INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: ***Multiple Sclerosis***
-August 2025-

Background:

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) provided a comprehensive, initial disease state review of pharmacotherapeutic agents for multiple sclerosis (MS). Currently, there are no medications for management of MS on the National Core Formulary. The NPTC reviewed the available evidence and the recent American, British and European guidelines for the management of MS.[1-3] Following clinical review and analysis, the NPTC made **no modifications** to the National Core Formulary.

Discussion:

Multiple sclerosis is a chronic, demyelinating inflammatory and neurodegenerative disease of the central nervous system with no cure.[4] The presentation is largely nonspecific, with a wide differential diagnosis and many other syndromes to exclude.[5] Individual case presentations and prognosis are highly variable and largely unpredictable. Diagnosis is most frequently confirmed with magnetic resonance imaging and analysis of the cerebrospinal fluid. MS can be classified into clinically isolated syndrome, primary progressive MS (PPMS), or the most common diagnosis of relapsing-remitting MS (RRMS). RRMS is characterized by periods of flares resulting in neurologic changes and then periods of remission. Most treatment guidelines focus on the management of RRMS and PPMS with non-pharmacologic therapy as well as disease-modifying therapies (DMT).

MS affects around 3 million people worldwide, primarily young adults between the ages of 20 to 40. It is more likely to occur in women, and historically has been identified as having a higher prevalence in those with northern European/ Caucasian ancestry.[6] Despite many other auto-immune disorders occurring at higher rates in the AI/AN population, MS is considered to have both low incidence and prevalence in American Indian/Alaska Natives (AI/AN), and there are few studies evaluating MS in AI/AN.[7]

Historically, pharmacologic management has been focused around treatment of symptoms with common medications such as gabapentin, cyclobenzaprine, and amitriptyline. Management of flares typically includes glucocorticoids.[8] There is no evidence that supplements or vitamins (such as vitamin D, gingko biloba, or omega-3s) affect the relapse rate or disease progression of MS.[9] Non-pharmacologic therapy for MS often includes aggressive physical and occupational therapy.

Disease-modifying therapies (DMT) were designed with the goal of preventing the frequencies of relapse and/or slowing disease progression. There are many factors to consider when selecting a regimen, such as patient characteristics, disease activity, drug safety, and accessibility of therapy. The initial DMTs, often referred to as “platform therapies”, include glatiramer and formulations of interferon-α. These therapies are often safer but considered to be a more conservative approach. Newer therapies provide higher efficacy, but often times with higher risk for adverse effects. Guidelines and expert consensus do not specifically recommend either safer/conservative route or the high efficacy/high risk route as a universal recommendation for all patients. There are no head-to-head trials directly comparing agents for MS, and they would likely have limited generalizability due to high variation between patient cases. There are many trials performing retrospective review of these agents, but no agent consistently yielded a probability of significantly improved safety, tolerability, and efficacy compared to other agents. All DMTs were superior to placebo in reducing relapse rate.[10-14]

Other drug classes include immune reconstitution therapies (alemtuzumab, cladribine); B-cell depleting or anti-CD20 therapies[15] (ocrelizumab, ofatumumab, ublituximab, rituximab); cell-trafficking therapies[16] (natalizumab); sphingosine-1-phosphate receptors[17] (S1PRs; oral agents fingolimod, siponimod, ozanimod, ponesimod); and other oral therapies such as dimethyl fumarate, teriflunomide, monomethyl fumarate, and diroximel fumarate. The immune reconstitution therapies, anti-CD20 therapies, and cell-trafficking therapies are considered as high-efficacy, with high risk. Of all high-efficacy DMTs, most retrospective reviews concluded that there were no major differences between individual therapies, and that natalizumab and ocrelizumab are among the safest.

Primary Patient or Treatment Goal:	Agent(s):
Minimize the risk of adverse events	Glatiramer, fingolimod, natalizumab, ocrelizumab
Highest prevention of relapse	Alemtuzumab, ocrelizumab, natalizumab
Convenient dosing	Infusions vs tablets, injection frequency (variable)
Safe in pregnancy	Glatiramer, interferons

Most patients will trial multiple agents, as the median time on any DMT is 4.3 years.[18] About 35% of patients discontinue due to adverse events, with interferons reportedly as the least tolerable. Another 30% switch due to lack of efficacy, primarily with platform therapies glatiramer and interferon. Patient considerations are one of the most important decision tools for selecting therapies. Safety considerations vary by drug class.[18-19] There are few safety concerns for platform therapies, but they are frequently switched due to disease progression or intolerance.

Adverse Event or Safety Concern:	Offending Agent(s):
Risk of progressive multifocal leukoencephalopathy	Natalizumab (highest risk), fingolimod, rituximab, ocrelizumab, dimethyl fumarate
Risk of developing malignancy, or should be discontinued if malignancy develops	Fingolimod, teriflunomide, alemtuzumab, dimethyl fumarate, mycophenolate, cyclophosphamide
Cardiovascular events (bradyarrhythmia, hypertension)	S1PRM (fingolimod)

Findings:

There is generally a low prevalence of MS in AI/AN populations. Management of MS is highly dependent on individual patient factors. There is no single agent recommended to treat MS and most patients require trials of multiple agents based on declining efficacy, intolerance or adverse effects. Given these findings, the NPTC made no changes at this time to the National Core Formulary.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov . For more information about the NPTC, please visit the NPTC website.

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