Preliminary 2015 Annual Meeting Scientific Program Announced

The latest and greatest scientific advances in neurology will debut at the world’s largest gathering of top neurologists April 18 through 25 in Washington, DC. This year’s Scientific Program will showcase more than 2,500 abstracts in a wide variety of formats: platform sessions, poster sessions, and e-Posters—all offering one-of-a-kind opportunities to meet with leading researchers and discuss their work.

For more information, visit the Annual Meeting website at AAN.com/view/AM15.

Get Help Planning Your Annual Meeting Itinerary, Earn 10 Free Self-assessment CME

*NeuroSAE Annual Meeting Edition Available Free to Members!*

If you’re attending the 2015 AAN Annual Meeting in Washington, DC, then you’ll want to be sure to include NeuroSAE® Annual Meeting Edition in your plans. Available free to AAN members, this convenient online program helps you assess your knowledge in major clinical areas of neurology and provides feedback and course suggestions by subspecialty area so you can build your ideal itinerary for the 2015 Annual Meeting. Upon successful completion of both the pre- and post-tests, participants receive 10 free self-assessment CME credits.

Webinars Explore New Health Care Models, Improving Referrals

Are you confused by changes in payment structures? Are you getting the referrals you need to maintain a healthy practice? Get the answers you need from experienced colleagues in these upcoming March practice management webinars.

**Webinar: Case Studies: Neurologists Succeeding in New Health Care Models**

Director: James N. Goldenberg, MD  
March 3 | 12:00 p.m.–1:30 p.m. ET  
Register by March 2

Continued on page 8 ▶
NEWS BRIEFS

Neurology® has appointed six additional members to the Editorial Board for 2015: Nathalie Jette, MD, MSc, FRCPC; Svetlana Lorenzano, MD, PhD, MSc; Jennifer J. Majersik, MD, MS; Phillip L. Pearl, MD, FAAN; B. Lee Peterlin, DO; and Nicole I. Wolf, MD, PhD.

A record number of Neurology Career Center job applications for 2014 produced a 19-percent increase over 2013.

Take a look at the 2014 AAN Year in Pictures at ow.ly/HjFZp—celebrating high points from the record-breaking Annual Meeting to former Vice President Walter Mondale’s visit to the AAN office.

*
AAN to Help Subspecialties Get Greater Recognition

In August 2012, the AAN issued a position statement on Definition of Neurology Subspecialty which listed subspecialties recognized by the United Council for Neurologic Subspecialties (UCNS) among other neurology subspecialties recognized by the medical community. However, we have heard from some UCNS diplomates who have encountered difficulties receiving reimbursement for “new patient” visits because their subspecialties are not listed in the Medicare Physician Specialty Codes. In addition, electronic health record (EHR) systems used by some hospitals recognize only CMS physician codes or subspecialties included in the National Uniform Claim Committee (NUCC) Health Care Provider Taxonomy code set, which lists only one UCNS subspecialty. Private insurers may refer to the CMS and NUCC lists in making reimbursement decisions.

To address these issues, I appointed a task force to consider the need for greater recognition of UCNS certification by health facilities, state regulators, and insurers—including Medicare and commercial insurers. Chaired by John C. Morris, MD, FAAN, the task force reported that a high proportion of neurologists choose to subspecialize, at least to some extent. In 2011, for example, 86 percent of neurology residents went on to obtain fellowship training, at least to some extent. It is therefore in the interest of the AAN to assist neurologists in reducing barriers to appropriate reimbursement for their subspecialty services. The report also pointed out that a critical issue for inclusion of a neurology subspecialty is likely to be obtaining a taxonomy code as a prerequisite for inclusion in the Medicare Physician Specialty Codes list. Therefore, the task force recommended that the AAN should coordinate an effort to seek expansion of the NUCC list to include more UCNS subspecialties. Based on the results of this initiative, the AAN could consider whether it would apply for recognition of additional neurologic subspecialties on the CMS Physician Specialty Codes list.

I believe that recognition of appropriate neurological subspecialties is critical to the health—perhaps even survival—of our specialty, just as medical subspecialties have been vital to extending the scope and capabilities of internal medicine. I think they also reflect an obligation we have to our patients: To assure they have access to the most up-to-date information regarding unusually complex and sometimes rare disorders. In speaking with colleagues in other fields as well as with patients and their families, I find that increasingly neurology is operationally viewed by practitioners, patients, and advocacy groups as a general specialty that deals broadly and capably with most disorders of the nervous system. For many years, however, some (and increasingly most) neurologists in academic departments have had subspecialty interests with expertise recognized locally, regionally, or nationally. Epilepsy and neuromuscular diseases were early examples of neurology subspecialties, each with its own professional and scientific society as well requiring examinations to demonstrate competence in unique technical aspects required for practice (EEG in the case of epilepsy, EMG in the case of neuromuscular disease).

UCNS is increasingly vital to this evolution and, as is so often the case, its development and subsequent growth have had to be adaptive and responsive to the environment existing at any point in time that we all practice in. But I will offer one example in which I believe UCNS was decisive to the survival of a vital new neurological subspecialty, and that is neurocritical care. Neurointensivists were initially a diverse group that generally worked within the environment of a medical ICU. As their number grew, however, and their value to the management of patients critically ill with neurological disorders or complications became more evident, they were increasingly perceived as a threat by many neurosurgeons, anesthesiologists, and medical intensivists. Efforts were made to limit their role and independence, and the most common strategy was to argue with hospital credentialing bodies that neurologists did not have training programs with uniform requirements nor was their expertise certified by any independent credentialing body. UCNS became the answer to those challenges, and I do not think it is an exaggeration to state that it is unlikely neurocritical care would have survived as an independent subspecialty without UCNS.

Recently, I wrote to the sponsoring organizations of UCNS subspecialties. In my letter, I said that our subspecialties may ask the Academy to submit applications for NUCC recognition on their behalf. Not all subspecialties will qualify for the AAN’s help. Instead, applications will be submitted sequentially by the Academy based on their likelihood of success. I also offered several ideas on how the subspecialties and the AAN can work together. This is a first step toward helping subspecialty diplomates find even greater value in their certifications. This initiative will be subject to continuous review that will inform our next steps, including a possible future effort to seek recognition by CMS. Its main purpose now, however, is to provide a forum for collaboration to influence policy through coordinated advocacy, medical education, and accreditation from a broad cross-specialty perspective. The Council of Medical Specialty Societies is the unified voice for medical specialty societies, created to improve the United States’ health care system and, most importantly, the health of the public. A Council of Neurological Subspecialty Societies would serve a similar purpose.

Please take a moment to learn more about this initiative at AAN.com/practice/payer-relations. ♦

Timothy A. Pedley, MD, FAAN
President, AAN
tpedley@aan.com
The AAN has published quality measurements for headache that can help neurologists improve their care, including appropriate medication use, overuse of treatments and therapies, patient-reported outcomes, and patient engagement and care coordination. The measurement set appeared in the January 13, 2015, print issue of Neurology®.

“The AAN partnered with the American Academy of Family Physicians to develop a set of performance measures for headache using the Physician Consortium for Performance Improvement (PCPI) national framework for measure development,” said Stephen C. Ross, MD, FAAN, a member of the AAN’s Section on Headache and Facial Pain. “In this era of intense focus on evidence-based and value-added practice of medicine, neurologists must rise to the challenge by leading efforts to develop quality measures for neurological conditions. Eighteen different medical organizations and patient advocacy groups joined together to work on the development of these measures with the purpose of improving care delivery and outcomes for patients with headache and migraine.”

The rigorous PCPI measure development framework includes:
- Multi-specialty, multi-disciplinary representation on the measure development panel
- Consideration of all relevant clinical guidelines
- Consideration of evidence ranking and strength of recommendation statements
- Development of technical specifications
- Solicitation of public comments

AAN members are encouraged to implement these quality measures within their practices and integrate them within their electronic health records. Documenting use of quality measures qualifies for certain payment incentives and prevents reduction in reimbursement. Potential uses for these measures include:
- Reduce practice and system variation
- Promote efficient use of resources
- Improve health outcomes for patients
- Promote quality improvement
- Measure quality to establish performance rates and benchmarks
- Recognize and reward for high levels of performance or improvement
- Engage patients
- Affirm the role of neurologists in the diagnosis and treatment of neurologic disorders

The measures also benefit residents and fellows learning the science and art of neurology, who will gain understanding as to how quality measurements can improve the care they deliver.

Visit AAN.com/practice/quality-measures/all-measures today to download your copy of the headache quality measurement set.
ARE YOUR PATIENTS LOOKING FOR A DIFFERENT ROUTE TO MIGRAINE RELIEF?

Your route to more information is zecuity.com

It’s in the delivery
Coming soon:
a non-oral treatment for migraine with or without aura in adults

ZECUITY is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use: Use only if a clear diagnosis of migraine has been established. If a patient has no response to the first migraine attack treated with ZECUITY reconsider the diagnosis of migraine before ZECUITY is administered to treat any subsequent attacks. ZECUITY is not intended for the prevention of migraine attacks.

IMPORTANT SAFETY INFORMATION
ZECUITY is contraindicated in patients with:

- Ischemic coronary artery disease (CAD) or coronary artery vasospasm, including Prinzmetal’s angina; or Wolff-Parkinson-White syndrome or other cardiac accessory conduction pathway disorders

- History of stroke, transient ischemic attack (TIA), or history of hemiplegic or basilar migraine; peripheral vascular disease; ischemic bowel disease; or uncontrolled hypertension

- Recent (i.e., within 24 hours) use of ergotamine-containing or ergot-type medication, or another 5-HT₁ agonist; or concurrent or recent (within 2 weeks) use of a MAO-A inhibitor

- Known hypersensitivity to sumatriptan or components of ZECUITY; severe hepatic impairment; or allergic contact dermatitis to ZECUITY

ZECUITY contains metal parts and must be removed before an MRI procedure.

Use of ZECUITY may lead to allergic contact dermatitis (ACD).

ZECUITY should be discontinued if ACD is suspected. Patients who develop ACD with ZECUITY and require treatment with sumatriptan via other routes should receive their first subsequent dose under close medical supervision.

Other serious adverse events associated with the use of ZECUITY or 5-HT₁ agonists include: myocardial ischemia/infarction, Prinzmetal’s angina, arrhythmias; chest, throat, neck and/or jaw pain/tightness/pressure; cerebral hemorrhage, subarachnoid hemorrhage, and stroke; peripheral vascular ischemia, gastrointestinal vascular ischemia/infarction, splenic infarction, and Raynaud’s syndrome; medication overuse headache; serotonin syndrome; significant elevation in blood pressure; anaphylactic/anaphylactoid reactions; and seizures.

ZECUITY should not be applied in areas near or over electrically-active implantable or body-worn medical devices.

The most common adverse reactions (≥ 5%) in a controlled single dose study were application site pain, paresthesia, pruritus, warmth, and discomfort.

Please see brief summary of Prescribing Information for ZECUITY on the following pages.
BRIEF SUMMARY OF PRESCRIBING INFORMATION FOR ZECUITY® (sumatriptan iontophoretic transdermal system)

INDICATIONS AND USAGE
ZECUITY is indicated for the acute treatment of migraine with or without aura in adults.

Limitations of Use:
- Use only if a clear diagnosis of migraine has been established.
- If a patient has no response to the first migraine attack treated with ZECUITY, reconsider the diagnosis of migraine before ZECUITY is administered to treat any subsequent attacks.
- ZECUITY is not intended for the prevention of migraine attacks.

CONTRAINdications
ZECUITY is contraindicated in patients with:
- Ischemic coronary artery disease (CAD) (angina pectoris, history of myocardial infarction, or documented silent ischemia) or coronary artery vasospasm, including Prinzmetal's angina [see Warnings and Precautions].
- Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders [see Warnings and Precautions].
- History of stroke, transient ischemic attack (TIA), or history of hemiplegic or basilar migraine because these patients are at a higher risk of stroke [see Warnings and Precautions].
- Peripheral vascular disease [see Warnings and Precautions].
- Ischemic bowel disease [see Warnings and Precautions].
- Uncontrolled hypertension [see Warnings and Precautions].
- Recent (i.e., within 2 weeks) use of ergotamine-containing medication, ergot-type medication (such as dihydroergotamine or methysergide), or another 5-hydroxytryptamine-(5-HT)- agonist [see Drug Interactions].
- Concurrent administration of an MAO-A inhibitor or recent (within 2 weeks) use of a MAO-A inhibitor [see Drug Interactions].
- Known hypersensitivity to sumatriptan or components of ZECUITY [see Warnings and Precautions].
- Severe hepatic impairment.
- Allergic contact dermatitis to ZECUITY [see Warnings and Precautions].

WARNINGS AND PRECAUTIONS
Risk of Injury During Magnetic Resonance Imaging (MRI) Procedure
ZECUITY contains metal parts and must be removed before an MRI procedure.

Allergic Contact Dermatitis
Use of ZECUITY may lead to allergic contact dermatitis (ACD). In two long-term open-label studies where patients were allowed to treat multiple migraine attacks for up to 1 year, the rate of ACD was 4%. ZECUITY should be discontinued if ACD is suspected. Erythema is commonly seen with use of ZECUITY and is not by itself an indication of sensitization. Following sensitization with ZECUITY, erythematous plaque and/or erythema-vesicular or erythema-to-bullous eruptions may develop. Clinical course is characterized by crescendo phenomenon of worsening pruritus and appearance over time with slower resolution to normal of affected skin areas.

Patients sensitized from use of ZECUITY, as evidenced by development of ACD, may develop systemic sensitization or other systemic reactions if sumatriptan-containing products are taken via other routes, e.g., orally or subcutaneously. It is possible that some patients who developed ACD with sumatriptan by exposure to ZECUITY, and who have developed systemic sensitization, may not be able to take sumatriptan in any form.

Patients who develop ACD with ZECUITY and require treatment with sumatriptan via other routes should receive their first subsequent dose under close medical supervision.

Myocardial Ischemia, Myocardial Infarction, and Prinzmetal’s Angina
The use of ZECUITY is contraindicated in patients with ischemic or vasospastic CAD. There have been rare reports of serious cardiac adverse reactions, including acute myocardial infarction, occurring within a few hours following administration of sumatriptan. Some of these reactions occurred in patients without known CAD. 5-HT1 agonists, including ZECUITY, may cause coronary artery vasospasm (Prinzmetal’s angina), even in patients without a history of CAD. Perform a cardiovascular evaluation in triptan-naive patients who have multiple cardiovascular risk factors (e.g., increased age, diabetes, hypertension, smoking, obesity, strong family history of CAD) prior to using ZECUITY. Do not use ZECUITY if there is evidence of CAD or coronary artery vasospasm [see Contraindications]. For patients with multiple cardiovascular risk factors who have a negative cardiovascular evaluation, consider using the first ZECUITY TDS in a medically supervised setting and performing an electrocardiogram (EKG) upon activation of ZECUITY. For such patients, consider periodic cardiovascular evaluation in intermittent long-term users of ZECUITY.

ARRHYTHMIAS
Life-threatening disturbances of cardiac rhythm, including ventricular tachycardia and ventricular fibrillation leading to death, have been reported within a few hours following the administration of 5-HT1 agonists. Discontinue ZECUITY if these disturbances occur. ZECUITY is contraindicated in patients with Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders [see Contraindications].

CHEST, THROAT, NECK AND/OR JAW PAIN/TIGHTNESS/pressure
Sensations of tightness, pain, pressure, and heaviness in the chest, throat, neck, and jaw commonly occur after treatment with sumatriptan and are usually non-cardiac

ZECUITY® (sumatriptan iontophoretic transdermal system) in origin. However, perform a cardiac evaluation if these patients are at high cardiac risk. The use of ZECUITY is contraindicated in patients shown with CAD and those with Prinzmetal’s variant angina [see Contraindications].

Cerebrovascular Events
Cerebral hemorrhage, subarachnoid hemorrhage, and stroke have occurred in patients treated with 5-HT1 agonists, and some have resulted in fatalities. In a number of cases, it appears possible that the cerebrovascular events were primary, the 5-HT1 agonist having been administered in the incorrect belief that the symptoms experienced were a consequence of migraine when they were not. As with other acute migraine therapies, before treating headaches in patients not previously diagnosed as migraineurs, and in migraineurs who present with atypical symptoms, exclude other potentially serious neurological conditions. ZECUITY is contraindicated in patients with a history of stroke or TIA [see Contraindications].

Other Icosapram Reactions
5-HT1 agonists, including ZECUITY, may cause non-coronary vasospastic reactions, such as peripheral vascular ischemia, gastrointestinal vascular ischemia and infarction (presenting with abdominal pain and bloody diarrhea), splenic infarction, and Raynaud’s syndrome. In patients who experience symptoms or signs suggestive of a vasospastic reaction following the use of any 5-HT1 agonist, rule out a vasospastic reaction before using ZECUITY [see Contraindications]. Reports of transient and permanent blindness and significant partial vision loss have been reported with the use of 5-HT1 agonists. Since visual disorders may be part of a migraine attack, a causal relationship between these events and the use of 5-HT1 agonists has not been clearly established.

Medication Overuse Headache
Overuse of acute migraine drugs (e.g., ergotamine, triptans, opioids, combination of drugs for 10 or more days per month) may lead to exacerbation of headache (medication overuse headache). Medication overuse headache may present as migraine-like daily headaches or as a marked increase in frequency of migraine attacks. Detoxification of patients, including withdrawal of the oversized drugs, and treatment of withdrawal symptoms (which often includes a transient worsening of headache) may be necessary.

Serotonin Syndrome
Serotonin syndrome may occur with triptans, including ZECUITY, particularly during coadministration with selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and MAO inhibitors [see Drug Interactions]. Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination), and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). The onset of symptoms usually occurs within minutes to hours of receiving a new or a greater dose of a serotonergic medication. Discontinue ZECUITY if serotonin syndrome is suspected.

Increase in Blood Pressure
Significant elevation in blood pressure, including hypertensive crisis with acute impairment of organ systems, has been reported on rare occasions in patients treated with 5-HT1 agonists, including patients without a history of hypertension.

Monitor blood pressure in patients treated with ZECUITY. ZECUITY is contraindicated in patients with uncontrolled hypertension [see Contraindications].

Electrolytically Active Implantable or Body-Worn Medical Devices
ZECUITY should not be applied in areas near or over electrolytically active implantable medical devices (e.g., implantable cardiac pacemaker, body-worn insulin pump, implantable deep brain stimulator).

ADVERSE REACTIONS
Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In two long-term, open-label studies in which patients were allowed to treat multiple migraine attacks for up to 1 year, 15% (99 out of 682) withdrew from the study because of adverse reaction. The most common adverse reactions leading to withdrawal were cardiovascular (4%) and application site pain (4%). The most common adverse reactions (≥ 5%) in a controlled single dose study were application site pain, paresthesia, pruritus, warmth, and discomfort.

Controlled single dose acute migraine study
This study used the adrenergic reaction that occurred at a frequency of 2% or greater in a controlled clinical study of ZECUITY in patients with acute migraine (Study 1).
Table 1: Adverse Reactions Reported by at least 2% of Patients in Study 1

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ZECUITY (n = 234)</th>
<th>Control (n = 235)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application site pain</td>
<td>26%</td>
<td>17%</td>
</tr>
<tr>
<td>Application site paresthesia</td>
<td>9%</td>
<td>16%</td>
</tr>
<tr>
<td>Application site pruritus</td>
<td>8%</td>
<td>7%</td>
</tr>
<tr>
<td>Application site warmth</td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>Application site discomfort</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Application site irritation</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Application site discoloration</td>
<td>3%</td>
<td>1%</td>
</tr>
</tbody>
</table>

The incidence of “atypical sensations” adverse events (paresthesia, sensation warm/cold) and “pain and other pressure sensations” (chest pain/tightness/pressure/hardness or neck/throat/jaw pain, tightness, pressure or hardness) was 2% each in ZECUITY-treated patients, vs. 0% in the control group. Application site bruising was reported in 2 ZECUITY-treated patients (0.9%) vs. no patient in the control group. Subgroup analyses of age (<41 years, >41 years), race (Caucasian, non-Caucasian) and body mass index (BMI) (≥25.7 mg/kg², >25.7 mg/kg²) showed no difference between subgroups for adverse events.

SKIN IRRITATION EXAMINATION

In Study 1, patients performed their own examination of the TDS application site at 4, 12, and 24 hours post TDS activation, and daily thereafter until resolution. The median time to “no redness” was 2.6 days for ZECUITY compared with 0.3 day in the control group.

**Application site reactions across clinical studies (Controlled single dose acute migraine study and long term safety studies)**

In the controlled and uncontrolled clinical studies combined (n = 796 unique ZECUITY-treated subjects), the frequency of application site reactions of clinical interest was: discoloration (5%), contact dermatitis (4%), irritation (4%), vesicles (3%), bruising (2%), and erosion (0.4%).

**DRUG INTERACTIONS**

**Ergot-Containing Drugs**

Ergot-containing drugs have been reported to cause prolonged vasospastic reactions. Because these effects may be additive, use of ergotamine-containing or ergot-type medications (like dihydroergotamine or methysergide) and ZECUITY within 24 hours of each other is contraindicated (see Contraindications).

**Monoamine Oxidase-A Inhibitors**

MAO-A inhibitors increase systemic exposure by 2-fold. Therefore, the use of ZECUITY in patients receiving MAO-A inhibitors is contraindicated (see Contraindications).

**Other 5-HT, Agonists**

Because their vasospastic effects may be additive, coadministration of ZECUITY and other 5-HT, agonists (e.g., triptans) within 24 hours of each other is contraindicated.

**Selective Serotonin Reuptake Inhibitors/Serotonin Norepinephrine Reuptake Inhibitors and Serotonin Syndrome**

Cases of serotonin syndrome have been reported during coadministration of triptans and SSRIs or SNRIs, SNRIs, TCAs, and MAO inhibitors (see Warnings and Precautions).

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**

Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women. ZECUITY should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Nursing Mothers**

It is not known whether sumatriptan is excreted in human milk following transdermal administration. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from ZECUITY, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

**Pediatric Use**

Safety and effectiveness in pediatric patients have not been established. Since clinical data to determine the frequency of serious adverse reactions in pediatric patients who might receive subcutaneous, oral, or intranasal sumatriptan are not presently available, the use of ZECUITY in patients under 18 years of age is not recommended.

**Geriatric Use**

Clinical trials of ZECUITY did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy. A cardiovascular evaluation is recommended for geriatric patients who have other cardiovascular risk factors prior to using ZECUITY (see Warnings and Precautions).

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Webinars Explore New Health Care Models, Improving Referrals

Continued from cover

- Understand the goals of new payment models
- Learn from neurology colleagues how they are being included in new payment models
- Understand successes and barriers for neurology participation in new payment models
- Learn tactics for working with payers

Webinar: Improving Your Referral Network
Director: Joel M. Kaufman, MD, FAAN
March 24, 12:00 p.m.–1:30 p.m. ET
Register by March 23
- Understand how referrals to you are impacted by your cost and quality
- Learn how primary care physicians use payer rankings of specialists in referral decisions
- Discover the importance of reviewing your payer star ratings
- Take away tips to keep referrals coming in

Save Big with Your 2015 Series Subscription!
AAN members can pay either $149 for each webinar—or subscribe to the entire 2015 series of 14 Practice Management Webinars for only $199. Subscriptions include convenient access to past webinar recordings from 2015 as well as all remaining live webinars for the year. Nonmembers pay $199 per webinar or $649 for a full subscription.

Participants are charged per phone line, so additional staff can listen in at no extra cost. Registrants can access both the live and recorded options for the webinar, giving them flexibility for last-minute changes in their work schedules. Slides are included with all webinar purchases. Physicians will earn 1.5 AMA PRA Category 1 Credits™ per webinar and non-physicians who attend will receive a certificate of completion. Learn more about these webinars and register at AAN.com/view/pmw15.

Don’t Miss This February 10 Webinar!
There still is time to register by February 9 for the webinar Coding for Neurodiagnostic Procedures Made Easy, hosted by Neil A. Busis, MD, FAAN, on Tuesday, February 10, from 12:00 p.m. to 1:30 p.m. ET. Avoid common errors and make sure you are coding appropriately for neurodiagnostic procedures including EMG and nerve conduction studies, and EEG procedures.
Two of the most trusted names in health care – Baylor Health Care System and Scott & White Healthcare – have become one: Baylor Scott & White Health. This new organization is the largest nonprofit health care system in Texas. Now we are one for knowledge. One for expertise. One for innovation. One for possibilities. And we share one vision: Creating healthier communities in the areas we serve. And that benefits us all.
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Neurology® Podcasts
Visit Neurology.org to listen to Neurology podcasts and earn 0.5 AMA PRA Category 1 CME Credits™ by answering the multiple-choice questions in the online podcast quiz.

New (Available February 1)
- Optimal achieved blood pressure in acute intracerebral hemorrhage: INTERACT2
  Michael D. Brogan, MD, and Craig Anderson, MD
- “Non-cognitive” symptoms of early Alzheimer disease: A longitudinal analysis
  Jeffrey M. Burns, MD, and Catherine Marie Roe, MD
- Olfactory dysfunction predicts early transition to a Lewy body disease in idiopathic RBD
  Binit B. Shah, MD, and Werner Poewe, MD
- Aspirin and intracerebral hemorrhage: Where are we now?
  Andrew M. Southerland, MD, MSc, and Reza Behrouz, DO

Recent
- Optimal combination secondary prevention drug treatment and stroke outcomes
  Andrew M. Southerland, MD, MSc, and Bruce Ovbiagele, MD, MSc, MAS
- Reduced trigeminovascular cyclicity in patients with menstrually-related migraine
  Andrew M. Southerland, MD, MSc, and Antoinette Maassen van den Brink, PhD
- Exercise for falls prevention in Parkinson disease: A randomized controlled trial
  Michelle Fullard, MD, BS, and Colleen Canning, PhD, MA, BPhy
- The spectrum of acute encephalitis: Causes, management and predictors of outcome
  Michael D. Brogan, MD, and Alejandro A. Rabinstein, MD

Neurology® Clinical Practice Podcasts
Visit Neurology.org/cp to access these podcasts on topical issues affecting neurologists in practice.

New
- Symptom exaggeration and symptom validity testing in persons with medically unexplained neurologic presentations
  John R. Corboy, MD; Joseph Lockhart, PhD, ABPP; and Saty Satya-Murti, MD

Recent
- NMDA receptor encephalitis causing reversible caudate changes on MRI and PET imaging
  David C. Anderson, MD, and William O. Tobin, PhD
- Long segment spinal cord involvement as initial clinical manifestation of sarcoidosis
  Richard L. Barbano, MD, PhD, and Jamie L. Adams, MD
- Capgras-like visual decomposition in Lewy body dementia with therapeutic response to donepezil
  John R. Corboy, MD, and Kinga Szigeti, MD, PhD
In the February/March issue of Neurology Now®, actor R.J. Mitte, formerly of “Breaking Bad” and currently in ABC’s “Switched at Birth,” discusses his life with cerebral palsy—battling childhood bullies, exceeding expectations as an actor with a physical disability, and how he manages his condition on and off-camera. Other topics include how physicians assess the signs of clinically isolated MS, what they are learning from neuroimaging, and what experts think about therapeutic next steps; how to disclose a neurologic illness and handle the stigma; patient tips for managing multiple medications; and where funds raised for the ALS ice bucket challenge are going.

Visit NeurologyNow.com for more information about the AAN’s free bimonthly magazine for neurology patients, their families, and caregivers. AAN members can adjust the number of free copies of Neurology Now received in their offices by contacting AAN Member Services at (800) 879-1960, or updating their member profile at AAN.com/view/profile.

The AAN’s Neurology® Clinical Practice likewise covers multiple areas in the February issue, ranging from Five New Things about ulnar neuropathy at the elbow, to symptom exaggeration and symptom validity testing in persons with medically unexplained neurologic presentations, and how Dutch neurologists involve families of critically ill patients in end-of-life care and decision-making. The latter is complemented by an editorial by David Y. Hwang, MD, and James L. Bernat, MD, on “Neurologists and End-of-life Decision-making: The Role of ‘Protective Paternalism.’”

Neurology: Clinical Practice, published six times a year, is available in print (for US members only), online, and for the iPad. Visit Neurology.org/cp for more information.

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Capitol Hill Report

Capitol Hill Report presents regular updates on legislative and regulatory actions and how the Academy ensures that the voice of neurology is heard on Capitol Hill. It is emailed to US members twice monthly and is posted at AAN.com/view/HillReport. Below are some recent highlights.

AAN Leadership Helps Open 114th Congress

By Terrence L. Cascino, MD, FAAN, AAN President Elect

Recently, I had the pleasure of walking the halls of Congress with Mike Amery of the AAN’s Washington, DC, office as a new Congress convened with the swearing-in of members of the 114th Congress.

I went to Washington to personally congratulate members on their elections, especially those who have been supportive of AAN positions in the past and have been supported by the AAN through the Academy’s political action committee, BrainPAC. It also offered the opportunity to introduce the AAN to some new members of Congress.

Throughout the day, we met with members of Congress from across the country, both Democrats and Republicans, and it was clear that they know the AAN, they personally know our lobbyists, and, most importantly, they know the issues that are critical to AAN members and their patients.

Along with my congratulations, I brought a message to these policymakers about data. We know that as neurologists we improve the health and lives of our patients, but improvement is often difficult to value. As president elect of the AAN, I am committed to improving the data we have to show the value of neurology. AAN members from all aspects of practice are working to generate quantifiable data through new, ambitious programs like a clinical data registry. The lawmakers I met are desperate to know what policies work and which do not and I assured them that the AAN is going to be there to help.

After a long day of seeing our DC team in action, it is clear to me that the AAN has the right formula for influencing the legislative process. A staff of political professionals in Washington joined by physician volunteers like myself is a powerful combination. Relationships built through day-to-day interactions by Mike and his DC colleague Derek Brandt open the doors for physician expertise to truly impact the conversation on policy.

By the end of the day, we had met with 30 congressional offices and I personally met with 19 members of Congress. Many of the pictures taken and tweeted can be seen at the AAN Facebook page. I hope you will take a look and see who the AAN is working with to improve the practice of neurology. •

AAN President Elect Terrence L. Cascino, MD, FAAN, with neurology champions Sen. Amy Klobuchar (D-MN) (above) and Rep. Gus Bilirakis (R-FL) (below).
Neurology Needs Your Votes in the AMA

The House of Delegates is the policy-setting body of the American Medical Association (AMA), which meets twice per year and is composed of representatives from state and county medical societies as well as specialty medical societies and other special groups such as designated agencies, medical students, and residents.

The number of delegates from each specialty society is determined by the number of AMA members in a given society’s membership. The states and specialties have a delegate (and alternate delegate) on a 1 per 1,000 basis after obtaining at least one delegate.

Currently, the AAN delegation to the AMA House of Delegates is allowed only three delegates and three alternate delegates.

“We need to increase the voice of neurology at the AMA House of Delegates,” said Shannon M. Kilgore, MD, chair of the AAN delegation. “And in order to do that, we need neurology members to ballot for the AAN.”

Although all AAN members who are AMA members can designate a specialty society to represent them, only one-third have done so. “Therefore, if all of our AMA members who feel the AAN best represents their interests would simply choose the AAN, we would gain representation right there, even without additional neurologists joining AMA,” said Kilgore. “Of course, every 1,000 additional AMA members results in another two people able to attend the meeting.”

Currently, the AAN delegation to the AMA House of Delegates includes Kilgore; Lyell K. Jones, MD, delegation vice chair; William C. Davison, MD, FAAN; and alternate delegates Joshua M. Cohen, MD, and Nicholas Elwood Johnson, MD. The empty third alternate position is in the process of being filled.

Greater representation for neurology at AMA meetings is vital to more effectively representing the specialty, according to Kilgore. “Were we to have a larger number of delegates, we could more effectively cover all the proceedings that happen during the House of Delegates meetings, as many issues are being discussed simultaneously. The ability to have the right person at the right hearing to offer key testimony is where the power of any delegation exists. With the size of our delegation, we cannot effectively cover every hearing and thus miss opportunities to offer the neurology perspective.”

Increased Size Brings Greater Influence, Connections

As delegate Lyell K. Jones, MD, said, “Part of the importance of delegation size is influence. Other delegations care about our opinion more if we’re bringing more delegates to the table.”

The current size of the AAN’s delegation of six means inherent limitations on how the group can adequately represent some states or regions of the United States and some types of practice or subspecialty. “If we had a larger delegation,” said Kilgore, “we would gain additional perspective inherent in our membership, as well as the increased geographic connections that these delegates would bring. These benefits increase neurology’s voice in an arena in which other much larger specialties direct the agenda, and thus, the resultant policy.

“Our delegation has been successful on many occasions in swaying the general opinion through carefully delivered testimony,” Kilgore continued. “However, on specialty vs. specialty issues, our ability to make an impact is directly tied to the strength of our numbers and geographic influence. As the AMA remains THE umbrella organization for advocacy in medicine, the AAN can leverage the size and resources of the AMA to advocate for our members and our patients in a way in which the AAN cannot do alone. By working through the AMA delegation to influence AMA policy, the AAN will be more successful in representing neurology.”

Vote for Neurology and the AAN!

Every member of the AMA is entitled to select, or ballot for, one national society to represent their views in the House of Delegates. Balloting is open to AMA members at any time. Members can check their balloting status and designate the AAN as their society at Tinyurl.com/BallotForAAN.

AAN, AMA Support Interstate Compact

In a win that will remove a significant barrier for telemedicine, the American Medical Association (AMA) will support the Federation of State Medical Board’s Interstate Compact for Medical Licensure. The vote took place at the recent 2014 Interim Meeting of the AMA House of Delegates. The AAN strongly supports the Interstate Compact; improving the license process allows members to practice more easily in multiple states via telemedicine.
Academy Announces AAN Board Nominations

The AAN Nominations Committee, chaired by former AAN President Robert C. Griggs, MD, FAAN, has announced the slate of nominees for AAN officer and director positions for the 2015–2017 term. These nominees will be presented to the voting membership for approval during the AAN’s 2015 Business Meeting on Monday, April 20, 2015, at 8:00 a.m. during the Annual Meeting in Washington, DC. Members are encouraged to attend the Business Meeting and participate in this election and other matters. The classes of membership entitled to vote on any matter during any business meeting of the Academy are Fellows and Active Members. Honorary and Senior members who had voting privileges in their most recent previous category of membership also are eligible to vote.

“The committee recognized the need to select board members who brought perspectives from as wide a range of interests as possible—community and academic practitioners as well as subspecialty interests,” said Griggs. “In addition, we considered it important to foster age, gender, and racial diversity. We had a remarkably talented group of neurologists to consider and believe we have proposed a cadre of leaders who will serve the interests of our membership exceedingly well.”

The Academy is comprised of two legal entities: the AAN and the AAN Institute. Most of the elected members of the AAN Board of Directors also serve ex officio on the Board of Directors of the AAN Institute, which includes an independent secretary-treasurer and additional members who serve in ex officio capacities. For informational purposes only, the slate below includes both AAN and AAN Institute proposed Board members including those who serve ex officio pursuant to the AAN and AAN Institute bylaws.

For more information, contact Donna Honeyman, Manager, Board and Officer Relations, at (612) 928-6055 or dhoneyman@aan.com.

Learn more about these new nominees by reading their bios at AAN.com/view/BoardSlate.

2015–2017 Proposed AAN Board Slate

Officers

President: Terrence L. Cascino, MD, FAAN

President Elect: Ralph L. Sacco, MD, FAAN

Vice President: James C. Stevens, MD, FAAN

Secretary: Aaron E. Miller, MD, FAAN

AAN Treasurer: Lisa M. Shulman, MD, FAAN

AAN Institute Secretary/Treasurer: Ann H. Tilton, MD, FAAN

Past President: Timothy A. Pedley, MD, FAAN
Directors

Allison Brashear, MD, MBA, FAAN
Neil A. Busis, MD, FAAN
Charles C. Flippen II, MD, FAAN
Carlayne E. Jackson, MD, FAAN
Elaine C. Jones, MD, FAAN

Janis Miyasaki, MD, MEd, FRCP, FAAN
John C. Morris, MD, FAAN
Stefan M. Pulst, MD, FAAN
Thomas R. Vidic, MD, FAAN

Ex Officio (voting)

Orly Avitzur, MD, MBA, FAAN, Chair, Medical Economics and Management Committee
Gregory D. Cascino, MD, FAAN, Chair, Member Engagement Committee
Lisa M. DeAngelis, MD, FAAN, Chair, Science Committee (only AAN Institute)
Robert A. Gross, MD, PhD, FAAN, Neurology® Journal Editor-in-Chief
Nicholas E. Johnson, MD, Chair, Government Relations Committee

John C. Mazziotta, MD, PhD, FAAN, Chair, American Brain Foundation (only AAN Institute)
Heidi B. Schwarz, MD, FAAN, Chair, Practice Committee (only AAN Institute)
A. Gordon Smith, MD, FAAN, Chair, Education Committee (only AAN Institute)

Ex Officio (non-voting)

Catherine M. Rydell, CAE, Executive Director/CEO
AAN Recognizes New Fellows of 2014

Congratulations to the following AAN members who have been recognized as Fellows of the American Academy of Neurology (FAAN) during 2014. Fellow status acknowledges exemplary work and achievements in the neurosciences, the clinical practice of neurology or academic/administrative neurology, in the AAN, and in the community. The Academy thanks the new class of Fellows for their dedication to their profession and their patients, and for their continued commitment to the vision and mission of the AAN.

For more information on how you can attain the prestigious FAAN status or nominate a colleague, visit AAN.com/membership/become-a-fellow.

2014 Fellows of the American Academy of Neurology

- Taoufik Alsadi, MD, FAAN
- Erastus Amayo, MD, FAAN
- Wayne Anderson, MD, FAAN
- Oliver Bandmann, MD, PhD, FAAN
- Ikshvanku Barot, MD, FAAN
- Christopher Boes, MD, FAAN
- Diego Cadavid, MD, FAAN
- Francisco Cardoso, MD, FAAN
- Jeffrey Chung, MD, FAAN
- Eduardo De Sousa, MD, FAAN
- Michael Elliott, MD, FAAN
- Murray Engel, MD, FAAN
- Marian Evatt, MD, FAAN
- Dominic Fee, MD, FAAN
- Wendy Galpern, MD, PhD, FAAN
- Christopher Gibbons, MD, FAAN
- David Greer, MD, FAAN
- Mustafa Hammad, MD, DO, FAAN
- Claire Henchcliffe, MD, PhD, FAAN
- Jennifer Hopp, MD, FAAN
- Sandra Horowitz, MD, FAAN
- Jihad Inshasi, MD, MBBS, FAAN
- Jeffrey Jackson, MD, FAAN
- Mamdouh Kalkatawi, MD, FAAN
- Walter Kukull, PhD, FAAN
- Jin Li, MD, PhD, FAAN
- Brandy Matthews, MD, FAAN
- Margaret McBride, MD, FAAN
- Marco Medina, MD, FAAN
- Man Mohan Mehandratta, MD, MBBS, FAAN
- Jose Merino, MD, MPhil, FAAN
- Leslie Morrison, MD, FAAN
- Gereon Nelles, MD, PhD, FAAN
- Darin Okuda, MD, FAAN
- Massimo Pandolfi, MD, FAAN
- Hema Patel, MD, FAAN
- Phillip Pearl, MD, FAAN
- Erik Perkins, MD, FAAN
- Daniel Potts, MD, FAAN
- Craig Powell, MD, PhD, FAAN
- Christopher Prusinski, DO, FAHA, FAAN
- Goran Rakocevic, MD, FAAN
- Richard Rison, MD, FAAN
- Howard Rowley, MD, FAAN
- Arman Sabet, MD, FAAN
- Saud Sadiq, MD, MB, FAAN
- Joseph Safdieh, MD, FAAN
- Markus Schuerks, MD, FAAN
- Sudha Seshadri, MD, FAAN
- Nitin Sethi, MD, MBBS, FAAN
- Prahlad Kumar Sethi, MD, FAAN
- Nutan Sharma, MD, PhD, FAAN
- Sanjay Singh, MD, FAAN
- Aneesh Singhal, MD, FAAN
- Nizam Souayah, MD, FAAN
- Jayashri Srinivasan, MD, PhD, MRCP, FAAN
- Michael Waters, MD, PhD, FAAN
- Allison Weathers, MD, FAAN

Pedro L. Ponce, MD, Named Honorary Member of the AAN

The AAN has bestowed Honorary Member status upon Pedro L. Ponce, MD, of Caracas, Venezuela. Ponce joins a small group of fewer than 60 current Honorary Members, the Academy’s most exclusive category. Ponce has been an AAN member since 1958 and became a Senior member in 2011.

He was nominated by Vladimir Hachinski, MD, president of the World Federation of Neurology (WFN) and AAN member. In his nominating letter, Hachinski cited numerous accomplishments by Ponce, including persuading the Venezuelan government to include a special section dedicated to neurology in the Ministry of Health. Ponce was the founder and president of the Venezuelan Neurological Society and was his country’s representative to the WFN for many years, culminating in his serving as vice president of the organization.

“Given his dedication to Latin America and world neurology and his commitment to the American Academy of Neurology, it would be both appropriate and very much appreciated by him if he were to be recognized as an Honorary Member,” said Hachinski.

In his letter to Ponce congratulating him on this honor, AAN President Timothy A. Pedley, MD, FAAN, noted, “Out of more than 28,000 current AAN members, you now join an exclusive pantheon of fewer than 60 giants of neurology who have made indelible marks on our profession, including a Nobel Prize recipient, groundbreaking researchers and academic leaders, and a dozen former AAN presidents. You should be as proud of your accomplishments as we are to have you in our midst.”
INDICATION
AUBAGIO® (teriflunomide) is indicated for the treatment of patients with relapsing forms of multiple sclerosis.

IMPORTANT SAFETY INFORMATION
WARNING: HEPATOTOXICITY AND RISK OF TERATOGENICITY
Severe liver injury including fatal liver failure has been reported in patients treated with leflunomide, which is indicated for rheumatoid arthritis. A similar risk would be expected for teriflunomide because recommended doses of teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. AUBAGIO is contraindicated in patients with severe hepatic impairment and in patients taking leflunomide. Concomitant use of AUBAGIO with other potentially hepatotoxic drugs may increase the risk of severe liver injury. Obtain transaminase and bilirubin levels within 6 months before initiation of AUBAGIO therapy. Monitor ALT levels at least monthly for 6 months after starting AUBAGIO. If drug-induced liver injury is suspected, discontinue AUBAGIO and start an accelerated elimination procedure with cholestyramine or charcoal. Patients with pre-existing liver disease may be at increased risk of developing elevated serum transaminases when taking AUBAGIO.

Based on animal data, AUBAGIO may cause major birth defects if used during pregnancy. Pregnancy must be excluded before starting AUBAGIO. AUBAGIO is contraindicated in pregnant women or women of childbearing potential who are not using reliable contraception. Pregnancy must be avoided during AUBAGIO treatment or prior to the completion of an accelerated elimination procedure after AUBAGIO treatment.

Please see Important Safety Information and Brief Summary of Full Prescribing Information, including boxed WARNING on the following pages.
INDICATION

AUBAGIO® (teriflunomide) is indicated for the treatment of patients with relapsing forms of multiple sclerosis.

IMPORTANT SAFETY INFORMATION

WARNING: HEPATOTOXICITY AND RISK OF TERATOGENICITY

Severe liver injury including fatal liver failure has been reported in patients treated with leflunomide, which is indicated for rheumatoid arthritis. A similar risk would be expected for teriflunomide because recommended doses of teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. AUBAGIO is contraindicated in patients with severe hepatic impairment and in patients taking leflunomide. Concomitant use of AUBAGIO with other potentially hepatotoxic drugs may increase the risk of severe liver injury. Obtain transaminase and bilirubin levels within 6 months before initiation of AUBAGIO therapy. Monitor ALT levels at least monthly for 6 months after starting AUBAGIO. If drug-induced liver injury is suspected, discontinue AUBAGIO and start an accelerated elimination procedure with cholestyramine or charcoal. Patients with pre-existing liver disease may be at increased risk of developing elevated serum transaminases when taking AUBAGIO.

Based on animal data, AUBAGIO may cause major birth defects if used during pregnancy. Pregnancy must be excluded before starting AUBAGIO. AUBAGIO is contraindicated in pregnant women or women of childbearing potential who are not using reliable contraception. Pregnancy must be avoided during AUBAGIO treatment or prior to the completion of an accelerated elimination procedure after AUBAGIO treatment.

Warnings and Precautions

Patients with pre-existing acute or chronic liver disease, or those with serum ALT >2 times the upper limit of normal (ULN) before initiating treatment, should not normally be treated with AUBAGIO. In clinical trials, if ALT elevation was >3 times the ULN on 2 consecutive tests, patients discontinued AUBAGIO and underwent accelerated elimination. Consider additional monitoring if co-administering AUBAGIO with other potentially hepatotoxic drugs; monitor patients who develop symptoms suggestive of hepatic dysfunction (eg, unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, jaundice and/or dark urine).

Before starting therapy, use of reliable contraception must be confirmed, and the patient counseled on risks to the fetus. Patients with delayed onset of menses or other reason to suspect pregnancy should immediately see their physician for pregnancy testing. Patients who become pregnant or wish to become pregnant should discontinue treatment, followed by accelerated elimination until plasma concentrations of <0.02 mcg/mL are verified, a level expected to pose minimal risk to the fetus. Women who become pregnant while taking AUBAGIO may enroll in the AUBAGIO pregnancy registry by calling 1-800-745-4447, option 2.

TOWER: The second pivotal Phase III trial for AUBAGIO that demonstrates and confirms the significant effect of AUBAGIO 14 mg on both sustained disability progression† and relapse rate in two Phase III trials†

- AUBAGIO 7 mg did not have a statistically significant effect on reduction of disability progression†

TOPIC: The first and only trial of an oral MS therapy that studied patients who had a first clinical event consistent with acute demyelination, occurring within 90 days of randomization†

Get the latest information at www.AubagioHCP.com

MS=multiple sclerosis.

*TOWER was a double-blind, placebo-controlled clinical trial in which a total of 1165 patients received AUBAGIO 7 mg (n=407), AUBAGIO 14 mg (n=370), or placebo (n=388). Patients were required to have a diagnosis of multiple sclerosis exhibiting a relapsing clinical course and to have experienced at least one relapse over the year preceding the trial, or at least two relapses over the two years preceding the trial.

†TOPIC was a double-blind, placebo-controlled clinical trial in which patients with relapsing MS received AUBAGIO 14 mg (n=214), AUBAGIO 7 mg (n=203), or placebo (n=197) once daily. Patients had a first clinical event consistent with acute demyelination within 90 days of randomization with 2 or more T2 lesions at least 3 mm in diameter characteristic of MS.

‡Sustained disability progression was defined as at least a 1-point increase from baseline EDSS score ≤5.5 (or at least a 0.5-point increase for those with a baseline EDSS score >5.5) sustained for at least 12 weeks.

Get the latest information at www.AubagioHCP.com

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Teriflunomide is eliminated slowly from the plasma—it takes an average of 8 months, or up to 2 years, to reach plasma concentrations <0.02 mcg/mL. Elimination may be accelerated by administration of cholestyramine or charcoal, but this may cause disease activity to return in patients who were responding to AUBAGIO.

Decreases in white blood cell counts, mainly of neutrophils and lymphocytes, and platelets have been reported with AUBAGIO. Obtain a complete blood cell count within 6 months before starting treatment, with further monitoring based on signs and symptoms of bone marrow suppression. AUBAGIO is not recommended for patients with severe immunodeficiency, bone marrow disease, or severe uncontrolled infections. Tuberculosis (TB) has been observed in clinical studies of AUBAGIO. Before starting treatment, screen patients for latent TB infection with a tuberculin test. Treatment in patients with acute or chronic infections should not be started until the infection(s) is resolved. Administration of live vaccines is not recommended. The risk of malignancy, particularly lymphoproliferative disorders, or infection may be increased with the use of some medications with immunosuppressive potential, including teriflunomide.

Peripheral neuropathy, including polyneuropathy and mononeuropathy, has been reported with AUBAGIO. Age >60 years, concomitant neurotoxic medications, and diabetes may increase the risk. If peripheral neuropathy is suspected, consider discontinuing treatment and performing accelerated elimination.

Interstitial lung disease and rare cases of Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported with leflunomide; a similar risk would be expected for teriflunomide. If a severe skin reaction develops with AUBAGIO, stop treatment and use accelerated elimination.

Blood pressure increases and hypertension have occurred with AUBAGIO. Measure blood pressure at treatment initiation and manage any elevations during treatment.

**Adverse Reactions:** The most frequent adverse reactions (≥10% and ≥2% greater than placebo) with AUBAGIO 7 mg and 14 mg and placebo, respectively, were headache (18% and 16% vs 15%), ALT increased (13% and 15% vs 9%), diarrhea (13% and 14% vs 8%), alopecia (10% and 13% vs 5%), and nausea (8% and 11% vs 7%).

**Drug Interactions:** Monitor patients when teriflunomide is coadministered with warfarin, or with drugs metabolized by CYP1A2, CYP2C8, substrates of OAT3 transporters, substrates of BCRP, or OATP1B1/1B3 transporters.

**Use in Specific Populations:** AUBAGIO is detected in human semen. To minimize any possible fetal risk, men not wishing to father a child and their female partners should use reliable contraception. Men wishing to father a child should discontinue therapy and undergo accelerated elimination, with verification of plasma concentrations <0.02 mcg/mL. Nursing mothers should not use AUBAGIO.

Please see Brief Summary of Full Prescribing Information, including boxed WARNING, on the following pages.
INDICATION
AUBAGIO® (teriflunomide) is indicated for the treatment of patients with relapsing forms of multiple sclerosis.

IMPORTANT SAFETY INFORMATION
WARNING: HEPATOTOXICITY AND RISK OF TERATOGENICITY
Severe liver injury including fatal liver failure has been reported in patients treated with leflunomide, which is indicated for rheumatoid arthritis. A similar risk would be expected for teriflunomide because recommended doses of teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. AUBAGIO is contraindicated in patients with severe hepatic impairment and in patients taking leflunomide. Concomitant use of AUBAGIO with other potentially hepatotoxic drugs may increase the risk of severe liver injury. Obtain transaminase and bilirubin levels within 6 months before initiation of AUBAGIO therapy. Monitor ALT levels at least monthly for 6 months after starting AUBAGIO. If drug-induced liver injury is suspected, discontinue AUBAGIO and start an accelerated elimination procedure with cholestyramine or charcoal. Patients with pre-existing liver disease may be at increased risk of developing elevated serum transaminases when taking AUBAGIO.

Based on animal data, AUBAGIO may cause major birth defects if used during pregnancy. Pregnancy must be excluded before starting AUBAGIO. AUBAGIO is contraindicated in pregnant women or women of childbearing potential who are not using reliable contraception. Pregnancy must be avoided during AUBAGIO treatment or prior to the completion of an accelerated elimination procedure after AUBAGIO treatment.

Please see Brief Summary of Full Prescribing Information, including boxed WARNING, on the following pages.

AUBAGIO® (teriflunomide) tablets, for oral use

Brief Summary of Prescribing Information

WARNINGS: HEPATOTOXICITY AND RISK OF TERATOGENICITY

Hepatotoxicity
Severe liver injury including fatal liver failure has been reported in patients treated with leflunomide, which is indicated for rheumatoid arthritis. A similar risk would be expected for teriflunomide because recommended doses of leflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. Concomitant use of AUBAGIO with other potentially hepatotoxic drugs may increase the risk of severe liver injury. Obtain transaminase and bilirubin levels within 6 months before initiation of AUBAGIO therapy. Monitor ALT levels at least monthly for six months after starting AUBAGIO [see Warnings and Precautions (5.1)]. If drug induced liver injury is suspected, discontinue AUBAGIO and start an accelerated elimination procedure with cholestyramine or charcoal [see Warnings and Precautions (5.3)].

AUBAGIO is contraindicated in patients with severe hepatic impairment (see Contraindications [4.1]). Patients with pre-existing liver disease may be at increased risk of developing elevated serum transaminases when taking AUBAGIO.

Risk of Teratogenicity
Based on animal data, AUBAGIO may cause major birth defects if used during pregnancy. Pregnancy must be excluded before starting AUBAGIO. AUBAGIO is contraindicated in pregnant women or women of childbearing potential who are not using reliable contraception. Pregnant women must be released from AUBAGIO treatment and undergo an accelerated elimination procedure before conception or for the completion of an accelerated elimination procedure after AUBAGIO treatment [see Contraindications (4.2), Warnings and Precautions (5.2), and Use in Specific Populations (8.1)].

1 INDICATIONS AND USAGE
AUBAGIO® is indicated for the treatment of patients with relapsing forms of multiple sclerosis.

2 DOSAGE AND ADMINISTRATION
The recommended dose of AUBAGIO is 7 mg or 14 mg orally once daily. AUBAGIO may be taken with or without food.

DOSAGE ADJUSTMENT
AUBAGIO may cause fetal harm when administered to a pregnant woman. AUBAGIO is contraindicated in patients with severe hepatic impairment (see Contraindications [4.1]). Patients with pre-existing liver disease may be at increased risk of developing elevated serum transaminases when taking AUBAGIO. Patients with pre-existing acute or chronic liver disease, or those with serum alanine aminotransferase (ALT) greater than two times the upper limit of normal (ULN) or bilirubin at least twice the ULN, should not be treated with AUBAGIO. AUBAGIO is contraindicated in patients with severe hepatic impairment [see Contraindications (4.1)].

In placebo-controlled trials, ALT greater than three times the ULN occurred in 6/165 (3.6%) of 4/1202 (0.3%) of patients receiving AUBAGIO 7 mg and 14 mg, respectively, and 38/997 (3.8%) of patients receiving placebo, during the treatment period. These elevations occurred mostly within the first year of treatment. Half of the cases returned to normal without drug discontinuation. In clinical trials, if ALT or bilirubin was greater than five times the ULN on two consecutive treatments, AUBAGIO was discontinued and patients underwent an accelerated elimination procedure [see Warnings and Precautions (5.3)]. Of the patients who underwent discontinuation and accelerated elimination in controlled trials, half returned to normal or near normal values within 2 months.

Obtain serum transaminase and bilirubin levels within 6 months before initiation of AUBAGIO therapy. Monitor ALT levels at least monthly for six months after starting AUBAGIO. Consider additional monitoring when AUBAGIO is given with other potentially hepatotoxic drugs. Consider discontinuing AUBAGIO if serum transaminase increase (greater than three times the ULN) is confirmed. Monitor serum transaminase and bilirubin on AUBAGIO therapy, particularly in patients who develop symptoms suggestive of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, jaundice, or dark urine. If liver injury is suspected to be AUBAGIO-induced, discontinue AUBAGIO and start an accelerated elimination procedure [see Warnings and Precautions (5.3)] and monitor liver function tests weekly until normalized. If AUBAGIO-induced liver injury is unlikely based on other probable cause being found, resumption of AUBAGIO therapy may be considered.

5.2 Use in Women of Childbearing Potential
There are no adequate and well-controlled studies evaluating AUBAGIO in pregnant women. However, based on animal studies, teriflunomide may increase the risk of teratogenic effects or fetal death when administered to a pregnant woman [see Contraindications (4.2)].

Women of childbearing potential must not be started on AUBAGIO until pregnancy is excluded and it has been confirmed that they are using reliable contraception. Before starting treatment with AUBAGIO, patients must be fully counseled on the potential for serious risk to the fetus. The patient must be advised that if there is any delay in onset of menses or any other reason to suspect pregnancy, they must notify their physician immediately for pregnancy testing and, if pregnant, the physician and patient must discuss the risk to the fetus. It is possible that rapidly lowering the plasma concentration of teriflunomide by instituting an accelerated elimination procedure may decrease the risk to the fetus from AUBAGIO. Pregnancy must be avoided during AUBAGIO treatment or prior to the completion of an accelerated elimination procedure.

5.3 Procedure for Accelerated Elimination of Teriflunomide
Teriflunomide is eliminated slowly from the plasma. Without an accelerated elimination procedure, this takes on average 2 years to reach plasma concentrations less than 0.02 mg/L. Human plasma concentrations of teriflunomide less than 0.02 mg/L (0.02 mcg/mL) are expected to have minimal risk [see Contraindications (4.2), Warnings and Precautions (5.2), and Use in Specific Populations (8.1)].

5.4 Bone Marrow Effects/Immune Suppression/Infections
White Blood Cell (WBC) count decrease
A mean decrease in white blood cell (WBC) count of approximately 15% (mainly neutrophils and lymphocytes) and in platelet count of approximately 10% was observed in leflunomide-controlled trials with 7 mg and 14 mg of AUBAGIO compared to placebo. The decrease in mean WBC count occurred during the first 6 weeks and WBC count remained low during treatment. In placebo-controlled studies, neutrophil count < 1.5 x 10^9/L was observed in 12% and 16% of patients receiving AUBAGIO 7 mg and 14 mg, respectively, compared with 7% of patients receiving placebo; lymphocyte count < 0.6 x 10^9/L was observed in 10% and 12% of patients
Intestinal lung disease may be fatal. Intestinal ulcer disease may occur acutely at any time during therapy and has a variable clinical presentation. New onset or worsening pulmonary symptoms, such as cough and dyspnea, with or without associated fever, may be a reason for discontinuation of the therapy and for further investigation as appropriate. If discontinuation of the drug is necessary, consider initiation of an accelerated elimination procedure [see Warnings and Precautions (5.3)].

5.9 Concomitant Use with Immunosuppressive or Immunomodulating Therapies

Co-administration with antineoplastic, or immunosuppressive therapies used for treatment of multiple sclerosis has not been evaluated. Safety studies in which AUBAGIO was concomitantly administered with other immune modulating therapies for up to one year (interferon beta, glatiramer acetate) did not reveal any specific safety concerns. The long term safety of these combinations in the treatment of multiple sclerosis has not been established.

In any situation in which the decision is made to switch from AUBAGIO to another agent with a known potential for hematologic suppression, it would be prudent to monitor for hematologic toxicity, because there will be overlap of systemic exposure to both compounds. Use of an accelerated elimination procedure may decrease this risk, but may also potentially result in return of disease activity if the patient had been responding to AUBAGIO treatment [see Warnings and Precautions (5.3)].

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the prescribing information:

- Hepatotoxicity [see Contraindications (4.1) and Warnings and Precautions (5.1)]
- Bone Marrow Effects/Immunosuppression Potential/Infections [see Warnings and Precautions (5.4)]
- Peripheral Neuropathy [see Warnings and Precautions (5.5)]
- Skin Reactions [see Warnings and Precautions (5.6)]
- Increased Blood Pressure [see Warnings and Precautions (5.7)]
- Respiratory Effects [see Warnings and Precautions (5.8)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

A total of 2047 patients receiving AUBAGIO (7 mg or 14 mg once daily) constituted the safety population in the pooled analysis of placebo controlled studies in patients with relapsing forms of multiple sclerosis; of these, 71% were female. The average age was 37 years.

Table 1 lists adverse reactions in placebo-controlled trials with rates that were at least 2% for AUBAGIO patients and also at least 2% above the rate in placebo patients.

Table 1. Adverse Reactions in Pooled Placebo-Controlled Studies in Patients with Relapsing Forms of Multiple Sclerosis

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>AUBAGIO 7 mg (N=1045)</th>
<th>AUBAGIO 14 mg (N=1002)</th>
<th>Placebo (N=997)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>18%</td>
<td>16%</td>
<td>15%</td>
</tr>
<tr>
<td>Increase in Alanine Aminotransferase</td>
<td>13%</td>
<td>15%</td>
<td>9%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>13%</td>
<td>14%</td>
<td>8%</td>
</tr>
<tr>
<td>Alopecia</td>
<td>10%</td>
<td>13%</td>
<td>5%</td>
</tr>
<tr>
<td>Nausea</td>
<td>8%</td>
<td>11%</td>
<td>7%</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>8%</td>
<td>9%</td>
<td>7%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>8%</td>
<td>6%</td>
<td>5%</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>4%</td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3%</td>
<td>4%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Cardiovascular deaths

Four cardiovascular deaths, including three sudden deaths, and one myocardial infarction in a patient with a history of hyperlipidemia and hypertension were reported among approximately 2600 patients exposed to AUBAGIO in the premarketing database. These cardiovascular deaths occurred during uncontrolled extension studies, one to nine years after initiation of treatment. A relationship between AUBAGIO and cardiovascular death has not been established.

Adverse Reactions

In placebo-controlled studies, creatinine values increased more than 100% over baseline in 8/1045 (0.8%) patients in the 7 mg AUBAGIO group and 6/1002 (0.6%) patients in the 14 mg AUBAGIO group versus 4/997 (0.4%) patients in the placebo group. These elevations were transient. Some elevations were accompanied by hyperkalemia. AUBAGIO may cause acute uric acid nephropathy with transient acute renal failure because AUBAGIO increases renal uric acid clearance.

Hyponatremia

In clinical trials, 18% of AUBAGIO-treated patients had hyponatremia with serum potassium levels of at least 0.6 mmol/L, compared to 7% of placebo-treated patients.
patients; 4% of AUBAGIO-treated patients had hypophosphatemia with serum phosphorus levels at least 0.3 mmol/L but less than 0.6 mmol/L, compared to 0.8% of placebo-treated patients. No patient in any treatment group had a serum phosphorus below 0.3 mmol/L.

7 DRUG INTERACTIONS

Effect of AUBAGIO on CYP2C8 substrates

Teriflunomide may be a weak inducer of CYP2C8 in vivo. In patients taking AUBAGIO, exposure of drugs metabolized by CYP2C8 (e.g., paeclitaxel, pioglitazone, repaglinide, rosiglitazone) may be increased. Monitor these patients and adjust the dose of the concomitant drug(s) metabolized by CYP2C8 as required [see Clinical Pharmacology (12.3) in the full prescribing information].

Effect of AUBAGIO on organic anion transporter 3 (OAT3) substrates

Teriflunomide inhibits the activity of OAT3 in vivo. In patients taking AUBAGIO, exposure of drugs which are OAT3 substrates (e.g., cefaclor, cimetidine, ciprofloxacin, penicillin G, ketoprofen, furosemide, methotrexate, zidovudine) may be increased. Monitor these patients and adjust the dose of the concomitant drug(s) which are OAT3 substrates as required [see Clinical Pharmacology (12.3) in the full prescribing information].

Effect of AUBAGIO on OATP1B1/1B3 substrates

Teriflunomide inhibits the activity of OATP1B1/1B3 in vivo. For a patient taking AUBAGIO, the dose of rosuvastatin should not exceed 10 mg once daily. For other substrates of OATP1B1/1B3 (e.g., mitoxantrone) and drugs in the OATP family (e.g., methotrexate, rifamycins), especially HMG-CoA reductase inhibitors (e.g., atorvastatin, pravastatin, repaglinide, and simvastatin), consider reducing the dose of these drugs and monitor patients closely for signs and symptoms of increased exposures to the drugs while patients are taking AUBAGIO [see Clinical Pharmacology (12.3) in the full prescribing information].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category X [see Contraindications (4.2) and Warnings and Precautions (5.2)].

When teriflunomide (oral doses of 1, 3, or 10 mg/kg/day) was administered to pregnant rats throughout the period of organogenesis, high incidences of fetal malformation (primarily craniofacial, and axial and appendicular skeletal defects) and embryofetal death were observed at doses not associated with maternal toxicity. Adverse effects on embryofetal development were observed following dosing at various stages throughout organogenesis. Maternal plasma exposure at the no-effect level (1.0 mg/kg/day) for embryofetal developmental toxicity in rats was less than that in humans at the maximum recommended human dose (MRHD, 14 mg /day).

Administration of teriflunomide (oral doses of 1, 3.5, or 12 mg/kg/day) to pregnant rabbits throughout organogenesis resulted in high incidences of fetal malformation (primarily craniofacial, and axial and appendicular skeletal defects) and embryofetal death at doses associated with minimal maternal toxicity. Maternal plasma exposure at the no-effect dose (1.0 mg/kg/day) for embryofetal developmental toxicity in rabbits was less than that in humans at the MRHD.

In studies in which teriflunomide (oral doses of 0.05, 0.1, 0.3, 0.6, or 1.0 mg/kg/day) was administered to rats during gestation and lactation, decreased growth, eye and skin abnormalities, and high incidences of malformation (primarily craniofacial, and axial and appendicular skeletal defects) and postnatal death were observed in the offspring at doses not associated with maternal toxicity. Maternal plasma exposure at the no-effect dose for pre- and postnatal developmental toxicity in rats (0.10 mg/kg/day) was less than that in humans at the MRHD.

In animal reproduction studies of leflunomide, embryolethality and teratogenic effects were observed in pregnant rat and rabbit at or below clinically relevant plasma teriflunomide exposures (AUC). In published reproduction studies in pregnant mice, leflunomide was embryolethal and increased the incidence of malformations (craniofacial defects, cardiac defects, and skeletal defects). Administration of exogenous uridine reduced the teratogenic effects in pregnant mice, supporting that the mode of action (inhibition of mitochondrial enzyme dihydroorotate dehydrogenase) is the same for therapeutic efficacy and developmental toxicity. At recommended doses in humans, teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide.

Use in Males

AUBAGIO is detected in human semen. Animal studies to specifically evaluate the risk of male-mediated fetal toxicity have not been conducted. To minimize any possible risk, men not wishing to father a child and their female partners should use reliable contraception. Men wishing to father a child should discontinue use of AUBAGIO and undergo an accelerated elimination procedure to decrease the plasma concentration of teriflunomide to less than 0.02 mg/L (0.02 mg/mL) [see Warnings and Precautions (5.3)].

8.2 Nursing Mothers

Teriflunomide was detected in rat milk following a single oral dose of teriflunomide. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from AUBAGIO a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Clinical studies of AUBAGIO did not include patients over 65 years old.

8.6 Hepatic Impairment

No dosage adjustment is necessary for patients with mild and moderate hepatic impairment. The pharmacokinetics of teriflunomide in severe hepatic impairment have not been evaluated. AUBAGIO is contraindicated in patients with severe hepatic impairment [see Contraindications (4.1) Warnings and Precautions (5.1), and Clinical Pharmacology (12.3) in the full prescribing information].

8.7 Renal Impairment

No dosage adjustment is necessary for patients with mild, moderate, and severe renal impairment [see Clinical Pharmacology (12.3) in the full prescribing information].

10 OVERDOSAGE

There is no experience regarding teriflunomide overdose or intoxication in humans. Teriflunomide 70 mg daily up to 14 days was well tolerated by healthy subjects. In the event of clinically significant overdose or toxicity, cholestyramine or activated charcoal is recommended to accelerate elimination [see Warnings and Precautions (5.3)].

Genzyme Corporation
500 Kendall Street
Cambridge, MA 02142
A SANOFI COMPANY

October 2014a

TER-BPLR-SA-OCT14 Revised: October 2014a
## Saturday, April 18

8:00 a.m.–12:00 p.m.  
**I1** New Windows into the Brain: Technological Advances in Frontline Neurologic Diagnosis via the Visual and Oculomotor Systems  
1:00 p.m.–5:00 p.m.  
**I2** Management of Asymptomatic Cerebrovascular Lesions

### Sunday, April 19

8:00 a.m.–12:00 p.m.  
**I3** Dopamine-mediated Neural Plasticity in Motor and Non-motor Circuits  
1:00 p.m.–5:00 p.m.  
**I4** Infectious, Paraneoplastic, and Autoimmune Encephalopathies: Advances in Clinical Diagnosis and Emerging Insights about Pathogenesis

### Monday, April 20

8:00 a.m.–12:00 p.m.  
**I5** Pediatric Neurotrauma: From Coma to Concussions  
1:00 p.m.–2:30 p.m.  
**S1** Section Topic Controversies: Antiplatelets, Anticoagulants, or Stenting for Acute Treatment of Cervical/Cranial Dissection?  
1:00 p.m.–2:45 p.m.  
**S2** Section Topic Controversies: Should All Brain Tumor Patients Receive Prophylactic Anti-epileptic Drugs?

### Tuesday, April 21

7:30 a.m.–12:00 p.m.  
**P2** Poster Session II  
9:00 a.m.–12:00 p.m.  
**I6** Future Therapies: How We Will Be Treating, Preventing, and Curing Epilepsy in the Year 2025  
2:00 p.m.–6:30 p.m.  
**P1** Poster Session I

### Wednesday, April 22

7:30 a.m.–12:00 p.m.  
**P4** Poster Session IV  
9:00 a.m.–12:00 p.m.  
**S20** Treatment Mechanisms in Multiple Sclerosis  
2:00 p.m.–3:45 p.m.  
**S22** Epilepsy/ Clinical Neurophysiology (EEG): Basic Science and Intraoperative Monitoring

## Conferences

### Scientific Platform Sessions

- **S1** Movement Disorders: Genetics Presentation of the Founders Award
- **S8** Aging, Dementia, Cognitive, and Behavioral Neurology: Basic Science Presentation of the Potamkin Prize for Research in Pick’s, Alzheimer’s Disease, and Related Diseases
- **S7** Movement Disorders: Genetics Presentation of the Founders Award
- **S9** General Neurology: Neurological Treatments and Therapeutics
- **S10** Pain and Palliative Care Presentation of the Mitchell B. Max Award for Neuropathic Pain
- **S12** Neuroimmune Mechanisms in Multiple Sclerosis
- **S13** Cerebrovascular Disease and Interventional Neurology: Epidemiology and Risk Factors Presentation of the Michael S. Pessin Stroke Leadership Prize
- **S14** Epilepsy/ Clinical Neurophysiology (EEG): Clinical Epilepsy
- **S15** Movement Disorders: Huntington’s Disease, Dystonia, and Atypical Parkinsonism
- **S16** Aging, Dementia, Cognitive, and Behavioral Neurology: Clinical Science
- **S17** Muscle and Anterior Horn Cell Diseases: Mechanisms and Biomarkers
- **S18** Neuro-oncology: Imaging and Quality of Life Presentation of the Neuro-oncology Investigator Award
- **S19** Neurologic Education
- **S15** Movement Disorders: Huntington’s Disease, Dystonia, and Atypical Parkinsonism
- **S16** Aging, Dementia, Cognitive, and Behavioral Neurology: Clinical Science
- **S17** Muscle and Anterior Horn Cell Diseases: Mechanisms and Biomarkers
- **S18** Neuro-oncology: Imaging and Quality of Life Presentation of the Neuro-oncology Investigator Award
- **S19** Neurologic Education
- **S20** Treatment Mechanisms in Multiple Sclerosis Presentation of the John Dystel Prize for Multiple Sclerosis Research
- **S21** Cerebrovascular Disease and Interventional Neurology: Prehospital and Acute Ischemic Stroke Treatment
- **S22** Epilepsy/ Clinical Neurophysiology (EEG): Basic Science and Intraoperative Monitoring Presentation of the Drei fuss-Penny Epilepsy Award
- **S23** Headache: Imaging and Physiology
- **S24** ALS: Mechanisms and Biomarkers Presentation of the Sheila Essey Award: An Award for ALS Research
- **S25** General Neurology Presentation of the S. Weir Mitchell Award
- **S26** Neuro-ophthalmology/ Neuro-otology
S27 Neuro Trauma, Critical Care, and Sports Neurology

S28 Neuro-rehabilitation

2:00 p.m.–6:00 p.m.
I9 Treating Dementia in an Age of Mixed Disease

2:00 p.m.–6:00 p.m.
I10 The Dynamic Brain in Health and Disease: Plasticity and Reprogramming

2:00 p.m.–6:30 p.m.
P5 Poster Session V

4:00 p.m.–5:45 p.m.
Platform Blitz Sessions

S29 Neuroimaging Correlates in Multiple Sclerosis

S30 Cerebrovascular Disease and Interventional Neurology: Diagnostics, Biomarkers, and Genetics

S31 Epilepsy/Clinical Neurophysiology (EEG): Epilepsy Therapy

S32 Movement Disorders: Tremor, Ataxia, and More

S33 Aging, Dementia, Cognitive, and Behavioral Neurology: Biomarkers and Pathology

S34 Neuromuscular Update

S35 Child Neurology and Developmental Neurology

S36 Neuroepidemiology: Movement Disorders, ALS, and Aging

S37 Global Health and Infectious Disease

6:00 p.m.–7:00 p.m.
Highlights in the Field

H1 Sleep

H2 Movement Disorders

H3 Global Health

H4 Stroke and Vascular Neurology

H5 Multiple Sclerosis

H6 Sports Neurology

H7 Neuromuscular

H8 Clinical Neurophysiology/Autonomic Disorders

H9 Neuro-oncology

H10 Women’s Issues in Neurology

H11 Critical Care and Emergency Neurology

6:00 p.m.–7:30 p.m.
Emerging Science Session

Thursday, April 23

7:30 a.m.–12:00 p.m.
P6 Poster Session VI

9:00 a.m.–12:00 p.m.
Frontiers in Neuroscience Plenary Session

1:00 p.m.–2:45 p.m.
Scientific Platform Sessions

S38 Diet and Hormonal Factors in Multiple Sclerosis

S39 Cerebrovascular Disease and Interventional Neurology: Intracerebral Hemorrhage

S40 Movement Disorders: Functional Imaging in Parkinson’s Disease Presentation of the Movement Disorders Research Award

S41 Aging, Dementia, Cognitive, and Behavioral Neurology: Imaging: Aging and Alzheimer’s Disease Presentation of the Norman Geschwind Prize in Behavioral Neurology

S42 New Developments in Peripheral Neuropathies

S43 Neuro-oncology: Basic Science and Clinical Trials

S44 History of Neurology Presentation of the Lawrence C. McHenry Award: An Award for the History of Neurology

S45 Neuroepidemiology: Multiple Sclerosis, Cerebrovascular, and Aging Presentation of the Bruce S. Schoenberg International Award in Neuroepidemiology

1:00 p.m.–5:00 p.m.
H11 The Promise of Novel Biomarker Approaches in Advancing Treatment

1:00 p.m.–5:00 p.m.
H12 Obesity and Neurological Disorders

Continued on page 30

Annual Meeting Abstract Listing Available This Month

A full listing of the scientific abstracts highlighting breakthrough research on the most critical issues facing neurologists will be available later this month.

Access 2015 abstracts one of three easy ways:

1. Watch for Annual Meeting Scientific Program Book
   Watch your mailbox in late February/early March for the 2015 Scientific Abstract Listing and Annual Meeting Information book, which includes titles and authors of all abstracts.

2. Browse Abstracts Online
   Visit AAN.com/view/AM15 in late February to browse abstracts online.

3. Browse Abstracts via the Annual Meeting Mobile App
   Tap in to the meeting wherever you are with the Annual Meeting mobile app—available for iPhone, iPad, and Android.

Continued on page 30
Conferences

Preliminary 2015 Annual Meeting Scientific Program Announced
Continued from page 29

2:00 p.m.–6:30 p.m.
P7 Poster Session VII

3:15 p.m.–5:00 p.m.
Scientific Platform Sessions
S46 Neuromyelitis Optica
S47 Cerebrovascular Disease and Interventional Neurology
S48 Parkinson’s Disease
  Presentation of the Jon Stolk Award in Movement Disorders
  for Young Investigators
S49 Aging, Dementia, Cognitive, and Behavioral Neurology: Imaging:
  Behavioral Neurology and Non-Alzheimer’s Disease Dementias
S50 Treatment Trials in Neuromuscular Diseases

S51 Headache: Epidemiology and Clinical
  Presentation of the Harold Wolff-John Graham Award:
  An Award for Headache/Facial Pain Research
S52 General Neurology: Neural Networks and Neuromodulation
S53 Sleep
  Presentation of the Wayne A. Hening Sleep Medicine Investigator Award
  Presentation of the Sleep Science Award

5:30 p.m.–6:30 p.m.
Highlights in the Field
H12 Geriatric Neurology
H13 Neuro-ophthalmology/Neuro-otology

H14 Neural Repair and Rehabilitation
H15 Behavioral Neurology
H16 Neuro-endocrinology
H17 Headache
H18 Epilepsy

5:30 p.m.–7:00 p.m.
Controversies in Neurology Plenary Session

Friday, April 24
12:00 p.m.–1:30 p.m.
Clinical Trials Plenary Session
4:30 p.m.–6:00 p.m.
Neurology Year in Review Plenary Session

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*Medical Students and Nurse Practitioner/Physician Assistant members at the lower dues rate not eligible.
AAN Gives Back in 2015 Through Neediest Kids Partnership

A quarter of a million students in the Washington, DC, metro area are at or below the poverty line. Education is the key to breaking the cycle of poverty, but for 37 percent of all metro area students, reality includes struggling to master algebra without a calculator, trouble reading the whiteboard without glasses, or facing bitter cold temperatures without a coat.

Due to the success of the “AAN Gives Back to Haiti” program during the 2014 Annual Meeting, the AAN is once again partnering with a charity during the 2015 meeting to help those in need. This year’s partner, the Neediest Kids, is an independent charity that addresses childhood poverty in the Washington, DC, metropolitan area. Through its Bridge to Success Program, Neediest Kids partners with local school districts throughout DC, Maryland, and Virginia to ensure that thousands of at-risk, low-income students get the basic essentials they need so they can get the education they deserve. A donation to the Neediest Kids Bridge to Success Program will help kids thrive by providing the following goods and services based on precise individual needs and without any delays or bureaucracy:

- Eye exams and eyeglasses
- Coats
- Clothes and shoes
- School uniforms
- Groceries
- Personal care items
- School supplies
- School fees
- Transportation
- Other necessities

“Because last year’s program was so well received by Annual Meeting attendees, we knew we wanted to host a similar program this year, and contribute to the community hosting our 2015 meeting,” said Stefan M. Pulst, MD, FAAN, Chair of the Meeting Management Committee that is responsible for selecting AAN Gives Back partners. “After learning about the huge impact that the Neediest Kids program has had on the DC area—helping more than 30,000 students and families last year alone—we knew this renowned program was the 2015 partner for us.”

AAN Gives Back will take place during the Annual Meeting, and attendees are encouraged to stop by the booth to make a donation, or visit AAN.com/view/AANGivesBack to donate online.

To learn more about the program, including a full listing of DC-area school partners, visit Neediestkids.org/about.

Get Help Planning Your Annual Meeting Itinerary, Earn 10 FREE Self-assessment CME

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To access the exam, visit AAN.com/view/NeuroSAEAM.
Hallucinations and delusions characterize Parkinson's disease (PD) psychosis, but silence may be a symptom, too. 1-3 Could your patients be hiding the real impact of what they're going through? Dig deeper at PDpsychosis.com.

What are your patients with PD psychosis holding back?

References:

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WHAT ARE YOUR PATIENTS WITH PD PSYCHOSIS HOLDING BACK?

Hallucinations and delusions characterize Parkinson’s disease (PD) psychosis, but silence may be a symptom, too.\(^1\)\(^2\)\(^3\)

Could your patients be hiding the real impact of what they’re going through?

Dig deeper at PDpsychosis.com.

Conferences

Highlights in the Field Sessions at Annual Meeting Encapsulate Year’s Best in Subspecialty Areas

Plan to attend the Highlights in the Field sessions for your areas of interest at the 2015 AAN Annual Meeting.

These sessions, coordinated by AAN sections, highlight important scientific research from the past year and other topics such as practice issues or education updates for your subspecialty or area of interest.

**Wednesday | April 22 | 6:00 p.m.–7:00 p.m.**
- Clinical Neurophysiology/Autonomic Disorders
- Critical Care and Emergency Neurology
- Global Health
- Movement Disorders
- Multiple Sclerosis
- Neuromuscular
- Neuro-oncology
- Sleep
- Sports Neurology
- Stroke and Vascular Neurology
- Women’s Issues in Neurology

**Thursday | April 23 | 5:30 p.m.–6:30 p.m.**
- Behavioral Neurology
- Epilepsy
- Geriatric Neurology
- Headache and Facial Pain
- Neuroendocrine
- Neuro-ophthalmology/Neuro-otology
- Neural Repair and Rehabilitation

The sessions are free of charge with Annual Meeting registration and are open to all attendees. No registration is required.

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Learn More About Spinal Cord Disorders in Continuum

Disorders of the spinal cord is the topic for February’s Continuum: Lifelong Learning in Neurology®. The issue offers participants an opportunity to earn up to 14 hours of AMA PRA Category 1 Credits™.

“The spinal cord is essential for neurologic function,” said Guest Editor Tracey A. Cho, MD, assistant professor of neurology at Massachusetts General Hospital/ Harvard Medical School. “A multitude of pathologic processes may injure the spinal cord, almost always leading to significant dysfunction for the patient. This issue provides neurologists with updated knowledge on how to recognize and treat diseases of the spinal cord with appropriate urgency and efficiency.”

Upon completion of this issue, participants will be able to:

- Define the spinal cord syndromes based on anatomic principles and apply that knowledge to localize spinal cord lesions
- Interpret common MRI abnormalities associated with various spinal cord disorders
- Recognize the clinical and radiographic features of cervical spondylotic myelopathy and formulate a timely and cost-effective management plan
- Describe vascular disorders of the spinal cord including infarction, hemorrhage, and arteriovenous fistula
- List the metabolic causes of myelopathy and explain the diagnostic and therapeutic approach to nutritional myelopathies
- Distinguish infectious from noninfectious causes of spinal cord dysfunction and recognize specific infectious myelopathies
- Describe the immune-mediated causes of myelitis and formulate the diagnostic and therapeutic approach to their management
- Define direct neoplastic involvement of the spinal cord in the parenchymal, subarachnoid, and epidural compartments, and list indirect causes of spinal cord injury in the setting of neoplasm
- Identify cauda equina syndrome and recognize the need for urgent evaluation and possible surgical management
- Discuss the life-threatening complications of acute spinal cord injury and integrate neurologic expertise in a multidisciplinary approach to management
- List the most common chronic neurologic complications of spinal cord injury and discuss the management of these complications

Continuum is published six times per year. Subscribe to Continuum by contacting Lippincott Williams & Wilkins at (800) 361-0633, (301) 223-2300 (international), or LWW.com/continuum. Junior members who are transitioning to Active or Associate memberships can receive a 50-percent discount on the already low member rate for Continuum subscriptions.

Tracey A. Cho, MD
Residents and Fellows: Check out Neurology’s Section for You

Residents and fellows can find articles, mystery cases, e-pearls, Teaching NeuroImages for education, and much more online at the Neurology® Resident & Fellow Section.

“Since we launched the Resident and Fellow Section 10 years ago, it has been highly successful, with tremendous growth in resident involvement, publications submitted and published, and projects undertaken,” said Section Editor Mitchell S.V. Elkind, MD, MS, FAAN, who works with Deputy Section Editor John J. Millichap, MD. “Our goal continues to be to promote scholarship in the field of neurology.”

New article submissions are encouraged. For more information on the Call for Authors or anything else related to the section, visit Neurology.org and select “For Residents & Fellows.”

Elkind and Millichap explain the process of submitting articles for the Neurology Residents and Fellows Section in a video at Neurology.org/site/feature/index.xhtml.

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Please see additional dosing information on titration, administration instructions, premedication for flu-like symptoms, and a Brief Summary of safety information on the adjacent pages.

Indication
PLEGRIDY™ (peginterferon beta-1a) is indicated for the treatment of patients with relapsing forms of multiple sclerosis.

Important Safety Information
- PLEGRIDY is contraindicated in patients with a history of hypersensitivity to natural or recombinant interferon beta or peginterferon, or any other component of the formulation.
- Severe hepatic injury, including hepatitis, autoimmune hepatitis, and rare cases of severe hepatic failure, have been reported with interferon beta. Asymptomatic elevation of hepatic transaminases has also been reported, and in some patients has recurred upon rechallenge with interferon beta.
- Depression, suicidal ideation, and suicide occur more frequently in patients receiving interferon beta than in patients receiving placebo.
- Seizures are associated with the use of interferon beta.
### Pivotal Phase III Clinical Trial Results*  
**OUTCOMES AT 48 WEEKS**

<table>
<thead>
<tr>
<th>Clinical endpoints</th>
<th>PLEGRIDY 125 micrograms every 14 days</th>
<th>Placebo</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=512</td>
<td>n=500</td>
<td></td>
</tr>
<tr>
<td>Annualized relapse rate (ARR)</td>
<td>0.26</td>
<td>0.40</td>
<td>0.0007</td>
</tr>
<tr>
<td>Relative reduction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients relapsed</td>
<td>0.19</td>
<td>0.29</td>
<td>0.0003</td>
</tr>
<tr>
<td>Relative risk reduction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disability progression</td>
<td>0.07</td>
<td>0.11</td>
<td>0.0383</td>
</tr>
<tr>
<td>Relative risk reduction</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MRI endpoints</th>
<th>PLEGRIDY 125 micrograms every 14 days</th>
<th>Placebo</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=457</td>
<td>n=476</td>
<td></td>
</tr>
<tr>
<td>Mean number of new or newly enlarging T2 hyperintense lesions</td>
<td>3.6</td>
<td>10.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Relative reduction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean number of Gd-enhancing lesions</td>
<td>0.2</td>
<td>1.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Relative reduction</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Primary outcome: ARR over 1 year; secondary outcomes: proportion of patients relapsing, number of new or newly enlarging T2 hyperintense lesions, and time to confirmed disability progression, defined as follows: if the baseline EDSS score was 0, a sustained 12-week increase in EDSS score of 1.5 points was required; if the baseline EDSS score was greater than 0, a sustained 12-week increase in EDSS score of 1 point was required.*

- Anaphylaxis and other serious allergic reactions are rare complications of treatment with interferon beta.
- Injection site reactions, including injection site necrosis, can occur with the use of subcutaneous interferon beta.
- Congestive heart failure, cardiomyopathy, and cardiomyopathy with congestive heart failure occur in patients receiving interferon beta.
- Interferon beta can cause decreased peripheral blood counts in all cell lines, including rare instances of pancytopenia and severe thrombocytopenia. Monitor patients for infections, bleeding, and symptoms of anemia. Monitor complete blood cell counts, differential white blood cell counts, and platelet counts during treatment.
- Autoimmune disorders of multiple target organs including idiopathic thrombocytopenia, hyper- and hypothyroidism, and autoimmune hepatitis have been reported with interferon beta.
- The most common adverse reactions associated with PLEGRIDY treatment are injection site erythema, influenza-like illness, pyrexia, headache, myalgia, chills, injection site pain, asthenia, injection site pruritus, and arthralgia.

**Please see the Brief Summary of Full Prescribing Information on the adjacent pages.**

PLEGRIDY™ (peginterferon beta-1a) injection, for subcutaneous injection

Brief Summary of Full Prescribing Information  Rx only.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information: PLEGRIDY is administered subcutaneously. The recommended dosage of PLEGRIDY is 125 micrograms injected subcutaneously every 14 days.

Treatment initiation: Patients should start treatment with 63 micrograms on day 1. On day 15 (14 days later), the dose is increased to 94 micrograms, reaching the full dose of 125 micrograms on day 29 (after another 14 days). Patients continue with the full dose (125 micrograms) every 14 days thereafter (see Table 1). A PLEGRIDY Starter Pack is available containing two prefilled pens or syringes: 63 micrograms (dose 1) and 94 micrograms (dose 2).

Table 1: Schedule for Dose Titration

<table>
<thead>
<tr>
<th>Dose</th>
<th>Time*</th>
<th>Amount (micrograms)</th>
<th>Color of Pen or Syringe Label</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose 1</td>
<td>On day 1</td>
<td>63</td>
<td>Orange</td>
</tr>
<tr>
<td>Dose 2</td>
<td>On day 15</td>
<td>94</td>
<td>Blue</td>
</tr>
<tr>
<td>Dose 3</td>
<td>On day 29 and every 14 days thereafter</td>
<td>125 (full dose)</td>
<td>Grey</td>
</tr>
</tbody>
</table>

*Dosed every 14 days

2.2 Important Administration Instructions (All Dosage Forms): Healthcare professionals should train patients in the proper technique for self-administering subcutaneous injections using the prefilled pen or syringe. Patients should be advised to rotate sites for subcutaneous injections. The usual sites for subcutaneous injections are abdomen, back of the upper arm, and thigh.

Each PLEGRIDY pen and syringe is provided with the needle pre-attached. Prefilled pens and syringes are for a single dose only and should be discarded after use.

2.3 Premedication for Flu-like Symptoms: Prophylactic and concurrent use of analgesics and/or antipyretics may prevent or ameliorate flu-like symptoms sometimes experienced during treatment with PLEGRIDY.

4 CONTRAINDICATIONS

PLEGRIDY (peginterferon beta-1a) is contraindicated in patients with a history of hypersensitivity to natural or recombinant interferon beta or peginterferon, or any other component of the formulation.

5 WARNINGS AND PRECAUTIONS

5.1 Hepatic Injury: Severe hepatic injury, including hepatitis, autoimmune hepatitis, and rare cases of severe hepatic failure, have been reported with interferon beta. Asymptomatic elevation of hepatic transaminases has also been reported, and in some patients has recurred upon rechallenge with interferon beta.

Elevations in hepatic enzymes and hepatic injury have been observed with the use of PLEGRIDY in clinical studies. The incidence of increases in hepatic transaminases was greater in patients taking PLEGRIDY than in those taking placebo. The incidence of elevations of alanine aminotransferase above 5 times the upper limit of normal was 1% in placebo-treated patients and 2% in PLEGRIDY-treated patients. The incidence of elevations of aspartate aminotransferase above 5 times the upper limit of normal was less than 1% in placebo-treated patients and less than 1% in PLEGRIDY-treated patients. Elevations of serum hepatic transaminases combined with elevated bilirubin occurred in 2 patients. Both cases resolved following discontinuation of PLEGRIDY. Monitor patients for signs and symptoms of hepatic injury.

5.2 Depression and Suicide: Depression, suicidal ideation, and suicide occur more frequently in patients receiving interferon beta than in patients receiving placebo.

In clinical studies, the overall incidence of adverse events related to depression and suicidal ideation in multiple sclerosis patients was 8% in both the PLEGRIDY and placebo groups. The incidence of serious events related to depression and suicidal ideation was similar and less than 1% in both groups.

Advise patients to report immediately any symptom of depression or suicidal ideation to their healthcare provider. If a patient develops depression or other severe psychiatric symptoms, consider stopping treatment with PLEGRIDY.

5.3 Seizures: Seizures are associated with the use of interferon beta. The incidence of seizures in multiple sclerosis clinical studies was less than 1% in patients receiving PLEGRIDY and placebo. Exercise caution when administering PLEGRIDY to patients with a seizure disorder.

5.4 Anaphylaxis and Other Allergic Reactions: Anaphylaxis and other serious allergic reactions are rare complications of treatment with interferon beta. Less than 1% of PLEGRIDY-treated patients experienced a serious allergic reaction such as angioedema or urticaria. Those who did have serious allergic reactions recovered promptly after treatment with antihistamines or corticosteroids. Discontinue PLEGRIDY if a serious allergic reaction occurs.

5.5 Injection Site Reactions: Injection site reactions, including injection site necrosis, can occur with the use of subcutaneous interferon beta.

In clinical studies, the incidence of injection site reactions (e.g., injection site erythema, pain, pruritus, or edema) was 66% in the PLEGRIDY group and 11% in the placebo group; the incidence of severe injection site reactions was 3% in the PLEGRIDY group and 0% in the placebo group. One patient out of 1468 patients who received PLEGRIDY in clinical studies experienced injection site necrosis. The injury resolved with standard medical treatment.

Decisions to discontinue therapy following necrosis at a single injection site should be based on the extent of the necrosis. For patients who continue therapy with PLEGRIDY after injection site necrosis has occurred, avoid administration of PLEGRIDY near the affected area until it is fully healed. If multiple lesions occur, discontinue PLEGRIDY until healing occurs.

5.6 Congestive Heart Failure: Congestive heart failure, cardiomyopathy, and cardiomyopathy with congestive heart failure occur in patients receiving interferon beta.

In clinical studies, the incidence of cardiovascular events was 7% in both PLEGRIDY and placebo treatment groups. No serious cardiovascular events were reported in the PLEGRIDY group.

Monitor patients with significant cardiac disease for worsening of their cardiac condition during initiation and continuation of treatment with PLEGRIDY.

5.7 Decreased Peripheral Blood Counts: Interferon beta can cause decreased peripheral blood counts in all cell lines, including rare instances of pancytopenia and severe thrombocytopenia.

In clinical studies, decreases in white blood cell counts below 3.0 x 10^3/L occurred in 7% of patients receiving PLEGRIDY and in 1% receiving placebo. There is no apparent association between decreases in white blood cell counts and an increased risk of infections or serious infections. The incidence of clinically significant decreases in lymphocyte counts (below 0.5 x 10^3/L), neutrophil counts (below 1.0 x 10^3/L), and platelet counts (below 100 x 10^3/L) were all less than 1% and similar in both placebo and PLEGRIDY groups. Two serious cases were reported in patients treated with PLEGRIDY: one patient (less than 1%) experienced severe thrombocytopenia (defined as a platelet count less than or equal to 10 x 10^3/L), and another patient (less than 1%) experienced severe neutropenia (defined as a neutrophil count less than or equal to 0.5 x 10^3/L). Both patients, cell counts recovered after discontinuation of PLEGRIDY. Compared to placebo, there were no significant differences in red blood cell counts in patients treated with PLEGRIDY.

Monitor patients for infections, bleeding, and symptoms of anemia. Monitor complete blood cell counts, differential white blood cell counts, and platelet counts during treatment with PLEGRIDY. Patients with myelosuppression may require more intensive monitoring of blood cell counts.
5.8 Autoimmune Disorders: Autoimmune disorders of multiple target organs including idiopathic thrombocytopenia, hypothyroidism, and autoimmune hepatitis have been reported with interferon beta. In clinical studies, the incidence of autoimmune disorders was less than 1% in both PLEGRIDY and placebo treatment groups. If patients develop a new autoimmune disorder, consider stopping PLEGRIDY.

6 ADVERSE REACTIONS

6.1 CLINICAL TRIALS EXPERIENCE

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of PLEGRIDY cannot be directly compared to rates in clinical trials of other drugs and may not reflect the rates observed in practice.

In clinical studies (Study 1 and Study 2), a total of 1468 patients with relapsing multiple sclerosis received PLEGRIDY for up to 177 weeks (41 months), with an overall exposure equivalent to 1932 person-years. A total of 1033 patients received at least 1 year, and 415 patients at least 2 years of treatment with PLEGRIDY. A total of 512 and 500 patients, respectively, received PLEGRIDY 125 micrograms every 14 days or every 28 days during the placebo-controlled phase of Study 1 (year 1). The experience in year 2 of Study 1 and in the 2-year safety extension study (Study 2) was consistent with the experience in the 1-year placebo-controlled phase of Study 1.

In the placebo-controlled phase of Study 1, the most common adverse drug reactions for PLEGRIDY 125 micrograms subcutaneously every 14 days were injection site erythema, influenza-like illness, pyrexia, headache, myalgia, chills, injection site pain, asthenia, injection site pruritus, and arthralgia (all had incidence more than 10% and at least 2% more than placebo). The most commonly reported adverse event leading to discontinuation in patients treated with PLEGRIDY 125 micrograms subcutaneously every 14 days was influenza-like illness (in less than 1% of patients).

Table 2 summarizes adverse reactions reported over 48 weeks from patients treated in the placebo-controlled phase of Study 1 who received subcutaneous PLEGRIDY 125 micrograms (n=512), or placebo (n=500), every 14 days.

Table 2: Adverse reactions in the 48-week placebo-controlled phase of Study 1 with an incidence 2% higher for PLEGRIDY than for placebo.

<table>
<thead>
<tr>
<th>Condition</th>
<th>PLEGRIDY (n=512)</th>
<th>Placebo (n=500)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>44</td>
<td>33</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Musculoskeletal and Connective Tissue Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myalgia</td>
<td>19</td>
<td>6</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>General Disorders and Administration Site Conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection site erythema</td>
<td>62</td>
<td>7</td>
</tr>
<tr>
<td>Influenza like illness</td>
<td>47</td>
<td>13</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>45</td>
<td>15</td>
</tr>
<tr>
<td>Chills</td>
<td>17</td>
<td>5</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>Asthenia</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>Injection site pruritus</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>Hyperthermia</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Pain</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Injection site edema</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Injection site warmth</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Injection site hematoma</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Injection site rash</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

7.1 General and Administration Site Conditions

There were no new patterns of adverse reactions or new reactions due to increased drug exposure in patients with severe renal impairment.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies in pregnant women. PLEGRIDY should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

PLEGRIDY has not been tested for developmental toxicity in pregnant animals. In monkeys given interferon beta by subcutaneous injection every other day during early pregnancy, no teratogenic or other adverse effects on fetal development were observed. Abortifacient activity was evident following 3 to 5 doses.

8.3 Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when PLEGRIDY is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Safety and effectiveness in geriatric patients have not been established.

8.6 Renal Impairment

Monitor for adverse reactions due to increased drug exposure in patients with severe renal impairment.

Immunogenicity

For therapeutic proteins, there is a potential for immunogenicity. In Study 1, fewer than 1% of patients treated with PLEGRIDY every 14 days for 1 year developed neutralizing antibodies. Approximately 7% of PLEGRIDY-treated patients developed antibodies to PEG. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to PLEGRIDY with the incidence of antibodies to other products may be misleading.

Flu-Like Symptoms

Influenza-like illness was experienced by 47% of patients receiving PLEGRIDY 125 micrograms every 14 days and 13% of patients receiving placebo. Fewer than 1% of PLEGRIDY-treated patients in Study 1 discontinued treatment due to flu-like symptoms.

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8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Safety and effectiveness in geriatric patients have not been established.

8.6 Renal Impairment

Monitor for adverse reactions due to increased drug exposure in patients with severe renal impairment.

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Body temperature increased</th>
<th>Alanine aminotransferase increased</th>
<th>Aspartate aminotransferase increased</th>
<th>Gamma-glutamyltransferase increased</th>
<th>Skin and Subcutaneous Tissue Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6</td>
<td>3</td>
<td>6</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

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Neurology Position with Central Maine Medical Center

Central Maine Medical Group is seeking a BE/BC neurologist to join an established adult neurology practice primarily associated with Central Maine Medical Center. A focused interest in stroke, muscle disease, headache/migraine, epilepsy, or movement disorders would be a welcome addition, but is not required. Our diagnostic capabilities include: 1.5T MRI, CT angio, EMG, Evoked Potentials, EEG, and 24-72 Hour Ambulatory EEG. We also have an active Telemetry service that is affiliated with Massachusetts General Hospital. Central Maine Medical Center is the flagship hospital of Central Maine Healthcare. The medical center has 250 inpatient beds and offers a broad range of services that include, among many, neurosurgery, a Level II trauma center, cardiovascular medicine, vascular and cardiac surgery, and medical and radiation oncology. The Central Maine Medical Group comprises of approximately 350 providers, approximately half of which are in primary care. The group delivers care across almost 2500 square miles at numerous outpatient sites and four hospitals. A competitive salary and attractive benefits package are enhanced by the scenic beauty and abundant outdoor adventure found in Maine. Interested candidates, please send CV to Julia Lauver, Central Maine Medical Center, 300 Main Street, Lewiston, ME 04240. Fax: 207/796-6696, e-mail: jlauffer@cmhc.org, or call: 800/445-7431.

NEUROLOGIST Neurologist - Bend, Oregon

Bend Memorial Clinic, a community leader for over 65 years, is a group of 116 health care providers backed by nurses, technicians, administrators, even greeters at the door, gathered together to provide head-to-toe care to our patients to help them live the best possible life. We offer approximately 25 specialties — from Cardiatics to Pediatrics to Urgent Care — and the very latest in medical technology, including the most advanced imaging and diagnostic equipment. Put this all together, and we give you what no other medical group this side of the Cascade can — Total Care™. We’re currently looking for a BE/BC Neurologist provider to work with four other Neurologists. Here, you’ll enjoy the benefits of an internal referral group and the security of a very competitive compensation package with an opportunity to become a shareholder within two years. We will consider any Fellowship trained Provider as well. Located on the sunny side of the state, Bend enjoys 300 days of sunshine and a wonderful high desert climate. World class skiing, renowned fishing and amazing golf, water sports, cycling and trail running are all part of a quality lifestyle for Central Oregon residents. Our community also offers excellent schools, a variety of cultural activities, great food and entertainment, and is noted as one of the best places to live for outdoor activity by Sunset Magazine, Bike Magazine, CNN, Newsweek and Golf Magazine. Join us today in Central Oregon, a paradise in which to live and practice. Please send your CV to Andi Miller, Director of Provider Recruitment: Amiller@bmctotalcare.com or call (541) 408-0324; www.bendmemorialclinic.com

Faculty Positions-Movement Disorders Specialist & Epileptologist

The Department of Neurology at the University of Missouri School of Medicine is recruiting faculty positions for a Movement Disorders Specialist and an Epileptologist. Expertise in the specific area is required as well as Board Certification/Board Eligibility in Neurology. Faculty rank will be commensurate with experience and qualifications. Salary and benefits are very competitive. MU Neurology has 19 faculty in Adult General Neurology with subspecialties covering Movement Disorders, Epilepsy, Neuromuscular, Sleep Medicine, Stroke, Dementia, Multiple Sclerosis, and Neuro-ICU. The Neurosciences Center, with more than 20 physician specialists, features the largest medical and surgical neurology care team in mid-Missouri. In addition to clinical opportunities, a wide range of academic opportunities are offered by the University’s Institute for Clinical and Translational Science. MU is nationally recognized as an AUA member. Interested physicians, please email your Curriculum Vitae to department administrator, Mrs. Zhang at zhangh@health.missouri.edu.

BC/BE Neurologist Adirondack Mountains - Lake Champlain Region – Upstate NY – CVPH Medical Center (www.cvph.org) in conjunction with Fletcher Allen Health Care (www.fach.org) is seeking two BE/BC neurologists to join its medical staff. One position is 80% clinical/20% academic and the other is 20% clinical/80% academic. Fletcher Allen Health Care is the academic medical center affiliated with the University of Vermont. Call is negotiable. CVPH (www.cvph.org) is a regional referral hospital which is recognized by Healthgrades as a Top 100 Hospital for Cardiac Care. Plattsburgh, NY (www.NorthCountryGoodLife.com) offers a family-oriented community on Lake Champlain, near the Adirondacks, Olympic-Lake Placid region and Montreal. Contact: Rebecca Larkin, 518-314-3025, rlarkin@cvhp.org.

Neurologist Tri-State Neurology, PLLC in Memphis, TN is currently seeking an enthusiastic and aggressive adult neurologist to join our team. The ideal candidate will be dedicated on providing superior quality care to patients and work as a team with staff and other physicians. Specific training in clinical neurophysiology and sleep is a plus. Our outpatient clinics have a very established and prominent referral network. There are also research and teaching opportunities for those interested in academic tenures. We do NCVE/MEMG, EEG, Botul, sleep studies, and physical therapy in office. We also have in office infusion center. We do hospital rounds also. The salary is based on training and experience and highly competitive. If you are interested in the opportunity, please call 901-628-3988 or email cmn2000@yahoo.com. You may also fax your resume to 901.820.0298. J-1 waiver is offered.

North Shore Region

The Ochsner Neuroscience Institute and St. Tammany Parish Hospital are actively recruiting BC/BE General Neurologists, as well as neurologists with subspecialty training. This is a unique opportunity to join a developing neuroscience program in a highly desirable location. Newly trained and experienced physicians are encouraged to apply. Competitive salary with comprehensive benefits. The Department of Neurology has a complement of 25 neurologists system-wide with subspecialty representation in stroke, neurocritical care, interventional neurology, neuromuscular disease, movement disorders, epilepsy, MS, headache, cognitive disorders, and sleep. We are a Top 25 Neuroscience Center in the latest US News and World Report rankings. The telestroke programs at Ochsner Neuroscience Institute and St. Tammany Parish Hospital are integrated with our large tertiary care center on Jefferson Highway in New Orleans. The North Shore practice will have access to our current subspecialists and will support the development of several subspecialty programs as well. Ochsner North Shore has over 150 providers with twelve locations in six communities—providing an excellent referral base. Ochsner Health System is southeast Louisiana’s largest non-profit, academic, multi-specialty, healthcare delivery system. Driven by a mission to Serve, Heal, Lead, Educate and Innovate, coordinated clinical and hospital patient care is provided across the region by Ochsner’s 13 owned, managed and affiliated hospitals and more than 40 health centers. Ochsner is the only Louisiana hospital recognized by 2014-15 U.S. News & World Report as a “Best Hospital” across nine specialty categories. www.ochsner.org CVs will be reviewed by Richard M. Zwelfer, M.D., System Chair of Neurology. E-mail: prorecruiting@ochsner.org or call (800) 488-2240. Ref. # ANENS01. Ochsner is an equal opportunity employer and all qualified applicants will receive consideration for employment without regard to race, color, religion, sex, national origin, sexual orientation, disability status, protected veteran status, or any other characteristic protected by law.

Neurology Openings with Dignity Health in Northern California

Join a Dignity Health Medical Group in Northern California. Do you desire: Work/life balance in California? Traditional employment model? Opportunity to develop a successful neurology practice? Multiple housing and community options based on lifestyle? Neurology practices include: opportunity to develop Neurology service within the group, telementeueurology services in place with Affiliate Group, Joint Commission-Certified Primary Stroke Centers, comfortable or no hospital call options, new clinic buildings within walking distance to our hospitals, our Medical Foundation is aligned with the one of the largest hospital systems in the nation and the largest hospital system in California. Compensation includes: competitive salary guarantee, excellent earning potential with RVU Productivity Model & Bonuses, generous time off. Community highlights include: proximity to San Francisco, Monterey and Sacramento, excellent top-ranked public and parochial schools, multi-cultural arts, cuisine and theater. Group locations: Merced, Red Bluff, Redding (Directorship option available), Stockton. For more information, please contact & send your CV to: Physician Recruiting, providers@dignityhealth.org; ph: 888.599.7787; www.dignityhealth.org/physician-careers.

Neurologists Ochsner Health System and The Ochsner Neuroscience Institute are actively recruiting BC/BE General Neurologists to join our expanding practice. Additional opportunities exist for neurologists with subspecialty training in the following areas: Epilepsy, Headache, Movement Disorders, Multiple Sclerosis, Neuromuscular, and Stroke/Vascular. This is a great opportunity to practice neurology in a collegial and patient-focused environment. Academic appointments are available at our affiliated institutions, including Tulane, LSU, and the University of Queensland. Opportunities exist at both of our hospitals in New Orleans, in addition to our Kenner, North Shore and West Bank facilities. Both newly trained and experienced physicians are encouraged to apply. We offer a highly competitive salary with comprehensive benefits. The Department of Neurology has a complement of 25 neurologists system-wide with subspecialty representation in stroke, neurocritical care, interventional neurology, neuromuscular disease, movement disorders, epilepsy, MS, headache, cognitive disorders, and sleep. We are a Top 25 Neuroscience Center in the latest US News and World Report rankings. Ochsner Health System is southeast Louisiana’s largest non-profit, academic, multi-specialty, healthcare delivery system. Driven by a mission
### Dates and Deadlines

<table>
<thead>
<tr>
<th>February 2015</th>
<th>March 2015</th>
<th>April 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FEBRUARY 10</strong>&lt;br&gt;Webinar: Coding for Neurodiagnostic Procedures Made Easy&lt;br&gt;(Register by February 9)&lt;br&gt;AAN.com/view/pmw15</td>
<td><strong>MARCH 3</strong>&lt;br&gt;Webinar: Case Studies: Neurologists Succeeding in New Health Care Models&lt;br&gt;(Register by March 2)&lt;br&gt;AAN.com/view/pmw15</td>
<td><strong>APRIL 15</strong>&lt;br&gt;Webinar: How PQRS Quality Measures Will Inform Value-based Payments&lt;br&gt;(Register by April 14)&lt;br&gt;AAN.com/view/pmw15</td>
</tr>
<tr>
<td><strong>FEBRUARY 16</strong>&lt;br&gt;Application Deadline: Clinical Neuromuscular Pathology Certification Examination&lt;br&gt;UCNS.org/go/subspecialty/neuromuscular/certification</td>
<td><strong>MARCH 13</strong>&lt;br&gt;Application Deadline: Leadership for Women&lt;br&gt;AAN.com/view/WomenLead&lt;br&gt;Application Deadline: Advanced Leadership for Women&lt;br&gt;AAN.com/view/AdvLead</td>
<td><strong>APRIL 18–25</strong>&lt;br&gt;AAN Annual Meeting&lt;br&gt;AAN.com/view/AM15</td>
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<td><strong>FEBRUARY 25</strong>&lt;br&gt;Submission Deadline: 2015 Neuro Film Festival Video&lt;br&gt;NeuroFilmFestival.com</td>
<td><strong>MARCH 18</strong>&lt;br&gt;Annual Meeting Hotel Deadline&lt;br&gt;AAN.com/view/AM15</td>
<td><strong>APRIL 20</strong>&lt;br&gt;AAN Business Meeting&lt;br&gt;AAN.com/view/BoardSlate</td>
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**Neurologists**<br>Well-established, quality oriented neuroscience group seeks to add additional neurologists. Opportunity for subspecialists and general neurologist. We are a multidisciplinary neuroscience group providing a strong team oriented environment and opportunities for professional growth. Our location offers easy access to the cultural institutions of Boston, the mountains, the ocean, as well as outstanding private and public school opportunities. Send CV to Howard M. Gardner, M.D., Medical Director, New England Neurological Associates, P.C., RIVERWALK, 354 Merrimack Street, Lawrence, MA 01843, or email to jtf@neneuro.com. Visit us on the web at www.neneuro.com

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