthy patients were randomized to receive orally inhalable Levadex, an intravenous version of the drug, or placebo. The company announced that Levadex did not have an effect on pulmonary artery pressure compared to placebo and caused less of an increase in pressure than the intravenous version of the drug. Further, there were no other clinically significant changes in any relevant cardiovascular parameters in the trial.

**Incobotulinum Toxin Approved, Now Available**

A new neurotoxin is now available on the US market. The FDA in July approved Xeomin (incobotulinum toxin A, Merz Pharmaceuticals) for the treatment of adults with cervical dystonia or blepharospasm. Xeomin, which does not require refrigeration prior to reconstitution, will be available in 50-unit and 100-unit vials allowing dosing flexibility for administration.

Merz announced in October that Xeomin is now commercially available in the US. “Over the years, botulinum toxin has become an important treatment for cervical dystonia and blepharospasm,” said Stephen Gollomp, MD, Clinical Professor of Neurology, Thomas Jefferson University, Philadelphia, and an investigator for Xeomin. “With the availability of Xeomin in the US, physicians and patients now have a new therapeutic option for the treatment of these conditions.”

**Acupuncture Not Useful for Stroke Recovery**

A meta-analysis published online in the Canadian Medical Association Journal (Sept. 27) found no data from “rigorous, randomized, sham-controlled trials to show a positive effect of acupuncture as a treatment for functional recovery after stroke.” Researchers found only 10 of 664 trials were controlled. They assessed the methodology quality of the trials using the Cochrane risk-of-bias criteria and the PEDro (Physiotherapy Evidence Database) scale. They found that, of the five studies that assessed functionality, there was not a significant difference in favor of acupuncture, with high heterogeneity. A post-hoc sensitivity analysis of three trials with low risk of bias did not show beneficial effects of acupuncture on activities of daily living at the end of the intervention period or after follow-up. For the chronic stage after stroke, three trials tested the effect of acupuncture on function according to the Modified Ashworth Scale, and all failed to show favorable effects.

**EU OKs DBS for Epilepsy**

The EU has awarded CE (Conformité Européenne) Mark to Medtronic for Deep Brain Stimulation (DBS) Therapy as adjunctive treatment for partial-onset seizures in adults with medically refractory epilepsy. Approval was based on data collected in Medtronic’s clinical trial called SANTÉ (Stimulation of the Anterior Nucleus of the Thalamus in Epilepsy), published online in Epilepsia (March 2010). For the trial, researchers randomized 110 patients with medically refractory partial seizures, including secondarily generalized seizures, to DBS or no stimulation. The baseline monthly median seizure frequency was 19.5. In the last month of the three-month blinded phase, the stimulated group had a 29 percent greater decline in seizures than did the control group, as projected by a generalized estimating equations (GEE) model (p = 0.002). The unadjusted median decline in seizure frequency was 14.5 percent in the control group and 40.4 percent in the stimulated group. Complex partial and "most severe" seizures were significantly reduced by stimulation. At two years, there was a 56 percent median percent decrease in seizure frequency; 54 per-

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**Worldwide Dementia Costs Rising**

Worldwide costs to treat dementia are staggering, according to Alzheimer’s Disease International, a group urging governments to increase research funding in efforts to combat the disease. According to a recent ADI study:

Global cost to treat dementia in 2010 .................. $604 billion
5604 B is equivalent to ....................... 1% worldwide GDP
Estimated annual cost of dementia treatment in 2030 .... $1 trillion
Anticipated number of affected patients by 2030 .... 66 million
cent of patients had a seizure reduction of at least 50 percent, and 14 patients were seizure-free for at least six months.

Medtronic DBS therapy is currently approved in Europe and the United States for the treatment of essential tremor and advanced Parkinson’s disease. It is also approved in Europe for dystonia and obsessive-compulsive disorder; in the US, for dystonia and treatment-resistant OCD, it is approved under a Humanitarian Device Exemption (HDE).

**TEMPO Strengthens Azilect’s Case**

New study findings confirm the long-term efficacy, safety, and tolerability of Azilect in patients with Parkinson’s disease and further demonstrate the benefits obtained with early treatment initiation. The TEMPO (TVP-1012) in Early Monotherapy for Parkinson’s Disease Outpatients trial and extension was a multicenter, double-blind, randomized, placebo-controlled, parallel group, delayed-start investigation of once-daily rasagiline in early PD, according to Lundbeck, a company behind Azilect. From the original cohort of 398 patients, 360 patients finished the double-blind phase of TEMPO, and 306 (85 percent) participated in the open-label extension. Patients were followed for up to 6.5 years with a mean of 3.5 ± 2.1 years. After 12 months, supplementary PD medications were added as required. At two years, nearly half (46 percent) of patients remaining in trial were maintained on Azilect monotherapy.

According to the company, overall, the average annual increase in UPDRS score for all patients taking Azilect (monotherapy or in combination) was less than two UPDRS units a year (compared to an increase of 8-12 UPDRS points per year, typically seen in untreated PD patients).

**Lamotrigine Neuroprotective in MS?**

Lamotrigine’s effect on cerebral volume of patients with secondary progressive multiple sclerosis does not vary from that of placebo over 24 months, but lamotrigine seems to cause early volume loss that reverses partially on discontinuation of treatment, according to a new phase II trial in *Lancet Neurology* (9(7):681-688).

For the study, 108 patients were analyzed for the primary endpoint: 52 receiving lamotrigine (target dose: 400mg/day) and 56 receiving placebo for two years. The authors say, “the mean change in partial (central) cerebral volume per year was -3.18mL (SD -1.25) in the lamotrigine group and -2.48mL (-0.97) in the placebo group (difference -0.71 mL, 95% CI -2.56 to 1.15; p=0·40).” Yet, in an exploratory modeling analysis, the researchers found that treatment with lamotrigine seemed to be associated with greater partial (central) cerebral volume loss than placebo in the first year (p=0.04), “and volume increased partially after treatment stopped (p=0.04). Lamotrigine treatment reduced the deterioration of the timed 25-foot walk (p=0·02) but did not affect other secondary clinical outcome measures.”

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**Clarification**

In the Special Report: “Inside the AED Development Process” that appeared in the July/August edition (vol. 9, no. 4, pp. 10-12), the following paragraph is misleading:

Currently, AEDs that come to market are indicated for add-on therapy. That indication results from the nature of clinical trials; it would be clearly unethical to relegate control patients with epilepsy to no treatment (placebo only), and questionably ethical to provide other patients a treatment that lacks a substantial body of human data to support its efficacy…Single-use indications for AEDs are not likely to emerge in the near future. “I’d be surprised if there is a change in the clinical or regulatory pathway for epilepsy drugs,” Dr. Zackheim says.

While the adjunctive therapy indication remains the most common route for initial FDA approval of an AED, formulations may subsequently pursue a single-use indication. Several AEDs have received approval for single-use indications, and, in fact, clinical trials are currently underway to ascertain the efficacy of lacosamide monotherapy.

Additionally, a statement by Dr. Zackheim contained a typographical error. It should have read:

He notes that reasonably establishing the safety and benefit of a drug requires “thousands of patient-years of exposure and years and years of experience.” Theoretical models provide more accurate predictions in the early stages of development, he says, but they become less reliable at predicting clinical outcomes in the “real world.”

We apologize for the oversights.