Topic Brief: Comparative Effectiveness and Safety of Disease Modifying Therapies for Multiple Sclerosis

Date: 12/05/2021
Nomination Number: 0950

Purpose: This document summarizes the information addressing a nomination submitted on May 14, 2021, through the Effective Health Care Website. This information was used to inform the Evidence-based Practice Center (EPC) Program decisions about whether to produce an evidence report on the topic, and if so, what type of evidence report would be most suitable.

Issue: Multiple sclerosis (MS) is a chronic immune mediated condition that affects nearly one million Americans and is associated with significant morbidity, mortality, and economic costs. Medications known as disease modifying therapies (DMTs) have been shown to reduce the activity and progression of MS. The American Academy of Neurology (AAN) recommends DMTs as a mainstay of MS treatment; however, the effectiveness and comparative effectiveness of individual therapies have not yet been sufficiently studied to fully inform clinician and patient decision-making. This nomination requests a new review comparing the effectiveness of existing DMTs for the treatment of adults with MS.[1]

Recommendation: Although treatment of MS is an important topic that merits consideration, the AAN recently reaffirmed their 2018 clinical guideline recommendations on the use of DMTs for adults with MS.[1] The AAN additionally expressed that their surveillance and assessment for new evidence published since 2018 would not change the current guideline recommendations. They will revisit the guidance in 2024 for consideration of an update. For this reason, the EPC Program will not develop a new evidence review for this topic at this time.

Background

Multiple sclerosis is a chronic immune mediated disease that impairs the central nervous system.[2] The condition is categorized into relapsing-remitting and progressive subtypes. Relapsing-remitting MS affects the majority (85-90%) of individuals, is diagnosed at a younger age (mean age of 30 years) and is characterized by a slow disease progression with periodic relapses which may improve with treatment. Progressive MS, which affects the remaining proportion of patients and typically presents later in life, is associated with a more rapid and steady disease course.[3]

An estimated 2.8 million individuals worldwide were affected by MS in 2020[4] and nearly one million Americans had MS in 2019.[5] This condition is the most common cause of nontraumatic disability in young adults and is associated with significant morbidity, mortality, and economic cost.[6] People with MS live on average seven to 14 years less when compared to the general population, and at least half die from causes directly related to MS.[7] Furthermore, most become unemployed due to an MS related disability within 15 years and about half require mobility

assistance within 20 years of diagnosis.[8] According to the National Multiple Sclerosis Society, the total cost of MS to the United States economy, including treatment expenses and costs related to a loss of productivity, exceeded $85 billion in 2019, and is projected to increase up to $10.5 billion in 2039.[9] The estimated lifetime cost of treatment for an individual patient exceeds $4 million, making MS the second most expensive chronic disease in the United States.[10]

Multiple sclerosis is not curable, therefore treatment focuses instead on reducing the frequency and severity of relapses and slowing the disease progression.[11] Disease modifying treatments have been a mainstay of MS treatment since the early 1990s after clinical trials demonstrated the efficacy of these medications in controlling the disease course.[1] As of 2021, a total of 21 DMTs have been approved by the United States Food and Drug Administration (FDA) for the treatment of MS.[12] The 2018 AAN guideline recommends initiating DMTs as early as possible after diagnosis and to continue treatment indefinitely in most MS patients.[1] At the same time, the guideline acknowledges a dearth of high-quality evidence regarding the comparative efficacy of individual DMTs and associated treatment strategies and calls for more research to inform evidence-based treatment recommendations in these areas. This nomination requested a comprehensive review of comparative effectiveness and safety of the existing DMTs to assist clinicians and patients in selecting treatment.

Assessment Methods

We assessed nomination for priority for a systematic review or other AHRQ EHC report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one.

1. Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. Establish the overall *importance* of a potential topic as representing a health or healthcare issue in the United States.
3. Determine the *desirability of new evidence review* by examining whether a new systematic review or other AHRQ product would be duplicative.
4. Assess the *potential impact* of a new systematic review or other AHRQ product.
5. Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. Determine the *potential value* of a new systematic review or other AHRQ product.

Summary of Selection Criteria Assessment

This nomination focuses on an FDA approved treatment for a medical condition that is prevalent in the United States and is associated with significant morbidity, mortality, and economic cost. However, the AAN recently reaffirmed their 2018 guideline on disease modifying therapies for adults with MS.[1] Because this guideline provides recommendations on treatment of MS and is informed by an evidence synthesis, AHRQ will not develop a new systematic review at this time.

Related Resources

We identified three recent reviews[13-15] and two additional clinical practice guidelines[16, 17] regarding the use of DMTs for the treatment of MS that may be useful to the nominator.

The two recent systematic reviews[13, 15] compared the efficacy and acceptability of DMTs in patients with relapsing-remitting MS. Another systematic overview of meta-analyses published in 2019 evaluated the efficacy of DMTs for reducing disability progression in MS.[14]

Additionally, two recent international clinical practice guidelines, one developed jointly by the European Committee of Treatment and Research in Multiple Sclerosis and the European Academy of Neurology,[16] and another by the Canadian Multiple Sclerosis Working Group,[17] addressed the comparative effectiveness of various DMTs and different treatment sequencing regimens for adults with MS.

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