2015 Annual Meeting Registration Opens This Month

Enhanced Registration Options

Registration opens this month for the 2015 Annual Meeting, set for April 18 through 25, at the Walter E. Washington Convention Center in Washington, DC.

The AAN is always working for you, our members, and looking for ways to improve your Annual Meeting experience. New for 2015 are the “Gold Registration Package.”

Keep the Benefits You Love, Gain Access to New

Renew Your Membership for 2015

It’s that time of year: Time to renew your valuable AAN membership for 2015. Be sure to renew before the end of the year to retain access to all of the exclusive member benefits upon which you’ve come to depend—and to make sure you don’t miss out on new member benefits coming your way in the new year!

Beginning January 1, 2015, the AAN is including as part of your already robust membership package FREE access to online learning programs designed specifically to help you take the necessary steps towards fulfilling your MOC requirements. Turn to page 32 for more details. Don’t miss out: Renew your membership today at AAN.com/dues!

Plan Your January Neurology Getaway Today!

Close your eyes and picture this: A warm January weekend in Arizona. Networking with your colleagues in a picturesque resort. Earning nearly 30 valuable CME credits. And, best of all, getting a comprehensive year-in-review of the best neurology science and education available.

Now, open your eyes and register for the AAN’s newest conference—Breakthroughs in Neurology: Translating Today’s Discoveries into Tomorrow’s Clinic. Join us!
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**News Briefs**

The AAN is helping you learn about the transition toward value-based payments with a new resource and a short AAN video series accessible at AAN.com/view/VBPM. These materials will help you understand how the Centers for Medicare & Medicaid Services measures the quality and costs of the care you provide in order to make adjustments to your future payments.

The AAN has summarized Current Procedural Terminology (CPT) coding changes impacting neurology in 2015 to allow members time to familiarize themselves with the changes before they take effect on January 1. View the changes at AAN.com/view/cpt. In addition, the Medical Economics and Management Committee seeks names of neurologists with experience and/or interest in getting involved in the AAN’s educational and advocacy activities around both procedural (CPT) coding and diagnosis (ICD-9/ICD-10) coding. To volunteer, contact Luana Ciccarelli at lciccarelli@aan.com.
Seeking Common Ground with CMS

The Academy has benefitted greatly from having staff on-site in Washington, DC, to advocate on behalf of our members and our patients. While ongoing efforts with members of Congress to pass legislation that will provide fair reimbursement for neurologists’ services and preserve patients’ access to necessary care might seem to receive the most attention, we’ve also made significant strides in recent years developing essential relationships with the other federal agencies involved in health care. Among the most notable of these have involved the leaders and staff of the Centers for Medicare & Medicaid Services (CMS).

Recently, I had the pleasure of meeting with Sean Cavanaugh, deputy administrator and director of the Center for Medicare at CMS. Mr. Cavanaugh is responsible for overseeing the regulation and payment of Medicare fee-for-service providers. I was joined by AAN President Elect Terrence Cascino, MD, FAAN; Past President Bruce Sigsbee, MD, FAAN; and Medical Economics and Management Committee Chair Orly Avitzur, MD, MBA, FAAN. AAN staff included Chief Executive Officer Catherine M. Rydell, CAE; Chief Health Policy Officer Rod Larson; Senior Director, Medical Economics and Quality Amanda Becker; and Regulatory Affairs Manager Daneen Grooms. We discussed a number of issues that are of concern to both the AAN and CMS.

Our message to Mr. Cavanaugh was that CMS has an important role to play, helping assure an adequate future supply of neurologists by implementing policies that properly value and recognize the role of neurologists.

We used our workforce data to illustrate the crisis that neurology is rapidly facing. We explained why neurology is having ever increasing difficulty attracting medical students—especially the best ones—into the specialty. In fact, neurology is experiencing the same workforce challenges as primary care. I shared with Mr. Cavanaugh the fact that many of the diseases impacting the Medicare population are diseases of the aging brain. Thus, as our population ages, disorders such as Alzheimer’s disease, stroke, and Parkinson’s disease increase at ever greater rates. These disorders represent a huge drain on Medicare resources, and this situation will continue to worsen until such time as effective treatments, or even cures, are found.

A second issue we discussed concerned the cost and quality of medical care. Simply put, internationally accepted measures of cost and quality place the US lowest in quality of medical care but highest in cost among industrialized western countries. As a result, it is clear that physicians who do not collect and use cost and quality data, and participate in new delivery and payment models, will become unable to compete effectively for market share and payer contracts, and thus eventually lose financial viability. To that end, we spoke with Mr. Cavanaugh and his team about the AAN’s longstanding commitment to developing relevant and useful neurology-specific quality measures. From the perspective of CMS and other policy makers, specialty societies which are held in the best regard demonstrate their commitment to improving the quality and value of care by creating clinical data registries. A registry is a structured way of collecting data on a set of patients in order to answer questions about treatments or procedures, practice patterns, and patient outcomes. CMS views collecting and analyzing quality data and interventions based on these data as essential to a high-value health care system.

The AAN and AAN Institute Boards of Directors recently approved developing a data registry focused on quality improvement. Such a registry pulls quality data directly from the electronic medical record of a practice or institution, and these data are then used in determining quality-and-value-based payments (e.g., PQRS), structuring contracts (e.g., ACOs), recertification (e.g., maintenance of certification), and internal quality improvement initiatives. At an aggregated level, such data should be able to benchmark quality across practices, regions, or nationally; inform
AAN Position Paper Evaluates Opioid Practice

There is increased attention to opioid prescription practices across medicine given the risks of addiction and adverse outcomes. A new AAN position paper addresses opioids for chronic, noncancer pain. The position paper Opioids for Chronic Noncancer Pain, written by Gary M. Franklin, MD, MPH, was published in the September 30, 2014, issue of Neurology®. It provides information on the health epidemic of prescription opioid related morbidity and mortality, including regulations, as well as, recommendations for neurologists in practice.

The objectives of the position paper are to review:
1. The key initiating causes of the epidemic,
2. The evidence for safety and effectiveness of opioids for chronic pain,
3. Federal and state policy responses, and
4. Recommendations for neurologists in practice to increase use of best practices/universal precautions most likely to improve effective and safe use of opioids, and to reduce the likelihood of severe adverse and overdose events.

“While there is evidence for significant short-term pain relief,” said Franklin, “there is no substantial evidence for maintenance of pain relief or improved function over long periods of time without incurring serious risk of overdose, dependence, or addiction.”

The rapidly emerging public health epidemic of prescription opioid related morbidity and mortality in the United States led the AAN’s Patient Safety Subcommittee to request a review of the related science and policy issues. More than 100,000 persons have died, directly or indirectly, from prescribed opioids in the United States since policies changed in the late 1990s. In the highest risk group aged 35–54, these deaths have exceeded mortality from both firearms and motor vehicle accidents.

To read the AAN’s position paper, visit AAN.com/public-policy/position-statements/position-and-policy-documents. For more information on how the AAN will present innovative information on how to safely use opioids in your practice at the AAN Annual Meeting in Washington, DC, visit AAN.com/practice/patient-safety.

Gary M. Franklin, MD, MPH
For the adjunctive treatment of seizures associated with LGS,

Add BANZEL® for powerful, broad spectrum efficacy in total seizure reduction

- 32.7% median reduction of total seizures in the BANZEL® group vs 11.7% for placebo ($P<0.002$)*1,2
- 42.5% median reduction in tonic-atonic seizures (drop attacks) in the BANZEL® group vs 1.4% increase for placebo ($P<0.0001$)*1,2

* A 12-week, randomized, double-blind, multicenter, placebo-controlled, parallel-group trial to assess the effectiveness of BANZEL (rufinamide) to reduce inadequately controlled seizures associated with LGS in patients (N=138, intent to treat) being treated with 1-3 concomitant stable-dose AEDs. These were primary efficacy endpoints in the pivotal trial.1-3

Indication:

BANZEL® (rufinamide) is indicated for the adjunctive treatment of seizures associated with Lennox-Gastaut syndrome (LGS) in children 4 years and older and adults.

Please see Important Safety Information below and Brief Summary of full Prescribing Information on the next page.

Important Safety Information

Contraindication:

BANZEL is contraindicated in patients with Familial Short QT syndrome.

Warnings:

AEDs increase the risk of suicidal thoughts or behavior in patients. Patients, their caregivers, and families should be informed of the risk and advised to monitor and report any emergence or worsening of depression, suicidal thoughts or behavior, or any unusual changes in mood or behavior, or thoughts of self-harm. If these symptoms occur, consider if it may be related to the AED or illness because epilepsy itself can increase these risks.

Use of BANZEL has been associated with central nervous system–related adverse reactions, such as somnolence or fatigue, coordination abnormalities, dizziness, gait disturbances, and ataxia.

Precautions:

Formal cardiac ECG studies demonstrated shortening of the QT interval (mean = 20 msec, for doses ≥ 2400 mg twice daily) with BANZEL. Caution should be used when administering BANZEL with other drugs that shorten the QT interval.

Multi-organ hypersensitivity syndrome has been reported in association with BANZEL therapy. In clinical trials, hypersensitivity reactions occurred in children less than 12 years of age and within 4 weeks of starting BANZEL therapy. In addition, rare cases of Drug Reaction with Eosinophilia and Systemic Symptoms and Stevens-Johnson syndrome have been reported in association with rufinamide therapy post marketing. If any of these reactions are suspected, BANZEL should be discontinued and alternative treatment started. All patients who develop a rash while taking BANZEL must be closely supervised.

As with all AEDs, BANZEL should be gradually withdrawn to minimize the risk of increased seizure frequency.

Adverse reactions:

In all patients with epilepsy treated in double-blind, adjunctive therapy studies, the most commonly observed (≥10%) adverse reactions with BANZEL vs placebo, respectively, were headache (25% vs 20%), dizziness (17% vs 10%), fatigue (15% vs 9%), somnolence (13% vs 9%), and nausea (11% vs 7%).


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Behaviors of concern should be reported immediately to healthcare providers. Patients, their caregivers, and families should be informed that AEDs increase the risk of suicidal thoughts and behavior. If suicidal thoughts or behavior emerge during treatment, the prescriber needs to consider whether the emergence of these behaviors is treatment-related or if it is a response to disease evolution or to other changes in the patient's life. The risk of suicidal thoughts or behavior was generally consistent among drugs in the data analyzed. The finding of a higher incidence of suicidal behavior or ideation among 27,863 AED-treated patients compared to 12,140 placebo-treated patients could be due to chance alone.

The increased risk of suicidal thoughts or behavior with AEDs was observed as early as one week after starting drug treatment. The estimated incidence rate of suicidal behavior or ideation among 27,863 AED-treated patients and 12,140 placebo-treated patients was 2.7 per 1000 patients treated (95% CI: 1.4, 3.9). The risk of suicidal behavior or ideation with AEDs was statistically significant compared to placebo (2.7 vs. 1.4 per 1000 patients treated).

Among patients with epilepsy, AEDs are most often used to treat generalized tonic-clonic seizures (grand mal), absence seizures, or myoclonic seizures. AEDs are also used to treat other seizure types, such as tonic seizures, clonic seizures, and atonic seizures. The most common side effects of AEDs are somnolence, drowsiness, dizziness, impaired coordination, and gastrointestional symptoms. The most serious side effect of AEDs is depression, which can lead to suicidal ideation or behavior. Other serious side effects include liver injury, aplastic anemia, and agranulocytosis. AEDs are associated with an increased risk of suicide and suicidal ideation, particularly in children and adolescents.

In conclusion, AEDs should be used with caution and close monitoring of patients for signs of suicidal ideation or behavior. Healthcare providers should educate patients and their families about the risks and benefits of AEDs and encourage open communication about the risks of suicide and suicidal ideation. Healthcare providers should also be alert for signs of depression and suicidal ideation, and should be prepared to intervene if necessary. AEDs are associated with an increased risk of suicide and suicidal ideation, particularly in children and adolescents.
In adult double-blind adjunctive clinical studies (up to 3200 mg/day), 3.5% of patients receiving BANZEL, as an adjunctive therapy and 1.5% of patients receiving a placebo complained of dizziness as an adverse event which was considered by the investigators to be drug-related. The adverse events most commonly leading to discontinuation of BANZEL (<1%) used as adjunctive therapy are presented in Table 5.

Table 5: Adverse Reactions Most Commonly Leading to Discontinuation in Double-Blind Adjunctive Trials (up to 3200 mg/day) in Adult Patients

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>BANZEL (N=823) vs Placebo (N=376)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizziness (3%)</td>
<td>2% vs 1%</td>
</tr>
<tr>
<td>Fatigue (2%)</td>
<td>2% vs 0%</td>
</tr>
<tr>
<td>Somnolence (7%)</td>
<td>0% vs 0%</td>
</tr>
</tbody>
</table>

Other Adverse Events Observed During Clinical Trials: BANZEL has been administered to 1788 individuals during all efficacy clinical trials (placebo-controlled and open-label). Adverse events occurring during these studies were recorded by the investigators using terminology of their own choice. To provide a clearer interpretation of the proportions of patients having adverse events, these events were grouped into standardized categories using the MedDRA dictionary. Adverse events occurring at least three times and considered possibly related to treatment are included in the System Organ Class/Preferred Terms table. Terms not included in the list are adverse events that, in the opinion of the investigator, were not drug-related. These terms have been included in the Table above. The following terms may be informative, those related to procedures and terms describing events common in the population. Some events occurring fewer than 3 times are also included based on their medical significance. Because the reports include events observed in open-label, uncontrolled observations, baseline characteristics, or severity of the condition, the events listed in the following table do not necessarily reflect those that would be observed in clinical practice.


Cardiac Disorders: Infrequent bundle branch block right, atrioventricular block first degree.

Metabolic and Nutritional Disorders: Frequent: decreased appetite, increased appetite.


6.2 Post-Marketing Experience

Decreased weight has been reported in patients receiving rufinamide both in the presence and absence of gastrointestinal symptoms.

7.2 DRUG INTERACTIONS

Based on in vitro studies, rufinamide shows little or no inhibition of most cytochrome P450 enzymes at clinically relevant concentrations, with weak inhibition of CYP 2E1. Drugs that are substrates of CYP 2E1 (e.g. chlorzoxazone) may have increased plasma levels of rifampicin, but no such studies have been done.

Based on in vivo drug interaction studies with trazodone and oral contraceptives, rufinamide is a weak inducer of the CYP 3A4 enzyme and can decrease exposure of drugs that are substrates of CYP 3A4 [see Drug Interactions (7.3)]. Rufinamide is metabolized by cytochrome P450. Drugs that may aid the activity of cytochrome P450 may increase plasma concentrations of rufinamide. Rufinamide has been shown to increase the area under the plasma concentration versus time curve (AUC) of midazolam, phenytoin, and phenobarbital, but not of diazepam, prazepam, clonazepam, or propranolol. Drug interactions occurring during clinical trials are presented in Table 7.

Table 7: Drug Interactions with BANZEL

<table>
<thead>
<tr>
<th>AED Co-administered</th>
<th>Influence of Rufinamide on CYP3A4 Activity</th>
<th>Influence of AED on Rufinamide</th>
<th>Pharmacokinetic Parameters of Rufinamide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>Decrease by 7 to 13%</td>
<td>Decrease by 19 to 26%</td>
<td>Decrease by 25 to 46%</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Decrease by 7 to 13%</td>
<td>No Effect</td>
<td>Independent of dose or concentration</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Decrease by 8 to 13%</td>
<td>Decrease by 25 to 46%</td>
<td>Independent of dose or concentration</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Decrease by 7 to 21%</td>
<td>Decrease by 25 to 46%</td>
<td>Independent of dose or concentration</td>
</tr>
<tr>
<td>Valproate</td>
<td>No Effect</td>
<td>No Effect</td>
<td>Independent of dose or concentration</td>
</tr>
<tr>
<td>Primidone</td>
<td>Not investigated</td>
<td>Decrease by 25 to 46%</td>
<td>Independent of dose or concentration</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Not investigated</td>
<td>No Effect</td>
<td>No Effect</td>
</tr>
</tbody>
</table>

A) Predictions are based on BANZEL concentrations at the maximum recommended dose of BANZEL.
B) Maximum changes predicted to be in children and in patients who achieve significantly higher levels of BANZEL, as the effect of rifampicin on these AEDs is concentration-dependent.
C) Larger effects in children at high doses/concentrations of AEDs.
D) Phenobarbital and primidone were treated as a single covalent phenobarbital-type inducer to examine the effect of these agents on BANZEL clearance.
E) All compounds of the benzodiazepine class were pooled to examine for ‘class effect’ on BANZEL clearance.
F) Any increase in plasma levels of rufinamide (Cmax, 15 μg/mL) is predicted to increase plasma levels of phenytoin by 7 to 21%. As phenytoin is known to have non-linear pharmacokinetics (clearance becomes saturated at higher doses), it is possible that exposure will be greater than the model prediction.

7.2.3 Effects of RUF on Other AEDs at BANZEL

Patient cytotoxicity of P450 enzyme inducers, such as carbamazepine, phenytoin, primidone, and phenobarbital appear to increase the clearance of BANZEL [see Table 6]. Given that the majority of clearance of BANZEL is via a non-CYP-dependent route, the observed decrease in blood levels seen with these drugs, phenytoin, phenobarbital, and primidone are unlikely to be entirely attributable to induction of a P450 enzyme. Other factors explaining this interaction are not understood. Any effects, where they occurred, were likely to be more marked in the pediatric population.

Phenobarbital, based on a population pharmacokinetic analysis, reduced the clearance of rufinamide was increased by 68% in children. In children, rufinamide might be administered to those who are known to have poor oral absorption or who are known to have low plasma clearance (e.g., the elderly). In children, rufinamide may be administered to those who are known to have low plasma clearance (e.g., the elderly). It is not known whether doses lower than the target doses are effective.

Phenytoin: The decrease in clearance of phenytoin estimated at typical levels of rufinamide (Cavss 15 μg/mL) is predicted to decrease by 25% to 46% in independent of dose or concentration of phenobarbital. The abuse and dependence potential of BANZEL has not been evaluated in human studies.

10. OVERDOSAGE

BANZEL is not readily expected to be excised in humans. Milk. Because of the potential for serious adverse reactions in nursing infants from BANZEL, if a decision is made to discontinue breastfeeding in the presence of rufinamide, BANZEL should be discontinued 2-4 hours before breast feeding. If the patient is breastfeeding, the transition to another AED should be made under close medical supervision. In clinical trials, BANZEL discontinuation was associated with no major signs or symptoms, no medical intervention was required, and the patient continued in the study at the target dose.

Treatment of Overdose: There is no specific antidote for overdose with BANZEL. If clinically indicated, elimination of unabsorbed drug should be attempted by induction of emesis or gastric lavage. Usual precautions should be observed to maintain the airway. General supportive care of the patient is indicated including monitoring of vital signs and observation of the clinical status of the patient. Hemodialysis: Standard hemodialysis procedures may result in limited clearance of rufinamide. Although there is no experience in treating overdose with hemodialysis, the procedure may be considered if indicated by the patient’s clinical status.

17. PATIENT COUNSELING INFORMATION

Patients should be advised to notify their physician if they experience a rash associated with fever.

BANZEL should be taken with food.

Patients should be advised about the potential for somnolence or dizziness and advised not to drive or operate machinery until they have gained sufficient experience on BANZEL to gauge whether it adversely affects their mental and/or psychomotor performance.

Female patients of childbearing age should be advised that the concurrent use of BANZEL with hormonal contraceptives may render this method of contraception less effective [see Drug Interactions (7.3)]. Additional non-hormonal forms of contraception are recommended when using BANZEL [see Information for Patients (7.7)].
IPAs Added to Menu of Reimbursement and Quality Care Options

To many, an “IPA” denotes a flavorful beverage imbued with a heady dose of hops. But neurologists soon may be raising their glasses to a different IPA—the independent practice association.

This flavor of IPA is being adopted by mid-sized neurology practices to address reimbursement concerns. It is an option that allows their practices to remain independent, yet align with other physicians. One example of an IPA was recently formed by Savannah Neurology Specialists in Georgia. The clinic has eight adult and two pediatric neurologists as well as four nurse practitioners.

Last year, in response to reimbursement changes moving from standard contracted fee-for-service (FFS) rates to quality and efficiency, or fee-for-value (FFV), the clinic came together with 17 private specialty practices to form Merit IPA. The IPA presently has 120 physician members representing 18 practices and specialties include orthopedics, vascular surgery, nephrology, oncology, ob-gyn, urology, and gastroenterology.

“There was very little accountable care organization (ACO) or other collaborative activity in our market, but there was a sense that change would come and that we, as private practices, wanted to be part of the conversation,” said Joanne S. Johansen, CMPE, chief operating officer for Merit IPA.

“Our primary goal was to provide a platform for working with key revenue sources in developing new and innovative ways to improve care while reducing costs and to do so while remaining independent, to deploy community clinical initiatives, and to share data to benchmark quality and episodic cost of care.”

The group’s initial steps involved hiring a consultant and an anti-trust attorney for guidance. After examining several structures, including an ACO, it was decided that a messenger model IPA would be the best initial structure.

“It would allow us to communicate with each other and to meet with payers as a collective group,” said Johansen. In the current messenger model, the IPA establishes a core fee schedule, which the membership votes to approve. The core fee schedule is a way to initiate a conversation with payers.
“Although we are not directly negotiating fee schedules, we have had several meetings with the payers and their medical directors to determine what their concerns are, top cost drivers, and what they are focusing on as they move to FFV reimbursement models via quality initiatives. We have also determined that we must move toward clinical integration in order to achieve our goals. Currently this is one of our top objectives as an IPA. As a result, data connectivity, clinical initiatives, and community partnerships are key in our current work plan as a group.”

Thus far, the group has formed a board and executive steering committee, clinical integration committee, finance committee, and credentialing committee. In the first six months, the clinical integration committee, composed of physicians and administrators, produced a white paper with five initiatives:

- Acute headache clinic
- Lower back pain clinic
- Peritoneal dialysis
- Clinical value pathways
- Dizziness/vertigo pathways

Formal work groups have been created to flesh out these initiatives. “It has been my privilege to observe the physicians on our clinical integration committee as they work on eliminating roadblocks to care and quality improvement,” said Johansen, who sits on that committee and the steering committee. “They are truly committed to this process and display an understanding that this is instrumental in surviving as an independent provider.”

In order to share data and benchmark, the group has chosen GRACHIE, a regional health information exchange out of Augusta, GA, due to its low cost and ability to interface with the diverse software systems among Merit’s providers. “We are using a tool that will help integrate all of our members and their respective EMR. This is vital in improving care coordination in our community,” Johansen said. “We are in the process of the technical assessment per practice to implement in a tiered fashion among the members.”

The IPA also has created savings for practices with malpractice discounts as well as discounts on answering services, reference laboratories, supplies, and IT services.

Anti-trust laws are an important consideration in forming an IPA, particularly when involving a significant number of specialists in one geographic area. Merit IPA exceeds the threshold, which means anti-trust rules apply and a different level of anti-trust review is triggered. The membership of an IPA can include 100 percent of specialists, but what matters is what the IPA does with the membership and how it uses its market power. As Merit moves to clinical integration, it will get another anti-trust review and formally apply to the FTC to see if it meets the standards.

As a business option, these IPAs are still brewing and may not be to every physician’s taste. But as health care reforms continue to create new partnerships and opportunities, the IPA may be more than just the flavor of the month.”

“Are You Certain? Or Just Guessing?”

“The Neurology Compensation and Productivity Report provides essential components to ensure every practice’s survival. The data provides me with valuable comparison information to ensure that I am not leaving money on the table. The survey also provides critical information that helps me understand how efficient (or not) my practice is.”

Brad Klein, MD, MBA
Abington Neurological Associates, Ltd.
AAN Member Since 2005

Be certain with the AAN 2014 Neurology Compensation and Productivity Report.

AAN.com/view/2014NeuroReport
Adjunctive therapy for patients ages 12 and up with partial-onset seizures

**NOVEL TARGET. NOVEL POTENTIAL.**

The first and only non-competitive AMPA receptor antagonist

**Demonstrated efficacy across all partial-onset seizures in clinical trials**

<table>
<thead>
<tr>
<th>MEDIAN % REDUCTION IN SEIZURE FREQUENCY FROM BASELINE (PLACEBO ADJUSTED)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Without Inducers</strong></td>
</tr>
<tr>
<td>4 mg/day</td>
</tr>
<tr>
<td>8 mg/day</td>
</tr>
<tr>
<td>12 mg/day</td>
</tr>
</tbody>
</table>

**One tablet, once-daily oral dosing at bedtime**

- Starting dosage is 2 mg once daily in patients not taking enzyme-inducing AEDs, and 4 mg in patients taking enzyme-inducing AEDs
- Increase dose based on clinical response and tolerability by a maximum of 2 mg once daily, no more frequently than every week, to a dose of 4 mg to 12 mg per day
- A dose of 12 mg once daily resulted in somewhat greater reductions in seizure rates than the dose of 8 mg once daily, but with a substantial increase in adverse reactions

---

* Pooled results of three randomized, double-blind, placebo-controlled, multicenter trials of FYCOMPA. All trials had a 6-week baseline period followed by a 19-week treatment period (6-week titration + 13 week maintenance), and patients were required to have ≥5 seizures at baseline to be randomized.†

- More than 85% of patients were taking 2-3 concomitant AEDs with or without concurrent VNS; approximately 50% were on at least one enzyme-inducing AED

- Primary endpoint was the percent change in seizure frequency per 28 days during the treatment period as compared to the baseline period

† Concomitant enzyme-inducing AEDs (carbamazepine, oxcarbazepine, or phenytoin) resulted in a substantial reduction in efficacy

‡ Antiepileptic drugs
Indication: FYCOMPA® (perampanel) is indicated as adjunctive therapy for the treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy aged 12 years and older.

Important Safety Information

WARNING: SERIOUS PSYCHIATRIC AND BEHAVIORAL REACTIONS

- Serious or life-threatening psychiatric and behavioral adverse reactions including aggression, hostility, irritability, anger, and homicidal ideation and threats have been reported in patients taking FYCOMPA.
- These reactions occurred in patients with and without prior psychiatric history, prior aggressive behavior, or concomitant use of medications associated with hostility and aggression.
- Advise patients and caregivers to contact a healthcare provider immediately if any of these reactions or changes in mood, behavior, or personality that are not typical for the patient are observed while taking FYCOMPA or after discontinuing FYCOMPA.
- Closely monitor patients particularly during the titration period and at higher doses.
- FYCOMPA should be reduced if these symptoms occur and should be discontinued immediately if symptoms are severe or are worsening.

Serious Psychiatric and Behavioral Reactions

Hostility- and aggression-related adverse reactions occurred in 12% and 20% of clinical trial patients randomized to receive FYCOMPA at doses of 8 mg and 12 mg/day, respectively, compared to 6% of patients in the placebo group. These effects were dose-related and generally appeared within the first 6 weeks of treatment, although new events continued to be observed through more than 37 weeks. These effects in FYCOMPA-treated patients led to dose reduction, interruption, or discontinuation more frequently than placebo-treated patients. The combination of alcohol and FYCOMPA significantly worsened mood and increased anger. Patients taking FYCOMPA should avoid the use of alcohol. Patients, their caregivers, and families should be informed that FYCOMPA may increase the risk of psychiatric events. Patients should be monitored during treatment and for at least one month after the last dose of FYCOMPA, and especially when taking higher doses and during the initial few weeks of drug therapy (titration period) or at other times of dose increases.

Suicidal Behavior and Ideation

Antiepileptic drugs (AEDs), including FYCOMPA, increase the risk of suicidal thoughts or behavior in patients. Anyone considering prescribing FYCOMPA or any other AED must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Patients, their caregivers, and families should be informed of the risk and advised to monitor and immediately report the emergence or worsening of depression, suicidal thoughts or behavior, thoughts about self-harm, and/or any unusual changes in mood or behavior. Should suicidal thoughts or behavior emerge during treatment, consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

Dizziness and Gait Disturbance

FYCOMPA caused dose-related increases in events related to dizziness and disturbance in gait or coordination. Dizziness and vertigo were reported in 35% and 47% of patients randomized to receive FYCOMPA at doses of 8 mg and 12 mg/day, respectively, compared to 10% of placebo-treated patients. Fatigue-related events were reported in 12% and 16% of patients randomized to receive FYCOMPA at doses of 8 mg and 12 mg/day, respectively, compared to 2% of placebo-treated patients. These adverse reactions occurred mostly during the titration phase.

Somnia/ence and Fatigue

FYCOMPA caused dose-dependent increases in somnolence and fatigue-related events. Somnolence was reported in 16% and 18% of patients randomized to receive FYCOMPA at doses of 8 mg and 12 mg/day, respectively, compared to 7% of placebo-treated patients. Fatigue-related events were reported in 12% and 15% of patients randomized to receive FYCOMPA at doses of 8 mg and 12 mg/day, respectively, compared to 5% of placebo-treated patients. In the controlled Phase 3 epilepsy clinical trials, these adverse reactions occurred mostly during the titration phase. Patients should be advised against engaging in hazardous activities requiring mental alertness, such as operating motor vehicles or dangerous machinery, until the effect of FYCOMPA is known.

Falls

Falls were reported in 5% and 10% of patients randomized to receive FYCOMPA at doses of 8 mg and 12 mg/day, respectively, compared to 3% of placebo-treated patients.

Withdrawal of AEDs

A gradual withdrawal is generally recommended with antiepileptic drugs to minimize the potential of increased seizure frequency.

Most Common Adverse Reactions

In clinical trials, the most frequently reported adverse reactions in patients receiving FYCOMPA 8 mg or 12 mg vs placebo (≥24% and at least 1% higher than the placebo group) included dizziness (36% vs 9%), somnolence (16% vs 7%), fatigue (10% vs 5%), irritability (9% vs 3%), falls (7% vs 3%), nausea (7% vs 5%), ataxia (5% vs 0%), balance disorder (4% vs 1%), gait disturbance (4% vs 1%), vertigo (4% vs 1%), and weight gain (4% vs 1%).

Drug Interactions

FYCOMPA may decrease the efficacy of contraceptives containing levonorgestrel. Plasma levels of FYCOMPA were decreased when administered with carbamazepine, phenytoin, or oxcarbazepine. Concomitant use with strong CYP3A inducers such as St. John’s wort and rifampin should be avoided. Multiple dosing of FYCOMPA 12 mg/day enhanced the effects of alcohol on vigilance and alertness, and increased levels of anger, confusion, and depression. These effects may also be seen when FYCOMPA is used in combination with other CNS depressants.

Pregnancy Category C and Lactation

FYCOMPA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Physicians are advised to recommend that pregnant patients taking FYCOMPA enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry. Caution should be exercised when FYCOMPA is administered to a nursing woman.

Hepatic and Renal Impairment

Use in patients with severe hepatic or severe renal impairment is not recommended. Dosage adjustments are recommended in patients with mild or moderate hepatic impairment. Use with caution in patients with moderate renal impairment.

Drug Abuse and Dependence

FYCOMPA is a Schedule III controlled drug substance and has the potential to be abused or lead to drug dependence.

Please see Brief Summary of full Prescribing Information on the next page for Boxed WARNING and additional Important Safety Information.

References:
**INDICATIONS AND USAGE**

FYCOMPA (perampanel) is indicated as adjunctive therapy for the treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy aged 12 years and older.

**DOSE AND ADMINISTRATION**

**Drug Interaction**

In the absence of an enzyme-inducing AEDs The recommended starting dosage of FYCOMPA is 2 mg/day, which can be increased up to 4 mg/day, and subsequently increased up to 12 mg/day, in 2 mg/day increments every 4 to 7 days, if required. The maximum recommended FYCOMPA dose is 12 mg/day.

**CONTRAINDICATIONS**

See Warnings and Precautions (5.3)

**WARNINGS AND PRECAUTIONS**

**Serious Psychiatric and Behavioral Reactions**

In the controlled Phase 3 epilepsy clinical trials, hostility- and aggression-related adverse reactions occurred in 19% and 20% of patients randomized to receive FYCOMPA at doses of 5 mg and 12 mg/day, respectively, compared to 9% of patients in the placebo group. These effects were dose-related and generally appeared within the first 6 weeks of treatment, although new events continued to be observed through more than 37 weeks. FYCOMPA-treated patients experienced more hostility- and aggression-related adverse reactions that were serious, severe, and led to dose reduction, interruption, and discontinuation more frequently than did placebo-treated patients. In general, in placebo-controlled Phase 3 epilepsy trials, neuropsychiatric events were reported more frequently in patients being treated with FYCOMPA than in patients taking placebo. These events included irritability, aggression, anxiety, and anger which occurred in 2% or greater of perampanel-treated patients and at a higher frequency than in placebo-treated patients. These events were observed with similar frequency and treatment and more commonly with placebo, included deliriousness, agitation, sleep behavior, and physical assault.

Some of these events were reported as serious and life-threatening. Hospitalization and/or death was reported in 38 FYCOMPA-treated patients in the controlled Phase 3 epilepsy trials and 3 placebo-treated patients. In the controlled Phase 3 epilepsy trials these events occurred in patients with and without prior psychiatric history, prior aggressive behavior, and/or concurrent treatment with another CNS depressant or other psychotropic medications.

Some patients experienced worsening of pre-existing psychiatric conditions. Patients with active psychiatric disorders and unstable recurrent affective disorders were excluded from the clinical trials. The combination of alcohol and perampanel significantly worsened mood and increased anger [see Drug Interactions (7.3)]. Patients taking FYCOMPA should avoid the use of alcohol. In healthy volunteers taking FYCOMPA, observed psychiatric events included paranoia, euphoric mood, agitation, anger, manic state, and disorientation/confusional state. In the non-placebo trials, psychiatric events that occurred in perampanel-treated subjects more often than placebo-treated subjects included disinhibition, delusion, and paranoia. Patients, their caregivers, and families should be informed that FYCOMPA may increase the risk of psychiatric events. Patients should be monitored during treatment and for at least one month after the last dose of FYCOMPA, and especially when taking higher doses and during the initial few weeks of drug therapy (titration period) or at other times of dose increases. Dose of FYCOMPA should be reduced if these symptoms occur or should be discontinued immediately if symptoms are severe or are worsening (5.1).

**Geriatric Use**

The safety and efficacy of FYCOMPA in patients 65 years of age and older have not been established. Use in this age group is not recommended. A certified poison control center should be contacted for updated information on the management of overdose with FYCOMPA.

**Pregnancy**

Animal studies have not been conducted with FYCOMPA. It is known that perampanel binds to the same high affinity human perampanel binding site found in the human brain. While it is not known whether perampanel crosses the placenta, the drug could be transferred from the mother to the fetus. The potential for perampanel to cause fetal harm when administered to a pregnant woman is unknown. For this reason, FYCOMPA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Lactation**

It is unknown if perampanel is excreted in human milk. Because many drugs are excreted in human milk, breastfeeding should be discontinued during treatment with FYCOMPA.

**Nursing Mothers**

The safety and efficacy of FYCOMPA in nursing mothers have not been established. For this reason, FYCOMPA should be used during breastfeeding only if the potential benefit justifies the potential risk to the nursing infant.

**Drug Abuse and Dependence**

Physical dependence

Sudden interruption or withdrawal of FYCOMPA may precipitate a syndrome that is characterized by withdrawal symptoms after abrupt discontinuation or a significant dose reduction of a drug. The severity of these withdrawal symptoms is related to the dose level of the drug. The symptoms following abrupt discontinuation of FYCOMPA may include anxiety, agitation, insomnia, and various autonomic symptoms (e.g., sweating, tachycardia, and hypertension).

**DRUG ABUSE AND DEPENDENCE**

The relative risk for suicidal thoughts or behavior was higher in clinical trials for epilepsy than in clinical trials for psychiatric or other conditions, but the absolute risk differences were similar for the epilepsy and psychiatric conditions. The risk of suicidal thoughts or behavior with FYCOMPA and other AEDs must be balanced against the risk of any AEDs.

**Renal Impairment**

The safety and efficacy of FYCOMPA in patients with renal impairment have not been established; however, because perampanel is eliminated through the kidneys, close clinical monitoring is recommended in patients with renal impairment.

**Hepatic Impairment**

The safety and efficacy of FYCOMPA in patients with hepatic impairment have not been established; however, because perampanel is metabolized through the liver, close clinical monitoring is recommended in patients with hepatic impairment.

**Table 1. Risk by indication for antiepileptic drugs in the pooled analysis**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Placeto Patients with Events Per 1000 Patients</th>
<th>Drug Patients with Events Per 1000 Patients</th>
<th>Relative Risk: Incidence of Events in Drug Patients/Incidence in Placebo Patients</th>
<th>Risk Difference: Additional Drug Patients with Events Per 1000 Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy</td>
<td>1.8</td>
<td>3.4</td>
<td>1.9</td>
<td>1.7</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>5.7</td>
<td>1.6</td>
<td>3.6</td>
<td>2.9</td>
</tr>
<tr>
<td>Other</td>
<td>1.0</td>
<td>1.6</td>
<td>0.9</td>
<td>0.7</td>
</tr>
<tr>
<td>Total</td>
<td>2.6</td>
<td>3.6</td>
<td>1.3</td>
<td>1.1</td>
</tr>
</tbody>
</table>

The relative risk for suicidal thoughts or behavior was higher in clinical trials for epilepsy than in clinical trials for psychiatric or other conditions, but the absolute risk differences were similar for the epilepsy and psychiatric conditions. The risk of suicidal thoughts or behavior with FYCOMPA and other AEDs must be balanced against the risk of any AEDs.

**ADVERSE REACTIONS**

The following adverse reactions are discussed in more detail in other sections of the prescribing information:

- Serious Psychiatric and Behavioral Reactions (see Warnings and Precautions (5.3))
- Somnolence and Fatigue (see Clinical Pharmacology (12.4))
- Neurologic Effects (see Warnings and Precautions (5.3))
- CNS Depressants (see Warnings and Precautions (5.3))
- Physical Dependence (see Warnings and Precautions (5.3))
- Infections and Infestations (see Warnings and Precautions (5.3))
- Other (see Warnings and Precautions (5.3))

**Table 2. Adverse Reactions in Pooled Double-blind Trials in Patients with Partial-Onset Seizures (Reactions ≥2% in Patients under 12 Years of Age in FYCOMPA Group and More Frequent than Placebo)**

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Placebo Patients</th>
<th>FYCOMPA Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary tract</td>
<td>4 (0)</td>
<td>12 (5)</td>
</tr>
<tr>
<td>Infections and Infestations</td>
<td>3 (2)</td>
<td>7 (4)</td>
</tr>
<tr>
<td>Injury, Poisoning and Procedural Complications</td>
<td>3 (2)</td>
<td>7 (4)</td>
</tr>
</tbody>
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<td>Other</td>
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<tr>
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<td>3.6</td>
<td>1.3</td>
<td>1.1</td>
</tr>
</tbody>
</table>

**Table 2. Adverse Reactions in Pooled Double-blind Trials in Patients with Partial-Onset Seizures (Reactions ≥2% in Patients under 12 Years of Age in FYCOMPA Group and More Frequent than Placebo)**

<table>
<thead>
<tr>
<th>Reaction</th>
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</thead>
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<td>7 (4)</td>
</tr>
<tr>
<td>Injury, Poisoning and Procedural Complications</td>
<td>3 (2)</td>
<td>7 (4)</td>
</tr>
</tbody>
</table>
Table 2. Adverse Reactions in Pooled Double-Mind Trials in Patients with Partial-Onset Seizures (Reactions: >2% of Patients in Highest FYCOMPA Dose (12 mg) Group and More Frequent than Placebo (cont.))

<table>
<thead>
<tr>
<th>Condition</th>
<th>Placebo (n=1,680)</th>
<th>8 mg FYCOMPA (n=1,343)</th>
<th>12 mg FYCOMPA (n=1,346)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>4 (0.2%)</td>
<td>5 (0.4%)</td>
<td>5 (0.4%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1 (0.0%)</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Weight gain</td>
<td>1 (0.0%)</td>
<td>1 (0.1%)</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>Liver function abnormality</td>
<td>0 (0.0%)</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Agranulocytosis</td>
<td>1 (0.0%)</td>
<td>2 (0.2%)</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>0 (0.0%)</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>1 (0.0%)</td>
<td>2 (0.2%)</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Urticaria</td>
<td>4 (0.2%)</td>
<td>5 (0.4%)</td>
<td>5 (0.4%)</td>
</tr>
<tr>
<td>Rash</td>
<td>1 (0.0%)</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Cough</td>
<td>0 (0.0%)</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Mucocutaneous/Connective tissue disorders</td>
<td>&lt;1 (0.0%)</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>0 (0.0%)</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Back pain</td>
<td>2 (0.1%)</td>
<td>2 (0.2%)</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>1 (0.0%)</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>2 (0.1%)</td>
<td>2 (0.2%)</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>1 (0.0%)</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Periorbital edema</td>
<td>1 (0.0%)</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
</tr>
</tbody>
</table>

Adverse Reactions (6.1)

Contraindications

- Concomitant use of FYCOMPA with a dose of 12 mg/d or reduced liver exposure by approximately 40% (see Clinical Pharmacology (2.3)). Use of FYCOMPA with oral or intravenous containing levetiracetam may render them less effective. Additional non-hormonal forms of contraception are recommended.
- Cytomegalovirus (CMV) infection: The concomitant use of known CMV enzyme inducers including carbamazepine, phenytoin, or acetazolamide with FYCOMPA decreased the plasma levels of perampanel by approximately 50–67% (see Clinical Pharmacology (2.3)). The start of FYCOMPA for the adjunctive therapy of partial-onset seizures in patients with CMV infection may need to be delayed.

Drug Interactions

- Concomitant use of FYCOMPA with citalopram, monotherapy, or acetazolamide with FYCOMPA decreased the plasma levels of perampanel by approximately 50–67% (see Clinical Pharmacology (2.3)). Use of FYCOMPA with oral or intravenous containing levetiracetam may render them less effective. Additional non-hormonal forms of contraception are recommended.
Register for Meaningful Use, Quality Improvement Webinars

The AAN offers two practice management webinars in November to help members stay informed with the latest developments in Meaningful Use and quality improvement.

Achieving Stage 2 Meaningful Use: Taking Your EHR Use to the Next Level
Date: November 4, 2014, from 12:00 p.m. to 1:30 p.m. ET
Registration deadline: November 3
Presenter: Allison L. Weathers, MD, FAAN

Upon completion of this webinar, participants should be able to:
- Understand the federal incentives that are available for the “meaningful” use of an EHR, and the requirements that must be met to obtain the incentives
- Recognize changes between Stage 1 and Stage 2 of the Medicare EHR Incentive Program
- Understand neurology-specific best practices and challenges in demonstrating meaningful use
- Calculate the consequences for physicians who do not meet meaningful use requirements
- Discover AAN resources

Quality Improvement: Beginning Steps in the Right Direction
Date: November 18, 2014, from 12:00 p.m. to 1:30 p.m. ET
Registration deadline: November 17
Presenter: Anup Patel, MD

Upon completion of this webinar, participants should be able to:
- Understand the language of quality improvement based on the Institute for Healthcare Improvement model
- Identify the tools and methods for planning and implementing quality improvement projects
- Examine quality improvement methods using an example from neurology

Still Time to Save and Access All 2014 Webinars!
AAN members can pay either $149 for each webinar—or subscribe to the entire 2014 series of 14 Practice Management Webinars for only $199. Subscriptions include convenient access to past webinar recordings from 2014 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 with 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/pmw14.

Free Webinar on 2015 Fee Schedule Offered on December 2

William S. Henderson, FAcMPE, will direct the FREE December webinar “Decoding the 2015 Medicare Physician Fee Schedule: Changes That Impact Neurology,” on Tuesday, December 2, from 12:00 p.m. to 1:30 p.m. ET. The webinar will be offered free to AAN members. The registration deadline is December 1.

Upon completion of this webinar, participants should be able to:
- Describe changes to payments in the Medicare Fee Schedule effective in January 2015
- Identify the opportunities and challenges relating to these fee schedule changes from a neurology perspective
- Discuss the impact of these changes to your practice
- Address other issues that relate to billing and reimbursement of neurology services

Register today for this important free webinar at AAN.com/view/pmw14.
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**New**
- Imaging prodromal Parkinson disease: The Parkinson associated risk syndrome study
  Alberto J. Espay, MD, MSc, and Danna L. Jennings, MD
- DPPX potassium channel antibody: Frequency, clinical accompaniments and outcomes in 20 patients
  Ted M. Burns, MD, and W. Oliver Tobin, MB, BCh, PhD
- Dietary treatment in adults with refractory epilepsy: A review
  Lara Vanessa Marcuse, MD, BA, and Pavel Klein, MB, BChir
- Her experiences and observations dealing with stroke recovery and rehabilitation
  Andy M. Southerland, MD, MSc, and Ms. Esmeralda Santiago

**Recent**
- Clinical and ethical judgment: A profound dilemma
  Daniel G. Lariviere, MD, and Ciro Ramos-Estebanez, MD, PhD
- Why brain death is considered death and why there should be no confusion
  Michael D. Brogan, MD; Christopher Montilla Burkle, MD, JD; and Eelco F. Wijdicks, MD, PhD
- Blood pressure management in stroke
  Bryan J. Eckerle, MD, and Ritvij Bowry, MD
- Cerebral amyloid angiopathy-related inflammation
  Prachi Mehndiratta, MD, and Aaron L. Berkowitz, MD, PhD

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  John R. Corboy, MD, and José G. Merino, MD
- Spinal Interventions
  John R. Corboy, MD, and J.D. Bartleson, MD
- Spotlight on Neuroinfectious Disease
  Chenjie Xia, MD, and David Clifford, MD

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Neurology on the Hill: Face-to-face Meetings Educate, Make Change Possible

For South Carolina neurologist Anil Yallapragada, MD, participating in his first Neurology on the Hill last March reinforced his growing awareness of the need for physicians to meet directly with those who enact medical policies that affect millions of neurology patients. By meeting face-to-face and developing relationships with lawmakers, neurologists stand a much better chance of influencing these policies.

"Neurology on the Hill was an extraordinary opportunity and experience to be a part of, not only as an active believer in the necessity of cooperation between those in medicine and legislation, but also as a neurologist early in my career who sees the effect health care laws have with my patients at the ground level. Throughout our training as physicians, focus is placed on nurturing compassion, instilling responsibility, and cultivating critical thinking and analysis. But I’ve realized that as a physician I also have a civic obligation just as vital to the well-being of my community, my patients, and their families. I believe there is a large void in physician participation across the board in government, both at the state and federal level. Too often laws are codified and regulations enacted without the consultation of the very patients and physicians who will be subject to these rules. We, as physicians, need to strengthen our voice and get involved."

Neurology on the Hill provided Yallapragada an excellent platform to achieve this goal. He also appreciated the experience as a starting point for physicians looking to gain experience in understanding the political aspects involved in the profession by talking directly to policy makers.

"The program was extraordinarily well organized, from education on the policy issues, to meeting the actual bill sponsors. There was even a mock interaction that trains medical professionals on how to approach and discuss the issues affecting our practice. During the actual day we were on Capitol Hill, it was an amazing experience to feel like we were truly participating in the democratic process firsthand. I was able to gain a deeper appreciation on how to connect with my lawmakers and their staff and provide them with the education they need to make the best decisions for their constituents."

"One experience that especially stands out is being asked by the chief of staff from Congressman Mark Sanford’s office to join the congressman for lunch to discuss the issues concerning our community. After the lunch, I met with him personally and we walked back together to his office at the Rayburn Building where I further engaged him about the serious burden of stroke we are dealing with in South Carolina. He was genuinely interested in learning about all the issues and asked many questions. Afterwards, he introduced me to his health policy advisor and we discussed my community’s concerns further. It was fulfilling to have such accessibility to our elected officials and share our concerns and suggestions on how we can improve a crippled system. I look forward to participating in Neurology on the Hill again in the future. It was a great experience, and I encourage more young neurologists to get involved because our patients are depending on us.”

Neurology on the Hill
March 2–3, 2015
Ritz-Carlton Pentagon City, Washington, DC

Application Deadline: December 3, 2014; Openings Are Limited!

Selected applicants will attend this two-day program to receive training from veteran advocates and AAN staff who will bring you up-to-date on recent issues. Then participants will go to the Hill for face-to-face meetings with congressional members and their staffs. The Academy will cover travel expenses and hotel accommodations. There is a general registration fee of $150, or $50 for residents, fellows, and members residing in the Washington, DC, area. Space fills quickly and a record number of AAN members attended last March, so apply today at AAN.com/view/2015NOH.
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.

Open Payments Data Released to the Public
The Centers for Medicare and Medicaid Services (CMS) has launched the Open Payments System online database. Now, the public can review the payments physicians and teaching hospitals receive from drug and medical device manufacturers. According to CMS, physicians and teaching hospitals received $3.5 billion between August 2013 and December 2013.

You should review the Open Payments database at CMS.gov/OpenPayments/index.html to see what was reported about you. If you find that there are data inaccuracies, you must contact the drug and medical device manufacturer directly as CMS will not get involved in these disputes. The AAN, however, wants to hear from our members. Please contact us at abecker@aan.com to share your experience or concerns with your data in the Open Payments database. Also, if you have not registered to review your data in Open Payments, you have until December 31. We urge you to do this so that you will be able to flag and correct any errors before the next data release in 2015.

The American Medical Association has provided some customizable talking points at http://ow.ly/CGokS for physicians to use in responding to inquires about the Open Payments data that we encourage you to review.

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Breakthroughs in Neurology

January 23–25, 2015
Phoenix, AZ

NEW AAN Conference

Translating Today’s Discoveries into Tomorrow’s Clinic
- 6 topic-intensive tracks
- 2 plenary sessions focusing on year-in-review of science and education and controversial issues
- Maintenance of Certification Exam Preparation Course
- 28.25 CME credits

Early Registration: December 19, 2014

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Plan Your January Neurology Getaway Today!

January 23 through 25, 2015, at the picturesque Pointe Hilton Tapatio Cliffs Resort in Phoenix, AZ, for an informative and rewarding weekend of neurology and earn up to 28.25 CME credits. And, if you act by December 19, you can save with significant early registration discounts. Learn more and register now at AAN.com/view/breakthroughs.

Highlights:

- Choose from six in-depth tracks—multiple sclerosis, stroke, epilepsy, headache, geriatric neurology, and sleep disorders—which combine an education course with an Integrated Neuroscience Session featuring invited speakers.

- Learn from expert faculty at evening plenary sessions:
  - Neurology Year in Review features the best science and education from the past year
  - Controversies in Neurology features a debate format with two speakers arguing one side of a current and controversial topic in neurology, followed by a rebuttal

- Prepare for your ABPN maintenance of certification exam and sharpen your skills on key topic areas in neurology by attending the full-day Maintenance of Certification Exam Preparation Course on Sunday, January 25—and earn 7.5 CME credits. See below for further details.

Remember, the deadline for the early registration discount is December 19, 2014. Registrations received after this date will be charged an additional fee. Make your plans today at register now at AAN.com/view/breakthroughs.

New Maintenance of Certification Exam Preparation Course

A new Maintenance of Certification Exam Preparation Course will debut at the Breakthroughs in Neurology conference on Sunday, January 25, 2015. The course provides 7.5 CME and is designed specifically for anyone preparing for board recertification in neurology. The program agenda includes eight 45-minute presentations by experts in the areas of neurology that are heavily weighted on the ABPN examination and those areas that have recently been added to the examination. Registered attendees will have the opportunity to take a pre-test in order to identify areas that require focused study and follow-up evaluation of improvement.

In addition, representatives from the ABPN and AAN will explain the new requirements for admission to the maintenance of certification examination and enrollment in the continuous maintenance of certification (C-MOC) after recertification. Learn more at AAN.com/view/breakthroughs.

The Pointe Hilton Tapatio Cliffs Resort, set in the granite bluffs of the Phoenix North Mountain Preserve, is a Spanish Mediterranean oasis overlooking Greater Phoenix. Many outdoor activities and attractions surround this natural haven. Relax at the Falls Water Village with its 40-foot waterfall, two massive free-form pools, a 138-foot enclosed waterslide—and plenty of sun-drenched terraces for lounging.
In treating patients with relapsing forms of MS

PROVEN EFFICACY, ONCE-DAILY

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.

AUBAGIO is available in 14 mg and 7 mg tablets.
SIGNIFICANT IMPACT ON DISABILITY PROGRESSION WITH AUBAGIO 14 mg

8 out of 10 patients were free of sustained disability progression at week 108 with AUBAGIO® (teriflunomide) 14 mg.

AUBAGIO 7 mg did not achieve statistical significance

- 17.3%, 18.6%, and 23.7% of patients experienced sustained disability progression at week 108 with AUBAGIO 14 mg, AUBAGIO 7 mg, and placebo, respectively (AUBAGIO 7 mg did not achieve statistical significance)

- A significant reduction in sustained disability progression was observed in 30% of patients treated with AUBAGIO 14 mg (P=0.03) versus placebo

  – AUBAGIO 7 mg (P=0.08) did not achieve a statistically significant reduction versus placebo

*In the double-blind, placebo-controlled Teriflunomide Multiple Sclerosis Oral (TEMSO) study, 1088 patients with relapsing forms of MS were randomized to receive AUBAGIO 14 mg (n=359), AUBAGIO 7 mg (n=366), or placebo (n=363) once daily for 108 weeks.

1 Sustained disability progression was defined as at least a 1-point increase from baseline Expanded Disability Status Scale (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.

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. Perform accelerated elimination 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 coadministering AUBAGIO with other potentially hepatotoxic drugs; monitor patients who develop symptoms suggestive of hepatic dysfunction (eg, unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine). If drug-induced liver injury is suspected, discontinue use of AUBAGIO, start accelerated elimination, and monitor liver tests weekly until normalized.

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. Women who become pregnant while taking AUBAGIO may enroll in the AUBAGIO pregnancy registry by calling 1-800-745-4447, option 2.

Teriflunomide is eliminated slowly from the plasma—it takes an average of 8 months, or up to 2 years in some patients, 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.

† Sustained disability progression was defined as at least a 1-point increase from baseline Expanded Disability Status Scale (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.

‡ In the double-blind, placebo-controlled Teriflunomide Multiple Sclerosis Oral (TEMSO) study, 1088 patients with relapsing forms of MS were randomized to receive AUBAGIO 14 mg (n=359), AUBAGIO 7 mg (n=366), or placebo (n=363) once daily for 108 weeks.

§ Significant reduction in sustained disability progression was observed in 30% of patients treated with AUBAGIO 14 mg (P=0.03) versus placebo.
SIGNIFICANT IMPACT ON DISEASE ACTIVITY
WITH AUBAGIO 14 mg\(^2,3\)

61% of patients
had zero relapses\(^2,3^*\)
over the course of the trial with AUBAGIO 14 mg

- AUBAGIO 14 mg and 7 mg (P<0.001) significantly reduced annualized relapse rate (ARR) by 31% versus placebo\(^1\)
- 60.6%, 57.8%, and 49.3% of patients remained relapse-free at week 108 with AUBAGIO 14 mg, AUBAGIO 7 mg, and placebo, respectively\(^1,3\)
- Consistent reductions of ARR noted in patient subgroups defined by sex, age, prior MS therapy, and baseline disease activity\(^1\)

**Safety profile evaluated in the TEMSO study\(^1,2^*\)**

- The most frequent adverse events (AEs) (incidence ≥10% and at a ≥2% greater incidence than placebo) with AUBAGIO 14 mg, AUBAGIO 7 mg, and placebo, respectively, were alanine aminotransferase (ALT) increased (14%, 12%, and 7%), alopecia (13%, 10%, and 3%), diarrhea (18%, 15%, and 9%), influenza (12%, 9%, and 10%), nausea (14%, 9%, and 7%), and paresthesia (10%, 9%, and 8%)

\(^1\)The corresponding hazard reduction was 28.1% (P=0.003) for the AUBAGIO 14 mg group and 24.4% (P=0.0104) for the AUBAGIO 7 mg group.\(^2\)

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 skin 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.

Transient acute renal failure and treatment-emergent hyperkalemia, as well as increased renal uric acid clearance, have been reported with AUBAGIO. Monitor renal function and potassium if symptoms of acute renal failure or hyperkalemia appear.

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.

Adverse Reactions: The most frequent adverse reactions (≥10% and ≥2% greater than placebo) with AUBAGIO 7 mg and 14 mg and placebo, respectively, were ALT increased (12% and 14% vs 7%), alopecia (10% and 13% vs 3%), diarrhea (15% and 18% vs 9%), influenza (9% and 12% vs 10%), nausea (9% and 14% vs 7%), and paresthesia (9% and 10% vs 8%)

\(^2\)The corresponding hazard reduction was 28.1% (P=0.003) for the AUBAGIO 14 mg group and 24.4% (P=0.0104) for the AUBAGIO 7 mg group.\(^3\)

KeepPlease see Brief Summary of Full Prescribing Information, including boxed WARNING, on the following pages.
AUBAGIO—THE ONCE-DAILY, ANY TIME OF DAY MS TABLET

- One tablet, once a day
- Can be taken any time, any place, with or without food
- No titration needed—patients can start and continue with the same dose
- Before initiating AUBAGIO® (teriflunomide) therapy, tests are recommended
  - Before starting therapy, exclude pregnancy, obtain transaminase and bilirubin levels (within 6 months), obtain complete blood cell count (CBC) (within 6 months), screen for latent tuberculosis infection with tuberculin skin test, and check blood pressure. During therapy, monitor alanine aminotransferase (ALT) levels at least monthly for 6 months and check blood pressure periodically.

$0 co-pay
for eligible commercially insured patients

GET STARTED TODAY

The AUBAGIO Start form acts as both a prescription and enrollment for patient support.

To learn more, contact MS One to One® at 1-855-MSOne2One (1-855-676-6326), visit the MS One to One HCP Portal, or speak with your Genzyme MS representative.

To start or switch your patients today, visit AubagioHCP.com.

Please see Important Safety Information on previous pages and Brief Summary of Full Prescribing Information, including boxed WARNING regarding hepatotoxicity and use in pregnancy, on the following pages.

AUBAGIO®
(teriflunomide) tablets for oral administration

Rx Only

Brief Summary of Prescribing Information

WARNING: 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 teriflunomide 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 the first 6 months after starting AUBAGIO [see Warnings and Precautions (5.1)]. If a 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. Pregnancy must be avoided during AUBAGIO treatment or prior to 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 [see Clinical Studies (14) in the full prescribing information].

2. DOSAGE AND ADMINISTRATION

The recommended dose of AUBAGIO is 7 mg or 14 mg orally once daily. AUBAGIO can be taken with or without food.

Monitoring to assess safety

- 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)].
- Obtain a complete blood cell count (CBC) within 6 months before the initiation of treatment with AUBAGIO. Further monitoring should be based on signs and symptoms of infection [see Warnings and Precautions (5.4)].
- Prior to initiating AUBAGIO, screen patients for latent tuberculosis infection with a tuberculin skin test [see Warnings and Precautions (5.4)].
- Check blood pressure before start of AUBAGIO treatment and periodically thereafter [see Warnings and Precautions (5.9)].

4. CONTRAINDICATIONS

4.1. Severe Hepatic Impairment

Patients with severe hepatic impairment [see Warnings and Precautions (5.1)].

4.2. Patients Who Are Pregnant or Women of Childbearing Potential Not Using Reliable Contraception

AUBAGIO may cause fetal harm when administered to a pregnant woman. In animal studies, teriflunomide has been shown to be selectively teratogenic and embryocidal in multiple species when administered during pregnancy at doses less than those used clinically. Nonclinical studies indicate further that the intended pharmacologic action of the drug is involved in the mechanism of developmental toxicity [see Use in Specific Populations (8.1)].

AUBAGIO is contraindicated in women who are pregnant or women of child-bearing potential not using reliable contraception. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus. If pregnancy occurs during treatment, the drug should be immediately discontinued and an alternative treatment should be started.

5. WARNINGS AND PRECAUTIONS

5.1 Hepatotoxicity

Severe liver injury including fatal liver failure and dysfunction has been reported in some 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. 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) before initiating treatment, should not normally 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 14/429 (3%) and 21/415 (5%) of patients on teriflunomide 7 mg and 14 mg, respectively, and 17/421 (4%) of patients on 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, ALT elevation was greater than three times the ULN on two consecutive tests. AUBAGIO was discontinued and patients underwent an accelerated elimination procedure [seeWARNINGS 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.

One patient in the controlled trials developed ALT 32 times the ULN and jaundice 5 months after initiation of AUBAGIO 14 mg treatment. The patient was hospitalized for 5 weeks and recovered after plasmapheresis and cholestyramine accelerated elimination procedure. Teriflunomide-induced liver injury in this patient could not be ruled out.

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, fatigue, anorexia, or jaundice and/or dark urine. If liver injury is suspected to be AUBAGIO-induced, discontinue teriflunomide and start an accelerated elimination procedure [see WARNINGS and Precautions (5.3)] and monitor liver tests weekly until normalized. If teriflunomide-induced liver injury is unlikely because some other probable cause has been found, resumption of teriflunomide therapy may be considered.

5.2 Use of Contraception

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 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 the physician immediately for pregnancy testing and, if positive, 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 [see Warnings and Precautions (5.3)].

Upon discontinuing AUBAGIO, it is recommended that all women of childbearing potential undergo an accelerated elimination procedure. Women receiving AUBAGIO treatment who wish to become pregnant must discontinue AUBAGIO and undergo an accelerated elimination procedure, which includes verifying that teriflunomide plasma concentrations less than 0.02 mg/L (0.02 mcg/mL). 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 (5.3), and Use in Specific Populations (8.1)].

5.3 Procedure for Accelerated Elimination of Teriflunomide

Teriflunomide is eliminated slowly from the plasma. Without an accelerated elimination procedure, it takes on average 8 months to reach plasma concentrations less than 0.02 mg/L, although because of individual variations in drug clearance it may take as long as 2 years. An accelerated elimination procedure could be used at any time after discontinuation of AUBAGIO. Elimination can be accelerated by either of the following procedures:

- Administration of cholestyramine 8 g every 8 hours for 11 days. If cholesteramine g three times a day is not well tolerated, cholestyramine 4 g three times a day can be used.
- Administration of 50 g oral activated charcoal powder every 12 hours for 11 days. If both elimination procedures are poorly tolerated, treatment days do not need to be consecutive unless there is a need to lower teriflunomide plasma concentration rapidly.

At the end of 11 days, both regimens successfully accelerated teriflunomide elimination, leading to more than 98% decrease in teriflunomide plasma concentrations. Use of the accelerated elimination procedure may potentiate disease activity if treatment is stopped. Use of the accelerated elimination procedure may result in return of disease activity if the patient had been responding to AUBAGIO treatment.

5.4 Bone Marrow Effects/Immunosuppression Potential/Infections

White Blood Cell (WBC) count decrease

A decrease in white blood cell (WBC) count of approximately 15% (mainly neutrophils) and lymphocytes and in platelet count of approximately 10% was observed in placebo-controlled trials with 7 mg and 14 mg of AUBAGIO. 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 <1.5×10^9/L was observed in 10% and 15% of patients on AUBAGIO 7 mg and 14 mg, respectively, compared with 5% of patients on placebo: lymphocyte count <0.8×10^9/L was observed in 7% and 10% of patients on AUBAGIO 7 mg and 14 mg, respectively, compared with 5% of patients on placebo. No cases of serious pancytopenia were reported in premarketing clinical trials of AUBAGIO but rare cases of pancytopenia, aplastic anemia, and thrombocytopenia have been reported in the postmarketing setting with leflunomide. A similar risk would be expected for teriflunomide [see Clinical Pharmacology (12.3) in the full prescribing information].

Obtain a complete blood cell count (CBC) within 6 months before the initiation of treatment with AUBAGIO. Further monitoring should be based on signs and symptoms suggestive of bone marrow suppression.

Risk of Infection / Tuberculosis Screening

Patients with active acute or chronic infections should not start treatment until the infection(s) is resolved. It is vital for patients with severe infection to consider suspending treatment with AUBAGIO and using an accelerated elimination procedure. Reassess the benefits and risks prior to resumption of therapy. Instruct patients receiving AUBAGIO to report symptoms of infections to a physician.

AUBAGIO is not recommended for patients with severe immunodeficiency, bone marrow disease, or severe, uncontrolled infections. Medications like teriflunomide that have immunosuppression potential may cause patients to be more susceptible to infections, including opportunistic infections.

In placebo-controlled studies of AUBAGIO, no overall increase in the risk of serious infections was observed with teriflunomide 7 mg (1.4%) or 14 mg (2.2%) compared to placebo (2.1%).
receiving leflunomide, especially Pneumocystis jiroveci, risk for peripheral neuropathy discontinuation. The other cases of peripheral neuropathy did not resolve with continued patients with polyneuropathy, one on each dose; one of them recovered following treatment AUBAGIO, respectively, compared with 0% on placebo. Treatment was discontinued in 2 AUBAGIO than in patients taking placebo. In one 108-week placebo-controlled study in 1086 Malignancy AUBAGIO should be considered when contemplating administration of a live vaccine after Vaccination has not been studied in patients with a positive tuberculosis screen, and the safety of AUBAGIO in individuals with latent tuberculosis infection is unknown. For patients testing positive in tuberculosis screening, treat by standard medical practice prior to therapy with AUBAGIO. No clinical data are available on the efficacy and safety of vaccinations in patients taking AUBAGIO. Vaccination with live vaccines is, however, not recommended. The long half-life of AUBAGIO should be considered when contemplating administration of a live vaccine after stopping AUBAGIO.

Malignancy

The risk of malignancy, particularly lymphoproliferative disorders, is increased with the use of some immunosuppressive medications. There is a potential for immunosuppression with teriflunomide. No apparent increase in the incidence of malignancies and lymphoproliferative disorders was reported in the AUBAGIO clinical trials, but larger and longer-term studies would be needed to determine whether there is an increased risk of malignancy or lymphoproliferative disorders with AUBAGIO. 

5.5 Peripheral Neuropathy

In placebo-controlled studies, peripheral neuropathy, including both polyneuropathy and mononeuropathy (e.g., carpal tunnel syndrome), was reported more frequently in patients taking AUBAGIO than in patients taking placebo. In one 108-week placebo-controlled study in 1086 patients taking AUBAGIO, the incidence of peripheral neuropathy confirmed by nerve conduction studies was 1.2% (4 patients) and 1.9% (6 patients) on 7 mg and 14 mg of AUBAGIO, respectively, compared with 0% on placebo. Treatment was discontinued in 2 patients with polyneuropathy, one on each dose, one of them recovered following treatment discontinuation. The other cases of peripheral neuropathy did not resolve with continued treatment. There have also been reports of peripheral neuropathy in patients receiving leflunomide. Age older than 60 years, concomitant neurotoxic medications, and diabetes may increase the risk for a peripheral neuropathy. If a patient taking AUBAGIO develops symptoms consistent with peripheral neuropathy, such as bilateral numbness or tingling of hands or feet, consider discontinuing AUBAGIO therapy and performing an accelerated elimination procedure [see Warnings and Precautions (5.3)].

5.6 Acute Renal Failure

In placebo-controlled trials, 10 of 844 (1.2%) of AUBAGIO-treated subjects had transient acute renal failure with a creatinine measurement increased by 100% or more of their baseline serum creatinine, compared to 0 of 421 placebo-treated subjects. Seven of the 10 subjects had a nadir serum creatinine level of >50% of baseline within 30 days of the last dose of AUBAGIO. In each of the 10 subjects, the serum creatinine level was normal on the next reported measurement (6–48 days from the increase in creatinine) with continued teriflunomide use. These increased creatinine measurements occurred between 12 weeks and 2 years after first dose of teriflunomide. Of the 6 subjects with available serum potassium measurements, 3 (50%) had hyperkalemia (measurements of 6.7, >7.3, and >7.3 mmol/L). No associated symptoms were documented. AUBAGIO causes increases in renal uric acid clearance with mean decreases in serum uric acid of 20–30%. Acute uric acid nephropathy is a likely explanation for the cases of transient acute renal failure seen with teriflunomide. Although symptoms associated with acute uric acid nephropathy, such as flank pain, were not reported, this information was not systematically collected. No inciting factors, such as dehydration, exercise, or increase in physical activity in the 30 days prior to the adverse event were reported, but this information was not systematically collected.

5.7 Hyperkalemia

In placebo-controlled trials, treatment-emergent hyperkalemia >7.0 mmol/L occurred in 8/829 (1.0%) of teriflunomide-treated subjects, compared to 1/414 (0.2%) of placebo-treated subjects. Two teriflunomide-treated subjects had hyperkalemia >7.0 mmol/L with acute renal failure. Possible causes in other cases were not documented. Check serum potassium level in AUBAGIO-treated patients with symptoms of hyperkalemia or with acute renal failure.

5.8 Skin Reactions

Rare cases of Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in patients with rheumatoid arthritis receiving leflunomide. A similar risk would be expected for teriflunomide [see Clinical Pharmacology (12.2) in the full prescribing information]. If a patient taking AUBAGIO develops any of these conditions, stop AUBAGIO therapy and perform an accelerated elimination procedure [see Warnings and Precautions (5.3)].

5.9 Blood Pressure Increase

In placebo-controlled studies, mean change from baseline in systolic blood pressure was 2.9 mmHg and 2.7 mmHg for AUBAGIO 7 mg and 14 mg, respectively, and -1.3 mmHg for placebo. The change from baseline in diastolic blood pressure was 1.4 mmHg and 1.3 mmHg for AUBAGIO 7 mg and 14 mg, respectively, and -0.9 mmHg for placebo. Hypertension was reported as an adverse reaction in 4% of patients treated with teriflunomide 7 mg or 14 mg of AUBAGIO, compared with 2% on placebo. Check blood pressure before start of AUBAGIO treatment and periodically thereafter. Elevated blood pressure should be appropriately managed during treatment with AUBAGIO.

5.10 Respiratory Effects

Intestinal lung disease and worsening of pre-existing intestinal lung disease have been reported during treatment with leflunomide. A similar risk would be expected for teriflunomide [see Clinical Pharmacology (12.3) in the full prescribing information]. Intestinal lung disease may be fatal. Intestinal lung disease may occur acutely at any time during therapy and has a variable presentation of 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)].

5.11 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 teriflunomide 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 [see Contraindications (4.2) and Warnings and Precautions (5.4)]
- Peripheral Neuropathy [see Warnings and Precautions (5.5)]
- Acute Renal Failure [see Warnings and Precautions (5.6)]
- Hyperkalemia [see Warnings and Precautions (5.7)]
- Serious Skin Reactions [see Warnings and Precautions (5.8)]
- Blood Pressure Effects [see Warnings and Precautions (5.9)]
- Respiratory Effects [see Warnings and Precautions (5.10)]

The most frequent adverse reactions for AUBAGIO (incidence ≥10% and ≥2% greater than placebo) in the placebo-controlled studies were ALT increased, alopecia, diarrhoea, influenza, nausea, and pancreatitis. Alopecia was the most common cause of discontinuation because of adverse events in controlled clinical trials as compared to placebo (0.5% and 1.4% of patients on AUBAGIO 7 mg and 14 mg, respectively, and 0% on placebo).

If desired, teriflunomide can be rapidly cleared from the body by the use of an accelerated elimination procedure [see Warnings and Precautions (5.3)].

6.1 Clinical Trial Experience

A total of 844 patients on teriflunomide (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 MS (RMS). Approximately 72% of patients were female and the mean age was 38 years. Study 1 was a 108-week placebo-controlled clinical study in 1086 RMS patients treated with teriflunomide 7 mg (n=368), teriflunomide 14 mg (n=358), or placebo (n=360).

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.

Table 1. Adverse Reactions in Study 1 (occurring in ≥2% of patients, and reported for teriflunomide 7 mg or 14 mg at ≥2% higher rate than for placebo)

<table>
<thead>
<tr>
<th>Preferred Term (%)</th>
<th>PRIMARY SYSTEM ORGAN CLASS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teriflunomide</td>
<td>14 mg (N=358)</td>
</tr>
<tr>
<td>INFECTIONS AND INFESTATIONS</td>
<td></td>
</tr>
<tr>
<td>Influenza</td>
<td>12%</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>9%</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>8%</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>6%</td>
</tr>
<tr>
<td>Cystitis</td>
<td>4%</td>
</tr>
<tr>
<td>Gastroenteritis viral</td>
<td>4%</td>
</tr>
<tr>
<td>Oral herpes</td>
<td>4%</td>
</tr>
<tr>
<td>BLOOD AND LYMPHATIC SYSTEM DISORDERS</td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>4%</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>1%</td>
</tr>
<tr>
<td>IMMUNE SYSTEM DISORDERS</td>
<td></td>
</tr>
<tr>
<td>Seasonal allergy</td>
<td>3%</td>
</tr>
<tr>
<td>PSYCHIATRIC DISORDERS</td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>4%</td>
</tr>
<tr>
<td>NEUROV SYSTEM DISORDERS</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>19%</td>
</tr>
<tr>
<td>Parasthesia</td>
<td>10%</td>
</tr>
<tr>
<td>Sciatica</td>
<td>3%</td>
</tr>
<tr>
<td>Burning sensation</td>
<td>3%</td>
</tr>
<tr>
<td>Cardiac tunnel syndrome</td>
<td>3%</td>
</tr>
<tr>
<td>EYE DISORDERS</td>
<td></td>
</tr>
<tr>
<td>Vision blurred</td>
<td>3%</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>1%</td>
</tr>
<tr>
<td>CARDIAC DISORDERS</td>
<td></td>
</tr>
<tr>
<td>Palpitations</td>
<td>2%</td>
</tr>
</tbody>
</table>
Table 1: Adverse Reactions in Study 1 (occurring in \( \geq 2\% \) of patients, and reported for teriflunomide 7 mg or 14 mg at \( \geq 2\% \) higher rate than for placebo) (continued)

<table>
<thead>
<tr>
<th>PRIMARY SYSTEM ORGAN CLASS</th>
<th>Preferred Term (%)</th>
<th>Teriflunomide 14 mg (N=358)</th>
<th>Teriflunomide 7 mg (N=368)</th>
<th>Placebo (N=360)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VASCULAR DISORDERS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>4%</td>
<td>4%</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td><strong>GASTROINTESTINAL DISORDERS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>18%</td>
<td>15%</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>14%</td>
<td>9%</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain upper</td>
<td>6%</td>
<td>5%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Toothache</td>
<td>4%</td>
<td>4%</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>1%</td>
<td>2%</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td><strong>SKIN AND SUBCUTANEOUS TISSUE DISORDERS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alopecia</td>
<td>13%</td>
<td>10%</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Acne</td>
<td>5%</td>
<td>1%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>3%</td>
<td>4%</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td><strong>MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>4%</td>
<td>5%</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Myalgia</td>
<td>5%</td>
<td>4%</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td><strong>INVESTIGATIONS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alanine aminotransferase</td>
<td>increased</td>
<td>14%</td>
<td>12%</td>
<td>7%</td>
</tr>
<tr>
<td>Gamma-glutamyltransferase</td>
<td>increased</td>
<td>3%</td>
<td>5%</td>
<td>1%</td>
</tr>
<tr>
<td>Aspartate aminotransferase</td>
<td>increased</td>
<td>3%</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Weight decreased</td>
<td>2%</td>
<td>3%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>Neutrophil count decreased</td>
<td>2%</td>
<td>3%</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td>White blood cell count decreased</td>
<td>1%</td>
<td>3%</td>
<td>0%</td>
<td></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 teriflunomide and cardiovascular death has not been established.

Hypophosphatemia
In clinical trials, 18% of teriflunomide-treated subjects had mild hypophosphatemia (\( \geq 0.6 \) mmol/L and < lower limit of normal), compared to 9% of placebo-treated subjects. 5% of teriflunomide-treated subjects had moderate hypophosphatemia (\( 0.3 \) mmol/L and < 0.6 mmol/L), compared to 1% of placebo-treated subjects. No subject in either treatment group had a serum phosphorus \( < 0.3 \) mmol/L.

7. DRUG INTERACTIONS

Effect of teriflunomide on CYP2C8 substrates
There was an increase in mean CYP2C8 T max and AUC (1.7- and 2.4-fold, respectively), following repeated doses of teriflunomide and a single dose of 0.25 mg repaglinide, suggesting that teriflunomide is an inhibitor of CYP2C8 in vivo. The magnitude of this inhibition could be higher at the recommended repaglinide dose. Therefore, monitoring patients with concomitant use of drugs metabolized by CYP2C8, such as repaglinide, pioglitazone, or rosiglitazone is recommended as they may have higher exposure.

Effect of teriflunomide on warfarin
A 25% decrease in peak international normalized ratio (INR) was observed when teriflunomide was coadministered with warfarin as compared with warfarin alone. Therefore, when warfarin is coadministered with teriflunomide, close INR follow-up and monitoring is recommended.

Effect of teriflunomide on oral contraceptives
There was an increase in mean ethinylestradiol C T max and AUC C 0–24, (1.58- and 1.54-fold, respectively) and levonorgestrel C T max and AUC C 0–24, (1.33- and 1.41-fold, respectively) following repeated doses of teriflunomide. Consideration should be given to the type or dose of oral contraceptives used in combination with teriflunomide.

Effect of teriflunomide on CYP1A2 substrates
Repeated doses of teriflunomide decreased mean C T max and AUC of caffeine (CYP1A2 substrate) by 18% and 55% respectively, suggesting that teriflunomide may be in vivo a weak inducer of CYP1A2. Therefore, patients should be monitored when teriflunomide is coadministered with drugs metabolized by CYP1A2 (such as duloxetine, alprazolam, theophylline, and tizanidine), as the efficacy of such drugs could be reduced.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Pregnancy Category X [see Contraindications (4.2) and Warnings and Precautions (5.3)]
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 MRHD. 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 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 (limb 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, axial skeletal, heart, and great vessel). Supplementation with exogenous uridine reduced the teratogenic effects in pregnant mice, suggesting 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.
Enhanced Registration Options

and “Silver Registration Package.” The Silver Registration Package allows you the opportunity to purchase all of your education courses for one flat rate. The Gold Registration Package includes the Silver Registration Package plus Annual Meeting On Demand, the AAN’s comprehensive digital library of the 2015 meeting featuring more than 500 hours of presentations and syllabi summaries from more than 160 programs that will be offered.

The itinerary planner available this month should make planning your week easier. Enhanced features for 2015 allow you to browse all programs and events by topic or keyword, view your schedule, and quickly add personal events and scientific sessions when the schedule is available in February.

“We’re thrilled to be bringing the 2015 meeting to the US capital,” said Meeting Management Committee Chair Stefan M. Pulst, MD, FAAN. “The 2014 meeting in Philadelphia broke attendance records and brought together the world’s best minds in neurology to experience exceptional education and breakthrough research, and take part in unlimited networking opportunities. With the lineup of offerings we’re planning for 2015, I have no doubt this year’s meeting will be just as spectacular.”

Added Pulst, “I hope you’ll join us—either for a few days, or all eight days—to take part in top CME opportunities in your subspecialty. Discover and share the latest scientific research, meet up with old friends, or make new, lasting connections. I look forward to seeing you in Washington, DC!”

Look for online registration to be available later this month at AAN.com/view/AM15.*

* Skills Workshops, Skills Pavilions, and Leadership Courses excluded from Gold and Silver Package pricing. Attendee must identify courses to be included as part of Gold and Silver Packages. Courses are subject to closure due to reaching maximum capacity.

** Total hours available subject to speakers’ permission.
Submit Abstracts for 2015 Emerging Science Program

Researchers with work conducted after the AAN abstract deadline have until February 3, 2015, to submit abstracts for consideration for the 2015 Annual Meeting Emerging Science program. Abstracts may be submitted online at AAN.com/view/15Abstracts.

The program highlights major research conducted after the abstract deadline of October 27. Key aspects of the research must have been conducted after the deadline. Work should be of major scientific importance, warranting expedited presentation and publication. The fee for abstract submission is $100 for AAN members and $200 for nonmembers. Junior and Student members may submit abstracts at no charge. The fee is based on the first author’s status.

For more information, contact science@aan.com or (612) 928-6088.

Call for Entries

Win $1,000 and a Trip to Washington, DC!

Submit a video to the Neuro Film Festival YouTube channel that makes the case for why more research is needed to find cures for Alzheimer’s disease, migraine, concussion, multiple sclerosis, Parkinson’s disease, epilepsy, ALS, stroke, and other brain diseases.

DEADLINE: February 25, 2015

NeuroFilmFestival.com
Guideline Examines Diagnosis, Treatment of Limb-Girdle, Distal Dystrophies

The AAN, in full collaboration with the American Association of Neuromuscular & Electrodiagnostic Medicine, has published the first of four evidence-based guidelines that will comprise a series of muscle disease guidelines. “Diagnosis and Treatment of Limb-Girdle and Distal Dystrophies” was published in the October 14, 2014, print issue of Neurology®. It is the first comprehensive evidence-based review of the scientific studies on diagnosis and treatment of limb-girdle muscular dystrophy (LGMD) and distal muscular dystrophy (distal MD).

“LGMD and distal MD are two diverse groups of disorders that many providers do not regularly see,” said lead author Pushpa Narayanaswami, MD, FAAN. “These types of rare muscle diseases can be difficult to diagnose. This complexity and unfamiliarity can lead to delays in diagnosis, inappropriate testing, and failure to screen for important comorbidities. A systematic approach to diagnosis and management can help neurologists focus treatment.”

Clinicians may avoid unnecessary tests or treatments by gathering key information needed for diagnosis, which includes knowledge of the clinical features that point to a certain phenotype such as patterns of muscle weakness, as well as information from blood tests, muscle biopsy findings, and evidence of cardiac and respiratory involvement, all of which can help direct genetic testing. “The guideline includes algorithms that provide a systematic means of directing the steps to making a diagnosis,” said senior author Anthony A. Amato, MD, FAAN.

The guideline also offers recommendations on what to consider for management of these disorders, including typical comorbidities and complications, and recommends clinicians refer patients with these disorders to multidisciplinary clinics designed specifically to care for patients with LGMD, distal MD, and other neuromuscular disorders in order to provide efficient and effective long-term care.

This guideline has been endorsed by the American Academy of Physical Medicine and Rehabilitation, the Child Neurology Society, the Jain Foundation, and the Muscular Dystrophy Association. Development of this guideline was funded in part by a grant from the Centers for Disease Control and Prevention.

Read the guideline and access PDF summaries for clinicians and patients, a clinical case example, and a slide presentation set at AAN.com/guidelines. For more information, email Julie Cox at jcox@aan.com or call (612) 928-6069.

Pushpa Narayanaswami, MBBS, DM, FAAN

Anthony A. Amato, MD, FAAN

Are You Getting Your AANe-news?

Don’t miss the latest news headlines from your Academy! As an exclusive member benefit, you should be receiving AANe-news™ the second and fourth Wednesday of each month if your email address is on file. If not, be sure to set your email filter to accept mailer@aan.com as a friendly address. Or update your email address at AAN.com/MemberProfile.

It’s Not Spam... It’s AANe-news!
Seeking Common Ground with CMS

Continued from page 3

the AAN’s future quality measure and guideline development efforts; support the AAN’s advocacy efforts; and demonstrate a commitment to improve the value of neurology.

To be sure, such a registry represents a significant financial investment for the AAN. Over three years, the cost to build and maintain the registry will range between $1.9–2.5 million. But the Boards of Directors believe this investment aligns with the AAN’s mission, goals, and its vitally important objective to demonstrate the value of neurology. In the year-long process to reach this decision, members of the Practice Committee thoroughly researched and discussed the need for a registry, the target audience, the likelihood of participation, alternative sources of quality and cost data, and business models. While there are still important challenges, such as encouraging member participation and adapting the technology to interact with diverse electronic health record products, the majority of our specialty society colleagues have found the data useful and meaningful on many levels.

We concluded the meeting by thanking CMS for supporting physicians who perform care coordination by agreeing to pay for these services in 2015 using the chronic care management codes. As principal care physicians, our role is often to coordinate all aspects of our patients’ care. We urged CMS to move forward with their proposal to eliminate the global surgical periods because it’s about fairness. Physicians should be paid for work they perform and document.

I view this meeting as a significant success because we were able to spend time on several issues of critical importance to our members. The meeting included several CMS senior officials from quality reporting, physician reimbursement, and the accountable care organization program. This spoke to me of greater familiarity with the Academy and a steadily growing and productive relationship with CMS.

Timothy A. Pedley, MD, FAAN
President, AAN
tpedley@aan.com
NEW! Beginning January 1, 2015: Additional MOC and CME Programs Are FREE* with AAN Membership!

Our members asked, and we listened! In a continued effort to support our members across their careers and make membership in the AAN an even more invaluable part of the neurology profession, the AAN is pleased to announce that beginning January 1, 2015**, the following online learning programs—designed specifically to help members take the necessary steps toward fulfilling their MOC requirements as mandated by the ABPN—will be included FREE* with AAN membership:

- **NeuroPiSM**: Provides 20 CME credits per module; designed to help neurologists meet the ABPN performance in practice clinical component requirements for maintenance of certification
- **NeuroSAE**: Provides 8 self-assessment CME credits per exam; designed to help neurologists meet the ABPN self-assessment requirement for maintenance of certification
- **NeuroLearnSM**: Provides 1–2 CME credits per course; designed to address relevant clinical and practice topics while offering a range of CME credits

Learn more at AAN.com/view/MOC.

* $0 purchase price excludes Student and Nurse Practitioner/Physician Assistant members at the lower dues rate. Free access is limited to one course per program at a time.

** This new AAN membership benefit will not go into effect until January 1, 2015; until then, you may purchase any of these programs using your current AAN member discount. No refunds will be given after January 1, 2015, for programs purchased before this date.

Meet Your Year-end CME Needs Quickly, Conveniently with Exclusive AAN Online Learning Programs

If you need important CME credits before the end of the year, then look no further than the AAN’s suite of exclusive online learning programs. These handy courses can be accessed from virtually anywhere—home or office—and allow you to meet your end-of-year CME needs, as well as take the necessary steps toward fulfilling your maintenance of certification (MOC) requirements, as mandated by the ABPN.

- **Annual Meeting On Demand Encore**
  This new and unique AAN online program expands on hot topics from the 2014 Annual Meeting—and offers two CME credits. The program’s flipped classroom teaching model allows participants to learn the foundational content online first, at their own pace, before attending a live session for an interactive discussion and application of the subject. Choose your favorite topic—or register for the entire series and get the third course for free! Available courses include: “Update in Spine Disorders” with live webinar scheduled for November 20, 2014; “Treatment Optimization for Relapsing MS” with recorded webinar; and “Sorting Through AEDs” with recorded webinar.

- **NeuroPiSM**
  This online performance improvement program meets the ABPN MOC Part 4 Performance in Practice clinical component requirements in addition to offering 20 CME credits. A new “Multiple Sclerosis: Symptoms Assessment” module is now available within the NeuroPi suite of excellent programs, all designed to help you improve your care strategies. Learn more about all of the available NeuroPi modules at AAN.com/view/NeuroPi. Available FREE with membership beginning January 1, 2015! See above for more information.

- **NeuroSAE**
  The AAN’s convenient online self-assessment examination assesses your knowledge of neurology to assist you in building your learning plan and compares your performance to other neurologists. A new Epilepsy Edition is now available featuring 150 questions based on the ABPN’s content outline for epilepsy medicine and offering eight self-assessment CME credits upon successful completion. Learn more about all of the available NeuroSAE modules at AAN.com/view/NeuroSAE. Available FREE with membership beginning January 1, 2015! See above for more information.

- **NeuroLearnSM**
  This exclusive multimedia suite of online education courses is designed to be taken at your own time and pace. These courses address relevant clinical neurology and timely practice topics, and offer up to two CME credits upon successful completion. The latest edition is “Sleep and the Practicing Neurologist: Mechanisms and Management.” Learn more about all of the available NeuroLearn editions at AAN.com/view/NeuroLearn. Available FREE with membership beginning January 1, 2015! See above for more information.
Continuum: Lifelong Learning in Neurology®
The AAN’s self-study journal provides up to 14 hours of AMA PRA Category 1 Credits™ per issue. Assess your knowledge online, on your mobile device, and in print. Continuum® is approved to meet the ABPN self-assessment and continuing medical education requirement for MOC. Available in print and online.

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Sports Neurology Topics Discussed on *Continuum* Audio

Concussion, neurologic emergencies in sports, peripheral nerve injuries in sports, and playing sports with neurologic conditions are among the topics discussed by experts in the new four-part *Continuum®* Audio series on sports neurology.

“With the continuing public interest in sports concussion, neurologists may appreciate this convenient format allowing them to have lively conversations with leading sports neurology experts,” said Daniel G. Larriviere, MD, JD, FAAN, host of this series. “The series also covers chronic traumatic encephalopathy and unusual sports-related neurologic conditions.”

The first two hours of the series are available this month; the second two hours will be available in December.

**Hour 1:**
- Definition of Concussion
  Christopher Giza, MD
- Diagnosis and Management of Sports Concussion
  Jeffrey S. Kutcher, MD
- Practice: Legal Issues in Return to Play After a Concussion
  Raman Malhotra, MD

**Hour 2:**
- Pediatric Issues in Sports Concussion
  Christopher Giza, MD
- Neurologic Emergencies in Sports
  Vernon B. Williams, MD
- Ethics
  Matthew Kirschen, MD, PhD

**Hour 3:**
- CTE and Other Long-term Sequelae
  Barry D. Jordan, MD
- Playing Sports with Neurologic Conditions
  Kevin E. Crutchfield, MD

**Hour 4:**
- Unusual Sports-related Neurologic Conditions
  Francis X. Conidi, MD, DO
- Peripheral Nerve Injuries in Sports
  Brian Hainline, MD, FAAN
- Exercise and Neurologic Disease
  Tad Dean Seifert, MD

*Continuum* Audio is an audio CME program based on discussions with the authors of articles published in *Continuum: Lifelong Learning in Neurology®*, the official CME journal of the AAN. *Continuum* Audio is available in multiple formats, including apps for iOS and Android devices. This program may be used to meet self-assessment and CME requirements for maintenance of certification as mandated by the American Board of Psychiatry and Neurology. To learn more and subscribe, visit audio-digest.org/continuum.
Reminder: November 20 Webinar Offers Update in Spine Disorders

The Annual Meeting On Demand Encore webinar featuring J.D. Bartleson, MD, FAAN; John Engstrom, MD, FAAN; and Charles Argoff, MD, is scheduled to take place on November 20, 2014, at 12:00 p.m. ET. The live webinar is the companion to the On Demand Encore recorded lecture “Update in Spine Disorders,” as presented during the 2014 Annual Meeting course “Neurology Update I.”

During the webinar, the faculty panel will present challenging cases and invite audience participation and questions. How do you assess spine disorders and address pain? Interact with the experts on evidence based clinical guidelines for patients with conditions affecting the lumbar spine.

Upon successful completion of both the recorded lecture and the webinar and submission of an assessment, participants will receive 2 CME credits toward their maintenance of certification requirements, as mandated by the American Board of Psychiatry and Neurology.

For those who can’t attend the live webinar, the recording will be accessible within the course. The course is accredited for three years.

To register for this and other Annual Meeting On Demand Encore programs, visit AAN.com/view/Encore.

UCNS Now Offers Clinical Neuromuscular Pathology Certification

The United Council for Neurologic Subspecialties (UCNS) is offering its first certification examination in clinical neuromuscular pathology.

Applications for the exam are available beginning November 1; the deadline to apply is February 16, 2015. The exam will be held the week of August 24 to 28, 2015. Clinical neuromuscular pathology is a subspecialty area of neurology defined by special competence in the interpretation of muscle and nerve pathology. It differs from neuropathology due to its focus on clinical management of neuromuscular disease.

For more information, visit UCNS.org or contact Todd Bulson at tbulson@ucns.org or (612) 928-6067.
Sixteen Members Selected for 2014–2015 Emerging Leaders Forum

The Academy has selected 16 AAN members from 267 interested candidates for the 2014–2015 Emerging Leaders Forum. This is the largest group yet to participate in the AAN’s highly competitive and innovative program designed to identify, orient, and cultivate talented, motivated young individuals into future Academy leaders.

The 10-month program will kick off this month at a meeting at the AAN Fall Conference in Las Vegas. Participants will be separated into two cohorts and will work on tasks, share experiences, learn, and network. Each cohort will be assigned a specific issue facing neurologists and be asked to investigate solutions to the problem. Each participant has been paired with a high-level AAN leader who will serve as a mentor throughout the duration of the program. The Emerging Leaders will meet again in April, 2015, at the 67th AAN Annual Meeting in Washington, DC, and then finally at the June 2015 AAN Board Meeting, where they will share the solutions to their cohort assignments.

Upon completion, participants will have gained enhanced skills to prepare them to assume leadership roles with the AAN. Successful participants will be eligible for placement on an AAN committee, subcommittee, or presidential task force.

For more information about the program, visit AAN.com/view/leadership, or contact Donna Honeyman at dhoneyman@aan.com or (612) 928-6055.

Congratulations to the 2014–2015 Class of Emerging Leaders!

Emerging Leaders

Erika Fullwood Augustine, MD – Rochester, NY
Stacey Clardy, MD, PhD – Park City, UT
Prabhu Dayal Emmady, MD – Cheyenne, WY
Amanda C. Guidon, MD – Boston, MA
Deborah Hall, MD, PhD – Chicago, IL
Ihtsham Haq, MD – Winston Salem, NC
Lyell K. Jones, MD – Rochester, MN
Adam Kelly, MD – Rochester, NY
Shannon M. Kilgore, MD – Palo Alto, CA
Mia T. Minen, MD – New York, NY
Augusto A. Miravalle, MD – Aurora, CO
Alexander Pantelyat, MD – Baltimore, MD
Tamara M. Pringsheim, MD – Calgary, AB
Kevin N. Sheth, MD – New Haven, CT
Parthasarathy Thirumala, MD – Pittsburgh, PA
David B. Watson, MD – Morgantown, WV

Mentors

Allison Brashear, MD, MBA, FAAN
Neil A. Busis, MD, FAAN
Terrence L. Cascino, MD, FAAN
Cynthia L. Comella, MD, FAAN
Lisa M. DeAngelis, MD, FAAN
Robert C. Griggs, MD, FAAN
Robert A. Gross, MD, PhD, FAAN
Carlayne E. Jackson, MD, FAAN
Ralph F. Jozefowicz, MD, FAAN
Janice M. Massey, MD, FAAN
Janis Miyasaki, MD, FAAN
Aaron E. Miller, MD, FAAN
John C. Morris, MD, FAAN
Ralph L. Sacco, MD, MS, FAHA, FAAN
James C. Stevens, MD, FAAN
Ann H. Tilton, MD, FAAN
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pletgridy™
(peginterferon beta-1a)

PLEGRIDY will be available in the coming months

Register for updates at PlegridyHCP.com

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08/14 PLG-1003686
Fading Memories. Undying Love.

As a father of four, grandfather of nine, and great-grandfather of nine, 79-year old Larry swore he would never get married again. Until he met Anne.

The couple married in 1994 and spent the next 20 years living a life they had once only dreamed of: A life filled with world travel, the best food and wine, love, laughter, and philanthropy. Until 2004, when Larry was diagnosed with Parkinson’s disease.

“I could deal with my own diagnosis,” he said. “But it was when Anne started becoming ill just three years later that my entire world was shattered.” Not willing to believe an early Alzheimer’s diagnosis, Larry took Anne on a tour of the best doctors money could buy. She eventually was diagnosed with Lewy body dementia in 2008. There was no denying Anne’s condition.

Today, Anne’s long-term memory is all but gone; she retains only a few recollections from when they first met. But despite her declining condition, Larry makes a point of reminding her, every day, of the wonderful trips they once took. He holds her hand, tells her he loves her, feeds her the chocolate candy she so loves, and, despite his own balance troubles and depression, vows to keep his promise that so long as she is alive Anne will never see the inside of a rest home or care facility.

“Anne used to be such a happy person,” Larry recalled, “but the disease has all but taken that away. I only wish I had met her sooner so we could have made more memories together.”

With 1 in 6 Americans suffering from brain disease, chances are you have a loved one who is suffering, too. Support research into causes, prevention, treatment, and cures at AmericanBrainFoundation.org.
Our Foundation. Our Future.

That is, if there is a future.

The current lack of available research funding is at a crisis, putting the future of neurology in jeopardy.

Your donation helps fund the future.

AmericanBrainFoundation.org
Visit the AAN’s Neurology Career Center to view hundreds of additional jobs and sign up for customized, confidential notifications when positions of interest are added.

Neurology Career Center

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 disorder would be a welcome addition, but is not required. Our diagnostic capabilities include: 1.5T MRI, CT angiogram, EMG, Evoked Potentials, EEG, and 24-72 Hour Ambulatory EEG. We also have an active Teleneurology 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/Cover Letter to Central Maine Medical Center, 350 Main Street, Lewiston, ME 04240. Fax: (207) 795-6696, email: JLauver@cmhc.org, or call: (800) 445-7431.

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 BC/BE 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 of the University of Vermont. CVPH Medical Center is a regional referral hospital which is recognized by Healthgrades as a Top 100 Hospital for Cardiac Care. Plattsburgh, NY (www.NorthernNewYorkGoodLife.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@cvph.org

Private Practice with Academic Responsibilities

A large, academically oriented Neurology group located on Long Island is interested in hiring another neurologist/Neurohospitalist. We are affiliated with three major teaching hospitals. An academic appointment will be obtained and resident and/or medical student teaching is required. While a subspecialty interest is an advantage, it is not a necessity. We seek a hard-working, well-trained person interested in clinical practice to join us. Please email resume/CV to dstrovs@gmail.com

Neurologist/Concussion Specialist

Well-established, multidisciplinary neuroscience medical group located north of Boston seeks Neurologist/Concussion Specialist with an interest in Head Injury or Sports Medicine. Unusual opportunity to be involved in a comprehensive head injury program that brings together resources in neurology, neurosurgery, physical medicine and rehabilitation, and psychiatry. Our services benefit from a close working relationship with local acute rehabilitation facilities. We offer a strongly collaborative environment and opportunities for professional growth. Send CV to Howard M. Gardner, MD, Medical Director, New England Neurological Associates, PC, RIVERWALK, 354 Merrimack Street, Lawrence, MA 01843, or email contact@neneuro.com. Visit us on the web at www.neneuro.com

Neurologists

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, MD, Medical Director, New England Neurological Associates, PC, RIVERWALK, 354 Merrimack Street, Lawrence, MA 01843, or email to jtf@neneuro.com. Visit us on the web at www.neneuro.com

Neurologists

Ochsner Health System and The Ochsner Neuroscience Institute are actively recruiting BC/BE General Neurologists, including Neuromuscular, to join our expanding practice. Additional opportunities exist for neurologists with subspecialty training in the following areas: Stroke/Vascular, Multiple Sclerosis, Neurocritical care, Pain, MS, 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 a physician-led, academic, multi-specialty, non-profit healthcare delivery system. We employ over 900 physicians, and our system includes 11 hospitals and more than 40 health centers. We also enjoy the advantage of practicing in a favorable malpractice environment in Louisiana. Please visit our website, www.ochsner.org for more information. CV’s will be reviewed by Richard M. Zweifler, MD, Chairman Department of Neurology. Email: profrecruiting@ochsner.org, Ref # AMSROZ. Information: (800) 488-2240. 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.

Neurologist (Bend, OR)

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 Cardiology to Pediatrics to Urgent Care—and the very latest in medical technology, including the most advanced imaging and diagnostic equipment. Put this together, and we give you what no other medical group this side of the Cascades can: Total Care. We’re currently looking for a BE/BC provider to work with four other Neurologists; an interest in General Neurology and Movement Disorder subspecialty training is a plus. Here, you’ll find a relaxed lifestyle, and we give you what no other medical group this side of the Cascades can: Total Care. We’re currently looking for a BE/BC provider to work with four other Neurologists; an interest in General Neurology and Movement Disorder subspecialty training is a plus. Here, you’ll find a comfortable or no hospital call options. New clinic building openings in 2015. Excellent top-ranked public and parochial schools. Multi-cultural arts, cuisine and theater. Group locations: Redding, Redding (Directorship option available), Red Bluff, Stockton. For more information, please contact & send your CV to Mary Weerts, Director of Provider Recruitment/Credentialing: mweerts@bmcotalcare.com or call (514) 706-2425, www.bendmemorialclinic.com

Neurology Positions with Central Maine Medical Center

Join a Dignity Health Medical Group in Northern California. Do you desire: Work/life balance in California? Traditional employment model? Opportunity to develop Neurology service within the group? Teleneurology services in place with Affiliated Group. Joint Commission-Certified Primary Stroke Center. Comfortable or no hospital call options. New clinic buildings within walking distance to our hospitals. The Medical Foundation is aligned with the fifth largest hospital provider 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: Low cost of living with 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, phone: (888) 599-7787. Website: www.dignityhealth.org/physician-careers

Neurology-Ophthalmology Position

New England Neurological Associates, PC, RIVERWALK, 354 Merrimack Street, Lawrence, MA 01843, or email contact@neneuro.com. Visit us on the web at www.neneuro.com

Neurologists

Ochsner Health System is a physician-led, academic, multi-specialty, non-profit healthcare delivery system. We employ over 900 physicians, and our system includes 11 hospitals and more than 40 health centers. We also enjoy the advantage of practicing in a favorable malpractice environment in Louisiana. Please visit our website, www.ochsner.org for more information. CV’s will be reviewed by Richard M. Zweifler, MD, Chairman Department of Neurology. Email: profrecruiting@ochsner.org, Ref # AMSROZ. Information: (800) 488-2240. 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.

Neurologist (Bend, OR)

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 Cardiology to Pediatrics to Urgent Care—and the very latest in medical technology, including the most advanced imaging and diagnostic equipment. Put this together, and we give you what no other medical group this side of the Cascades can: Total Care. We’re currently looking for a BE/BC provider to work with four other Neurologists; an interest in General Neurology and Movement Disorder subspecialty training is a plus. Here, you’ll find a comfortable or no hospital call options. New clinic building openings in 2015. Excellent top-ranked public and parochial schools. Multi-cultural arts, cuisine and theater. Group locations: Redding, Redding (Directorship option available), Red Bluff, Stockton. For more information, please contact & send your CV to Mary Weerts, Director of Provider Recruitment/Credentialing: mweerts@bmcotalcare.com or call (514) 706-2425, www.bendmemorialclinic.com

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. Teleneurology services in place with Affiliated Group. Joint Commission-Certified Primary Stroke Center. Comfortable or no hospital call options. New clinic buildings within walking distance to our hospitals. The Medical Foundation is aligned with the fifth largest hospital provider 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: Low cost of living with 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, phone: (888) 599-7787. Website: www.dignityhealth.org/physician-careers
Neuroimaging Fellowship: Flexible one year Fellowship in Neuroimaging: Winchester Neurological Consultants, Inc., in conjunction with Virginia Commonwealth University and Winchester Medical Center, is offering a clinical Neuroimaging Fellowship for BC/BE neurology graduates that can be completed in one or two years. Located approximately an hour from Washington, DC, our United Council of Neurologic Subspecialties fully accredited fellowship offers extensive training in the performance and interpretation of diagnostic inpatient and outpatient MRI, CT, Doppler, TCD, and myelography, utilizing four state of the art MRI scanners and four multi-slice CT units. Responsibilities include supervision and interpretation of imaging, assisting with acute stroke protocols, and direct patient care. Initial availability July 1, 2015. Research interests are encouraged. Salary is $60,000.00 plus benefits. There is also an option to combine the imaging fellowship with a NeuroHospitalist Fellowship over a two year training period with a salary of $80,000.00 per year. CVs should be emailed to pcapone@winchesternurological.com.

Dates and Deadlines

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<th>NOVEMBER 2014</th>
<th>DECEMBER 2014</th>
<th>JANUARY 2015</th>
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<td><strong>DECEMBER 1</strong></td>
<td><strong>JANUARY 31</strong></td>
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<td>AAN Fall Conference</td>
<td>Registration Deadline: RITE® Examination</td>
<td>Application Deadline: 2016 A.B. Baker Award for Lifetime Achievement in Neurologic Education</td>
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<td>AAN.com/view/RITE</td>
<td>AAN.com/membership/sections/ab-baker</td>
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<td><strong>NOVEMBER 3</strong></td>
<td><strong>DECEMBER 2</strong></td>
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<td>Application Deadline: Viste Patient Advocate of the Year Award</td>
<td>Webinar: Decoding the 2015 Medicare Physician Fee Schedule—Changes That Impact Neurology</td>
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<td><strong>NOVEMBER 4</strong></td>
<td><strong>DECEMBER 3</strong></td>
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<td>Webinar: Achieving Stage 2 Meaningful Use—Taking Your EHR Use to the Next Level</td>
<td>Application Deadline: Neurology on the Hill</td>
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<td>(Register by November 3)</td>
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<td>AAN.com/view/pmw14</td>
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<td><strong>DECEMBER 19</strong></td>
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<td>FREE Webinar: What Does the New Congress Mean for Your Practice?</td>
<td>Early Registration Deadline: Breakthroughs in Neurology Conference</td>
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<td>(Register by November 17)</td>
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<td>AAN.com/view/14PostElection</td>
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<td><strong>NOVEMBER 18</strong></td>
<td><strong>DECEMBER 31</strong></td>
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<td>Webinar: Quality Improvement—Beginning Steps in the Right Direction</td>
<td>Application Deadline: AAN Safety and Quality Awards</td>
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<td>(Register by November 17)</td>
<td>AAN.com/view/2015PTAwards</td>
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<td>AAN.com/view/pmw14</td>
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<td><strong>NOVEMBER 20</strong></td>
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<td>Webinar: Annual Meeting On Demand Encore: Update in Spine Disorders</td>
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<td>AAN.com/view/Encore</td>
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Neurology Resources
Wherever You Go
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for your smartphone

AANnews® Classified Advertising
The AAN offers a complete package of print, online, and in-person recruitment advertising opportunities. Visit AAN.com/careers for all AAN options, rates, and deadlines.

Ad copy for the January 2015 print edition of AANews must be submitted by December 1, 2014. The same deadline applies to changes/cancellations. The American Academy of Neurology reserves the right to decline, withdraw, or edit advertisements at its discretion. Every care is taken to avoid mistakes, but the responsibility for clerical or printer errors does not exceed the cost of the ad.
TECFIDERA™ (dimethyl fumarate) delayed-release capsules, for oral use

Brief Summary of Full Prescribing Information

1 INDICATIONS AND USAGE

TECFIDERA is indicated for the treatment of patients with relapsing forms of multiple sclerosis.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Lymphopenia

TECFIDERA may decrease lymphocyte counts [see Adverse Reactions (6.1)]. In the MS placebo controlled trials, mean lymphocyte counts decreased by approximately 30% during the first year of treatment with TECFIDERA and then remained stable. Four weeks after stopping TECFIDERA, mean lymphocyte counts increased but did not return to baseline. Six percent (6%) of TECFIDERA patients and <1% of placebo patients experienced lymphocyte counts <0.5x10^9/L (lower limit of normal 0.91x10^9/L). The incidence of infections (60% vs 58%) and serious infections (2% vs 2%) was similar in patients treated with TECFIDERA or placebo, respectively. There was no increased incidence of serious infections observed in patients with lymphocyte counts <0.8x10^9/L or 0.5x10^9/L.

Before initiating treatment with TECFIDERA, a recent CBC (i.e., within 6 months) should be available. A CBC is recommended annually, and as clinically indicated. Withholding treatment should be considered in patients with serious infections until the infection(s) is resolved. TECFIDERA has not been studied in patients with pre-existing low lymphocyte counts.

5.2 Flushing

TECFIDERA may cause flushing (e.g., warmth, redness, itching, and/or burning sensation). In clinical trials, 40% of TECFIDERA treated patients experienced flushing. Flushing symptoms generally began soon after initiating TECFIDERA and usually improved or resolved over time. In the majority of patients who experienced flushing, it was mild or moderate in severity. Three percent (3%) of patients discontinued TECFIDERA for flushing and <1% had serious flushing symptoms that were not life-threatening but led to hospitalization. Administration of TECFIDERA with food may reduce the incidence of flushing.

6 ADVERSE REACTIONS

The following important adverse reactions are described elsewhere in labeling: Lymphopenia, Flushing [see Warnings and Precautions (5.1, 5.2)].

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in 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.

The most common adverse reactions (incidence ≥10% and ≥2% more than placebo) for TECFIDERA were flushing, abdominal pain, diarrhea, and nausea.

Adverse Reactions in Placebo-Controlled Trials

In the two well-controlled studies demonstrating effectiveness, 1529 patients received TECFIDERA with an overall exposure of 2244 person-years [see Clinical Studies (14)].

The adverse reactions presented in the table below are based on safety information from 769 patients treated with TECFIDERA 240 mg twice a day and 771 placebo-treated patients.

Table 1: Adverse Reactions in Study 1 and 2 reported for TECFIDERA 240 mg BID at ≥ 2% higher incidence than placebo

<table>
<thead>
<tr>
<th>Category</th>
<th>TECFIDERA %</th>
<th>Placebo %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and Lymphatic System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>2</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>Nausea</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Vomiting</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Vascular Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flushing</td>
<td>40</td>
<td>6</td>
</tr>
<tr>
<td>Skin and Subcutaneous Tissue Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Rash</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Erythema</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Investigations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin urine present</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>4</td>
<td>2</td>
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</tbody>
</table>

Gastrointestinal Disorders

TECFIDERA caused GI events (e.g., nausea, vomiting, diarrhea, abdominal pain, and dyspepsia). The incidence of GI events was higher early in the course of treatment (primarily in month 1) and usually decreased over time in patients treated with TECFIDERA compared with placebo. Four percent (4%) of patients treated with TECFIDERA and less than 1% of placebo patients discontinued due to gastrointestinal events. The incidence of serious GI events was 1% in patients treated with TECFIDERA.

Hepatic Transaminases

An increased incidence of elevations of hepatic transaminases in patients treated with TECFIDERA was seen primarily during the first six months of treatment, and most patients with elevations had levels < 3 times the upper limit of normal (ULN). Elevations of alanine aminotransferase and aspartate aminotransferase to ≥ 3 times the ULN occurred in a small number of patients treated with both TECFIDERA and placebo and were balanced between groups. There were no elevations in transaminases ≥ 3 times the ULN with concomitant elevations in total bilirubin > 2 times the ULN. Discontinuations due to elevated hepatic transaminases were < 1% and were similar in patients treated with TECFIDERA or placebo.

Eosinophilia

A transient increase in mean eosinophil counts was seen during the first 2 months of therapy.
Adverse Reactions in Placebo-Controlled and Uncontrolled Studies

In placebo-controlled and uncontrolled clinical studies, a total of 2513 patients have received TECFIDERA and been followed for periods up to 4 years with an overall exposure of 4603 person-years. Approximately 1162 patients have received more than 2 years of treatment with TECFIDERA. The adverse reaction profile of TECFIDERA in the uncontrolled clinical studies was consistent with the experience in the placebo-controlled clinical trials.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies in pregnant women. In animals, adverse effects on offspring survival, growth, sexual maturation, and neurobehavorial function were observed when dimethyl fumarate (DMF) was administered during pregnancy and lactation at clinically relevant doses. TECFIDERA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

In rats administered DMF orally (25, 100, 250 mg/kg/day) throughout organogenesis, embryofetal toxicity (reduced fetal body weight and delayed ossification) were observed at the highest dose tested. This dose also produced evidence of maternal toxicity (reduced body weight). Plasma exposure (AUC) for monomethyl fumarate (MMF), the major circulating metabolite, at the no-effect dose is approximately three times that in humans at the recommended human dose (RHD) of 480 mg/day. In rabbits administered DMF orally (25, 75, and 150 mg/kg/day) throughout organogenesis, embryolethality and decreased maternal body weight were observed at the highest dose tested. The plasma AUC for MMF at the no-effect dose is approximately 5 times that in humans at the RHD.

Oral administration of DMF (25, 100, and 250 mg/kg/day) to rats throughout organogenesis and lactation resulted in increased lethality, persistent reductions in body weight, delayed sexual maturation (male and female pups), and reduced testicular weight at the highest dose tested. Neurobehavioral impairment was observed at all doses. A no-effect dose for developmental toxicity was not identified. The lowest dose tested was associated with plasma AUC for MMF lower than that in humans at the RHD.

Pregnancy Registry

There is a pregnancy registry that monitors pregnancy outcomes in women exposed to TECFIDERA during pregnancy. Encourage patients to enroll by calling 1-800-456-2255.

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 TECFIDERA is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Clinical studies of TECFIDERA did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information)

17.1 Dosage

Inform patients that they will be provided two strengths of TECFIDERA when starting treatment: 120 mg capsules for the 7 day starter dose and 240 mg capsules for the maintenance dose, both to be taken twice daily. Inform patients to swallow TECFIDERA capsules whole and intact. Inform patients to not crush, chew, or sprinkle capsule contents on food. Inform patients that TECFIDERA can be taken with or without food [see Dosage and Administration (2.1)].

17.2 Flushing and Gastrointestinal (GI) Reactions

Flushing and GI reactions (abdominal pain, diarrhea, and nausea) are the most common reactions, especially at the initiation of therapy, and may decrease over time. Advise patients to contact their healthcare provider if they experience persistent and/or severe flushing or GI reactions, as taking TECFIDERA with food may help [see Adverse Reactions (6.1)].

17.3 Pregnancy and Pregnancy Registry

Instruct patients that if they are pregnant or plan to become pregnant while taking TECFIDERA they should inform their physician. Encourage patients to enroll in the TECFIDERA Pregnancy Registry if they become pregnant while taking TECFIDERA. Advise patients to call 1-800-456-2255 for more information [see Use in Specific Populations (8.1)].

17.4 Lymphocyte Counts

Inform patients that TECFIDERA may decrease lymphocyte counts. A recent blood test (i.e., within 6 months) should be available before they start therapy to identify patients with pre-existing low lymphocyte counts. Blood tests are also recommended annually, and as clinically indicated [see Warnings and Precautions (5.1), Adverse Reactions (6.1)].
For your patients with relapsing multiple sclerosis

Start at the Tecfidera level

MEANINGFUL EFFICACY

In the 2-year DEFINE* trial vs placebo (n=408), Tecfidera (n=410) cut risk and frequency of relapses† in half.
PPR: 49% relative risk reduction, placebo 46%, Tecfidera 27% [P<0.0001].
ARR: 53% relative reduction, placebo 0.364, Tecfidera 0.172 [P<0.0001].

SAFETY STUDIED IN 2 CLINICAL TRIALS

The most common adverse reactions were flushing and gastrointestinal events. CBCs are recommended, as Tecfidera may decrease lymphocyte counts.†

INDICATION

Tecfidera® (dimethyl fumarate) is indicated for the treatment of patients with relapsing forms of multiple sclerosis.

IMPORTANT SAFETY INFORMATION

• Tecfidera may decrease lymphocyte counts; in clinical trials there was a mean decrease of ~30% in lymphocyte counts during the first year which then remained stable. Four weeks after stopping Tecfidera, mean lymphocyte counts increased but not to baseline. Six percent of Tecfidera patients and <1% of placebo patients had lymphocyte counts <0.5x10⁹/L. Tecfidera has not been studied in patients with pre-existing low lymphocyte counts.

• The incidence of infections and serious infections was similar in patients treated with Tecfidera or placebo. Consider withholding treatment in patients with serious infections until resolved. A complete blood count is recommended within 6 months before initiating treatment, annually, and as clinically indicated.

• Tecfidera may cause flushing (e.g., warmth, redness, itching, and/or burning sensation). 40% of patients taking Tecfidera reported flushing which was mostly mild to moderate in severity. Three percent of patients discontinued Tecfidera for flushing and <1% had serious flushing events that led to hospitalization. Taking Tecfidera with food may reduce flushing.

• Tecfidera may cause gastrointestinal [GI] events (e.g., nausea, vomiting, diarrhea, abdominal pain, and dyspepsia). Four percent of Tecfidera patients and <1% placebo patients discontinued due to GI events. The incidence of serious GI events was 1%. The most common adverse reactions associated with Tecfidera versus placebo are flushing (40% vs 6%) and GI events: abdominal pain (18% vs 10%), diarrhea (14% vs 11%), nausea (12% vs 9%).

• Elevations in hepatic transaminases have been reported. A transient increase in mean eosinophil counts was seen during the first two months. Tecfidera should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Encourage patients who become pregnant while taking Tecfidera to enroll in the Tecfidera pregnancy registry by calling 1-800-456-2255.

For additional important safety information, please see Brief Summary of full Prescribing Information on the preceding pages.

For more information, please visit TecfideraHCP.com.