2017 AAN Award Applications Opening This Month

Have you or someone you know been conducting research that may be advancing the field of neurology? If so, now is the time to start thinking about applying—or nominating a colleague—for one of more than 20 prestigious AAN awards to be presented at the 2017 AAN Annual Meeting in Boston, MA, April 22 through 29. Online applications will be available later this month at AAN.com/view/17Awards, and the application deadline is October 26, 2016.

Prestigious AAN awards honor the best research and achievements by neurologists and neuroscientists around the globe with prizes and other compensation, such as complimentary travel expenses and registration for the Annual Meeting. AAN awards recognize scientists at all stages of their careers for a variety of activities. *

Fall Conference Early Registration Savings End September 8

Don’t wait: Early registration savings for the 2016 AAN Fall Conference end September 8. Visit AAN.com/view/fall today to save $100 or more.

For the first time, the Fall Conference is offering a single-rate registration that includes most education programs and eliminates the need to select courses in advance, allowing you the flexibility to move between sessions as you wish. Secure your spot for the weekend of October 14 through 16 at The Cosmopolitan of Las Vegas where you’ll be sure to get the very latest clinical advances in neurology and practice management from experts in the field while earning up to 15.75 CME credits before year-end. *

AAN Scores Regulatory Advocacy Victories with CMS Proposed Fee Schedule

Last month, the Centers for Medicare & Medicaid Services (CMS) released its proposed 2017 Medicare Physician Fee Schedule, which contains a number of important victories for neurologists. Together, these represent a major step forward for the reimbursement of neurologic care and highlights the work of the AAN’s proactive advocacy on behalf of neurologists with federal regulators.

In the proposal, CMS shows a strong interest in improving the payment accuracy for care and services in this rule, as underscored by comments from CMS Acting Administrator Andy Slavitt: “Doctors will be compensated for spending more time with their patients, serving their patients’ needs outside of the office visit, and better coordinating care. These changes will

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In June, the Neurology® Podcast reached 10 million total downloads since this member benefit was introduced in September 2007. The AAN’s Neurology Now® and Neurology Today® garnered top awards from APEX, an annual competition recognizing excellence in print, web, electronic, and social media. Neurology Now received the top honor, the Grand Award for Writing, for the article, “Dementia 101” (December/January 2015). Neurology Today won the Award of Excellence for News Writing for the article, “When Academic Neurologists Leave, Who Owns Their Research? Sometimes, Not Always, It’s a Tug of War Between Institutions” (Oct. 8, 2015).

The American Society of Association Executives has recognized the AAN’s Brain Health Fair with a silver award in its latest Power of A Awards competition. The Power of A is an annual award that recognizes a select number of associations that distinguish themselves with innovative, effective, and broad-reaching programs and activities that positively impact America and the world. The awards recognize and celebrate the extraordinary contributions associations make to society by enriching lives, creating a competitive workforce, preparing society for the future, driving innovation, and making a better world. •
President’s Column

Increased Support of Research Continues AAN’s Long Commitment to Treatments and Cures

The AAN’s commitment to research stretches back to the earliest days of the Academy, when our founder A.B. Baker advocated to Congress for the creation of what was then known as the National Institute for Neurological Diseases and Blindness and helped install Dr. Pearce Bailey as its first director. Now, it’s known as the National Institute of Neurological Disorders and Stroke and AAN member Walter J. Koroshetz, MD, FAAN, is its chief.

Recently, the Academy’s board and staff put into place a significant expansion of our investment in research. In 2015, the AAN research program funded $2,400,000 to recipients. In 2016, the amount is $2,800,000—an increase of $400,000—and in 2017, the plans are to add $1.1 million in additional funds. The AAN research programs include money from the AAN Institute, the American Brain Foundation, association partners, the pharmaceutical industry, and AAN members.

I’d like to highlight four awards—two of them new—that underscore the AAN’s pledge to support all types of research across all career levels and discovery stages:

$130,000 Practice Research Training Scholarship

Also previously known as a fellowship, this scholarship provides $55,000 per year for two years, plus a $10,000 per year stipend to support education and research-related costs to support training in clinical practice research.

The application deadline for these awards is October 1, 2016. We also have awards specifically for research in ALS, Alzheimer’s, ataxia, epilepsy, multiple sclerosis, muscular dystrophy, Parkinson’s disease, stroke, and Tourette syndrome with varying application deadlines. I encourage eligible researchers to learn more about these and other Academy research grants at AAN.com/research-and-awards.

The brain remains the least-understood—and arguably the most important—organ of the human body, and the human and financial cost of neurologic disease is so tremendously high. These Academy programs, as modest as they may be in the overall funding of brain research, play a vital role in our profession’s ongoing search for answers and the nurturing of the next generations of investigators. We always will strive to do more, and we always will be proud of doing as much as we can.

Terrence L. Cascino, MD, FAAN
President, American Academy of Neurology
tcascino@aan.com
Meet Your Leader

Janis M. Miyasaki, MD, MEd, FRCPC, FAAN

This is the latest in a series of profiles of members of the Board of Directors for the AAN and AAN Institute.

Janis M. Miyasaki, MD, MEd, FRCPC, FAAN, is a member of the division of neurology at the University of Alberta, Canada, and active in provincial initiatives in palliative care for neurologic patients. Her AAN activities include work on many committees, including the Practice Committee, Practice Improvement Subcommittee, Patient Safety Subcommittee, Education Committee, and as co-chair of the Technology and Therapeutics Subcommittee (now the Guideline Development Subcommittee).

What experiences and viewpoints do you bring to this role?

After a movement disorders fellowship at the University of Toronto, I began community neurology practice as a solo practitioner for four years. We did 1 in 4 call one week at a time. In 1999, I joined the University of Toronto faculty full time as an educator. Since 2014, I have been at the University of Alberta as a clinical investigator. Through my local institutions, I have served on the board of the hospital, acted in finance and audit, quality improvement, and hospital accreditation. I am currently involved in academic evaluation for promotion and management of the Department of Medicine. In addition, I am maintaining an active research program and am the Director of the Movement Disorders Program. In terms of the AAN, I have been actively involved since 2000 writing guidelines or serving on multiple committees and subcommittees including as co-chair on the Practice Committee, the forerunner of the Guidelines Development Subcommittee, and the Education Committee.

From your experiences as an AAN leader, what is one of the more common misperceptions members may have about the Academy?

One of the most common is that we are a closed group of academic neurologists. In every committee, subcommittee, and workgroup on which I have served there has been a private practice physician. The challenge is the time commitment for many members, as the work is intensive, often requires a short turn around for every committee member, and if you do not contribute, you will not be asked to serve for a second term. Both private practice physicians and academic neurologists who serve in these capacities dedicate a huge amount of time without compensation. Unlike other societies, the AAN does not pay the expenses of the Board to attend the Annual Meeting—leadership takes stewardship of member funds seriously.

Another common misperception is that the AAN is imposing standards of care on neurologists including maintenance of certification. The AAN was anticipating the changes and trying to provide support for members to maintain certification. We are not the ABPN.

In your view, how does the AAN benefit the field of neurology most?

The AAN provides leadership to anticipate changes in the practice of medicine, to advocate for the importance of neurology to government and third-party payers, and represent neurologists with other medical societies.

Members also value guidelines because they synthesize large amounts of information to provide the best possible care based on the highest level of evidence—this is important for members and the public.

Another important role for the AAN is to provide high-quality education that is engaging and uses the latest technology to keep members’ knowledge and skills up-to-date. The last AAN Annual Meeting provided a seismic change: a single registration fee and access to nearly all courses (excluding those requiring small groups for skills). This was very popular and, in speaking to attendees, nearly universally appreciated. One attendee said he was so excited he got up every morning for the 6:30 a.m. courses, which he had never done in the past.

How should members evaluate the success of the AAN and the Board of Directors in supporting their careers and neurology in general?

Continued on page 12

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NOW APPROVED FOR RELAPSING FORMS OF MS

**Indication**
ZINBRYTA is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of ZINBRYTA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

**Important Safety Information**

**Contraindications**
ZINBRYTA is contraindicated in patients with pre-existing hepatic disease or hepatic impairment, including alanine aminotransferase (ALT) or aspartate aminotransferase (AST) at least 2 times the upper limit of normal (ULN); a history of autoimmune hepatitis or other autoimmune condition involving the liver; or a history of hypersensitivity to daclizumab or any other components of the formulation.

**WARNING: HEPATIC INJURY INCLUDING AUTOIMMUNE HEPATITIS and OTHER IMMUNE-MEDIATED DISORDERS**

**Hepatic Injury Including Autoimmune Hepatitis**
- ZINBRYTA can cause severe liver injury including life-threatening events, liver failure, and autoimmune hepatitis. Obtain transaminase and bilirubin levels before initiation of ZINBRYTA. Monitor and evaluate transaminase and bilirubin levels monthly and for 6 months after the last dose
- ZINBRYTA is contraindicated in patients with pre-existing hepatic disease or hepatic impairment

**Other Immune-Mediated Disorders**
- Immune-mediated disorders including skin reactions, lymphadenopathy, non-infectious colitis, and other immune-mediated disorders can occur with ZINBRYTA

These conditions may require treatment with systemic corticosteroids or immunosuppressive medication

ZINBRYTA is available only through a restricted distribution program called the ZINBRYTA REMS Program

Please see the following pages for additional Important Safety Information and Brief Summary of Full Prescribing Information, including BOXED WARNING.
In clinical studies, ZINBRYTA significantly reduced annualized relapse rates compared with AVONEX® (interferon beta-1a) and placebo.

**DECIDE pivotal clinical trial: outcome up to 144 weeks**

<table>
<thead>
<tr>
<th>Primary Endpoint</th>
<th>ZINBRYTA 150 mg (n=919)</th>
<th>AVONEX 30 mcg (n=922)</th>
<th>P-value</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annualized relapse rate up to 144 weeks</td>
<td>0.216</td>
<td>0.393</td>
<td>&lt;0.0001</td>
<td>45% relative reduction</td>
</tr>
</tbody>
</table>

**Study Design:** DECIDE was a randomized, double-blind, active control study that compared ZINBRYTA 150 mg subcutaneous (n=919) every 4 weeks to AVONEX 30 mcg intramuscular (n=922) weekly. Treatment continued for 96 to 144 weeks. The primary outcome measure was the annualized relapse rate (ARR). Additional outcome measures included the proportion of patients relapsed, the proportion of patients who experienced confirmed disability progression (CDP), and the number of new or newly enlarging T2 hyperintense lesions. The study included RMS patients with an Expanded Disability Status Scale (EDSS) score 0.0-5.0 who had either: 1) ≥2 relapses during the prior 3 years and ≥1 relapse in the year prior to randomization; or 2) ≥1 clinical relapses and ≥1 new T1 gadolinium (Gd)-enhancing or T2 hyperintense MRI lesions within the prior 2 years with at least one of these events in the prior 12 months. Patients with progressive forms of MS were excluded.

**SELECT pivotal clinical trial: outcome at 52 weeks**

<table>
<thead>
<tr>
<th>Primary Endpoint</th>
<th>ZINBRYTA 150 mg (n=208)</th>
<th>Placebo (n=204)</th>
<th>P-value</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annualized relapse rate at 52 weeks</td>
<td>0.211</td>
<td>0.458</td>
<td>&lt;0.0001</td>
<td>54% relative reduction</td>
</tr>
</tbody>
</table>

**Study Design:** SELECT was a randomized, double-blind, placebo-controlled study that compared ZINBRYTA 150 mg subcutaneous (n=208) every 4 weeks to placebo (n=204). Treatment duration was 52 weeks. The primary outcome measure was the annualized relapse rate (ARR) at Week 52. Additional outcome measures included new T1 Gd-enhancing lesions between Weeks 8 to 24, the proportion of patients relapsed, the proportion of patients who experienced 12-week CDP and the number of new or newly enlarging T2 hyperintense lesions. The study included RMS patients with an EDSS score 0.0-5.0 who had experienced ≥1 relapse in the year prior to randomization or who had ≥1 T1 gadolinium (Gd)-enhancing or T2 hyperintense MRI lesions within the prior 2 years with at least one of these events in the prior 12 months. Patients with progressive forms of MS were excluded.

**Important Safety Information (Continued)**

**Hepatic Injury**

ZINBRYTA can cause life-threatening severe liver injury, including liver failure and autoimmune hepatitis. In controlled studies, serious drug-related hepatic injury occurred in 0.7% of ZINBRYTA-treated patients compared with 0.4% of AVONEX-treated patients (Study 1) and in 1.0% of ZINBRYTA-treated patients compared with no injury in placebo patients (Study 2). A fatal case of autoimmune hepatitis occurred in a patient re-initiating ZINBRYTA after a planned 6 month treatment interruption period. The incidence of increases in hepatic transaminases was greater in patients taking ZINBRYTA than in those taking AVONEX or placebo. Prior to starting treatment with ZINBRYTA, obtain serum transaminases (ALT and AST) and total bilirubin levels. Test transaminase levels and total bilirubin monthly and assess before the next dose of ZINBRYTA. Follow transaminase levels and total bilirubin monthly for 6 months after the last dose of ZINBRYTA. If a patient develops clinical signs or symptoms suggestive of hepatic dysfunction (e.g., unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine), promptly measure serum transaminases and total bilirubin and interrupt or discontinue treatment with ZINBRYTA, as appropriate. Discontinue ZINBRYTA if autoimmune hepatitis is suspected. Caution should be used when using hepatotoxic drugs, including non-prescription drugs, herbal products, and dietary supplements, concomitantly with ZINBRYTA.

**Immune-Mediated Disorders**

Treatment with ZINBRYTA increases the risk of immune-mediated disorders, including autoimmune disorders such as autoimmune hepatitis. Across all clinical studies (controlled and open-label), immune-mediated disorders occurred in 28% of patients on ZINBRYTA, the most common of which were skin reactions and lymphadenopathy. In the active-control study (Study 1), immune-mediated disorders were observed in 32% of ZINBRYTA-treated patients compared with 12% for AVONEX-treated patients.

Some patients required invasive procedures for diagnosis (e.g., colonoscopy, liver biopsy, kidney biopsy, lung biopsy), hospitalization for fluid replacement or blood transfusion, or prolonged treatment with systemic corticosteroids or immunosuppressant drugs. Some of these events did not resolve after stopping ZINBRYTA during study follow-up. Prescribers should be vigilant regarding emergent immune mediated disorders. For suspected immune-mediated disorders, ensure adequate evaluation to confirm etiology or to exclude other causes. If a patient develops a serious immune disorder, consider stopping ZINBRYTA and refer the patient to an appropriate specialist for further evaluation and treatment.

(continued on adjacent page)
- ZINBRYTA causes skin reactions. In clinical trials, skin reactions occurred in 37% of ZINBRYTA-treated patients compared with 19% of AVONEX-treated patients (Study 1) and in 18% of ZINBRYTA-treated patients compared with 13% of patients on placebo (Study 2). Skin reactions occurred at any time during treatment with ZINBRYTA. If a patient develops a serious diffuse or inflammatory rash, it is recommended that a dermatologist evaluate the patient before the next dose of ZINBRYTA. Discontinuation of ZINBRYTA may be appropriate.

- ZINBRYTA increases the incidence of lymphadenopathy. In controlled studies, lymphadenopathy or lymphadenitis occurred in 6% of ZINBRYTA-treated patients compared with 1% of AVONEX-treated patients (Study 1) and in 2% of ZINBRYTA-treated patients compared with 1% of placebo-treated patients (Study 2).

- An increased incidence of serious colitis (less than 1%) was reported in patients treated with ZINBRYTA compared with none for patients treated with AVONEX or placebo in clinical trials.

- A wide variety of other immune-mediated disorders, some serious, have occurred infrequently with the use of ZINBRYTA. If a patient develops a serious immune disorder, consider stopping ZINBRYTA.

ZINBRYTA REMS Program
ZINBRYTA is available only through a restricted program called the ZINBRYTA REMS Program, because of the risks of hepatic injury including autoimmune hepatitis, and other immune-mediated disorders. Only certified prescribers and pharmacies and patients enrolled in the REMS program can prescribe, dispense or receive ZINBRYTA.

Acute Hypersensitivity
ZINBRYTA can cause anaphylaxis, angioedema, and urticaria after the first dose or at any time during treatment. Discontinue and do not re-start ZINBRYTA if anaphylaxis or other allergic reactions occur.

Infections
ZINBRYTA increases the risk for infections. The most common types of infections observed were upper respiratory tract infections, urinary tract infections and viral infections. Avoid initiating ZINBRYTA in patients with severe active infection until the infection is fully controlled. If serious infection develops, consider withholding treatment with ZINBRYTA until the infection resolves.

- Vaccination with live vaccines is not recommended during treatment and up to 4 months after discontinuation of ZINBRYTA

Depression and Suicide
In controlled trials, depression-related events occurred in 10% of ZINBRYTA-treated patients compared with 8% of AVONEX-treated patients (Study 1) and in 7% of ZINBRYTA-treated patients compared with 2% of patients taking placebo (Study 2). Administer ZINBRYTA with caution to patients with previous or current depressive disorders. Advise patients and/or caregivers to immediately report any symptoms of new or worsening depression and/or suicidal ideation. If a patient develops severe depression and/or suicidal ideation, consider discontinuation of ZINBRYTA.

Adverse Reactions
The most common adverse reactions (incidence at least 5% and at least 2% higher incidence than comparator) that occurred in ZINBRYTA-treated patients were nasopharyngitis, upper respiratory tract infection, rash, influenza, dermatitis, oropharyngeal pain, bronchitis, eczema, and lymphadenopathy compared with AVONEX; and upper respiratory tract infection, depression, rash, pharyngitis, and increased ALT compared with placebo.

Please see Full Prescribing Information including Boxed Warning and Medication Guide for additional Important Safety Information.

23 Assessment Prior to Initiating ZINBRYTA

2.3 Assessment Prior to Initiating ZINBRYTA

Hepatic Assessment: Prior to initiating ZINBRYTA, obtain and evaluate the following: Serum transaminases (alanine aminotransferase (ALT) and aspartate aminotransferase (AST)) and total bilirubin levels. Initiation of ZINBRYTA is contraindicated in patients with pre-existing hepatic disease or hepatic impairment including ALT or AST at least 2 times the ULN (see Contraindications (4) and Warnings and Precautions (5.1)).

Assessment for Tuberculosis and Other Infections: Evaluate patients at high risk for tuberculosis infection prior to initiating treatment with ZINBRYTA (see Warnings and Precautions (5.3)). For patients testing positive for tuberculosis, treat tuberculosis by standard medical practice prior to therapy with ZINBRYTA. Avoid initiating ZINBRYTA in patients with tuberculosis or other severe active infection (see Warnings and Precautions (5.3)).

Prior to initiating ZINBRYTA, screen patients for Hepatitis B and C. ZINBRYTA is contraindicated in patients with pre-existing hepatic disease (see Contraindications (4)).

Vaccinations: Because vaccination with live vaccines is not recommended during treatment and up to 4 months after discontinuation of treatment, consider any necessary immunization with live vaccines prior to treatment with ZINBRYTA (see Warnings and Precautions (5.5)).

2.4 Laboratory Testing and Monitoring to Assess Safety After Initiating ZINBRYTA

Conduct the following laboratory tests at periodic intervals to monitor for early signs of potentially serious adverse effects:

Liver Tests: Test transaminase levels and total bilirubin monthly and assess before the next dose of ZINBRYTA. Follow transaminase levels and total bilirubin monthly for 6 months after the last dose of ZINBRYTA. In case of elevation in transaminases or total bilirubin, treatment interruption or discontinuation may be required (see Dosage and Administration (2.4) and Warnings and Precautions (5.1)).

- Other Immune-Mediated Disorders

In addition to autoimmune hepatitis, immune-mediated disorders such as skin reactions, lymphadenopathy, and non-infectious colitis can occur in patients treated with ZINBRYTA. Overall, serious immune-mediated conditions were observed in 5% of patients treated with ZINBRYTA (see Warnings and Precautions (5.2)).

- If a patient develops a serious immune-mediated disorder, consider stopping ZINBRYTA and refer the patient to a specialist to ensure comprehensive diagnostic evaluation and appropriate treatment.

Some patients required systemic corticosteroids or other immunosuppressant treatment for autoimmune hepatitis or other immune-mediated disorders and continued this treatment after the last dose of ZINBRYTA (see Warnings and Precautions (5.1, 2.2)).

Because of the risks of hepatic injury, including autoimmune hepatitis, and autoimmune hepatitis. In controlled studies, serious drug-related hepatic disorders. For suspected immune-mediated disorders, ensure adequate monitoring: Prior to starting treatment with ZINBRYTA, obtain serum transaminases (ALT and AST) and bilirubin levels (see Dosage and Administration (2.3)).

Test transaminase levels and total bilirubin monthly and assess before the next dose of ZINBRYTA. Follow transaminase levels and total bilirubin monthly for 6 months after the last dose of ZINBRYTA. In case of elevation in transaminases or total bilirubin, treatment interruption or discontinuation may be required (see Dosage and Administration (2.4) and Warnings and Precautions (5.1)).

Table 1: ZINBRYTA Treatment Modification for Liver Test Abnormalities

<table>
<thead>
<tr>
<th>Elevated Transaminases and/or Total Bilirubin (see Warnings and Precautions (5.1))</th>
<th>Lab Value(s)</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT or AST greater than 5 times ULN OR Total bilirubin greater than 2 times ULN</td>
<td>Interrupt ZINBRYTA therapy and investigate for other etiologies of abnormal lab value(s)</td>
<td></td>
</tr>
<tr>
<td>ALT or AST greater than or equal to 3 but less than 5 times ULN AND total bilirubin greater than 1.5 but less than 2 times ULN</td>
<td>If no other etiologies are identified, then discontinue ZINBRYTA. If other etiologies are identified, re-assess the overall risk/benefit profile of ZINBRYTA in the patient and consider whether to resume ZINBRYTA when both AST or ALT are less than 2 times ULN and total bilirubin is less than or equal to ULN.</td>
<td></td>
</tr>
</tbody>
</table>

In clinical trials, permanent discontinuation of therapy was required if the patient had liver test abnormalities resulting in suspension of study treatment for at least 8 consecutive weeks. ULN = upper limit of normal

3 DOSE FORMS AND STRENGTHS

Injection: 150 mg/mL solution in a single-dose prefilled syringe. ZINBRYTA is a sterile, preservative-free, colorless to slightly yellow, clear to slightly opalescent solution.

4 CONTRAINDICATIONS

ZINBRYTA is contraindicated in patients with:

- Pre-existing hepatic disease or hepatic impairment, including ALT or AST at least 2 times the ULN, because ZINBRYTA could exacerbate existing liver dysfunction (see Dosage and Administration (2.3) and Warnings and Precautions (5.1)).

- A history of autoimmune hepatitis or other autoimmune condition involving the liver (see Warnings and Precautions (5.1)).

- A history of hypersensitivity to daclizumab or any other components of the formulation. Use in such patients may result in anaphylaxis or life-threatening multi-organ hypersensitivity (see Warnings and Precautions (5.4)).

1 INDICATIONS AND USAGE

ZINBRYTA is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (MS). Because of its safety profile, the use of ZINBRYTA should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

The recommended dosage of ZINBRYTA is 150 milligrams injected subcutaneously once monthly (see Dosage and Administration (2.3, 2.4)).

Instruct patients to inject a missed dose as soon as possible but no more than two weeks late. After two weeks, skip the missed dose and take the next dose on schedule. Administer only one dose at a time.

2.2 Important Administration Instructions

ZINBRYTA is for subcutaneous use only.

Train patients in the proper technique for self-administering subcutaneous injections using the prefilled syringe. Thirty minutes prior to injection, remove ZINBRYTA from the refrigerator to allow the drug to warm to room temperature. Do not use external heat sources such as hot water to warm ZINBRYTA. Do not place ZINBRYTA back into the refrigerator after allowing it to warm to room temperature (see How Supplied/Storage and Handling (16.2)).

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. ZINBRYTA is a colorless to slightly yellow, clear to slightly opalescent solution. Do not use ZINBRYTA if it is cloudy or there are visible particles.

Sites for injection include the thigh, abdomen, and back of the upper arm. Use each prefilled syringe one time and then place in a sharps disposal container for disposal according to community guidelines (see How Supplied/Storage and Handling (16.3)).
5 WARNINGS AND PRECAUTIONS

5.1 Hepatic Injury

ZINBRYTA can cause life-threatening severe liver injury, including liver failure and autoimmune hepatitis. In controlled studies, serious drug-related hepatic injury occurred in 0.7% of ZINBRYTA-treated patients compared with 0.4% of AVONEX-treated patients (Study 1) and 1% of ZINBRYTA-treated patients compared with no injury in placebo patients (Study 2). Across all clinical studies (controlled and open-label), serious drug-related hepatic injury occurred in 1% of ZINBRYTA-treated patients, with monthly monitoring of transaminases and total bilirubin. The incidence of discontinuation due to drug-related hepatic injury was 5% in ZINBRYTA-treated patients and 4% in AVONEX-treated patients.

Autoimmune Hepatitis: Across all clinical studies (controlled and open-label), 0.3% of ZINBRYTA-treated patients developed autoimmune hepatitis. One fatal case of autoimmune hepatitis occurred in a patient re-initiating ZINBRYTA after a planned 6 month treatment interruption period. This patient subsequently received two doses of ZINBRYTA in the presence of persisting alanine aminotransferase levels (ALT) more than 5 times the upper limit of normal (ULN).

Transaminase and Total Bilirubin Elevations: The incidence of increases in hepatic transaminases was greater in patients taking ZINBRYTA than in those taking AVONEX or placebo. The incidence of ALT or AST elevations above 5 times the ULN was 6% in ZINBRYTA-treated patients compared with 3% in AVONEX-treated patients (Study 1) and 4% in ZINBRYTA-treated patients compared with 1% in patients on placebo (Study 2). Less than 1% of ZINBRYTA-treated patients had ALT or AST greater than 20 times the ULN. Elevations of hepatic transaminases of at least 3 times the ULN combined with elevated bilirubin at least 2 times the ULN and alkaline phosphatase less than 2 times the ULN occurred in 0.7% of ZINBRYTA-treated patients compared with 0.1% of AVONEX-treated patients. In clinical trials, serum transaminase elevations occurred during treatment and up to 4 months after the last dose of ZINBRYTA.

Monitoring: Prior to starting treatment with ZINBRYTA, obtain serum transaminases (ALT and AST) and total bilirubin levels (see Contraindications (4)).

Test transaminase levels and total bilirubin monthly and assess before the next dose of ZINBRYTA. Follow transaminase levels and total bilirubin monthly for 6 months after the last dose of ZINBRYTA. Treatment modifications are recommended based on serum transaminase and total bilirubin values (see Dosage and Administration (2.4)).

If a patient develops clinical signs or symptoms suggestive of hepatic dysfunction (e.g., unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine), promptly measure serum transaminases and total bilirubin and interrupt or discontinue treatment with ZINBRYTA, as appropriate. Patients with prolonged elevations of serum transaminases should be evaluated for other possible causes, such as infection, and a specialist should evaluate the patient (see Table 1). Discontinue ZINBRYTA if autoimmune hepatitis is suspected. Treatment of autoimmune hepatitis with systemic corticosteroids and other immunosuppressant drugs may be required. Some patients may need long-term immunosuppression.

Risk of Hepatic Injury with Concomitant Use of Other Hepatotoxic Drugs: Caution should be used when using hepatotoxic drugs, including nonprescription products, concomitantly with ZINBRYTA. Some required several months for resolution after the last dose of ZINBRYTA. In clinical trials, discontinuation because of liver injury was more frequent in ZINBRYTA-treated patients compared to AVONEX-treated patients, and in 7% of ZINBRYTA-treated patients compared to 3% of patients on placebo. Dermatitis occurred more frequently in ZINBRYTA-treated patients compared to AVONEX-treated patients or to patients on placebo, and eczema was observed more frequently in ZINBRYTA-treated patients compared to AVONEX-treated patients (see Adverse Reactions (6.1)).

5.2 Immune-Mediated Disorders

Treatment with ZINBRYTA increases the risk of immune-mediated disorders, including autoimmune disorders such as autoimmune hepatitis. Across all clinical studies (controlled and open-label), immune-mediated disorders occurred in 28% of patients on ZINBRYTA, the most common of which were skin reactions and lymphadenopathy. In the active-control study (Study 1), immune-mediated disorders were observed in 32% of ZINBRYTA-treated patients compared with 12% for AVONEX-treated patients. In Study 1, serious immune-mediated disorders were observed in 4% of patients treated with ZINBRYTA compared with less than 1% for AVONEX-treated patients. In the placebo-controlled study (Study 2), immune-mediated disorders were observed in 13% of ZINBRYTA-treated patients compared with 5% of placebo-treated patients. In Study 2, serious immune-mediated disorders were observed in 0.5% of ZINBRYTA-treated patients and in 0.5% of placebo-treated patients. In some cases, patients had concurrent or sequential occurring disorders while taking ZINBRYTA.

Some patients required invasive procedures for diagnosis (e.g., colonoscopy, liver biopsy, kidney biopsy, lung biopsy), hospitalization for fluid replacement or blood transfusions, or prolonged treatment with systemic corticosteroids or immunosuppressant drugs. Some of these events did not resolve after stopping ZINBRYTA during study follow-up. Prescribers should be vigilant regarding emergent immune-mediated disorders. For suspected immune-mediated disorders, ensure adequate evaluation to confirm etiology or to exclude other causes. If a patient develops a serious immune-mediated disorder, consider stopping ZINBRYTA and refer the patient to an appropriate specialist for further evaluation and treatment.

Skin Reactions: ZINBRYTA causes skin reactions. In clinical trials, skin reactions occurred in 37% of ZINBRYTA-treated patients compared with 19% of AVONEX-treated patients (Study 1) and in 18% of ZINBRYTA-treated patients compared with 13% of patients on placebo (Study 2). Skin reactions occurred at any time during treatment with ZINBRYTA. Rash occurred in 12% of ZINBRYTA-treated patients compared to 4% of AVONEX-treated patients, and in 4% of ZINBRYTA-treated patients compared to 3% of patients on placebo. Dermatitis occurred more frequently in ZINBRYTA-treated patients compared to AVONEX-treated patients or to patients on placebo, and eczema was observed more frequently in ZINBRYTA-treated patients compared to AVONEX-treated patients (see Adverse Reactions (6.1)).

Other Immune-Mediated Disorders: A wide variety of other immune-mediated disorders, some serious, have occurred infrequently with the use of ZINBRYTA. These include single organ or systemic multi-organ inflammatory reactions. Many events occurred in only one patient, and the relationship to ZINBRYTA is unknown (see Adverse Reactions (6.1)). Some required treatment with systemic corticosteroids. Some required several months for resolution after the last dose of ZINBRYTA.

For suspected immune-mediated disorders, ensure adequate evaluation to confirm etiology or to exclude other causes. If a patient develops a serious immune-mediated disorder, consider stopping ZINBRYTA and refer the patient to an appropriate specialist for further evaluation and treatment.

5.3 ZINBRYTA REMS Program

ZINBRYTA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ZINBRYTA REMS Program, because of the risks of hepatic injury including autoimmune hepatitis, and other immune-mediated disorders (see Warnings and Precautions (5.1, 5.2)).

Notable requirements of the ZINBRYTA REMS Program include the following:

- Prescribers must be certified with the program by enrolling and completing training.
- Patients must enroll in the program and comply with ongoing monitoring requirements (see Warnings and Precautions (5.1, 5.2)).
- Pharmacists must be certified with the program and must only dispense to patients who are authorized to receive ZINBRYTA.

Further information, including a list of qualified pharmacies/distributors, is available at 1-800-456-2255.

5.4 Acute Hypersensitivity

ZINBRYTA can cause anaphylaxis, angioedema, and urticaria after the first dose or at any time during treatment. Discontinue and do not restart ZINBRYTA if anaphylaxis or other allergic reactions occur (see Contraindications (4)).
5.5 Infections
ZINBRYTA increases the risk for infections. In controlled trials, infections occurred in 65% of ZINBRYTA-treated patients compared with 57% of AVONEX-treated patients (Study 1) and in 50% of ZINBRYTA-treated patients compared with 44% of patients taking placebo (Study 2). Serious infections occurred in 4% of ZINBRYTA-treated patients compared with 2% of AVONEX-treated patients (Study 1) and in 3% of ZINBRYTA-treated patients compared with none on placebo (Study 2).

The most common types of infections observed were upper respiratory tract infections, urinary tract infections and viral infections.

In clinical trials, cases of tuberculosis occurred in countries where tuberculosis is endemic. Evaluate high-risk patients for tuberculosis infection prior to initiating treatment with ZINBRYTA. For patients testing positive for tuberculosis, treat by standard medical practice prior to therapy with ZINBRYTA (see Dosage and Administration (2.3)).

Avoid initiating ZINBRYTA in patients with severe active infection until the infection is fully controlled. If serious infection develops, consider withholding treatment with ZINBRYTA until the infection resolves.

Vaccination: The safety of immunization with live viral vaccines during treatment with ZINBRYTA has not been studied. Vaccination with live vaccines is not recommended during treatment and up to 4 months after discontinuation of ZINBRYTA (see Dosage and Administration (2.3)).

5.6 Depression and Suicide
Depression-related events occurred more frequently in patients receiving ZINBRYTA than in patients receiving AVONEX or placebo. In controlled trials, depression-related events occurred in 10% of ZINBRYTA-treated patients compared with 8% of AVONEX-treated patients (Study 1) and in 7% of ZINBRYTA-treated patients compared with 2% of patients taking placebo (Study 2). In Study 1, serious events related to depression, including suicidal ideation or suicide attempt, occurred in 0.4% of ZINBRYTA-treated patients and in 0.7% of AVONEX-treated patients. None occurred in Study 2 (placebo-controlled).

Administer ZINBRYTA with caution to patients with previous or current depressive disorders. Advise patients and/or caregivers to immediately report any symptoms of new or worsening depression and/or suicidal ideation to their healthcare provider.

If a patient develops severe depression and/or suicidal ideation, consider discontinuation of ZINBRYTA.

6 ADVERSE REACTIONS
The following serious adverse reactions are described elsewhere in labeling:

• Hepatic Injury [see Warnings and Precautions (5.1)]
• Immune-Mediated Disorders [see Warnings and Precautions (5.2)]
• Acute Hypersensitivity [see Warnings and Precautions (5.4)]
• Infections [see Warnings and Precautions (5.5)]
• Depression and Suicide [see Warnings and Precautions (5.6)]

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of ZINBRYTA cannot be directly compared with rates in clinical trials of other drugs and may not reflect the rates observed in practice.

In all controlled and uncontrolled trials performed in patients with relapsing multiple sclerosis, 2236 patients received ZINBRYTA for a total of 5214 person-years. Of these patients, 1576 received ZINBRYTA for at least 1 year, 1259 for at least 2 years, and 888 for at least 3 years. In the controlled studies, approximately 67% were female; 92% were Caucasian, and the mean age was 36 years at study entry.

In the active-controlled study (Study 1), 919 patients received ZINBRYTA (150 mg SQ, every 4 weeks) and 922 patients received AVONEX (interferon beta-1a 30 mcg IM, weekly) for a minimum of 2 years and up to 3 years, with 1952 person-years of exposure to ZINBRYTA; the median length of treatment was approximately 27 months. The adverse reactions from Study 2 are presented in Table 2.

In the placebo-controlled study (Study 2), 417 patients received ZINBRYTA with 423 person-years of exposure, of which 208 received 150 mg, and 204 received placebo every 4 weeks for up to 1 year; the median length of treatment was approximately 11 months. The adverse reactions from Study 2 are presented in Table 3.

The most common adverse reactions (incidence at least 5% and at least 2% higher incidence than comparator) that occurred in ZINBRYTA-treated patients were nasopharyngitis, upper respiratory tract infection, rash, influenza, dermatitis, oropharyngeal pain, bronchitis, eczema, and lymphadenopathy compared with AVONEX; and upper respiratory tract infection, depression, rash, pharyngitis, and increased alanine aminotransferase (ALT) compared with placebo.

The most common adverse reactions leading to discontinuation in up to 5% of patients treated with ZINBRYTA were hepatic events including elevations of serum transaminases and cutaneous events.

Patients were excluded from the clinical studies for abnormal laboratory values including hemoglobin, complete blood count with differential, serum transaminases, or serum creatinine. Patients were excluded if they had a history of seizure disorder or of having a seizure within 6 months of beginning the study, or suicidal ideation or severe depression within 3 months of beginning the study. During Study 1, concomitant use of ZINBRYTA with the hepatotoxic drugs valproic acid, carbamazepine, lamotrigine, phenytoin, sunitizol, and propylthiouracil was not permitted except in patients already receiving the drugs at the time of study entry.

In clinical studies, serum chemistry was evaluated at baseline and monthly. Hematology was evaluated at baseline, monthly for 6 months, and then every 3 months. Thyroid function was measured at baseline and every 6 months.

### Table 2: Adverse Reactions in Adults with RMS with an Incidence at Least 2% More for ZINBRYTA 150 mg SQ Every 4 Weeks than AVONEX 30 mcg IM Once Weekly (Study 1)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ZINBRYTA 150 mg SQ Every 4 Weeks N = 919 %</th>
<th>AVONEX 30 mg IM Once Weekly N = 922 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngitis</td>
<td>25</td>
<td>21</td>
</tr>
<tr>
<td>Upper respiratory tract infection¹</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>Rash¹</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Influenza</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Dermatitis¹</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Oropharyngeal pain</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Eczema¹</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>5</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Tonsillitis</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Acne</td>
<td>3</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

¹ includes upper respiratory tract infection and viral upper respiratory tract infection

### Table 3: Adverse Reactions in Adults with RMS with an Incidence at Least 2% More for ZINBRYTA 150 mg SQ Every 4 Weeks than Placebo (Study 2)

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ZINBRYTA 150 mg SQ Every 4 Weeks N = 208 %</th>
<th>Placebo N = 204 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper respiratory tract infection</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Depression¹</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Rash¹</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Increased ALT</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Anemia</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Increased AST</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Dermatitis¹</td>
<td>3</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

¹ includes depressed mood and depression

Includes erythematous rash, exfoliative rash, maculopapular rash, papular rash, pruritic rash, rash, and vesicular rash

Includes allergic dermatitis, atopic dermatitis, bullous dermatitis, dermatitis, exfoliative dermatitis, and seborrheic dermatitis

Includes dyshidrotic eczema, eczema, and nummular eczema

Other clinically relevant adverse reactions observed at <2% difference included abnormal liver function test, decreased lymphocyte count, diarrhea, dry skin, erythema, folliculitis, increased hepatic enzyme, laryngitis, lymphadenitis, pneumonia, pruritus, psoriasis, respiratory tract infection, skin exfoliation, toxic skin eruption, and viral infection.
Clinical studies of ZINBRYTA did not include patients with ALT or AST more than two times the ULN. Patients with signs and symptoms of hepatic impairment may be at increased risk for hepatotoxicity from ZINBRYTA [see Dosage and Administration (2.3, 2.4), Contraindications (4), and Warnings and Precautions (5.1)].

17 PATIENT COUNSELING INFORMATION
Adviser the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Hepatic Injury: Inform the patient of the risk of severe hepatic injury associated with ZINBRYTA. Advise patients of the symptoms of hepatic dysfunction, and instruct patients to report such symptoms to their healthcare provider immediately [see Warnings and Precautions (5.1)].

Discuss with the patient the importance of measuring hepatic laboratory values and having them evaluated by the healthcare provider monthly while taking ZINBRYTA and for up to 6 months after the last dose of ZINBRYTA.

Discuss with the patient the risk of concomitant use of other hepatotoxic medications, over the counter medications, herbal products, or dietary supplements.

Inform the patient that they will be given a ZINBRYTA Patient Wallet Card that they should carry with them at all times. This card describes symptoms which, if experienced, should prompt the patient to immediately seek medical evaluation.

Advise the patient to show the ZINBRYTA Patient Wallet Card to other treating healthcare providers.

Immune-Mediated Disorders: Advise patients that ZINBRYTA can cause their immune system to attack healthy cells in their body and that this can affect any organ system.

Skin Reactions: Advise patients that ZINBRYTA can cause dermatologic reactions that can range from mild rashes to serious reactions that could require treatment with other medications or result in hospitalization. Instruct patients to seek immediate medical attention if dermatologic reactions occur [see Warnings and Precautions (5.2)].

Lymphadenopathy: Inform patients that ZINBRYTA may cause lymphadenopathy that can range from mild events that can resolve on their own to serious lymphadenopathy that may require invasive procedures for diagnosis. Inform patients of the symptoms and instruct patients to contact their healthcare provider if they develop lymphadenopathy [see Warnings and Precautions (5.2)].

Non-Infectious Colitis: Inform patients that ZINBRYTA may cause gastrointestinal reactions that may be serious and could require treatment. Advise patients of the symptoms of colitis and instruct patients to promptly contact their healthcare provider if they experience these symptoms [see Warnings and Precautions (5.2)].

ZINBRYTA REMS Program
ZINBRYTA is available only through a restricted program called the ZINBRYTA REMS Program [see Warnings and Precautions (5.3)]. Inform the patient of the following notable requirements:

• Patients must enroll in the program and comply with ongoing monitoring requirements [see Warnings and Precautions (5.5, 5.2)].

ZINBRYTA is available only from certified pharmacies participating in the program. Therefore, provide patients with the telephone number and website for information on how to obtain the product.

8.1 Pregnancy
Risk Summary: There are no adequate data on the developmental risk associated with use of ZINBRYTA in pregnant women. Administration of ZINBRYTA to monkeys during gestation resulted in embryofetal death and increased risk for hepatotoxicity from ZINBRYTA [see Warnings and Precautions (5.1)].

8.3 Lactation
Risk Summary: There are no data on the presence of daclizumab in human milk, the effects on the breastfed child, or the effects of the drug on milk production. Daclizumab was excreted in the milk of ZINBRYTA-treated monkeys. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for ZINBRYTA and any potential adverse effects on the breastfed child from ZINBRYTA or from the underlying maternal condition.

8.4 Pediatric Use
Safety and effectiveness of ZINBRYTA in patients less than 17 years old have not been established. Use of ZINBRYTA is not recommended in pediatric patients due to the risks of hepatic injury and immune-mediated disorders [see Warnings and Precautions (5.1, 5.2)].

8.5 Geriatric Use
Clinical studies of ZINBRYTA did not include a sufficient number of patients aged 65 and over to determine whether they respond differently than younger patients.

8.6 Hepatic Impairment
Clinical trials did not include patients with ALT or AST more than two times the ULN.
Meet Your Leader

Janis M. Miyasaki, MD, MEd, FRCPC, FAAN

In order to evaluate the AAN and Board performance, you need to be informed. Keeping up-to-date with Neurology Today and also the website can help members make an informed decision. Get involved in the AAN—there is no better way to understand than to participate. There are many opportunities to participate including reviewing guidelines prior to publication, participating in focus groups, on up to full committee membership. There are also many leadership training opportunities that help you in many aspects of your life. I participated in the Palatucci Advocacy Leadership Forum and use those skills every day.

How do you deal with the challenges of balancing the demands of your work and personal life?

First, I haven’t always been successful in having work-life balance. Wanting to spend time with my son as a single mother helped me. One night, he was at his dad’s and I stayed at work to catch up and thought, “Isn’t it great that I’m getting all this work done?” It was 8:00 p.m. That wasn’t great. I realized it as soon as I thought it.

He is now at university, and I have a stepson also at university. I still work too many hours and say ‘yes’ too often, but I also exercise (since I keep telling my Parkinson patients to do so). In fact, my advice to my patients to be their best is probably good advice for me to follow: keep socially engaged, connect to your community, read widely, debate politics, and do hobbies. This last one is for all physicians: Appreciate your families (especially your spouse). They also sacrifice for your profession.

Access Your New Neurology Compensation and Productivity Report

The AAN’s 2016 Neurology Compensation and Productivity Report and customizable results dashboard, based on 2015 data, is now available.

This is the fourth—and only—annual report exclusively detailing the neurology profession and gives you the power to compare US neurologist salaries and practice characteristics by subspecialty, practice setting, and more! The report and customizable results dashboard will enable you to see what other practices are doing to more efficiently streamline their work and find new areas of growth.

US participants who completed the 2016 Neurology Compensation and Productivity Survey can access the online report and customizable dashboard for free. Access to the report and customizable results dashboard is also available for purchase for $600 by members who did not complete the survey.

Whether you are a physician or practice administrator in a large or small practice setting, you can:

- Discover fair market value based on your subspecialty, region, and practice type
- Create charts and graphs and download them right to your desktop
- Assess patient and practice management principles and implement efficiencies that ultimately can help improve the quality of patient care

Cohort Testing of Axon Registry Accomplishes “Push” Milestone

Recently, the neurology department of the University of Miami successfully packaged up patient records and sent the data files to the Axon Registry™ using a secure and encrypted file transfer process. The university is the first of 28 practices participating with the Axon Registry pilot that are testing the “push method” of data transfer. This “push method” is the alternative method for institutions or practices that have tight security policies about what third-party software can be installed on their computer systems. Other pilot participants have been successfully using the “pull method,” where required software is installed on the users’ computer system and the registry extracts the necessary data from clinic files.

AAN President Elect Ralph L. Sacco, MD, MS, FAAN, FAHA, is the chair of the neurology department at the University of Miami’s Miller School of Medicine. It may not be surprising that his team is on the forefront of this effort to harness data that could improve the delivery of health care to people with brain disease.

“As president elect of the AAN, I feel strongly about this major initiative to improve the quality of care for our patients as well as provide help to our clinical neurologists,” said Sacco. “It was very important to me to be an early adopter in my department and get firsthand knowledge of the power of the Axon Registry.”

Sacco tasked his neurology department colleague Salim I. Dib, MD, to champion the registry project. Dib created a cross-departmental team, determining key stakeholders and understanding the team’s weaknesses and strengths prior to beginning of the registry project.

“Identifying a representative from the neurology clinic—our nurse manager—to work closely with IT and the Patient Safety and Quality Office proved to be very valuable,” said Dib. Weekly meetings were held to coordinate efforts among neurology, IT, informatics, and patient safety staff. They also worked closely with the AAN’s registry provider FIGMD. The result of the three-month effort was the development of an automated process to send appropriate patient data files to the Axon Registry.

“We are proud of the excellent work performed by the University of Miami staff involved in this project,” said Sacco.

For more information on the Axon Registry, visit AAN.com/view/Axon.

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Available by August 1

- Neurology: A Low-cost, Tablet-based Option for Prehospital Neurologic Assessment: the iTREAT Study
  Kevin M. Barrett, MD, MSc, and Andrew M. Southerland, MD, MSc
- Neurology: Zika Virus-associated Guillain-Barré Syndrome Variant in Haiti
  Stephen N. Donahue, MD, and Aaron L. Berkowitz, MD, PhD
- Neurology: Executive Summary: International Consensus Guidance for Management of Myasthenia Gravis
  Ted M. Burns, MD, and Donald B. Sanders, MD
- Neurology: Clinical Practice: Alice in Wonderland Syndrome: a Systematic Review
  David A. Lapides, HS, and Jan Dirk Blom, MD, PhD
MACRA Introduces New Component: Clinical Practice Improvement Activities

Under the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA), the Centers for Medicare & Medicaid Services have added a new component to quality payment programs for providers: Clinical Practice Improvement Activities (CPIAs). This new element is part of the Merit-based Incentive Payment System (MIPS), which replaces older CMS programs: the Physician Quality Reporting System (PQRS), the Value-based Payment Modifier (VBPM), and Meaningful Use of Electronic Health Records (MU).

Implementation of MIPS begins in 2017. At least that is when physician participation really begins. Data collected in 2017 will inform payment adjustments starting in 2019, the official start of MACRA.

Under MIPS, each provider (or group) will receive a single composite score based on achievements in the following four areas. The composite score will determine future provider payment bonuses and penalties.

1. Quality (formerly PQRS)
2. Resource Use (formerly VBPM)
3. Advancing Care Information (formerly MU of EHR)
4. Clinical Practice Improvement Activities (new)

Clinical Practice Improvement Activities (CPIAs) are formalized quality or practice redesign activities that lead to improved population health and patient outcomes, lower costs, and/or better patient experience of care. Physicians will choose from a broad inventory of over 90 potential activities to fulfill the requirement for CPIAs. Proposed examples of CPIAs include:

- Care coordination
- Expanded practice hours
- Telehealth services
- Chronic care management programs
- Use of a registry to track population outcomes
- Improved transitions of care

CPIAs take collecting quality data to the next level and require providers to use their quality data to make improvements in care.

The AAN supports a broad inventory of proposed CPIAs and recommends that CMS continue to allow for flexibility in CPIAs. Neurologists are possibly well positioned to perform several of the proposed CPIAs, such as:

- Collection of patient experience and satisfaction data, e.g., through the Consumer Assessment of Healthcare Providers and Systems (CAHPS) survey.
- Management of patients with stroke in a systemic anticoagulation program.
- Collaborate with Quality Improvement organizations to improve the health status of communities affected by Alzheimer’s.
- Participation in clinical trials and data registries for neurologic drugs.
- Reconciling and coordinating medication use, including for opioid drugs.
- Participating in the Transforming Clinical Practices Initiative.
- Linking patients with neurologic disorders to sources of home- and community-based social services.
- Participation in qualified clinical data registries.
- Performing CPIAs that integrate behavioral and mental health with primary care for individuals with chronic conditions.

The AAN’s Axon Registry has been recognized by CMS as a qualified clinical data registry and can help members meet these requirements once they are determined by CMS. Learn more about the Axon Registry at AAN.com/view/Axon.

The AAN provides members with numerous resources to help members understand quality improvement initiatives and how to put them into practice at AAN.com/practice/quality-measures. More information on MACRA is available at AAN.com/view/macra.
Don’t let patients get lost in the noise of RMS

RMS = relapsing forms of multiple sclerosis.
QUIETING MS

for your patients with relapsing MS

* AUBAGIO is effective across key measures of disease activity: sustained disability progression (14 mg only), annualized relapse rate, and MRI activity. Overall discontinuation rates due to adverse events were 12.5% with AUBAGIO 14 mg, 11.2% with AUBAGIO 7 mg, and 7.5% with placebo, and treatment discontinuation rates due to common adverse events were ≤3.3% in the pooled clinical trials.1,2

INDICATION

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

IMPORTANT SAFETY INFORMATION

WARNING: HEPATOTOXICITY AND RISK OF TERATOGENICITY

Severe liver injury including fatal liver failure has been reported in patients treated with leflunomide, which is indicated for rheumatoid arthritis. A similar risk would be expected for teriflunomide because recommended doses of teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. AUBAGIO is contraindicated in patients with severe hepatic impairment and in patients taking leflunomide. Concomitant use of AUBAGIO with other potentially hepatotoxic drugs may increase the risk of severe liver injury. Obtain transaminase and bilirubin levels within 6 months before initiation of AUBAGIO therapy. Monitor ALT levels at least monthly for 6 months after starting AUBAGIO. If drug-induced liver injury is suspected, discontinue AUBAGIO and start an accelerated elimination procedure with cholestyramine or charcoal. Patients with pre-existing liver disease may be at increased risk of developing elevated serum transaminases when taking AUBAGIO. Based on animal data, AUBAGIO may cause major birth defects if used during pregnancy. Pregnancy must be excluded before starting AUBAGIO. AUBAGIO is contraindicated in pregnant women or women of childbearing potential who are not using reliable contraception. Pregnancy must be avoided during AUBAGIO treatment or prior to the completion of an accelerated elimination procedure after AUBAGIO treatment.

Warnings and Precautions

Patients with pre-existing acute or chronic liver disease, or those with serum ALT >2 times the upper limit of normal (ULN) before initiating treatment, should not normally be treated with AUBAGIO. In clinical trials, if ALT elevation was >3 times the ULN on 2 consecutive tests, patients discontinued AUBAGIO and underwent accelerated elimination. Consider additional monitoring if co-administering AUBAGIO with other potentially hepatotoxic drugs; monitor patients who develop symptoms suggestive of hepatic dysfunction (eg, unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine). Before starting therapy, use of reliable contraception must be confirmed, and the patient counseled on risks to the fetus. Patients with delayed onset of menses or other reason to suspect pregnancy should immediately see their physician for pregnancy testing. Patients who become pregnant or wish to become pregnant should discontinue treatment, followed by accelerated elimination until plasma concentrations of <0.02 mcg/mL are verified, a level expected to pose minimal risk to the fetus. Women who become pregnant while taking AUBAGIO may enroll in the AUBAGIO pregnancy registry by calling 1-800-745-4447, option 2.

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

Decreases in white blood cell counts, mainly of neutrophils and lymphocytes, and platelets have been
AUBAGIO® (teriflunomide) was proven again and again to reduce key measures of disease activity: sustained disability progression (14 mg only), annualized relapse rate, and MRI activity.

- AUBAGIO 14 mg is the only oral RMS therapy with 2 pivotal Phase III trials that show a significant reduction in the risk of sustained disability accumulation.
  - AUBAGIO 7 mg did not demonstrate a significant reduction in risk of sustained disability progression in either trial.
- 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.
- AUBAGIO has demonstrated a consistent safety profile across 4 separate trials in 2047 patients.
- One daily tablet that can be taken with or without food.
- Health care professionals should run certain tests before prescribing AUBAGIO and should monitor patient liver enzyme levels monthly for the first 6 months.

TEMSO: A double-blind, placebo-controlled trial in patients with relapsing forms of MS (N=1088). Patients were randomized to receive AUBAGIO 14 mg (n=359), AUBAGIO 7 mg (n=366), or placebo (n=363) once daily for 108 weeks.

TOWER: A double-blind, placebo-controlled trial in patients with relapsing forms of MS (N=1169). Patients were randomized to receive AUBAGIO 14 mg (n=372), AUBAGIO 7 mg (n=408), or placebo (n=389) once daily with results for up to 40 months of treatment.

TOPIC: A double-blind, placebo-controlled clinical trial in patients with relapsing MS (N=618). Patients were randomized to receive AUBAGIO 14 mg (n=216), AUBAGIO 7 mg (n=205), or placebo (n=197) once daily for 108 weeks. Patients had a first clinical event consistent with acute demyelination occurring within 90 days of randomization with 2 or more T2 lesions at least 3 mm in diameter characteristic of MS.

Study 4: A randomized, double-blind, placebo-controlled trial in patients with relapsing forms of MS (N=179). Patients were randomized to receive AUBAGIO 14 mg (n=57), AUBAGIO 7 mg (n=61), or placebo (n=61) once daily for 36 weeks.

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

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

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

Please see Brief Summary of Full Prescribing Information, including boxed WARNING regarding hepatotoxicity and use in pregnancy, on the following pages.
AUBAGIO® (teriflunomide) and MS One to One® may help your patients manage their RMS

Getting started: the AUBAGIO Start form is both a prescription for AUBAGIO and enrollment for support offered by MS One to One.

For more information, visit www.AubagioHCP.com or call 1-855-MSOne2One (1-855-676-6326).

AUBAGIO is effective across key measures of disease activity: sustained disability progression (14 mg only), annualized relapse rate, and MRI activity. Overall discontinuation rates due to adverse events were 12.5% with AUBAGIO 14 mg, 11.2% with AUBAGIO 7 mg, and 7.5% with placebo, and treatment discontinuation rates due to common adverse events were ≤3.3% in the pooled clinical trials.1,2

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.


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AUBAGIO® (teriflunomide) tablets, for oral use

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 hepatotxicity. Obtain transaminase and bilirubin levels within 6 months before initiation of AUBAGIO therapy. Monitor ALT levels at least monthly for six months after starting AUBAGIO [see Warnings and Precautions (5.1)]. If drug induced liver injury is suspected, discontinue AUBAGIO and start an accelerated elimination procedure with cholestyramine or charcoal [see Warnings and Precautions (5.3)]. AUBAGIO is contraindicated in patients with severe hepatic impairment [see Contraindications (4)]. 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 excluded during AUBAGIO treatment or prior to the completion of an accelerated elimination procedure after AUBAGIO treatment [see Contraindications (4), Warnings and Precautions (5.2), and Use in Specific Populations (8.1)].

1 **INDICATIONS AND USAGE**

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

2 **DOSEAGE 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 treatment. 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 or blood test for mycobacterium tuberculosis infection [see Warnings and Precautions (5.4)].
- Check blood pressure before start of AUBAGIO treatment and periodically thereafter [see Warnings and Precautions (5.7)].

4 **CONTRAINDICATIONS**

AUBAGIO is contraindicated in:

- Patients with severe hepatic impairment [see Warnings and Precautions (5.1)].
- Pregnant women or women of childbearing potential not using reliable contraception. AUBAGIO may cause fetal harm [see Warnings and Precautions (5.2) and Use in Specific Populations (8.1)].
- Patients with a history of a hypersensitivity reaction to teriflunomide, leflunomide, or any of the inactive ingredients in AUBAGIO. Reactions have included anaphylaxis, angioedema, and serious skin reactions [see Warnings and Precautions (5.5)].
- Co-administration with leflunomide [see Clinical Pharmacology (12.3 in the full prescribing information)].

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 liver disease may be at increased risk of developing elevated serum transaminases when taking AUBAGIO. AUBAGIO was discontinued and patients underwent an accelerated elimination procedure [see Warnings and Precautions (5.3)]. Of the patients who underwent discontinuation and accelerated elimination in controlled trials, half returned to normal or near normal values within 2 months.

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. AUBAGIO-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 AUBAGIO and start an accelerated elimination procedure [see Warnings and Precautions (5.3)] and monitor liver tests weekly until normalized. If AUBAGIO-induced liver injury is unlikely because some other probable cause has been found, resumption of AUBAGIO therapy may be considered.

5.2 Use in Women of Childbearing Potential

There are no adequate and well-controlled studies evaluating AUBAGIO in pregnant women. However, based on animal studies, teriflunomide may increase the risk of teratogenic effects or fetal death when administered to a pregnant woman [see Contraindications (4)].

Women of childbearing potential must not be started on AUBAGIO until pregnancy is excluded and it has been confirmed that they are using reliable contraception. Before starting treatment with AUBAGIO, patients must be fully counseled on the potential for serious risk to the fetus. The patient must be advised that if there is any delay in onset of menses or any other reason to suspect pregnancy, they must notify 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 verification of 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), Warnings and Precautions (5.5) 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 cholestyramine 8 g three times a day is not well tolerated, cholestyramine 4 g three times a day can be tolerated.
- Administration of 50 g oral activated charcoal powder every 12 hours for 11 days.

If either elimination procedure is 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 potentially result in return of disease activity if the patient had been responding to AUBAGIO treatment.

5.4 Bone Marrow Effects/Immunosuppression Potential/Infections

**Bone Marrow Effects**

A mean decrease in white blood cell (WBC) count of approximately 15% (mainly neutrophils and lymphocytes) and in platelet count of approximately 10% was observed in placebo-controlled trials with 7 mg and 14 mg of AUBAGIO compared to baseline. 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 < 1.5x10^9/L was observed in 12% and 16% of patients receiving AUBAGIO 7 mg and 14 mg, respectively, and those receiving placebo; lymphocyte count < 0.8x10^9/L was observed in 10% and 12% of patients receiving AUBAGIO 7 mg and 14 mg, respectively, compared with 6% of patients receiving placebo. No cases of serious pancytopenia were reported in premarketing clinical trials of AUBAGIO but rare cases of pancytopenia and agranulocytosis have been reported in the postmarketing setting with leflunomide. A similar risk would be expected for AUBAGIO [see Clinical Pharmacology, 12.3 in the full prescribing information]. Cases of thrombocytopenia with AUBAGIO, including rare cases with platelet counts less than 50,000/mm^3, have been reported in the postmarketing setting. 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. If a patient develops a serious infection 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 AUBAGIO 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 AUBAGIO 7 mg (2.2%) or 14 mg (2.7%) compared to placebo. However, in one fatal case of varicella pneumonia, patients infected in a patient taking AUBAGIO 14 mg for 1.7 years. Fatal infections have been reported in the post-marketing setting in patients receiving leflunomide, especially Pneumocystis jiroveci pneumonia and aspergillosis. Most of the reports were confined by concomitant immunosuppressant therapy and/or concomitant illness which, in addition to rheumatoid disease, may predispose patients to infection. In clinical studies with AUBAGIO, cytomegalovirus hepatitis reactivation has been observed.

In clinical studies with AUBAGIO, cases of tuberculosis have been observed. Prior to initiating AUBAGIO, screen patients for latent tuberculosis infection with a tuberculin skin test or with a blood test for mycobacterium tuberculosis infection. AUBAGIO has not been studied in patients with a positive tuberculin 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.

Vaccination

No clinical data are available on the efficacy and safety of live vaccinations in patients taking AUBAGIO. Vaccination with live vaccines is 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 AUBAGIO. 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 Hypersensitivity and Serious Skin Reactions

AUBAGIO can cause anaphylaxis and severe allergic reactions [see Contraindications (4)]. Signs and symptoms have included dyspnea, urticaria, and angioedema including lips, eyes, throat, and tongue. Cases of serious skin reactions, including cases of Stevens-Johnson syndrome (SJS) and a fatal case of toxic epidermal necrolysis (TEN), have been reported with AUBAGIO.

In patients treated with leflunomide, the parent compound, very rare cases of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) have also been reported. Inform patients of the signs and symptoms of anaphylaxis and angioedema and signs and symptoms that may signal a serious skin reaction. Inform patients that a fever along with other signs of drug rash (e.g., rash, lymphadenopathy, or hepatic dysfunction) may be drug-related. Instruct patients to discontinue AUBAGIO and seek immediate medical care should these signs and symptoms occur. Discontinue AUBAGIO, unless the reactions are clearly not drug-related, and begin an accelerated elimination procedure immediately [see Warnings and Precautions (5.5)]. In such cases, patients should not be re-exposed to teriflunomide [see Contraindications (4)].

5.6 Peripheral Neuropathy

In placebo-controlled studies, peripheral neuropathy, including both polyneuropathy and mononeuropathy (e.g., carpal tunnel syndrome), occurred more frequently in patients taking AUBAGIO than in patients taking placebo. The incidence of peripheral neuropathy confirmed by nerve conduction studies was 1.4% (13 patients) and 1.9% (17 patients) of patients receiving 7 mg and 14 mg of AUBAGIO, respectively, compared with 0.4% receiving placebo (4 patients).

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

Table 1 lists adverse reactions in placebo-controlled trials with rates that were at least 2% for AUBAGIO patients and also at least 2% above the rate in placebo patients. The most common reactions of any grade were headache (40%), fever (23%), and bone pain (14%). Cases of anaphylaxis, anaphylactoid reaction, and angioedema have been reported during treatment with leflunomide. Interstitial lung disease may be drug-related. Instruct patients to discontinue AUBAGIO and seek immediate medical care should these signs and symptoms occur. Discontinue AUBAGIO, unless the reactions are clearly not drug-related, and begin an accelerated elimination procedure immediately [see Warnings and Precautions (5.5)]. In such cases, patients should not be re-exposed to teriflunomide [see Contraindications (4)].

5.7 Increased Blood Pressure

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

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>AUBAGIO 7</th>
<th>AUBAGIO 14</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>18%</td>
<td>16%</td>
<td>15%</td>
</tr>
<tr>
<td>Increase in Alanine transaminase</td>
<td>13%</td>
<td>15%</td>
<td>9%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>13%</td>
<td>14%</td>
<td>8%</td>
</tr>
<tr>
<td>Anemia</td>
<td>10%</td>
<td>13%</td>
<td>5%</td>
</tr>
<tr>
<td>Nausea</td>
<td>8%</td>
<td>11%</td>
<td>7%</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>8%</td>
<td>9%</td>
<td>7%</td>
</tr>
<tr>
<td>Anthralgia</td>
<td>8%</td>
<td>6%</td>
<td>5%</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>4%</td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3%</td>
<td>4%</td>
<td>2%</td>
</tr>
</tbody>
</table>
patients in the 14 mg AUBAGIO group versus 4/997 (0.4%) patients in the placebo group. These elevations were transient. Some elevations were accompanied by hyperkalemia. AUBAGIO may cause acute urea nitrogenophathy with transient acute renal failure because AUBAGIO increases renal urea nitrogen clearance.

**Hypophosphatemia**

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

### 6.2 Use in Specific Populations

#### 6.2.1 Pregnancy

Pregnancy Category X [see Contraindications (4) and Warnings and Precautions (5.2)]. When teriflunomide (oral doses of 1, 3, or 10 mg/kg/day) was administered to pregnant rats throughout the period of organogenesis, high incidences of fetal malformations (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. 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. Use in Males

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

**Pregnancy Registry**

Although AUBAGIO is contraindicated in pregnancy, a pregnancy registry has been established to monitor fetal outcomes of pregnant women exposed to AUBAGIO. Physicians are encouraged to enroll pregnant women in the AUBAGIO pregnancy registry, or pregnant women may enroll themselves, by calling 1-800-745-4447, option 2.

#### 6.3 Nursing Mothers

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

#### 6.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

#### 6.5 Geriatric Use

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

#### 6.6 Hepatic Impairment

No dosage adjustment is necessary for patients with mild and moderate hepatic impairment. The pharmacokinetics of teriflunomide in severe hepatic impairment have not been evaluated. AUBAGIO is contraindicated in patients with severe hepatic impairment [see Contraindications (4) Warnings and Precautions (5.1), and Clinical Pharmacology (12.3 in the full prescribing information)].

#### 6.7 Renal Impairment

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

### 8 USE IN SPECIFIC POPULATIONS

#### 8.1 Pregnancy

Pregnancy Category X [see Contraindications (4) and Warnings and Precautions (5.2)]. When teriflunomide (oral doses of 1, 3, and 10 mg/kg/day) was administered to pregnant rats throughout the period of organogenesis, high incidences of fetal malformations (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 recommended human dose (MRHD, 14 mg /day). Administration of teriflunomide (oral doses of 1, 3.5, or 12 mg/kg/day) to pregnant rabbits throughout organogenesis resulted in high incidences of fetal malformation (primarily craniofacial, and axial and appendicular skeletal defects) and embryofetal death at doses associated with minimal maternal toxicity. Maternal plasma exposure at the no-effect dose (1.0 mg/kg/day) for embryofetal developmental toxicity in rabbits was less than that in humans at the MRHD. In studies in which teriflunomide (oral doses of 0.05, 0.1, 0.3, 0.6, and 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.
Improve Your Bottom Line by Using Benchmarks

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August 10, 2016 | 12:00–1:00 p.m. ET
Deadline to Register: August 9
Directors: David A. Evans, MBA, and Brad C. Klein, MD, MBA, FAAN

Objectives
- Learn how to identify practice inefficiencies
- Locate and interpret available data sources
- Apply process improvements using meaningful data

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New Issues Help Your Practice and Your Patients

The August-September issue of Neurology Now® features multitalented Cedric the Entertainer, who has made it his mission to educate others about diabetic nerve pain after this serious diabetes complication sidelined his father for more than a year.

Do neurologists who have a disease that they treat their patients for have greater empathy or insights because of their shared condition? Can stroke specialists predict outcomes based on severity and location of a stroke and how well patients do in rehab? These questions are examined in two feature stories.

Neurology Now is a free benefit for AAN members and their patients. AAN members may elect to receive multiple copies to distribute to their patients, who also can subscribe for free. Visit NeurologyNow.com to learn more or access your AAN member profile to adjust the number of copies you receive.

Multiple sclerosis is the focus of two articles and an accompanying editorial in the new issue of Neurology® Clinical Practice. Radiologically isolated syndrome, clinically isolated syndrome, and relapsing-remitting multiple sclerosis are the focus of “Consensus Opinion of US Neurologists on Practice Patterns in RIS, CIS, and RRMS: Evolution of Treatment Practices,” while a second article examines the development and approval of generic disease-modifying therapies for MS.

Other topics of interest to practicing neurologists include the article “Knowledge Translation of an Online Tool to Determine Candidacy for Epilepsy Surgery Evaluation.” Readers also can learn Five New Things about neurometabolic disorders and tuberous sclerosis complex.

Neurology: Clinical Practice, published six times a year, is available in print (for US members only), online, and for the iPad and Android. Visit Neurology.org/cp for more information.
AAN Scores Regulatory Advocacy Victories with CMS Proposed Fee Schedule

Continued from cover

deliver improved health outcomes that matter to the patient.”

According to the proposed rule, neurologists will receive a one-percent increase in allowed charges. Other positive aspects of the proposed rule include:

**Billing Code Revisions**

CMS is proposing several revisions to the Physician Fee Schedule billing code set to more accurately recognize the work of cognitive specialties like neurology. Historically, care management and cognitive work has been “bundled” into the E/M visit codes used by all specialties. Additional efforts were not recognized outside of the E/M visit. To improve payment accuracy for such care, CMS proposes new codes that separately pay for chronic care management.

**E/M Services**

CMS also is proposing to address non-face-to-face prolonged E/M services. In the proposed rule, CMS acknowledges the efforts of stakeholders like the AAN. We have previously requested payment for non-face-to-face time spent outside of E/M. CMS agrees that existing codes, which are currently non-covered, would provide a means to recognize the additional resource costs of physicians when they spend an extraordinary amount of time outside the in-person office visit caring for the individual needs of their patients. Accordingly, beginning in 2017, CMS proposes to begin paying for CPT add-on codes 99358 and 99359 for non-face-to-face prolonged service. The services would be furnished on the same day by the same physician as the companion E/M code.

**Cognitive Impairment**

CMS proposes separate payment for assessing and creating a care plan for beneficiaries with cognitive impairment in the creation of new code GPPP6. The CPT Editorial Panel approved a similar code scheduled to be included in the 2018 CPT code set, so CMS intends for their code to be temporary.

**Chronic Care Management Services**

For 2017, CMS also proposes a new add-on code, GPPP7, that would improve payment for visits that initiate chronic care management (CCM) services. The code would be billable for beneficiaries who require extensive face-to-face assessment and care planning by the billing practitioner (as opposed to clinical staff), through an add-on code to the initiating visit. CMS acknowledges this proposal will more appropriately recognize the relative resource costs for the work of the billing practitioner in initiating CCM services—specifically for extensive work assessing the beneficiary and establishing the CCM care plan that is reasonable and necessary, and that is not accounted for in the billed initiating visit.

**Teleneurology and Critical Care Consultation**

CMS recognizes the potential benefit of critical care consultation services that are furnished remotely. CMS specifically notes that telestroke is an approach that allows a neurologist to provide remote treatment to stroke victims. The agency further explains that teleneurology offers consultations for neurological problems from a remote location and may be initiated by a physician or patient for conditions such as headaches, dementia, strokes, multiple sclerosis, and epilepsy. CMS is proposing to make payment through critical care consultations furnished via telehealth using new G-codes described (GTTT1 and GTTT2) and also for advance care planning services.

“These decisions by CMS are a result of our proactive regulatory advocacy strategy that champions practicing neurologists and their patients,” said Orly Avitzur, MD, MBA, FAAN, chair of the AAN’s Medical and Economics Management Committee. “AAN volunteer members and staff work daily to develop a proactive relationship with officials at CMS and other federal regulatory agencies. We have taken your concerns directly to Medicare’s leaders and we are succeeding in having your voice heard by those in power, and this success is reflected in the proposals in this year’s Fee Schedule.”
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.

On July 6, the Centers for Medicare & Medicaid Services (CMS) proposal contained a big success on the regulatory advocacy front for the AAN. In response to our continued pressure, CMS proposed to again shorten the electronic health records (EHR) meaningful use reporting period to 90 days in 2016.

Similar to 2015, CMS is proposing an EHR reporting period of any continuous 90-day period between January 1, and December 31, 2016. This comes after the AAN and other stakeholders continuously stressed the need for a 90-day reporting period. CMS further determined that eligible providers (EPs) that have not successfully demonstrated meaningful use in a prior year may attest to Modified Stage 2 rather than the Stage 3 objectives by October 1, 2017.

CMS is also proposing hardship exceptions for certain EPs that have not successfully demonstrated meaningful use in a prior year, intend to attest to meaningful use for an EHR reporting period in 2017, and intend to transition to MIPS and report on measures specified for the advancing care information performance category under the MIPS as proposed in 2017. These EPs may apply for a significant hardship exception from the 2018 payment adjustment. Visit AAN.com/practice/medicare for additional details on the meaningful use program.

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1 AAN Accreditation Statement: The American Academy of Neurology Institute (the education subsidiary of the AAN) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. AAN Designation Statement: The AANI designates this enduring material for a maximum of 147.5 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

2 Hard Drive does not include all the functionality available online, such as Advanced Search, Recently Viewed, MP3 Downloads, Bookmarks, Syllabi files, iPoster files, and CME testing.
AAN Members Organize Runnin’ for Research in Three States

There is nothing particularly new about holding races or walks to raise funds to support medical research. Unless you don’t have such a race in your community. Or, one to support a particular health need.

David B. Watson, MD, FAAN, a 2011 graduate of the AAN’s Palatucci Advocacy Leadership Forum (PALF), seized on the opportunity to launch such a fundraising race—Runnin’ for Research—in Morgantown, WV, where he is interim neurology chair and director of the Headache Center at the West Virginia University. And since the first race in 2014, he has enlisted two more “PALFers,” Brian M. Plato, DO, (class of 2013) in Louisville, KY, and Jennifer Bickel, MD, (class of 2012 and faculty in 2016) in Kansas City, MO. All three AAN advocates are now in the midst of organizing a Runnin’ for Research event in their respective cities to be held on October 8, 2016.

Watson, a 2015 Emerging Leaders Forum graduate, recently shared with AANnews the genesis of Runnin’ for Research and how the event has grown.

Why did you start this race?

I was looking for a way to contribute to the migraine community and headache and migraine research in particular. I had started a personal health kick and was running a lot of 5Ks. It seemed like a fun and somewhat straightforward way to raise money and awareness. I didn’t know at the time how much effort it would take, but with the help of a lot of volunteers we were able to pull it off. I used my PALF training in that I made an action plan, used local media and social media for advertising, and worked with a variety of groups for sponsorships.

When was the inaugural race and how many have you held?

The first race was April 2014 in Morgantown. At the time it was called AHMA Runnin’ for Research. The American Headache and Migraine Association (AHMA) is the patient arm of the American Headache Society and they helped by providing some upfront money and they acted as the parent organization as an established 501(c)(3) organization. We had one race that year, then expanded to two the following year with the addition of Louisville. In 2016, we are adding Kansas City, MO. We are open to expanding to as many sites as we can throughout the US.

Has participation grown over the years?

Our first year we had 132 participants. Last year, the Morgantown race was down to just under 100 due to very poor weather, but with the addition of the Louisville race our total participation exceeded 150. This does not include the volunteers at each site.

How much have you raised in total and who has received the funds?

In year one, we were able to donate approximately $6,000. Last year, we raised about $20,000. Of that amount, $17,000 was donated to the American Migraine Foundation at the annual meeting of the American Headache Society. Some was made available to help patients attend conferences. Some was saved as a reserve for this year and beyond so we could have start-up funds for new locations. This year some will likely go to AHMA as well.

Have the races attracted any business sponsorships or media support?

Most of the fundraising comes from business sponsorships. For example, this year we have large sponsorships from Teva, Allergan, Avanir, and eNeura as well as our hospitals at each site have been significant contributors. Local businesses have also been generous with sponsorships in past years. We have had local newspaper coverage but nothing beyond this so far. This year we will be trying to get local TV and radio coverage.

In 2016, with the help of the West Virginia Law School and a grant from the AAN to help support Palatucci Forum graduates’ projects, Runnin’ for Research Inc. became an independent 501(c)(3) organization and registered business in the state of West Virginia. This allows for better flexibility and expansion. The AHMA and AHS were wonderful partners and we likely would not have done this without them.

What would you recommend to members who might want to start similar races?

First, be sure you really want to do it. Second, get a team in place to help. Pick a worthy cause (many of these, like the MS Society, already have race organizations that may be able to help). Get started early—you likely need a minimum of six months, if not more, to actually get it all put together. The most important first decisions are date, location, and distance. If you are not experienced with 5K events, enter a few to see what you like and don’t like.

Watson has developed a PDF file guidebook available to AAN members who are interested in establishing a similar race in their communities. He can be contacted at dwatson@hsc.wvu.edu.
What is the best way to diagnose atypical parkinsonian syndromes? What are the best treatments for neuropsychiatric issues in Parkinson’s disease? How should I manage movement disorders that present during childhood? Get answers to these questions and more with the latest issue of *Continuum: Lifelong Learning in Neurology*. Participants can earn up to 14 hours of AMA PRA Category 1 Credit™ (12 of which apply to MOC Self-Assessment credit).

“This update on movement disorders will help the practicing neurologist recognize and manage both common and rare movement disorders,” said Guest Editor Susan H. Fox, MBChB, MRCP(UK), PhD, of the University of Toronto. “Clinical phenomenology remains key to the correct diagnosis. This edition focuses on clinical skills as well as advances in biomarkers such as genetics and imaging. Each section covers important updates on current and new treatments and management strategies.”

Articles include:

- Diagnostic Approach to Atypical Parkinsonian Syndromes, by Nikolaus R. McFarland, MD, PhD
- Diagnosis and Management of Tremor, by Elan D. Louis, MD, MS, FAAN
- Movement Disorders Presenting in Childhood, by Manju A. Kurian, PhD; Russell C. Dale, PhD
- Chorea, by Tiago A. Mestre, MSc, MD
- Ataxia, by Tetsuo Ashizawa, MD, FAAN; Guangbin Xia, MD, PhD
- Diagnosis and Management of Dystonia, by Vicki Shanker, MD; Susan B. Bressman, MD, FAAN
- Wilson Disease, by Ronald F. Pfeiffer, MD, FAAN
- Ethics of Preclinical Dopamine Transporter Imaging, by Thomas I. Cochrane, MD, MBA
- Incorporating Parkinson Disease Quality Measures Into Practice, by Raghav Govindarajan, MD
- Chemodenervation Coding for Neurologists, by Allan D. Wu, MD; Dawn Eliashiv, MD, FAAN; Marc Nuwer, MD, PhD, FAAN

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

The AAN hosted its fifth annual bike helmet giveaway the weekend of the June Board meeting in Minneapolis. Staff volunteers fit and gave away 1,000 bike helmets to the local community at the AAN headquarters, in conjunction with the Mill City Farmers Market healthy brain food day. The popular seasonal event also raised nearly $900 in donations to the American Brain Foundation. In acknowledgement of the day, Minneapolis Mayor Betsy Hodges proclaimed June 25, 2016, as Brain Health Awareness Day in the city.

The AAN donated an additional 1,000 helmets to the Minneapolis Police Department Bike Cops for Kids, SPOKES/Cycles for Change, Downtown Congregation to End Homelessness, Venture North, NorthPoint Health & Wellness Center, and Minnesota Brain Injury Alliance to extend its impact on Minnesotans' brain health.

To further engage the community, the AAN sponsored a piano through Pianos on Parade, a summer program from the Minneapolis Downtown Council to connect city employees, residents, and visitors with downtown spaces in creative ways. The piano, which was painted by a local artist in a brain-meets-music motif—reinforcing how music is sometimes used as supplemental therapy for neurologic disorders such as Parkinson’s disease and dementia—was placed the month of June in the sensory garden in front of the AAN headquarters for the public to play.
AAN Leadership Programs Gain Expanded Industry Support

The AAN recognizes the value of partnering with industry on projects of common interest that focus on improving the quality of patient care. The Industry Roundtable (IRT) partners with the AAN to share vision, intellect, and financial resources in four key areas: Education, Research, Sponsorship, and Leadership.

The many challenges in today’s health care environment create a special need for great leadership, and the AAN has committed itself to helping members meet their leadership potential across their professional lives, from medical school to retirement.

“The Academy has long recognized that we need to cultivate leaders to build neurology’s future,” said AAN President Terrence L. Cascino, MD, FAAN. “Leaders take people places that they wouldn’t go on their own—in turn advancing the profession of neurology and meeting the growing needs of patients.”

To this end, the AAN recently expanded its Leadership Programs to include eight opportunities geared toward different demographics and career stages: Diversity Leadership, Enhanced Resident Scholarship, Emerging Leaders, Leadership University, Minority Medical Student Scholarship, Palatucci Advocacy Leadership, Transforming Leaders, and Women in Leadership.

“But we can’t do it alone,” said Jonathan P. Hosey, MD, FAAN, physician liaison to the AAN’s Industry Roundtable. “Which is why, along with this programmatic expansion, so, too, has industry’s financial support expanded, with an impressive $575,000 in support for the 2016 programs alone.”

The result is that more AAN members are now able to experience the programs’ career- and life-changing impacts.

No one knows this better than Temitayo Oyegbile, MD, PhD, assistant professor at Georgetown University Hospital in Washington, DC, and current Diversity Leadership Program participant. Oyegbile’s program kicked off with “Academy 101,” a full-day of training on Academy organization and structure taught by leadership and staff—including a segment led by Hosey on the role of the IRT. Her keen interest in the role of industry within the AAN inspired Hosey to extend an invitation to Oyegbile to attend a special presentation to industry during the recent Annual Meeting in Vancouver. The meeting gave Oyegbile a unique opportunity to experience the AAN industry partnership in action, share with industry supporters how much the leadership program means to her, and thank them personally for helping make it all happen.

“It was exceptionally rewarding to be able to share with industry partners how amazing the Diversity Leadership Program has been,” said Oyegbile. “The investment the Academy and its industry partners are making in the Leadership Programs indicates not only that they are truly committed to building the neurology leaders of tomorrow, but also in including diversity within the Academy. This has been so impressive and I am truly grateful for this opportunity.”

Hosey understands the importance of making AAN members—and particularly direct beneficiaries such as Oyegbile—aware of industry’s role in creating a strong future for neurology. “I was impressed by Dr. Oyegbile’s interest in and enthusiasm for how important it is to develop industry relationships built on transparency and trust, and then innovating and working together to achieve mutual goals. In light of continued scarcity in funding over the past few years, relationships like the IRT are essential to providing the highest level of education and cutting-edge science that is critical to advancing the highest quality patient-centered care—and I was thrilled to see how much Dr. Oyegbile appreciates that and is eager to learn more.”
The AAN has updated its 2004 guideline on the management of patients with a heart defect called a patent foramen ovale (PFO) and an ischemic stroke or transient ischemic attack (TIA) of unknown cause.

“Practice Advisory: Recurrent Stroke with Patent Foramen Ovale (Update of Practice Parameter)” was published online in Neurology® on July 27, and it will appear in the August 23, 2016, print issue of Neurology.

The updated guideline, now designated as a practice advisory, is based on the best available evidence. It recommends that PFO closure should not be routinely offered to patients with cryptogenic ischemic stroke outside of a research setting. This practice advisory is intended to reduce the inappropriate use of off-label atrial septal closure devices. Compared with typical secondary stroke prevention measures, including medication to reduce blood clots, these devices have limited (i.e., low) evidence to support their use.

“Patients with stroke or TIA should have a careful evaluation to determine the cause and to optimize secondary stroke prevention,” said Steven R. Messé, MD, FAAN, FAHA, author of the practice advisory. “Because PFO is fairly prevalent in the general population and the high rate of alternative etiologies for recurrent strokes in the prospective studies of PFO, other causes must be excluded before attributing the stroke to PFO.”

Read the practice advisory and access PDF summaries for clinicians and patients, a clinician video, and a slide set on AAN.com. For more information, contact Julie Cox at jcox@aann.com or (612) 928-6069.
From the beginning of his career, Bradford B. Worrall, MD, MSc, FAAN, has focused on the role that genes play in cerebrovascular disease. Along the way, the American Brain Foundation has gone from supporting Worrall’s research career with a Clinical Research Training Fellowship to receiving support from him through generous donations of his time as a volunteer and his financial gifts to benefit other promising young researchers.

Worrall, who is professor of neurology and public health sciences at the University of Virginia and also serves as the deputy editor of Neurology®, talks about his relationship with the American Brain Foundation.

Why do you support the American Brain Foundation?
I have long felt a debt to the Academy and the American Brain Foundation for the support it has shown me over the years. As one of the earliest recipients of what was then called the AAN Foundation Clinical Research Training Fellowship, I believe that the investment the foundation made in me and my career has paid forward a thousand times over. The AAN also recognized me with the Michael S. Pessin Stroke Leadership Award in my mid-career, again validating the work that I was doing and continue to do in cerebrovascular research. As a more senior researcher with the grey in the beard to show for it, I am happy to make investments in the next generation of academics.

How has receiving a Clinical Research Training Fellowship (CRTF) affected your career?
There is no way to put it other than the CRTF was the foundation of my academic career. It was the first grant I ever received. It allowed me to stay on after my stroke fellowship at the University of Virginia and get my initial faculty job. The funding also allowed me to pursue a master’s degree in health evaluation sciences/epidemiology, which has anchored my career in methodological rigor.

What has resulted from your fellowship research?
The AAN CRTF led to an NIH-funded pilot and feasibility grant, which led to my K-08, which led to…you get the picture. The seed money, the training, and the actual research done were each crucial to who I am now.

Tell us a little about your current research.
My research has focused on applying genetic tools to understand cerebrovascular disease. My most recent work was a huge collaboration with a team of scientists across the globe examining the genomes of tens of thousands of stroke patients and far more control subjects. The research has identified a new gene associated with strokes that result from large artery atherosclerosis and other genetic risk factors for ischemic stroke. Now our colleagues are working on testing drugs targeted to these genes. It’s a really exciting time. There’s real potential that one or more of these findings may lead to new treatments.

Why do you feel it is important to continue funding Clinical Research Training Fellowships?
We are at a time when the need for inventive and creative ideas in neurological research has never been higher. We need the best minds, period. The road to a career as a physician-scientist has always been challenging. However, fewer are choosing this path. At the beginning of medical school or residency, many express an interest in an academic research career. But those who consider academics have fewer opportunities to experience research firsthand during residency with the constraints of duty hours, the rigors of core competencies, and the growing clinical workload. The other substantial consideration is academic debt. At the end of residency training, many just cannot see a path into academics from a logistical, financial, or personal perspective. The CRTF provides an entry point—that first foothold on the climb. This has always been a crucial juncture, as it was for me, but I think it is now more important than ever.
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 atoversight. The practice is located in a beautiful residential community with excellent schools, parks and recreational opportunities. Send CV to Howard J. Ormont, Practice Administrator, or call: (207) 795-5696; email: Mallott2@cmhc.org, or call: (800) 445-7431. Not a J1 Opportunity.

Neurologist: Excellent Opportunity in NY

Excellent Opportunity in Neurology. St. Peter’s Health Partner’s Medical Associates, PC., is accepting applications for 2 new full-time Neurology positions for 2016 placement. Positions include general neurology and hospital-based neurology (neuro-hospitalist). These are excellent opportunities to join an expanding team of six physicians as the organization develops its neuroscience service line across the Capital District of NY. Applicants should be able to perform EMG/NCS and EEG. Some sleep study reading is available. We have beautiful new office space and are heavily investing in our infrastructure. We offer a supportive practice environment with established patient bases with strong demand. These are exciting opportunities to join a dynamic and growing organization as it takes its neurology program to the next level of integration. Find out more and apply online at www.sphma.org

Neurology Opportunities in Madison, WI

Dean Clinic, a 450+ physician multi-specialty group, is recruiting for two general Neurologists, a Neuro-Hospitalist, and a Pediatric Neurologist. Our physicians enjoy a work/life balance through flexible call schedules and a four-day work week. Dean Clinic draws from an 18-county service area with a population of 1.3 million people. There is a guaranteed two-year salary, signing bonus, and an outstanding fringe benefits package. Dean is an Equal Opportunity Employer and Affirmative Action Employer. All qualified applicants will receive consideration for employment without regard to race, color, religion, sex, or national origin. Madison consistently ranks as one of the most livable mid-size cities in the United States. Verona is a popular suburb to the west and the home of Epic, the premier EHR company. For more information about this position: Christopher Kashnig, Dean Clinic, 1808 W Beltline Hwy, Madison, WI 53713. Phone: (608) 250-1474 Cell: (608) 212-6348, Fax: (608) 250-1554, email: christopher.kashnig@deancareers.com

Stoke Director and Epilepsy Neurologist–Seattle Area

Overlake Medical Clinics (OMC) is seeking a Stoke Director and General Neurologist with Epilepsy experience for our expanding, hospital owned multi-specialty group located on Seattle’s eastside. We have expanded our Neuroscience program into a Neuroscience Institute and seek a fellowship trained Neurologist to develop a comprehensive stroke program. The physician will work as a Stoke Neurologist and then as a Stoke physician in our outpatient neurology and stroke clinic. The Epilepsy Neurologist is a full-time outpatient position. Overlake, WA is in a thriving community with major high-tech and health care employers. Overlake is a new hospital nearing one million by 2019. Overlake Medical Center is a financially stable, community, non-profit hospital with positive operating margins. Discharge growth has been steady at 7% this year. Our outpatient clinic structure continues to expand with double-digit growth over the past three years. Overlake Medical Clinics (OMC) now employs 120 providers. Benefits: salary guarantee during first two years; directorship monthly stipend; annual performance bonuses; relocation assistance; employed position with excellent benefits with retirement plan; malpractice + tail coverage; significant growth opportunities with new EPIC EMR plus advanced neuroservices. Email: chris.thompson@overlakehospital.org

BC/BE Neurologist: A multispecialty neurology group has an exceptional opportunity for a BC/BE neurologist to join an established, progressive neurology practice of six physicians. Our office is located in a thriving North Shore residential community with excellent schools, parks and recreation. We are 20 minutes from Manhattan, easily accessible by train and parkways. We are affiliated with three (3) major teaching hospitals where there are ample opportunities for professional development. We provide a myriad of neurological services within our practice including EMG, Transcranial Doppler, Carotid Doppler, EEG, Ambulatory EEG, Video EEG and VNG testing. We also have an on-site MRI within our state-of-the-art facility. Excellent salary, benefits and productivity incentives. Interested candidates including graduating residents and fellows should email their CV to ajormont@neurologiland.com or fax to (518) 487-4950; at: Andrew J. Ormont, Practice Administrator

Neurologists Well-established, quality oriented neurosciences group seeks to add additional neurologists. Opportunity for subspecialists and general neurologist. We are a multidisciplinary neurosciences group providing a strong training environment and opportunities for professional growth. Our location offers easy access to the cultural institutions of Boston, 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

Behavioral Neurology Fellowship

The University of Texas Southwestern Medical Center, in Dallas, Texas is offering a 1 or 2 year combined clinical and research fellowship in Behavioral Neurology & Neuropsychiatry accredited by the United Council for Neurologic Subspecialties, starting July 2016 and July 2017. The core faculty includes 5 behavioral neurologists and neuropsychologists. Access to subspecialty clinics in cognitive & memory disorders, geriatric psychiatry, neuropsychology, TBI/concussion, and movement disorders are available. UTSW has the only Texas-based NIA-funded Alzheimer’s Disease Center and active clinical and translational research programs. Exposure to the evaluation, diagnosis and treatment of a wide range of neurodegenerative disorders, including mild cognitive impairment, frontotemporal Dementias and Dementia with Lewy Bodies, movement disorders, and traumatic brain injury is provided. Weekly didactics and diagnostic consensus conferences, along with monthly neuropathological presentations are provided as part of the fellowship experience. Please contact Jameelah Shaheed (214) 648-2835 or email neurofellowship@utsouthwestern.edu. You may also visit http://www.utsouthwestern.edu/education/medical/ neuroscience/physician/fellowship-programs/behavioral-neurology.html

Fellowship in Neuroimaging

Winchester Neurological Consultants, Inc., in conjunction with Virginia Commonwealth University and Winchester Medical Center, is offering a clinical Neuroradiology 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 accrued 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. Availability: immediate. Research interests are encouraged. Salary is $60,000.00 per year, with bonus and there is also an opportunity to combine the imaging fellowship with a NeuroHospitalist Fellowship over a two year training period with a salary of $80,000.00 per year. CV’s should be emailed to jtf@winchesterneurological.com

Northwest Permanente—Multiple Neurology Openings

Help Build a Gateway to Better Health. At Northwest Permanente, PC., we want every patient we see to receive the medical care they need to live long and thrive. You’ll benefit from a comprehensive network of support services and a talented team of colleagues dedicated to the highest standard of medical care and patient care within our self-governed, physician-led, multi-specialty group of over 1,500 physicians, surgeons and clinicians who care for over 240,000 members throughout Oregon and Southwest Washington. Opportunities are available for individuals with subspecialty, general neurology and inpatient hospitalist responsibilities. Clinical excellence and an interest in helping to pioneer new ways of providing the right neurological care at the right time for the right person will be essential to these positions. We invite you to join our 11 Neurologist department that is pioneing integrated medical practice and is leading the way to the future of medical care. Opportunities in the Pacific Northwest: Movement & Epileptologist Neurologist, Vascular Neurologist, General Neurologist. Join us in the beautiful Pacific Northwest and enjoy a competitive salary in addition to an extensive benefit package which includes medical, dental, disability and life insurance; company funded/generous retirement plans; vacation, sabbatical and educational leave; and professional liability coverage. Physicians who are Board Certified are also eligible for Senior Physician and Shareholder standing after approximately three years with the group. To apply, please visit our Web site at: http://nvp KeystoneNeurology.com. For more information, call Shelonda at (800) 813-3783. No J1 Opportunities. We are an equal opportunity employer and value diversity within our organization.

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### Dates and Deadlines

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Get the recognition you deserve. Add the esteemed Fellow of the AAN (FAAN) designation to your already impressive credentials.

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