# Updated American Academy Guidelines on the Use of Disease-modifying Therapies in Multiple Sclerosis—What's New?

An Expert Interview with Alexander Rae-Grant

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*DOI: https://doi.org/10.17925/USN.2018.14.2.76*

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**Keywords**

American Academy of Neurology (AAN), disease-modifying therapy, guideline, multiple sclerosis, recommendations

**Disclosure**: Alexander Rae-Grant is a member of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology (AAN), and lead author of the 2018 AAN practice guideline on disease-modifying therapy for multiple sclerosis discussed in this interview.

**Review Process**: This is an expert interview and, as such, has not undergone the journal's standard peer review process.

**Acknowledgment**: Medical writing assistance was provided by Katrina Mountfort of Touch Medical Media and was supported by Touch Medical Media.

**Authorship:** The named author meets the International Committee of Medical Journal Editors (ICMJE) criteria for authorship of this manuscript, takes responsibility for the integrity of the work as a whole, and has given final approval for the version to be published.



**Received**: October 8, 2018

**Published Online**: November 6, 2018

**Citation**: *US Neurology.* 2018;14(2):76–7

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**Support**: No funding was received in the publication of this article.

Recently released guidelines on the use of disease-modifying therapies (DMTs) in patients with multiple sclerosis (MS) include guidance on starting, switching, and stopping treatment. The guidelines, which were produced by a multidisciplinary panel and endorsed by the Multiple Sclerosis Association of America and the National Multiple Sclerosis Society, were presented at the American Academy of Neurology (AAN) 2018 Annual Meeting and published in *Neurology*.[1] Included within the guidelines are recommendations for patients with relapsing-remitting MS, secondary progressive MS, and primary progressive MS, as well as those with clinically isolated syndrome of demyelination. In an expert interview, the lead author Alexander Rae-Grant discusses the major recommendations of the guidelines.

## Q. What are the recommendations of the new AAN guidelines in terms of when to prescribe DMTs for MS?

The guidelines are focused on personalizing the decision about when to start DMTs, which DMT to start, and how to start DMTs. Each individual with MS has different medical issues, different risk tolerances, and different preferences that need to be considered and acted upon when deciding on a DMT. Ultimately a shared decision-making model is the best one for this kind of long-term disease and patient management.

The guidelines recommend initiation of DMTs for people with relapsing MS, particularly those with recent clinical or magnetic resonance imaging (MRI) disease activity. In addition, people with a single demyelinating event who have two or more brain lesions characteristic of MS are recommended to be offered DMTs due to the high risk of continuing to have clinical and or MRI disease activity. The guideline also recommends offering ocrelizumab to people with primary progressive MS who are likely to benefit from such therapy.

## Q. What treatments are recommended for patients with highly active MS?

Highly active MS has not been clearly defined, but the panel considered people who had had multiple recent relapses particularly with an active MRI pattern to be highly active. Subgroup analysis for large pivotal studies of alemtuzumab, fingolimod and natalizumab showed benefit in this group,

and so the panel recommend these medications for highly active MS. It is possible that other medicines with higher efficacy may be beneficial, but the panel did not have data directed at the highly active group to point to in recommendations for other medicines.

## Q. What factors should be considered when switching DMTs?

The panel had less evidence from the systematic review for switching than for the starting recommendations. However, the panel did recommend that in people with MS on a DMT who have been on medicine long enough for it to take effect, and who had been adherent to therapy, who have one or more relapses, or two or more unequivocally new MRI lesions, or who have progressive disability, clinicians should discuss switching to another DMT. Again, the same factors come into play as with the initial decision for DMTs; patient preference, comorbid conditions that may be affected by particular DMTs, and patient risk aversion.

## Q. When should treatment discontinuation be recommended?

The panel had limited data to guide stopping decisions from the systematic review. However, the panel did feel that there must be a group of people with MS for whom the burden of further treatment outweighed the benefit. The panel did struggle with precisely who this might be. They did not come to full consensus on the recommendation for stopping, but clinicians may advise discontinuation in people with secondary progressive MS who do not have ongoing relapses (or gadolinium-enhanced lesions on MRI activity) and have not been ambulatory (Expanded Disability Status Scale score seven or greater) for at least 2 years. The thinking was this group may have the least benefit and the most risk from continued treatment. I note that this was a level C recommendation, which does not in any way compel the clinician to follow the recommendation. Each person with MS is different and the doctor-patient conversation is paramount in decision-making.

## Q. What aspects of treatment were identified as needing further research?

The panel felt strongly that more data were needed for whether starting a highly effective therapy early, rather than a stepped care approach, was better. In addition, the panel felt that more data were needed for safety of DMTs in pregnancy, particularly newer agents being critical. Finally, the committee felt that pragmatic clinical trials of stopping medications versus continuing medication were important. Of course, longer term studies are always needed but continue to be a difficult type of study to conduct. The panel is encouraged that work is already underway in all of these critical directions. ❑

1. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: Disease-modifying therapies for adults with multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018;90:777–88.