Esteemed Lecturers Named for 2017 Presidential Plenary Session

An impressive lineup of speakers has been confirmed for the 2017 Presidential Plenary Session at the 69th Annual Meeting in Boston, MA, April 22 through 28. The always popular session will be open to all registered attendees and take place on Sunday, April 23, from 9:15 a.m. to 12:00 p.m. Science Committee Chair Lisa DeAngelis, MD, FAAN, will moderate key lectures.

Science Committee Chair
Lisa DeAngelis, MD, FAAN, introduced speakers at the 2016 Annual Meeting in Vancouver.

Submit Abstracts for Annual Meeting by October 24

The deadline is approaching to submit abstracts for the 2017 AAN Annual Meeting in Boston, MA. Abstracts are accepted in all areas of neurology and neuroscience and submissions are due by 11:59 p.m. CT on October 24. To submit an abstract(s), complete the online form at AAN.com/View/17Abstracts. For more information, contact science@aan.com or (612) 928-6088.

WEBINAR: Don’t Just Phone It in: A Guide to Teleneurology

Teleneurology is an emerging field in neurology and affords an opportunity to increase patient access to care. However, it is a complex endeavor, and knowing state-of-the-art methods is the key to success. In this webinar, Eric Anderson, MD, PhD—whose practice relies solely on teleneurology services—will offer an interactive presentation designed to empower you to decide if teleneurology will work for you and your practice.

WEBINAR: Don’t Just Phone It in: A Guide to Teleneurology

October 11, 2016, 12:00–1:00 p.m. ET
Deadline to Register: October 10

Continued on page 11 ▶
**PUBLICATION**

The Vision of the AAN is to be indispensable to our members.

The Mission of the AAN is to promote the highest quality patient-centered neurologic care and enhance member career satisfaction.

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President’s Column

New Help for Solo and Small Practices

About a year ago, we launched the Solo and Small Practice Task Force, chaired by Board Vice President and practicing neurologist James C. Stevens, MD, FAAN. The group was charged with reviewing existing AAN products and services and identifying major issues affecting solo and small practices, whose neurologists make up 30 percent of our current AAN membership in the US.

The Task Force members reviewed current data and AAN resources available to assist this group of members, identified gaps in programs and services, and this summer they made their final report to the Board of Directors. In total, the Task Force made 25 recommendations to the Board that spanned eight important topic areas:

1. Running Your Practice
2. Advocacy
3. Communications
4. New Payment Models
5. Practice Management Education
6. Coding and Reimbursement
7. Recruiting and Hiring
8. Representation in AAN Activities

The Task Force prioritized the recommendations in order of importance. The number one suggestion to the AAN leadership was to consider the development of a toll-free practice help hotline and/or email address with a rapid response. Among other recommendations, the AAN will continue to strengthen existing efforts in these areas:

- Advocating for reduced administrative burdens on physicians (e.g., MOC, Prior Authorization, and Meaningful Use of Electronic Health Records) should remain a top priority for the AAN.
- One of the guiding principles of the AAN’s efforts around health care payment reform (MACRA) and alternative payment model frameworks should be to consider ease of implementation by members in solo and small practices.
- The AAN should encourage advocacy activities (e.g., email action alerts), leadership programs, and other micro-volunteerism opportunities as first steps for getting involved to members in this segment who are less likely to be able to take large amounts of time away from their practice.
- The leadership of the AAN should be cognizant of the percentage of AAN members in solo and small practice and seek to achieve a goal of proportionate representation on committees as well as the Board of Directors to reflect this segment of the membership.

We are currently evaluating these thoughtful recommendations as part of our consideration of developing an enduring strategy for engaging with members in solo and small practices. We have more control over internal changes than we do over Congress or the Centers for Medicare & Medicaid Services (CMS), of course. Legislative and regulatory advocacy takes time and considerable effort. But we have built a strong foundation and our influence has

Continued on page 31 >
Whether it’s your patients’ first step or their next,

POWERED FOR RESULTS
Made for every day

TECFIDERA is one pill, twice a day.1

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

Important Safety Information
TECFIDERA is contraindicated in patients with known hypersensitivity to dimethyl fumarate or any of the excipients of TECFIDERA. TECFIDERA can cause anaphylaxis and angioedema after the first dose or at any time during treatment. Patients experiencing signs and symptoms of anaphylaxis and angioedema (which have included difficulty breathing, urticaria, and swelling of the throat and tongue) should discontinue TECFIDERA and seek immediate medical care.

Progressive multifocal leukoencephalopathy (PML) has occurred in patients with MS treated with TECFIDERA. PML is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. A fatal case of PML occurred in a patient who received TECFIDERA in a clinical trial. PML has also occurred in the postmarketing setting in the presence of lymphopenia (<0.8 x10^9/L) persisting for more than 6 months. While the role of lymphopenia in these cases is uncertain, the majority of cases occurred in patients with lymphocyte counts <0.5x10^9/L. The symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes. At the first sign or symptom suggestive of PML, withhold TECFIDERA and perform an appropriate diagnostic evaluation. MRI findings may be apparent before clinical signs or symptoms.

TECFIDERA may decrease lymphocyte counts; in clinical trials there was a mean decrease of ~30% in lymphocyte counts during the first year which then remained stable. Four weeks after stopping TECFIDERA, mean lymphocyte counts increased but not to baseline. Six percent of TECFIDERA patients and <1% of placebo patients had lymphocyte counts <0.5x10^9/L. TECFIDERA has not been studied in patients with pre-existing low lymphocyte counts.

There was no increased incidence of serious infections observed in patients with lymphocyte counts <0.8x10^9/L or ≤0.5x10^9/L in controlled trials, although one patient in an extension study developed PML in the setting of prolonged lymphopenia (lymphocyte counts predominantly <0.5x10^9/L for 3.5 years). In controlled and uncontrolled clinical trials, 2% of patients experienced lymphocyte counts <0.5x10^9/L for at least six months. In these patients, the majority of lymphocyte counts remained <0.5x10^9/L with continued therapy. A complete blood count including lymphocyte count should be obtained before initiating treatment, 6 months after starting, every 6 to 12 months thereafter and as clinically indicated. Consider treatment interruption if lymphocyte counts <0.5x10^9/L persist for more than six months and follow lymphocyte counts until lymphopenia is resolved. Consider withholding treatment in patients with serious infections until resolved. Decisions about whether or not to restart TECFIDERA should be based on clinical circumstances.

TECFIDERA may cause flushing (e.g. warmth, redness, itching, and/or burning sensation). 40% of patients taking TECFIDERA reported flushing, which was mostly mild to moderate in severity. Three percent of patients discontinued
With TECFIDERA, half as many patients relapsed in the 2-year DEFINE* trial†

**PROPONPT OF PATIENTS RELAPSED‡**

<table>
<thead>
<tr>
<th>Time on Study (Weeks)</th>
<th>Proportion of Patients Relapsed</th>
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<tr>
<td>BL</td>
<td>PLACEO 46%</td>
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<tr>
<td>12</td>
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<td>84</td>
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<tr>
<td>96</td>
<td>TECFIDERA 27%</td>
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</tbody>
</table>

** n=408**
** n=410**

**RELATIVE RISK REDUCTION**

P<0.0001

TECFIDERA for flushing and <1% had serious flushing events that led to hospitalization. Taking TECFIDERA with food may reduce flushing. Alternatively, administration of non-enteric coated aspirin prior to dosing may reduce the incidence or severity of flushing.

TECFIDERA may cause gastrointestinal (GI) events (e.g., nausea, vomiting, diarrhea, abdominal pain, and dyspepsia). Four percent of TECFIDERA patients and <1% of placebo patients discontinued due to GI events. The incidence of serious GI events was 1%. The most common adverse reactions associated with TECFIDERA versus placebo are flushing (40% vs 6%) and GI events: abdominal pain (18% vs 10%), diarrhea (14% vs 11%), nausea (12% vs 9%). Elevations in hepatic transaminases have been reported. A transient increase in mean eosinophil counts was seen during the first two months. TECFIDERA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Encourage patients who become pregnant while taking TECFIDERA to enroll in the TECFIDERA pregnancy registry by calling 1-866-810-1462 or visiting www.TECFIDERApregnancyregistry.com.

For additional important safety information, please see adjacent Brief Summary of full Prescribing Information.

*Determination of the Efficacy and Safety of Oral Fumarate in Relapsing-Remitting MS, a 2-year, randomized, double-blind, placebo-controlled study in 1234 patients with relapsing-remitting multiple sclerosis (RRMS). 1,2

1 Included patients who had experienced at least 1 relapse over the year preceding the trial or had a brain magnetic resonance imaging (MRI) scan demonstrating at least 1 gadolinium-enhancing (Gd+) lesion within 6 weeks of randomization and had an Expanded Disability Status Scale (EDSS) score ranging from 0 to 5.1

2 Relapses were defined as new or recurrent neurologic symptoms not associated with fever or infection that lasted for at least 24 hours and were accompanied by new objective neurologic findings.‡

‡ Based on number of prescriptions from IMS NPA™ Weekly Data (September 27, 2013 to December 31, 2015).


For more information, visit TECFIDERAHCP.COM
TECFIDERA® (dimethyl fumarate) delayed-release capsules, for oral use

Brief Summary of Full Prescribing Information

1 INDICATIONS AND USAGE

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

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

The starting dose for TECFIDERA is 120 mg twice a day orally. After 7 days, the dose should be increased to the maintenance dose of 240 mg twice a day orally. Temporary dose reductions to 120 mg twice a day may be considered for individuals who do not tolerate the maintenance dose. Within 4 weeks, the recommended dose of 240 mg twice a day should be resumed. Discontinuation of TECFIDERA should be considered for patients unable to tolerate return to the maintenance dose. The incidence of flushing may be reduced by administration of TECFIDERA with food. Alternatively, administration of non-enteric coated aspirin (up to a dose of 325 mg) 30 minutes prior to TECFIDERA dosing may reduce the incidence or severity of flushing [see Clinical Pharmacology (12.3)].

TECFIDERA should be swallowed whole and intact. TECFIDERA should not be crushed or chewed and the capsule contents should not be sprinkled on food. TECFIDERA can be taken with or without food.

2.2 Blood Test Prior to Initiation of Therapy

Obtain a complete blood cell count (CBC) including lymphocyte count before initiation of therapy [see Warnings and Precautions (5.3)].

3 DOSAGE FORMS AND STRENGTHS

TECFIDERA is available as hard gelatin delayed-release capsules containing 120 mg or 240 mg of dimethyl fumarate. The 120 mg capsules have a green cap and white body, printed with “BG-12 120 mg” in black ink on the body. The 240 mg capsules have a green cap and a green body, printed with “BG-12 240 mg” in black ink on the body.

4 CONTRAINDICATIONS

TECFIDERA is contraindicated in patients with known hypersensitivity to dimethyl fumarate or to any of the excipients of TECFIDERA. Reactions have included anaphylaxis and angioedema [see Warnings and Precautions (5.1)].

5 WARNINGS AND PRECAUTIONS

5.1 Anaphylaxis and Angioedema

TECFIDERA can cause anaphylaxis and angioedema after the first dose or at any time during treatment. Signs and symptoms have included difficulty breathing, urticaria, and swelling of the throat and tongue. Patients should be instructed to discontinue TECFIDERA and seek immediate medical care if they experience symptoms or signs of anaphylaxis or angioedema.

5.2 Progressive Multifocal Leuкоencephalopathy

Progressive multifocal leukoencephalopathy (PML) has occurred in patients with MS treated with TECFIDERA. PML is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. A fatal outcome of PML occurred in a patient who received TECFIDERA for 4 years while enrolled in a clinical trial. During the clinical trial, the patient experienced prolonged lymphopenia (lymphocyte counts predominantly <0.5x10^9/L for 3.5 years) while taking TECFIDERA [see Warnings and Precautions (5.3)]. The patient had no other identifiable systemic medical conditions resulting in compromised immune system function and had not previously been treated with natalizumab, which has a known association with PML. The patient was also not taking any immunosuppressive or immunomodulatory medications concomitantly.

PML has also occurred in the postmarketing setting in the presence of lymphopenia (<0.8x10^9/L) persisting for more than 6 months. While the role of lymphopenia in these cases is uncertain, the majority of cases occurred in patients with lymphocyte counts <0.5x10^9/L.

At the first sign or symptom suggestive of PML, withhold TECFIDERA and perform an appropriate diagnostic evaluation. MRI findings may be apparent before clinical signs or symptoms. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limb movement and coordination, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.

5.3 Lymphopenia

TECFIDERA may decrease lymphocyte counts. In the MS placebo controlled trials, mean lymphocyte counts decreased by approximately 30% during the first year of treatment with TECFIDERA and then remained stable. Four weeks after stopping TECFIDERA, mean lymphocyte counts increased but did not return to baseline. Six percent (6%) of TECFIDERA patients and <1% of placebo patients experienced lymphocyte counts <0.5x10^9/L. The incidence of infections (60% vs 58%) and serious infections (2% vs 2%) was similar in patients treated with TECFIDERA or placebo, respectively. There was no increased incidence of serious infections observed in patients with lymphocyte counts <0.5x10^9/L in controlled trials, although one patient in an extension study developed PML in the setting of prolonged lymphopenia (lymphocyte counts predominantly <0.5x10^9/L for 3.5 years) [see Warnings and Precautions (5.2)]. In controlled and uncontrolled clinical trials, 2% of patients experienced lymphocyte counts <0.5x10^9/L for at least six months, and in this group the majority of lymphocyte counts remained <0.5x10^9/L with continued therapy. TECFIDERA has not been studied in patients with pre-existing low lymphocyte counts.

Obtain a CBC, including lymphocyte count, before initiating treatment with TECFIDERA, 6 months after starting treatment, and then every 6 to 12 months thereafter, and as clinically indicated. Consider interruption of TECFIDERA in patients with lymphocyte counts less than 0.5x10^9/L persisting for more than six months. Given the potential for delayed recovery of lymphocyte counts, continue to obtain lymphocyte counts until their recovery if TECFIDERA is discontinued or interrupted due to lymphopenia. Consider withholding treatment from patients with serious infections until resolution. Decisions about whether or not to restart TECFIDERA should be individualized based on clinical circumstances.

5.4 Flushing

TECFIDERA may cause flushing (e.g., warmth, redness, itching, and/ or burning sensation). In clinical trials, 40% of TECFIDERA treated patients experienced flushing. Flushing symptoms generally began soon after initiating TECFIDERA and usually improved or resolved over time. In the majority of patients who experienced flushing, it was mild or moderate in severity. Three percent (3%) of patients discontinued TECFIDERA for flushing and <1% had serious flushing symptoms that were not life-threatening but led to hospitalization. Administration of TECFIDERA with food may reduce the incidence of flushing. Alternatively, administration of non-enteric coated aspirin (up to a dose of 325 mg) 30 minutes prior to TECFIDERA dosing may reduce the incidence or severity of flushing [see Dosing and Administration (2.1) and Clinical Pharmacology (12.3)].

6 ADVERSE REACTIONS

The following important adverse reactions are described elsewhere in labeling: Anaphylaxis and Angioedema (5.1), Progressive multifocal leukoencephalopathy (5.2), Lymphopenia (5.3), Flushing (5.4) [see Warnings and Precautions].

6.1 Clinical Trials Experience

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

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

Adverse Reactions in Placebo-Controlled Trials

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

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

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

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>TECFIDERA N=769</th>
<th>Placebo N=771</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flushing</td>
<td>40%</td>
<td>6%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>18%</td>
<td>10%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>14%</td>
<td>11%</td>
</tr>
<tr>
<td>Nausea</td>
<td>12%</td>
<td>6%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>9%</td>
<td>5%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>8%</td>
<td>4%</td>
</tr>
<tr>
<td>Rash</td>
<td>8%</td>
<td>3%</td>
</tr>
<tr>
<td>Albumin urine present</td>
<td>6%</td>
<td>4%</td>
</tr>
<tr>
<td>Erythema</td>
<td>5%</td>
<td>1%</td>
</tr>
<tr>
<td>Dysepsia</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>2%</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>
TECFIDERA caused GI events (e.g., nausea, vomiting, diarrhea, abdominal pain, and dyspepsia). The incidence of GI events was higher early in the course of treatment (primarily in month 1) and usually decreased over time in patients treated with TECFIDERA compared with placebo. Four percent (4%) of patients treated with TECFIDERA and less than 1% of placebo patients discontinued due to gastrointestinal events. The incidence of serious GI events was 1% in patients treated with TECFIDERA.

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

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

Eosinophilia
A transient increase in mean eosinophil counts was seen during the first 2 months of therapy.

Adverse Reactions in Placebo-Controlled and Uncontrolled Studies
In placebo-controlled and uncontrolled clinical studies, a total of 2913 patients have received TECFIDERA and been followed for periods up to 4 years with an overall exposure of 4603 person-years. Approximately 1162 patients have received more than 2 years of treatment with TECFIDERA. The adverse reaction profile of TECFIDERA in the uncontrolled clinical studies was consistent with the experience in the placebo-controlled clinical trials.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

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

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

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

Pregnancy Registry
There is a pregnancy registry that monitors pregnancy outcomes in women exposed to TECFIDERA during pregnancy. Encourage patients to enroll by calling 1-866-810-1462 or visiting www.TECFIDERAPregnancyRegistry.com.

8.3 Nursing Mothers

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

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

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

17 PATIENT COUNSELING INFORMATION

Adverse events that may be considered related to TECFIDERA are listed in the following table. These events were described as serious, severe, or life-threatening by the investigator.

Anaphylaxis and Angioedema
Adverse events that may be considered related to TECFIDERA are listed in the following table. These events were described as serious, severe, or life-threatening by the investigator.

Progressive Multifocal Leukoencephalopathy
Inform patients that progressive multifocal leukoencephalopathy (PML) has occurred in patients who received TECFIDERA. Inform the patient that PML is characterized by a progression of deficits and usually leads to death or severe disability over weeks or months. Instruct the patient of the importance of contacting their doctor if they develop any symptoms suggestive of PML. Inform the patient that typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.

Lymphocyte Counts
Inform patients that TECFIDERA may decrease lymphocyte counts. A blood test should be obtained before they start therapy. Blood tests are also recommended after 6 months of treatment, every 6 to 12 months thereafter, and as clinically indicated.

Flushing and Gastrointestinal (GI) Reactions
Flushing and GI reactions (abdominal pain, diarrhea, and nausea) are the most common reactions, especially at the initiation of therapy, and may decrease over time. Advise patients to contact their healthcare provider if they experience persistent and/or severe flushing or GI reactions. Advise patients experiencing flushing that taking TECFIDERA with food or taking a non-enteric coated aspirin prior to taking TECFIDERA may help.

Pregnancy and Pregnancy Registry
Instruct patients that if they are pregnant or plan to become pregnant while taking TECFIDERA they should inform their physician. Encourage patients to enroll in the TECFIDERA Pregnancy Registry if they become pregnant while taking TECFIDERA. Advise patients to call 1-866-810-1462 or visit www.TECFIDERAPregnancyRegistry.com for more information.

Manufactured by:
Biogen
Cambridge, MA 02142

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2/2016
What moved you to join the Board of Directors? What experiences and viewpoints do you bring to this role?

For much of my first two decades as an AAN member, my participation largely was limited to the Annual Meeting in the form of scientific presentations and education courses. As I began to attend Committee on Sections meetings during my leadership of the Geriatric Neurology Section, I was brought to the attention of Francis Kitteridge, MD, FAAN, who was president of the AAN in 2001. He appointed me to the Commission on Subspecialty Certification. This commission, chaired by Stephen Sergay, MB BCH, FAAN, ultimately developed and implemented the concept of the United Council of Neurologic Subspecialties (UCNS). The motivation for the UCNS was to accredit training programs and certify physicians in neurologic subspecialties, for which such accreditation and certification was not available through the American Board of Medical Subspecialties. During Dr. Sergay’s term as AAN president in 2006, I was appointed as chair of the Committee on Sections, in part to encourage appropriate sections to apply for UCNS membership.

Because the president elect of the AAN attended the annual meeting of the Committee on Sections, I thus was able to interact with key AAN leaders (Drs. Robert Griggs, Bruce Sigsbee, and Timothy Pedley) who impressed me with their dedication to the AAN and with their vision to ensure that it would remain indispensable to its members. The opportunity to contribute to that vision as a director of the AAN motivated me to join the Board.

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

My sense is that there are two major misperceptions. First, some members believe that the AAN as an organization functions relatively independently of the wishes of its membership; a common refrain is that the AAN’s fees for membership and for the Annual Meeting are too high. In reality, providing value to its members is a core principle of the AAN leadership and staff. Member feedback is very carefully considered in all major decisions. There has been a concerted effort to better communicate these decisions to improve awareness of all that the AAN provides its members and how it strives to do so in a cost efficient manner. The AAN staff are truly committed to being “indispensable” to AAN members and individually and as a group are highly effective and supportive of the AAN’s mission. The AAN is very fortunate to have such a talented staff.

The second misperception is that the AAN focuses too much on subspecialty neurologists to the detriment of general neurologists. The AAN is dedicated to serving all of its members, and recognizes that many neurologists in practice function as general neurologists, even if they also provide subspecialty services. A sizeable number of general neurologists currently serve on the Board of Directors. Many current AAN initiatives, including addressing physician “burnout,” supporting “Emerging Leaders” and “Transforming Leaders,” and working to develop the Axon Registry that will demonstrate the value of practicing neurologists, are very relevant for general neurologists.

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

The AAN is the only professional organization to represent all neurologists. It thus is by far the most powerful advocate for our profession and our patients. In recent years, it has worked to ensure that its leadership reflects the diversity of its membership in regard to age, sex, race, and ethnicity, and to maintain an appropriate balance between academia and practice.

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

The AAN’s efforts to support the careers of its members can be measured in multiple ways. The Annual Meeting and affiliated meetings (e.g., the Fall Conference and the Breakthroughs in Neurology conference) provide scientific advances, education, and networking. The BrainPAC enables the AAN to advocate for the entire profession. Career development is strongly supported by the American Brain Foundation’s Clinical Research Training Fellowships and, with a recent grant from the Conrad Hilton Foundation, now aims to increase the percentage of medical students who enter neurology training. The Continuum® series provides lifelong learning for neurologists.

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

I have been blessed with a most supportive wife and family. As our children have all “launched,” it makes it easier for my wife to accompany me on at least some of my professional travel, which notably improves my personal life.

John C. Morris, MD, FAAN

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

John C. Morris, MD, FAAN, is the Harvey A. and Dorismae Hacker Friedman Distinguished Professor of Neurology, professor of pathology and immunology, professor of physical therapy, and professor of occupational therapy at Washington University. He also is the director and principal investigator of the Charles F. and Joanne Knight Alzheimer’s Disease Research Center at Washington University School of Medicine in St. Louis, MO. Since 2009, Morris has served on the Meeting Management Committee, and has been on the Editorial Board of Neurology Now® since 2015. He was on the Potamkin Prize Subcommittee from 2008 to 2014, chairing it from 2012 to 2014. He also chaired the 2013 UCNS Task Force. He chaired the Committee on Sections Executive Committee (2006–2012) and the Executive Council for Sections and Subspecialties (2012–2013).
“Meaningful Use” Is Now “Advancing Care Information” Under MACRA

Under the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA), the Centers for Medicare & Medicaid Services has created a quality payment program for providers. The Merit-based Incentive Payment System (MIPS), one of the payment pathways under MACRA, replaces older CMS programs: the Physician Quality Reporting System (PQRS), the Value-based Payment Modifier (VBPM), and Meaningful Use of Electronic Health Records (MU). So does this mean those older programs, like Meaningful Use, are going away? Not exactly.

Under MIPS, Meaningful Use will transition into a new program called Advancing Care Information (ACI). ACI is one of four components that will be used to form one composite score that will determine future provider payment bonuses or penalties.

What is the difference between MU and ACI? ACI aligns with other CMS reporting programs and no longer requires reporting quality measures as part of this category. It streamlines measures and allows for customization so a physician or clinician can choose which measures best fit their practice. And it emphasizes interoperability, information exchange, and security measures.

The ACI category initially will account for 25 percent of the total MIPS score. Since the ACI aims to be more flexible than the former MU program, there are multiple paths to receive the maximum score in this category.

A complete list of objectives and measures is expected to be delivered in the final MACRA rule due in early November. There will be objectives and measures to attest to, based on the EHR’s year of certification. The proposed objectives and measures align closely with Modified Stage 2 or Stage 3 of Meaningful Use, depending on the certification edition year.

What can you do now?

- Start or continue to participate in Meaningful Use in 2016
- Determine if your EHR is certified to the 2014 or 2015 edition by visiting https://chpl.healthit.gov/#/search
- Watch for communication from the AAN to help guide you through 2017 participation
- Visit AAN.com/view/MACRA for additional tools and resources developed by the AAN

CMS on MACRA: “Pick Your Pace” in 2017

As the AAN urged in our April comment letter to the Centers for Medicare & Medicaid Services (CMS) on the proposed MACRA regulations, the agency formally acknowledged last month the many challenges facing physician practices during the implementation phase of MACRA. CMS subsequently released its proposed plan to make available four choices that will empower physicians to pick their pace of participation in the first MACRA performance period that begins on January 1, 2017.

Under the proposed plan, choosing any one of the four options would ensure that you do not receive a negative payment adjustment (payment penalty) in 2019 based on your 2017 data:

- Full-year reporting that begins on January 1;
- Partial-year reporting for a reduced number of days;
- A “test” option under which physicians can report minimal amounts of data; or
- Participating in an advanced alternative payment model (APM).

Additional supporting details about each of the options are expected to be released in the final rule, due on or before November 1. The plan will provide a pathway for those not quite ready for full implementation to avoid negative payment adjustments, while allowing those who are prepared to retain the option to achieve bonus payments. This plan signals that CMS is willing to hear and take action on our concerns, particularly when it comes to ensuring the highest chance of success in new payment systems for our members in solo and small practices. Learn more about MACRA at AAN.com/view/MACRA.
Be Aware of New and Revised ICD-10-CM Codes

While the Centers for Medicare & Medicaid Services (CMS) has announced numerous new and revised ICD-10-CM codes for implementation on October 1, 2016, the number of codes impacting neurology is minimal. Perhaps of most significance to neurologists is the addition of a bilateral option (G56.03) when coding for carpal tunnel syndrome. Other revisions of interests include:

- Addition of autism spectrum disorder under code F84.0 (Autistic disorder).
- Addition of bilateral option to various lesions of specific nerves codes.
- Addition of Use Additional code instruction under I63 (Cerebral infarction) to indicate National Institutes of Health Stroke Scale score if known.
- Addition of bilateral option for Cerebral Infarction codes.
- Addition of new codes to capture cognitive deficits following nontraumatic subarachnoid, intracerebral, or intracranial hemorrhage as well as following cerebral infarction and other cerebrovascular diseases. These codes are found under I69 (Sequelae of cerebrovascular diseases).

It is important to note that CMS’s one-year grace period for diagnosis coding errors expired on October 1, 2016. During the first year of implementation, CMS established a grace period with the following criteria: If a valid ICD-10 code from the right family (three-character category) was submitted, CMS would process and not audit valid codes. While diagnosis coding to the correct level of specificity is the goal for all claims, the expiration of the grace period provides additional incentive to neurologists and their billing staff to select the most appropriate code for a given service.

As October 1 signifies the effective date of new diagnosis codes, it is also a good time to revisit a common point of confusion: Excludes1 and Excludes2 notes. To clarify, an Excludes1 note means the excluded code should never be used with the code above the Excludes1 note. The two conditions cannot occur together. An Excludes2 note means the excluded condition is not part of the condition the code represents; however, a patient may have both conditions simultaneously. Both the code and excluded code can be reported together when appropriate.

NEED ICD-10 Help?

Are you coding to the highest level of specificity to ensure you are reimbursed correctly and without delay? If not, check out the AAN’s recorded webinar “Get Caught Up: The ICD-10-CM Crosswalk Is Now a Cross-run.” This webinar reviews principles of the coding system and answers questions on specific best practices. Hear how more detailed documentation will benefit both clinicians and billing staff and can help when selecting the appropriate ICD-10-CM code. Learn how to review claims denials on the line item level as well as coverage policies for relevant diagnosis coding information. Visit AAN.com/view/pmw16 to register today.
Practice

Zika, Guillain-Barré Syndrome Webinar and Materials Now in Spanish

With the outbreak of Zika virus infections, there have been an increased number of reports of Guillain-Barré syndrome (GBS). The Centers for Disease Control and Prevention (CDC) has been partnering with international, national, and state organizations to best educate providers and the public about Zika virus. With the CDC, the AAN has developed a webinar for health care providers on the diagnosis, management, and treatment of GBS. Because of the prevalence of Zika virus in the Commonwealth of Puerto Rico, materials from the AAN’s June 17 webinar have been translated into Spanish. Members have access to the presentation slides in Spanish, and they may view a recording of the live webinar with Spanish subtitles. Other available resources translated into Spanish include:

- 2003 GBS guideline
- 2003 GBS clinician summary
- 2003 GBS patient summary

Stay informed about the Zika virus and access the tools and resources at AAN.com/zika-virus.

Webinar Connects You with Teleneurology

Directors: Eric Anderson, MD, PhD, and David A. Evans, MBA

Objectives

- Describe the applications and delivery models for the various forms of telemedicine and mobile health
- Understand the role of telemedicine and medical apps in the care continuum
- Learn how to code correctly for telemedicine for Medicare, Medicaid, and private payers
- Understand how neurology’s role in telemedicine neurology is growing
- Discuss legal and regulatory issues associated with telemedicine

Enjoy New Reduced 2016 Member Pricing!

- AAN members pay only $99 per webinar (save $50 each from 2015 fee) or subscribe to the complete 2016 webinar series for only $189 (save $10 from 2015 subscription)
- New and convenient one-hour sessions
- If you have scheduling conflicts, registration gives you access for one year to the recorded webinar if you miss the live event

Physicians will earn 1 AMA PRA Category 1 Credit™ per webinar and non-physicians will receive a certificate of completion

Includes presentation slides and access to recording

To initiate a 2016 subscription, simply start registering for a single webinar and the option to subscribe to all 10 live webinars will be presented. The 2016 subscription offer does not include registration for webinars presented in 2015, which must be made in a separate transaction.

Visit AAN.com/view/pmw16 for more information or to register.

Coming in November

Join us on November 8 for the practice management webinar “Getting the Most out of Your Technology: HIT and Your Patients,” directed by Allison L. Weathers, MD, FAAN. Learn more and register at AAN.com/view/pmw16.
New Issues Spotlight Aphasia, Burnout, and Decompressive Craniectomy

The October/November issue of Neurology Now® profiles actress Kimberly Williams-Paisley, whose mother has primary progressive aphasia. Williams-Paisley has written a book about her mother’s journey called Where the Light Gets In. Other featured articles address what to expect after a stroke and provide expert perspectives on the current state and future potential for stem cell therapy to treat neurologic conditions.

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.

Neurology® Clinical Practice offers two thought-provoking editorials. The timely topic of “Chipping Away at Neurologist Burnout, One Refill Request at a Time” addresses a problem experienced by many neurologists. The second editorial, “Decompressive Craniectomy in Malignant Middle Cerebral Artery Infarction: To Be, or Not to Be?” is complemented by the article “Early Decompressive Craniectomy for Malignant Cerebral Infarction: Meta-analysis and Clinical Decision Algorithm.” Other articles assess MACRA and the future of value-based care, five new things about Parkinson’s disease and cognitive impairment, and much more.

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 Collaborates on New Concussion Training for NFL Players

Prior to the beginning of the National Football League season, every NFL player received new concussion training from the NFL Players Association (NFLPA), including a video created in collaboration with the AAN. The video is endorsed by the American Brain Foundation.

“You only get one brain,” said AAN President Terrence L. Cascino, MD, FAAN. “When it comes to concussion—we want all athletes at all levels to remember ‘when in doubt, check it out.’”

The training includes an educational video for players and their families on how to recognize a concussion, essential facts about this brain injury, and the NFL concussion protocols that have been implemented for their health and safety. The training also covers how it will be determined when it may be safe for a player suspected of having a concussion or having already been diagnosed with a concussion to return to play.

“Concussion is really serious stuff. This is your brain—this is your mind—this is you. Don’t risk you,” said Thom Mayer, MD, NFLPA medical director.

“Once a potential injury has been identified, the NFL and the NFLPA have worked together to create evidence-based protocols to take you through a process that ensures you are safe to return to play,” said AAN member Jeffrey Kutcher, MD, FAAN, an advisor to the NFLPA.

“All of the people who are watching this game are trying to make it safer and trying to make it easier for a player, if he has a concussion, to have it diagnosed and treated properly, and if possible, preventing those concussions in the first place,” said Mayer.

Players are also being encouraged to speak up if they suspect a concussion.

“Simply going to the athletic trainer or the team physician, letting them know ‘hey, I got ringing in my ears after that hit,’ or ‘I’m seeing double a little bit, I think I need to be checked out,’” said Mayer.

Former NFL football player and AAN concussion spokesperson Ben Utecht retired early from the game due to the effects of too many concussions. Featured in the video, he tells viewers, “Your skill is what’s going to keep you on the field. So don’t be afraid, if in fact you ever face concussion, to speak up about it.”

Visit AAN.com/concussion for a wealth of resources—including the Academy’s Concussion Quick Check mobile app—to help coaches, athletes, and families recognize the signs of concussion.
Neurology Now Books Series Adds Epilepsy Title

The AAN's Neurology Now™ Books series now includes the newly published Navigating Life with Epilepsy, by David C. Spencer, MD, FAAN.

The book provides clearly written, easily grasped information about what epilepsy is, how it is diagnosed and treated, and how patients and caregivers can manage the disorder to enhance daily living. The author discusses treatment options and considerations ranging from medication to diets to surgery, and what outcomes patients may expect.

Navigating Life with Epilepsy is available to AAN members for only $13.95 ($19.95 list price) at The AAN Store® at AAN.com/AANStore/navigating-life-with-epilepsy.

Both the Neurology Now Books series and Neurology Now® magazine focus on the needs of people with neurologic disorders. The goal is to provide patients and their families and caregivers with the information they need to confront the day-to-day challenges of living with a neurologic condition. Other titles in the book series deal with Parkinson’s disease, brain tumor, stroke, and multiple sclerosis.

Set Yourself Apart

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

Learn how at AAN.com/view/FAAN.
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.

The AAN DC staff spent the seven weeks during Congress’ recess meeting with congressional staff about the Furthering Access to Stroke Telemedicine Act (HR 2799). The bill would allow Medicare to pay for stroke consultations via telemedicine in urban and suburban areas. Medicare already pays for these services in rural hospitals.

Our work paid off as we were informed by the author of the bill, Rep. Morgan Griffith (R-VA), that 14 more members of Congress had informed him that they were signing on as cosponsors. This brings the bill up to 159 cosponsors and we expect many more.

The advocacy staff had a discussion with key staff from the House Energy & Commerce Committee and learned there is concern that there may not be a final health care bill moving before Congress adjourns at the end of September.

Legislation impacting health care rarely moves through Congress as a standalone bill. Various ideas are packaged together into a larger bill. We have been eyeing several potential legislative vehicles for the FAST Act, such as the 21st Century Cures bill that passed the House earlier, but E&C Chairman Fred Upton (R-MI) indicated that there is no way the House and Senate will come to a final agreement with the Senate on 21st Century Cures before the elections. If the House is able to put something together before adjournment, we are ready to add the FAST Act.

On the Senate side, Senior Legislative Counsel Mike Amery joined AAN Government Relations Committee Chair Nicholas Johnson, MD, for a meeting with Senate Finance Committee staff. The committee is chaired by Johnson’s home state Senator Orrin Hatch (R-UT). Johnson has been working with Hatch’s office to get a cost analysis of the bill which is essential prior to moving forward.

If there are no more health-related bills that move through the current Congress, we will start again in the next session. This will be disappointing, but we will be well on our way. •
Across the spectrum of neurology,
Continuum is central
to your education and practice.

When questions arise, rely on Continuum: Lifelong Learning in Neurology® as the most comprehensive and authoritative go-to resource for the practicing neurology professional.

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Subscribe or renew today and receive 65% off with your AAN member discount at LWW.com/continuum.
January Breakthroughs in Neurology Conference Aims to Help Attendees Translate Today’s Discoveries into Tomorrow’s Clinics

Registration is open for the 2017 Breakthroughs in Neurology Conference, set to take place January 13 through 16 at the Sheraton Grand at Wild Horse Pass in Phoenix, AZ. This popular conference offers a unique and convenient opportunity to get a year-in-review of the best neurology science and education; network with faculty and colleagues; and earn up to 27 CME, 11.25 of which qualify for self-assessment CME—all at a beautiful warm-weather retreat.

“Whether you seek the latest practice management guidance, unparalleled science and education programs led by expert faculty, help preparing for ABPN board recertification, or specialty leadership skills training for women neurologists, the Breakthroughs in Neurology Conference has it—and then some,” said AAN Science Committee Chair Lisa M. DeAngelis, MD, FAAN.

Program Highlights:

- **NEW! Neuroscience in the Clinic Sessions (NICS):** Learn how to incorporate the latest scientific research into your daily practice. A mix of scientists and clinicians will present panel discussions on real-life cases covering a variety of disease states.

- **NEW! Curbside Consults:** Bring your challenging cases to discuss one-on-one with an expert in aging/dementia, neuro-oncology, or movement disorders.

- **Best of the Annual Meeting:** Hear from top leading researchers within the Hot Topics and Controversies Plenary Sessions.

- **Neurology MOC Prep Course:** Get help preparing for the ABPN recertification exam.

- **Leadership for Women:** Gain inspiration and training to grow your leadership potential.

- **Practice Management Programs:** Discover hot topics such as MACRA and MIPS requirements.

Early Registration and Hotel Deadline: December 1, 2016

Visit AAN.com/view/breakthroughs today to secure your spot—and save! •
Brush Up on Neuroimaging Skills with Continuum

Neuroimaging of conditions such as pituitary disorders, congenital malformations, and intracranial cysts is covered in the latest issue of Continuum: Lifelong Learning in Neurology®, along with overviews of imaging technologies. Participants can earn up to 14 hours of AMA PRA Category 1 Credit™ (12 of which apply to MOC Self-Assessment credit).

“Neuroimaging has evolved through the years beyond anatomic and basic tissue imaging into a field that provides detailed information on biological processes of diseases, becoming an intricate part of clinical neurology and a major tool in the neurosciences,” said Laszlo L. Mechtler, MD, FAAN, and guest editor of the issue with Joshua P. Klein, MD, PhD, FANA, FAAN, of Harvard Medical School in Boston. “This issue strikes a balance between more conventional and exciting new imaging technologies.”

Articles include:
- Introduction to Magnetic Resonance Imaging for Neurologists, by Ernst-Wilhelm Radue, MD; Matthias Weigel, PhD; Roland Wiest, MD; Horst Urbach, MD
- Imaging of Ischemic Stroke, by Michelle P. Lin, MD, MPH; David S. Liebeskind, MD, FAAN
- Imaging of Hemorrhagic Stroke, by Ryan Hakimi, DO, MS; Ankur Garg, MD
- Imaging for Adults With Seizures and Epilepsy, by Samuel Lapalme-Remis, MDCM, MA, FRCP; Gregory D. Cascio, MD, FAAN
- Imaging of Congenital Malformations, by Jennifer W. McVige, MA, MD
- Imaging in Patients With Visual Symptoms, by Gabriella Szatmáry, MD, PhD
- Imaging of Brain Tumors, by Mirza A Baig, DO; Joshua P. Klein, MD, PhD, FANA, FAAN; Laszlo L. Mechtler, MD, FAAN
- Imaging of Intracranial Cysts, by Bela Ajtai, MD, PhD; John A. Bertelson, MD
- Imaging of Pituitary and Parasellar Disorders, by Robert Fenstermaker, MD, FACS, FAANS; Ajay Abad, MD
- Imaging of Spinal Cord Disorders, by Karanbir Singh, MD; Laszlo L. Mechtler, MD, FAAN; Joshua P. Klein, MD, PhD, FANA, FAAN
- Imaging of Central Nervous System Demyelinating Disorders, by Konstantin Balashov, MD, PhD, FAAN
- Positron Emission Tomography and Single-Photon Emission Computed Tomography in Neurology, by Robert S. Miletich, MD, PhD, FAAAS
- Ultrasound in Neurology, by Georgios Tsivgoulis, MD, PhD, MSc, RVT; Andrei V. Alexandrov, MD, RVT
- Potential Safety Issues Related to the Use of Gadolinium-based Contrast Agents, by Nandor K. Pinter, MD; Joshua P. Klein, MD, PhD, FANA, FAAN; Laszlo L. Mechtler, MD, FAAN
- Legal Implications of Physician Investment and Ownership in Health Care Enterprises, by Rachel V. Rose, JD, MBA; Joseph S. Kass, MD, JD, FAAN
- Safety Considerations in Magnetic Resonance Imaging of Patients With Implanted Medical Devices, by Marcus Ponce de Leon, MD, FAAN
- Coding in Neuroimaging, by Joseph V. Fritz, PhD; Bennett Myers, MD

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Don’t let patients get lost in the noise of RMS

RMS—relapsing forms of multiple sclerosis.
QUIETING MS
Quietly*
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

MS=multiple sclerosis.

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.

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\(^1,3,4\).  
  - AUBAGIO 7 mg did not demonstrate a significant reduction in risk of sustained disability progression in either trial\(^1\).
- Sustained disability progression was defined as at least a 1-point increase from baseline Expanded Disability Status Scale (EDSS) score ≤5.5 (or at least a 0.5-point increase for those with a baseline EDSS score >5.5) sustained for at least 12 weeks\(^1\).
- AUBAGIO has demonstrated a consistent safety profile across 4 separate trials in 2047 patients\(^1\).
- One daily tablet that can be taken with or without food\(^1\).
- Health care professionals should run certain tests before prescribing AUBAGIO and should monitor patient liver enzyme levels monthly for the first 6 months\(^1\).

**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.\(^1\)

**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.\(^1,5\)

**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.\(^1,6\)

**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.\(^1\)

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.

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.

**WARNING: HEPATOTOXICITY and RISK OF TERATOGENICITY**

**Hepatotoxicity**

Severe liver injury including fatal liver failure has been reported in patients treated with leflunomide, which is indicated for rheumatoid arthritis. A similar risk would be expected for teriflunomide because recommended doses of teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. Concomitant use of AUBAGIO with other potentially hepatotoxic drugs may increase the risk of severe liver injury. Obtain transaminase and bilirubin levels within 6 months before initiation of AUBAGIO therapy. Monitor ALT levels at least monthly for 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 [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 before starting 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)].

**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 cholestyramine [see Warnings and Precautions (5.5)].
- Co-administration with leflunomide [see Drug Interactions (7.5)].
- Use in women of childbearing potential who are not using reliable contraception. Pregnancy must be excluded before starting AUBAGIO. AUBAGIO is contraindicated in pregnant women or women of childbearing potential who are not using reliable contraception. [see Warnings and Precautions (5.5)].
- ◆ Use in women of childbearing potential who are not using reliable contraception. Pregnancy must be excluded before starting AUBAGIO. AUBAGIO is contraindicated in pregnant women or women of childbearing potential who are not using reliable contraception. [see Warnings and Precautions (5.5)].

**5 WARNINGS AND PRECAUTIONS**

**5.1 Hepatotoxicity**

Severe liver injury including fatal liver failure and dysfunction has been reported in some patients treated with leflunomide, which is indicated for rheumatoid arthritis. A similar risk would be expected for teriflunomide because recommended doses of teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. Patients with pre-existing liver disease may be at increased risk of developing elevated serum transaminases when taking AUBAGIO. Patients with pre-existing acute or chronic liver disease, or those with serum alanine aminotransferase (ALT) greater than two times the upper limit of normal (ULN) before initiating treatment, should not normally be treated with AUBAGIO. AUBAGIO is contraindicated in patients with severe hepatic impairment [see Contraindications (4)].

**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 AUBAGIO, patients with pre-existing acute or chronic liver disease, or those with serum alanine aminotransferase (ALT) greater than two times the upper limit of normal (ULN) before initiating treatment, should not normally be treated with AUBAGIO. 

**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 before meals and 8 g three times a day can be used.
- 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 <1.5 x 10⁹/L was observed in 12% and 16% of patients receiving AUBAGIO 7 mg and 14 mg, respectively, compared with 7% of patients receiving placebo; lymphocyte count <0.6 x 10⁹/L was observed in 10% and 12% of patients receiving AUBAGIO 7 mg and 14 mg, respectively, with 6% of patients receiving placebo. No cases of serious pancytopenia were reported in premarketing trials. Two cases of pancytopenia with AUBAGIO compared to placebo 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/mm³, 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 Fatal and Life-Threatening Infections

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 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 (2.2%). However, one fatal case of klebsiella pneumonia sepsis occurred in a patient taking AUBAGIO 14 mg for 17 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 confounded by concomitant immunosuppressant therapy and/or comorbid 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 taking AUBAGIO 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 following serious adverse reactions are described elsewhere in the prescribing information:

- Hepatotoxicity [see Contraindications (4) and Warnings and Precautions (5.1)]
- Bone Marrow Effects/Immunosuppression Potential/Infections [see Warnings and Precautions (5.4)]
- Hypersensitivity and Serious Skin Reactions [see Contraindications (4) and Warnings and Precautions (5.5)]
- Peripheral Neuropathy [see Warnings and Precautions (5.6)]
- Increased Blood Pressure [see Warnings and Precautions (5.7)]
- Respiratory Effects [see Warnings and Precautions (5.8)]

6 Clinical Trials Experience

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

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

Table 1 lists adverse reactions in placebo-controlled trials with rates that were at least 2% for AUBAGIO patients and also at least 2% above the rate in placebo patients. The most common were headache, an increase in ALT, diarhoea, alopecia, and arthralgia. The adverse reaction most commonly associated with discontinuation was an increase in ALT (3.3%, 2.6%, and 2.3% of all patients in the AUBAGIO 7 mg, AUBAGIO 14 mg, and placebo treatment arms, respectively).

<table>
<thead>
<tr>
<th>Table 1. Adverse Reactions in Pooled Placebo-Controlled Studies in Patients with Relapsing Forms of Multiple Sclerosis</th>
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<tbody>
<tr>
<td><strong>AUBAGIO 7 mg</strong></td>
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<tr>
<td>------------------</td>
</tr>
<tr>
<td>Headache</td>
</tr>
<tr>
<td>Increase in Alanine</td>
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<tr>
<td>Aminotransferase</td>
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<td>Diarhoea</td>
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<td>Paresthesia</td>
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<td>Arthralgia</td>
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<td>Neutropenia</td>
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</table>

6.3 Cardiovascular Death

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

6.4 Acute Renal Failure

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

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

6.2 Post Marketing Experience

The following adverse reactions have been identified during post approval use of AUBAGIO. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Hypersensitivity reactions, some of which were severe, such as anaphylaxis and angioedema [see Warnings and Precautions (5.3)]
- Severe skin reactions, including toxic epidermal necrolysis and Stevens-Johnson syndrome [see Warnings and Precautions (5.3)]
- Thrombocytopenia [see Warnings and Precautions (5.3)]
- Intestinal lung disease [see Warnings and Precautions (5.8)]
- Pancreatitis

7 DRUG INTERACTIONS

Effect of AUBAGIO on CYP2C8 substrates
Teriflunomide is an inhibitor of CYP2C8 in vivo. In patients taking AUBAGIO, exposure of drugs metabolized by CYP2C8 (e.g., paxilaxil, pioglitazone, repaglinide, metformin) may be increased. Monitor these patients and adjust the dose of the concomitant drug(s) metabolized by CYP2C8 as required [see Clinical Pharmacology (12.3 in the full prescribing information)].

Effect of AUBAGIO on warfarin
Coadministration of AUBAGIO with warfarin requires close monitoring of the international normalized ratio (INR) because AUBAGIO may decrease peak INR by approximately 25%.

Effect of AUBAGIO on oral contraceptives
AUBAGIO may increase the systemic exposures of ethinylestradiol and levonorgestrel. Consideration should be given to the type or dose of contraceptives used in combination with AUBAGIO [see Clinical Pharmacology (12.3 in the full prescribing information)].

Effect of AUBAGIO on CYP1A2 substrates
Teriflunomide may be a weak inducer of CYP1A2 in vivo. In patients taking AUBAGIO, exposure of drugs metabolized by CYP1A2 (e.g., alosetron, duloxetine, theophylline, tizanidine) may be reduced. Monitor these patients and adjust the dose of the concomitant drug(s) metabolized by CYP1A2 as required [see Clinical Pharmacology (12.3 in the full prescribing information)].

Effect of AUBAGIO on organic anion transporter 3 (OAT3) substrates
Teriflunomide inhibits the activity of OAT3 in vivo. In patients taking AUBAGIO, exposure of drugs which are OAT3 substrates (e.g., cefaclor, cimetidine, ciprofloxacin, penicillin G, ketoprofen, furosemide, metothrexate, zidovudine) may be increased. Monitor these patients and adjust the dose of the concomitant drug(s) which are OAT3 substrates as required [see Clinical Pharmacology (12.3 in the full prescribing information)].

Effect of AUBAGIO on BCRP and organic anion transporting polypeptide B1 and B3 (OATP1B1/B3) substrates
Teriflunomide inhibits the activity of BCRP and OATP1B1/B3 in vivo. For a patient taking AUBAGIO, the dose of rosuvastatin should not exceed 10 mg once daily. For other substrates of BCRP (e.g., mitoxantrone) and drugs in the OATP family (e.g., methotrexate, rifampin), especially HMG-Co reductase inhibitors (e.g., atorvastatin, nateglinide, pravastatin, repaglinide, and simvastatin), consider reducing the dose of these drugs and monitor patients closely for signs and symptoms of increased exposures to the drugs while patients are taking AUBAGIO [see Clinical Pharmacology (12.3 in the full prescribing information)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category X [see Contraindications (4) 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 maximum recommended human dose (MRHD, 14 mg /day).

Administration of teriflunomide (oral doses of 1, 3.5, or 12 mg/kg/day) to pregnant rabbits throughout organogenesis resulted in high incidences of fetal malformations (primarily craniofacial, and axial and appendicular skeletal defects) and embryofetal death at doses associated with minimal maternal toxicity. Maternal plasma exposure at the no-effect dose (1.0 mg/kg/day) for embryofetal developmental toxicity in rabbits was less than that in humans at the MRHD. In studies in which teriflunomide (oral doses of 0.05, 0.1, 0.3, 0.6, or 1.0 mg/kg/day) was administered to rats during gestation and lactation, decreased growth, eye and skin abnormalities, and high incidences of malformation (limb defects) and postnatal death were observed in the offspring at doses not associated with maternal toxicity.
2017 NeuroSAE Annual Meeting Edition Launches this Month
Offers 10 Free Self-assessment CME to AAN Members

The latest Annual Meeting edition of the AAN’s popular self-assessment examination launches later this month. If you’re attending the 2017 Annual Meeting, then you’ll want to be sure and include the new NeuroSAE® Annual Meeting Edition in your plans. Available free to AAN members, this convenient online program helps you assess your knowledge in major clinical areas of neurology and provides course suggestions by subspecialty area to help you build your ideal itinerary for the Annual Meeting.

How it works:

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Pre-test</th>
<th>Take pre-test by April 22, 2017</th>
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<tbody>
<tr>
<td>Step 2</td>
<td>Annual Meeting</td>
<td>Attend Annual Meeting April 22–28, 2017</td>
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<tr>
<td>Step 3</td>
<td>Post-test</td>
<td>Take post-test by July 29, 2017</td>
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Apply Now for UCNS Neuro-oncology Certification or Recertification

Applications are open for certification and recertification in Neuro-oncology through the United Council for Neurologic Subspecialties (UCNS). The deadline to apply is January 17, 2017. The examination is scheduled for the week of August 7 to 11, 2017.

Because UCNS offers examinations once every two years, all Neuro-oncology diplomates certified in 2008 must apply to take the 2017 recertification exam.

For more information, contact Todd Bulson at tbulson@ucns.org or visit UCNS.org.
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AAN.com/view/17awards
Research & Awards

White Paper Cites Need for Nonhuman Primates in Medical Research

The use of animals in medical research has been a controversial issue in the public for some time. Recently, the Foundation for Biomedical Research, in collaboration with the AAN, the Society for Neuroscience, and other organizations, published a white paper on the topic. “The Critical Role of Nonhuman Primates in Medical Research” makes the case for continued need of animals in research, particularly nonhuman primates (NHP). It cites a number of major medical accomplishments that were assisted by research monkeys, which make up less than one percent of testing animals, but have a significant impact despite the small population.

The paper states that because of significant differences between the brains of primates and rodents, it is necessary to rely on monkeys. Because of their more direct similarities to humans, the use of primates in research has helped scientists understand what therapies or treatments are ready for prime-time in a much more assured sense than seeing benefit in an organism such as a rodent, cat, or worm, which also are used. This seems especially true for vaccination research—a critical situation when facing an outbreak like the Zika virus, where a vaccine is urgently needed.

To learn more about the role of nonhuman primates in research, read the paper at AAN.com/research-and-awards/animals-in-research.

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October 26 is the deadline to apply for one of the 25 prestigious 2017 AAN awards representing the most esteemed recognition of scientists—at all stages of their careers—who have made the most notable advancements in the field of neuroscience across a variety of disease states. In addition to career-enhancing recognition, AAN awards offer prizes and other compensation, such as complimentary travel and registration the 2017 AAN Annual Meeting in Boston, April 22 through 28.

View the full listing of award opportunities and apply, or nominate a well-deserving colleague, at AAN.com/view/17Awards.

The 2016 Minority Scholars Recipients.

Rufus O. Akinyemi, MBBS, MSc, PhD, MWACP, FMCP, received the Bruce S. Schoenberg International Award in Neuroepidemiology.

Riley Bove, MD, accepted the Neuroendocrine Research Award.

Rufus O. Akinyemi, MBBS, MSc, PhD, MWACP, FMCP, received the Bruce S. Schoenberg International Award in Neuroepidemiology.
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Learn more and apply or nominate by visiting AAN.com/view/FAAN. For more information, contact AAN Member Services at memberservices@aan.com or (800) 879-1960.

Congratulate These New FAANs!

The AAN congratulates the following 72 members who were named Fellows between May and August 2016.

Jason Lamar Aldred, MD, FAAN
Adel Alhazzani, MD, FRCPC, FAAN
Shireen Al-Qureshi, MD, FRCP, FAAN
Hany M. Aref, MD, FAAN
Brenda Banwell, MD, FAAN
Reza Behrouz, DO, FAAN
Dario Beltran, MD, FAAN
Bibiana Bielekova, MD, FAAN
David M. Biondi, DO, FAAN
Andrew Biondo, DO, FAAN
Thomas H. Brannagan III, MD, FAAN
K.C. Brennan, MD, FAAN
Steven M. Bromley, MD, FAAN
Amy R. Brooks-Kayal, MD, FAAN
Kevin J. Callerame, MD, FAAN
Marc Cantillon, MD, FAAN
Jerome H. Chin, MD, PhD, MPH, FAAN
John Y. Choi, MD, FAAN
Asha Das, MD, FAAN
Ted M. Dawson, MD, PhD, FAAN
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Cheryl Ann Jay, MD, FAAN
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Olga Klepitskaya, MD, FAAN
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Maureen Leehey, MD, FAAN
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Ashkan Mowla, MD, FAAN
Kazuma Nakagawa, MD, FAAN
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Mustafa S. Siddiqui, MD, FAAN
Lauren Seeberger, MD, FAAN
Manuel Seijo-Martinez, MD, PhD, FAAN
Gorazd B. Stokin, MD, PhD, FAAN
Stephen P. Suggs, MD, FAAN
John B. Townsend, MD, FAAN
Mark H. Tuszynski, MD, PhD, FAAN
Roxanne M. Valentino, MD, FAAN
Paul C. Van Ness, MD, FAAN
Bert B. Vargas, MD, FAAN
Ryan R. Walsh, MD, PhD, FAAN
Pedro Weisleder, MD, PhD, FAAN
Charles Zollinger, MD, FAAN •
New Help for Solo and Small Practices

grown because we are passionate about being proactive and asserting the views and needs of our practicing members. For example, a July 13, 2016, article on the widely read “Policy & Medicine” website lauded our in-depth response—just one of nearly 4,000 comments—to CMS’s proposed MACRA rules: “The American Academy of Neurology’s (AAN) comment letter was one of the most substantial and included a thorough legal and policy rationale for the inclusion of quality-related CME as a CPIA [Clinical Practice Improvement Activity].” (PolicyMed.com/2016/07/cms-receives-hundreds-of-comments-to-include-cme-in-macra.html). The article quoted heavily from our response to CMS, attesting to the strength of our voice and respect for our views as we continue to fight for members in practice and protect the neurology profession.

Members have a role to play, too: Stay informed and speak up. Often, after answering a “Why doesn’t the AAN...?” question from a member, the member’s response is “Great, I didn’t know the Academy was doing that” or “Thanks, I wasn’t aware of those resources.” Time is precious for all of us, but if you don’t take a few minutes to regularly visit AAN.com or read AAN emails, AANe-news™, or AANnews®, or join in the conversations on our Synapse online communities, you may miss out on significant information, tools, and programs that can help you regain time with your patients, make your practice more efficient, and ensure you will be properly reimbursed for your work. And please make your voice heard by responding to our advocacy action alert emails, because your participation adds credence to our efforts. If you have issues or concerns you want to relay to the Academy, please contact me at the email below or Member Services at memberservices@aan.com.

The goals of the Solo and Small Practice Task Force’s recommendations are to recommit the AAN to being indispensable to its members in solo and small practice by supporting them to remain in the practice of their choosing. We want to ensure that all of our members—in every type of practice arrangement—recognize the Academy’s commitment to them. Watch for more news on progress around implementing the recommendations of the Task Force in the weeks and months ahead. *

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

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President’s Column
MORE OPTIONS
ZERO CO-PAY*
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Give Your Topiramate Patients MORE with **Qudexy® XR**!

### Comparison of Features:

<table>
<thead>
<tr>
<th>Feature</th>
<th>Qudexy® XR¹</th>
<th>Topamax® (topiramate) Tablets²</th>
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<tr>
<td>100% Extended-Release Bead Formulation</td>
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<td>Smooth Pharmacokinetic Profile</td>
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<tr>
<td>5 Dosage Strengths, Including 150 mg</td>
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*Eligible Patients Pay $0. Covers $200/Prescription, Maximum Annual Savings of $2,400.

Visit us at hcp-options.QudexyXR.com
AAN members are invited to Standing Strong, a special once-in-a-lifetime evening benefiting brain disease research. The event takes place October 26 at the new U.S. Bank Stadium in Minneapolis, home of the Minnesota Vikings football team and site of the 2018 Super Bowl.

Artist Susan Schneider Williams, widow of beloved actor Robin Williams and member of the American Brain Foundation Board of Directors, will be the keynote speaker. She will share the struggles Williams faced with Parkinson’s and Lewy body disease before his untimely death in 2015.

The evening also will feature a musical performance by Ben Utecht, former NFL tight end, Super Bowl champion, and concussion sufferer. Utecht is the national concussion advocate for the American Brain Foundation and also serves on its Board. Attendees of Standing Strong will receive a copy of Utecht’s new book, Counting the Days While My Mind Slips Away.

This is the foundation’s third Standing Strong benefit, and it’s very personal to Utecht. It was his brainchild and the first two events took place at the University of Minnesota, where Utecht played four seasons with the Gophers. “This was born out of the relationship I have with the American Brain Foundation and the AAN. My story, which is now a book, is accompanied by my song “Standing Strong,” about the trials we face in everyday life. For me, that trial is traumatic brain injury, for others it may be different brain disorders and disease. My hope is that my personal story can help people realize the importance of finding cures.”

Utecht has enjoyed his mission as an ambassador for concussion awareness and brain health as he shares his story about the effects of five known concussions on his brain—and his life and family. “It’s been very successful. What we try to do with Standing Strong is connect people with their brains. I combine inspirational storytelling and specifically asking for help. When you do a good job bringing people into the lives of those affected, such as myself and my family, it has a very high impact. We’ve seen that in the last few years Standing Strong has been growing.”

His recently published memoir will help him get his message out farther. “This is what can happen with a book that touches people’s lives. The reach is very broad. I just hope the book connects with people and can be used along with Standing Strong to help people have a stronger appreciation for their minds and memories. I was very vulnerable with this book, talking about how things became confused in my own life because of concussions. I hope it really gets people to understand how much more funding and focus we need in the fight against brain disease.”

The Standing Strong benefit offers a rare, exclusive behind-the-scenes tour of the state-of-the-art U.S. Bank Stadium, including areas typically off-limits to the general public.

Tickets for this exciting event to support brain disease research are $125 per individual and $220 per couple. Standing Strong will take place from 6:30 p.m. to 10:00 p.m. on Wednesday, October 26. Members may RSVP by October 12 to ABF.convio.net/StandingStrong.
The American Brain Foundation is committed to bringing researchers and donors together to defeat brain disease. Join us today to help speed progress on the road to a cure.

AmericanBrainFoundation.org/cure
If neuroscience professionals could zip to one spot to search job openings, find mentors, research salaries, explore articles and webinars, and ensure their interviewing skills are up to par, where would they go? The answer: The American Academy of Neurology’s online Neurology Career Center at AAN.com/careers, a one-stop site created exclusively for the 30,000 professionals comprising the AAN.

The AAN’s Neurology Career Center is a multi-purpose, user-friendly toolbox of open job postings and career-related resources, including 400+ jobs posted at any given time. The site is a well-traveled path to job offers: Last year, it boasted more than 1 million views and 1,600 job applications submitted. According to a 2012 Career Center user survey, the average seeker applied for five jobs on the site, received three offers, and accepted one.

Targeted, thorough job searching
Still, not all AAN members may be aware of the Career Center or the varied benefits—like a neurology-centered focus, and the time and effort career-searching members can save through using it. Consider, for instance, the job search feature. “When members use other sites, even with a key word search using ‘Neurology,’ it’s going to bring up other material that has no interest to them,” states AAN Career Services Manager Amy Schoch, who helped launch the resource in 2011.

By contrast, the Neurology Career Center features only neurology-related job openings. Plus, a search mechanism allows members to list their subspecialties, preserve their searches, and await and acquire information on openings that may not yet be listed. “It will pull up positions of interest so they can actually dig down a deeper level,” Schoch states. “Then, they can save their search—for example, ‘Stroke in New York City.’ If a position opens up, they’ll receive an email notification: ‘You might be interested in this job from the Neurology Career Center’ and they can just click on a link.”

Private vs. public profiles
Unsolicited contact from employers and recruiters can waste time and clog up the search process. The AAN Neurology Career Center privacy setting was designed to eliminate such obstructions. Through this handy option, members can flag their profiles as private, thus ensuring contact only from employers to whom they have sent applications. According to Schoch, about 90 percent of users choose to create a private profile. And it works, says Schoch, who set up a test profile in 2011 that has never received any unwanted emails or phone calls.

On the other hand, AAN members who feel too busy to search the site can opt for a public profile, which allows Career Center advertisers to explore their information. “If they don’t have time, it’s a way to say, ‘I want the job to find me,’” Schoch explains.

Multiple CVs? No problem
Since the majority of neurology residents accept fellowships and pursue subspecialties, it’s common to have two CVs—one for general neurology, another for a subspecialty. Enter the storage function, a nifty feature that lets members save up to six documents online—including CVs, letters of reference, and publications—for fast, efficient future search processes. “When they apply for their jobs, it’s really easy,” Schoch states. “They click on the ‘Apply’ button, answer three questions, and they’re done.”

Planning ahead while staying current
Those not actively seeking a new position can still use the site to investigate what’s available, or to set up job alerts—a wise move considering that many larger hospitals and universities forecast for specialists they’ll need. Physicians in training can reach out to a facility, mention the available positions advertised now, and inquire about similar needs down the line, Schoch explains.

Members in training can also peruse postings to identify the capabilities employers need as a way to guide their decisions about residencies or other training. Established professionals, too, may find scanning job postings to be useful. “It’s helpful for them to keep tabs on their competition: For example, if they launch a new Stroke Center will that impact their patient base?” Schoch explains.

How else can the site help you stay current? Articles and webinars cover a range of career-relevant topics, from contract negotiation to strength-based interviewing. A salary calculator tool helps AAN junior members project earnings using data compiled by actual AAN members. And all members can take advantage of discounted CV reviews and interview coaching sessions year-round.
Help and be helped
A seasoned neurologist able to help new residents. An immigrant physician seeking visa advice. A resident considering starting a practice. All are good reasons to seek a mentor relationship through the AAN Career Center. Since 2012, more than 200 mentorships have been arranged through AAN Mentor Connect, the mentoring program that helps neurologists anywhere, at any career stage, to link up. Mentees create profiles and search a list of available mentors, who also create profiles but don’t conduct searching. Coordinating is up to the pairs, who determine when, where, and how they will meet. Some do so in person; others use email, phone calls, Skype, or other methods.

“It’s open-ended, offering anything anyone needs for mentoring, at any stage of their career,” Schoch explains. For example, residents who are parents of young children may need work-life balance tips, she says, while neurologists in rural settings may wish to dialogue with other neurologists in similar locales.

Don’t Forget to Participate in Neurology Career Week
The AAN’s popular Neurology Career Week takes place October 3 to 7. Academy members seeking new job opportunities and work search insights will want to take advantage of some exclusive offers, including a chance to win $500 in a sweepstakes for those who create or update their job search profile by October 7. To learn more about Neurology Career Week, visit AAN.com/careers.

Find Your Next Job
AAN.com/careers

Fill Your Open Job
The hottest jobs meet the top candidates at the AAN Neurology Career Center.
Two Stroke (Vascular) Neurology positions – Assistant, Associate or Full Professor

The Department of Neurology at the University of Washington is seeking two neurologists with expertise in vascular neurology to join the Comprehensive Stroke Center at Harborview Medical Center. The Stroke Program at Harborview represents a dynamic environment to practice Vascular Neurology, both inpatient and outpatient. A TeleStroke program is in place and expanding. You will interact with eight Vascular Neurosurgery, a Level II trauma center, two Interventional Neuroradiologists, and an outstanding Emergency Department. These are both full-time appointments and will be at the Assistant Professor rank (without tenure for reasons due to funding, job code 0113) in the clinician-educator academic pathway. Candidates with exceptional qualifications may be considered for appointment at the rank of Associate Professor (without tenure for reasons due to funding, job code 0112) or Professor (without tenure for reasons due to funding, job code 0111). Submit a letter of interest and curriculum vitae: Kass Klemz, Assistant to the Chairman, University of Washington, Department of Neurology, Box 356465, Seattle, WA 98195. Email: kass@uw.edu

These positions are open until filled. University of Washington is an affirmative action and equal opportunity employer. All qualified applicants will receive consideration for employment without regard to race, color, religion, sex, sexual orientation, gender identity, national origin, age, protected veteran or disabled status, or genetic information.

Neurology Position with Central Maine Medical Center

Central Maine Medical Group is seeking a BE/BC neurologist to join an established adult neurology practice primarily associated with Central Maine Medical Center. A focused interest in stroke, muscle disease, headache/migraine, epilepsy, or movement disorder would be a welcome addition, but is not required. Our diagnostic capabilities include: 1.5T MRI, CT angiography, EMG, Evoked Potentials, EEG, and 24-72 Hour Ambulatory EEG. We also have an active Teleneurology service that is affiliated with Massachusetts General Hospital. Central Maine Medical Center is the flagship hospital of Central Maine Healthcare. The medical center has 250 inpatient beds and offers a broad range of services that include, among many, neurosurgery, a Level II trauma center, cardiovascular medicine, vascular and cardiac surgery, and medical and radiation oncology. The Central Maine Medical Group comprises of approximately 350 providers, approximately half of which are in primary care. The group delivers care across almost 2500 square miles at numerous outpatient sites and four hospitals. A competitive salary and attractive benefits package are enhanced by the scenic beauty and abundant outdoor adventure found in Maine. Interested candidates, please send a CV to Gina Mallozzi, Central Maine Medical Center, 300 Main Street, Lewiston, ME 04240. Fax: (207) 795-5696, email: MallozziGi@cmhc.org, or call: (800) 445-7431. Not a J1 Opportunity.

Neurologists

Well-established, quality oriented neuroscience group seeks to add additional neurologists. Opportunity for subspecialists and general neurologist. We are a multidisciplinary neuroscience group providing a strong team oriented environment and opportunities for professional growth. Our location offers easy access to the cultural institutions of Boston, as well as outstanding private and public school opportunities. Send CV to Howard M. Gardner, MD, Medical Director, New England Neurological Associates, PC, RIVERWALK, 354 Merrimack Street, Lawrence, MA 01843, or email to jtf@neneuro.com. Visit us on the web at www.neneuro.com

Neurologists

Lowell Massachusetts, just 30 minutes from Boston; 5-person practice looking for well qualified neurologists to join fast growing medical community. This involves state of the art diagnosis and treatment opportunities with affiliation to Boston teaching hospital. We look forward to hearing from you. If interested, contact Jonathan Moray, MD, at jonathan.moray@neneuro.com or jtf@neneuro.com

Fellowship in Neuroimaging Winchester Neurological Consultants, Inc., in conjunction with Virginia Commonwealth University and Winchester Medical Center, is offering a clinical Neuroimaging Fellowship for BC/BE neurology graduates that can be completed in one or two years. Located approximately an hour from Washington, DC, our United Council of Neurologic Subspecialties fully accredited fellowship offers extensive training in the performance and interpretation of diagnostic 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 plus benefits. CV’s should be emailed to gsteele@winchesterneurological.com

Northwest Permanente—Multiple Neurology Openings

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 who share your passion for medicine and patient care within our self-governed, physician-led, multi-specialty group of over 1,500 physicians, surgeons, and other licensed professionals. Opportunities are available for individuals with subspecialty, general neurology and inpatient hospital 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 pioneering integrated medical practice and is leading the way to the future of medical care. Opportunities in the Pacific Northwest: Movement & Epilepsy 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 Website at http://nwp.kpphysiciancareers.com. For more information, call Shelonda at (800) 813-3763. No J1 opportunities. We are an equal opportunity employer and value diversity within our organization.

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Ad copy for the December 2016 print edition of AANnews must be submitted by November 1, 2016. The same deadline applies to changes/cancellations.

The American Academy of Neurology reserves the right to decline, withdraw, or edit advertisements at its discretion. Every care is taken to avoid mistakes, but the responsibility for clerical or printer errors does not exceed the cost of the ad.
NOW APPROVED AND AVAILABLE FOR RELAPSING FORMS OF MS

Zinbryta™
(daclizumab)
150 mg Subcutaneous Injection

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
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.

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.

Please see the following pages for additional Important Safety Information and Brief Summary of Full Prescribing Information, including BOXED WARNING.
In clinical studies, ZINBRYTA (daclizumab) significantly reduced the annualized relapse rate 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 (n=919)</th>
<th>AVONEX (n=922)</th>
<th>P-value</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annualized relapse rate</td>
<td>0.216</td>
<td>0.393</td>
<td>&lt;0.0001</td>
<td>45% relative reduction</td>
</tr>
</tbody>
</table>

*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 Score (EDSS) score of 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 (n=208)</th>
<th>Placebo (n=204)</th>
<th>P-value</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annualized relapse rate</td>
<td>0.211</td>
<td>0.458</td>
<td>&lt;0.0001</td>
<td>54% relative reduction</td>
</tr>
</tbody>
</table>

*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 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 of 0.0-5.0 who had either ≥2 relapses during the prior 3 years and ≥1 relapse in the year prior to randomization or who had ≥1 T1 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. (Continued on next page)
Important Safety Information (Continued)

Immune-Mediated Disorders (Continued)

If a patient develops a serious immune disorder, consider stopping ZINBRYTA and refer the patient to an appropriate specialist for further evaluation and treatment.

- 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 Brief Summary of Full Prescribing Information including BOXED WARNING on following pages.


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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 (5.5)]. 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 (5.5)].

Prior to initiation of 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, 5.2)].

Because of the risks of hepatic injury, including autoimmune hepatitis, and other immune-mediated disorders, ZINBRYTA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ZINBRYTA REMS Program [see Warnings and Precautions (5.3)].

Table 1: ZINBRYTA Treatment Modification for Liver Test Abnormalities

<table>
<thead>
<tr>
<th>Elevated Transaminases and/or Total Bilirubin</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT or AST greater than 5 times ULN OR</td>
<td>If no other etiologies are identified, then discontinue ZINBRYTA.</td>
</tr>
<tr>
<td>Total bilirubin greater than 2 times ULN OR</td>
<td>Interrupt ZINBRYTA therapy and investigate for other etiologies of abnormal lab value(s).</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 other etiologies are identified, re-assess the overall risk-benefit profile of ZINBRYTA in the patient and consider whether to resume ZINBRYTA when both ALT or AST are less than 2 times ULN and total bilirubin is less than or equal to ULN.</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)].
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. A serious drug-related hepatic injury occurred in 0.3% of ZINBRYTA-treated patients compared with 0.1% of AVONEX-treated patients. The incidence of severe liver injury was 0.7% in ZINBRYTA-treated patients and 0.1% 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 2% of ZINBRYTA-treated patients compared with 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. Also, carefully consider the need for the use of herbal products or dietary supplements that can cause hepatotoxicity [see Drug Interactions (7.1)].

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 lymphopoenopathy. 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. The incidence of serious immune-mediated disorders was 4% of ZINBRYTA-treated patients compared with 0.4% of AVONEX-treated patients. In the placebo-controlled study (Study 2), immune-mediated disorders were observed in 3% of ZINBRYTA-treated patients compared with 0.1% of placebo-treated patients. In Study 2, serious immune-mediated disorders were observed in 0.5% of ZINBRYTA-treated patients and 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 management 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-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. Rashes occurred in 11% of ZINBRYTA-treated patients compared to 2% of AVONEX-treated patients. If a patient develops a serious skin reaction (e.g., life-threatening severe liver injury, including liver failure and autoimmune hepatitis), discontinue ZINBRYTA and do not restart ZINBRYTA if the need for the use of herbal products or dietary supplements that can cause hepatotoxicity [see Drug Interactions (7.1)].

Other Immune-Mediated Disorders: A wide variety of other immune-mediated disorders, some serious, have occurred infrequently with the use of ZINBRYTA. They 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)].
- Pharmacies 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)].

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)].
5.5 Infections

ZINBRYTA increases the risk for infections. In controlled trials, infections occurred in 69% 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 1 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, concurrent use of ZINBRYTA with the hepatotoxic drugs valproic acid, carbamazepine, lamotrigine, phenytoin, isoniazid, 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 mcg 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 infection</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>Rash</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Influenza</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Dermatitis</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>Eczema</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
2 includes erythematous rash, exfoliative rash, macular rash, maculopapular rash, papular rash, pruritic rash, rash, and vesicular rash
3 includes allergic dermatitis, atopic dermatitis, bullous dermatitis, dermatitis, exfoliative dermatitis, and seborrheic dermatitis
4 includes dyshidrotic eczema, eczema, and nummular eczema

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>Depression</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Rash</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>Dermatitis</td>
<td>3</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

1 includes depressed mood and depression
2 includes erythematous rash, exfoliative rash, macular rash, maculopapular rash, papular rash, pruritic rash, rash, and vesicular rash
3 includes allergic dermatitis, atopic dermatitis, bullous dermatitis, dermatitis, exfoliative dermatitis, and seborrheic dermatitis

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, piorrhea, respiratory tract infection, skin exfoliation, toxic skin eruption, and viral infection.
Seizures: In Study 1, seizures occurred in 1% of ZINBRYTA-treated patients, compared with 0.3% of AVONEX-treated patients. In Study 2, no seizures occurred in either treatment group.

Immunemediated Disorders: Types of immune-mediated or autoimmune conditions that were observed in 2 or more ZINBRYTA-treated patients include type 1 diabetes, celiac disease, autoimmune thyroiditis, immune hemolytic anemia, thrombocytopenia, pancreatitis, glomerulonephritis, sarcoidosis, rheumatoid arthritis, thyroiditis, and sialadenitis [see Warnings and Precautions (5.2)]. The relationship of these events to ZINBRYTA is unknown.

Breast Cancer: In controlled studies, 1 ZINBRYTA-treated woman developed breast cancer compared with none in the AVONEX-treated group. Across all controlled and open-label clinical studies, 8 of 1485 (0.5%) ZINBRYTA-treated women developed breast cancer, and 1 of 751 (0.1%) ZINBRYTA-treated men developed breast cancer. It is unclear whether this represents an incidence increase over background rate.

6.2 Immunogenicity
As with all therapeutic proteins, there is potential for immunogenicity. In Study 1, patients were tested for anti-drug (daclizumab) antibodies at Week 4 and approximately every 3 months thereafter. Anti-drug antibodies and neutralizing antibodies were observed in 19% (175/913) and 8% (71/913) of patients, respectively. Anti-drug antibody responses were transient in 12% (110/913) of patients and persistent in 7% (65/913) of patients. Anti-drug and neutralizing antibody responses predominantly occurred during the first year of treatment, and their frequency declined with continued ZINBRYTA treatment.

In patients with neutralizing antibodies, daclizumab clearance was increased on average by 19% [see Clinical Pharmacology (12.3)]. There was no apparent correlation of anti-drug antibody or neutralizing antibody development to clinical response, adverse reactions, or pharmacodynamic profile of ZINBRYTA. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to daclizumab with the incidence of antibodies to other products may be misleading.

7 Drug Interactions
7.1 Hepatotoxic Drugs
Caution should be used when using hepatotoxic drugs, including nonprescription products, concomitantly with ZINBRYTA. Carefully consider the need for the use of herbal products or dietary supplements that can cause hepatotoxicity [see Warnings and Precautions (5.1)].

8 Use in Specific Populations
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 reduced fetal growth at maternal exposures greater than 30 times that expected clinically [see Data]. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2.4% and 15-20%, respectively. The background risk of major birth defects and miscarriage for the indicated population is unknown.

Data: Animal Data: In monkeys administered ZINBRYTA (0, 10, 50, or 200 mg/kg) weekly by subcutaneous injection during organogenesis (gestation days 20 through 50), there was a decrease in fetal body weight and crown-rump length, and an increase in embryofetal death at the highest dose tested. Plasma exposure (AUC) at the no-effect dose of 50 mg/kg was approximately 30 times that in humans at the recommended human dose (RHD) of 150 mg. In monkeys administered ZINBRYTA (50 mg/kg) weekly by subcutaneous injection from gestation day 50 to birth, there were no effects on pre- or postnatal development for up to 6 months after birth. Plasma exposure (AUC) at the administered dose was 55 times that in humans at the RHD.

8.2 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. 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 before they start 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.

Adviser 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 (5.1, 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.

Allergic Reactions and Anaphylaxis: Advise patients of the symptoms of allergic reactions and anaphylaxis, and instruct patients to seek immediate medical attention if these symptoms occur [see Warnings and Precautions (5.4)].

Risk of Infections: Inform patients that they may be more likely to get infections when taking ZINBRYTA, and that they should contact their healthcare provider if they develop symptoms of infection [see Warnings and Precautions (5.5)].

Depression and Suicide: Advise patients of the symptoms of depression and suicidal ideation as they have occurred with the use of ZINBRYTA and instruct patients to report symptoms of depression or thoughts of suicide to their healthcare provider immediately [see Warnings and Precautions (5.6)].

Instructions for Self-injection Technique and Procedures: Provide appropriate instruction for methods of self-injection, including careful review of the ZINBRYTA Instructions for Use. Instruct the patient in the use of aseptic technique when administering ZINBRYTA. Inform the patient that a healthcare provider should show them or their caregiver how to inject ZINBRYTA before administering the first dose. Tell the patient not to re-use needles or syringes, and instruct the patient on safe disposal procedures. Inform the patient to dispose of used needles and syringes in a puncture-resistant container.

Manufactured by: Biogen Inc. Cambridge, MA 02142 U.S. License # 1697

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## Dates and Deadlines

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### October 1
- Application Deadline: 2017 AAN Research Program Awards and Scholarships
  - [AAN.com/view/ResearchProgram](AAN.com/view/ResearchProgram)

### October 1
- Application Available: UCNS Neuro-oncology Certification and Recertification Examinations
  - [UCNS.org/go/subspecialty/neo-oncology/certification](UCNS.org/go/subspecialty/neo-oncology/certification)

### October 3–7
- Neurology Career Week
  - [AAN.com/careers](AAN.com/careers)

### October 11
- Webinar: Don’t Just Phone It In: A Guide to Teleneurology
  - (Register by October 10)
  - [AAN.com/view/pmw16](AAN.com/view/pmw16)

### October 14–16
- 2016 Fall Conference / Las Vegas, NV
  - [AAN.com/view/Fall](AAN.com/view/Fall)

### October 24
- Submission Deadline: 2017 AAN Annual Meeting Abstracts
  - [AAN.com/view/AM17](AAN.com/view/AM17)

### October 26
- Application Deadline: AAN Scientific Awards
  - [AAN.com/view/17Awards](AAN.com/view/17Awards)

### November 8
- Webinar: Getting the Most Out of Your Technology: HIT and Your Patients
  - (Register by November 7)
  - [AAN.com/view/pmw16](AAN.com/view/pmw16)

### November 20
- Application Deadline: 2017 Neurology on the Hill
  - [AAN.com/view/2017NOH](AAN.com/view/2017NOH)

### November 30
- Application Deadline: Fellow Scholarship to the Annual Meeting

### November 30
- Nomination Deadline: Resident Scholarship to the Annual Meeting
  - [AAN.com/research-and-awards/resident-scholarship-to-the-annual-meeting](AAN.com/research-and-awards/resident-scholarship-to-the-annual-meeting)

### November 30
- Nomination Deadline: Program Director Recognition Award

### November 30
- Application Deadline: Program Coordinator Recognition Award

### DECEMBER 1
- Application Deadline: UCNS Fellowship Program Accreditation
  - [UCNS.org](UCNS.org)

### DECEMBER 1
- Registration Deadline: RITE® (Residency In-service Training Examination) Exam
  - [AAN.com/trainees/resident-resources/residency-in-service-training-examination](AAN.com/trainees/resident-resources/residency-in-service-training-examination)

### DECEMBER 1
- Early Registration Deadline: Breakthroughs in Neurology
  - [AAN.com/view/Breakthroughs](AAN.com/view/Breakthroughs)

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## SAVE THE DATES!

**January 13–16, 2017**
- Breakthroughs in Neurology, Phoenix, AZ
  - [AAN.com/view/Breakthroughs](AAN.com/view/Breakthroughs)

**April 22–28, 2017**
- AAN Annual Meeting, Boston
  - [AAN.com/view/AM17](AAN.com/view/AM17)