# Wyoming Drug Utilization Review

# Treatment of Multiple Sclerosis

# Written by Noah Paiz PharmD, 2025

# Introduction

Multiple Sclerosis (MS) is a devasting chronic autoimmune inflammatory disease. The pathology of MS is characterized by the demyelination of axons in the central nervous system (CNS) with loss of oligodendrocytes and astroglia scarring.<sup>1,2</sup> MS is one of the most common neurological diseases found in the general population.<sup>3</sup> Wyoming ranks far higher than the national average with estimates of one in 350 having MS compared to the national average of one in 750.<sup>4</sup>

The exact cause of MS is not yet understood. However, it is believed to be an autoimmune disorder with various environmental factors, genetic predispositions (HLA-DR2), and past viral infections, such as the Epstein Barr virus, contributing to the overall development of the disease.<sup>1,2</sup> Additionally, there are many risk factors that can contribute to developing MS including female sex, younger age, living farther away from the equator, smoking, stress, and low serum vitamin D levels.<sup>1,2</sup>

# Pathophysiology

There is ongoing debate whether inflammation or formation of MS lesions are responsible for the progression of the disease. Autoreactive T cells and B cells, specifically CD3-positive T cells, appear to serve a primary role in the pathogenesis of the disease.<sup>5</sup> These autoreactive cells migrate into the CNS where they target antigens found in the myelin sheath triggering an immune response and destabilizing axons. The brain's repair process activates astrocytes to produce glial scars, resulting in plaques. In the early stages of MS perivenous plaques expand into the white matter of the brain.<sup>5</sup>The previously described process causes the formation of "Dawson Fingers", commonly associated lesions found in MRI scans of patients with MS.<sup>5</sup>

# Diagnosis

The presentation of MS varies from person to person due to the location of the lesions. The typical symptoms of MS include spasticity, fatigue, optic neuritis, bladder dysfunction, muscle weakness, and walking difficulties.<sup>1,2</sup> The diagnosis of MS can be challenging. Providers will have to consider past medical history, patient reported symptoms, and objective criteria.<sup>2</sup> McDonald's criteria is one of the most utilized tools for diagnosis of MS. McDonald's criteria incorporates patient reported symptoms and MRI findings of lesions involvement of 2 or more areas of the CNS seen in different timepoints.<sup>6</sup> Furthermore, MS has been labeled into several different subtypes: relapsing-remitting MS (RRMS), a pattern of relapses and remissions followed by recovery; secondary progressive MS (SPMS), gradual worsening of neurologic symptoms after an initial episode with continuous worsening with or without relapse; and primary progressive MS (PPMS), a strong continuous neurological decline from the beginning of presentation.<sup>7</sup>

# Pharmalogical therapy

McDonald criteria have allowed for quicker diagnosis of MS, expediting the use of pharmacological therapies. The accepted treatment between the international and domestic guidelines is to start disease modifying therapy (DMT) as soon as a diagnosis is given to limit the inflammatory process that occurs during an active event of MS.<sup>8,9</sup> Any DMT therapy can be considered as first-line therapy. Treatment of MS is

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considered personalized medication therapy where the individual's disease activity, preference for route of administration, tolerability, and efficacy are taken into consideration.<sup>8</sup> The goals of therapy for MS include slowing the progression of the disease, managing symptoms, reducing the number of relapses, and increasing the quality of life of the patient.<sup>8</sup> Unfortunately, no pharmaceutical agent solves the root cause of MS but rather focuses on slowing down disease progression and symptom management.<sup>8</sup> Below you will find all the current DMT available on the market. The chart was adopted from the American Journal of Health-System Pharmacy.<sup>10</sup>

# Disease Modifying Therapy<sup>9</sup>

Drug	Maintenance dose	Efficacy in reducing annualized relapse rate
Interferon B-1a (Avonex, Rebif)	30 mg IM once weekly or 44 mcg SQ 3 times Weekly	32%
Interferon B-1b (Betaseron, Extavia)	0.25 mg SQ every other day	33%
Pegylated interferon B1-a (Plegridy)	125 mg SQ every14 days	36%
Glatiramer (Copaxone)	20 mg SQ daily or 40 mg SQ 3 times weekly	34%
Ofatumumab (Kesimpta)	20 mg SQ monthly	50%
Mitoxantrone (Novatrone)	12 mg/m2 IV every 3 months; maximum lifetime cumulative dose of 140 mg/m2	91%
Natalizumab (Tysabri)	300 mg IV over 1 hour every 30 days	68%
Almetuzmab (Lemtrada)	12 mg IV for 5 consecutive days (first course); after 1 year, 12 mg IV for 3 consecutive days (second course)	55%
Ocrelizumab (Ocrevus)	600 mg IV every 6 months	47%
Fingolimod (Gilenya)	0.5 mg by mouth daily	54%
Siponimod (Mayzent)	Based on patient's CYP2C9 genotype: 1-2 mg by mouth daily	52%
Ozanimod (Zeposia)	0.92 mg by mouth daily	38% to 48%
Ponesimod (Ponvory)	20 mg by mouth daily	
Dimethyl fumarate (Tecfidera)	240 mg by mouth twice daily	53%
Diroximel fumarate (Vumerity)	462 mg by mouth twice daily	53%
Monomethyl fumarate (Bafiertam)	190 mg by mouth twice daily	53%
Teriflunomide (Aubagio)	7 or 14 mg by mouth daily	31%
Cladribine (Mavenclad)	3.5 mg/kg by mouth over a 2-year treatment course: 1.75 mg/ kg each year divided over 2 cycles lasting 4 to 5 consecutive days 23 to 27 days apart	57%

Pharmacotherapy for MS has grown complex with the addition of new pharmalogical DMT agents coming to the market. There are three main categories of agents used in the treatment of MS including injectable medications, oral medications and infusion therapy.<sup>12</sup> In the MS community, injectable medications are often considered less effective than other dosage forms, primarily because they tend to be older drugs that have since been improved upon. However, older medications are generally better tolerated in terms of side effects.<sup>12</sup>The side effect profile of each agent will depend on its unique mechanism of action. For example, fingolimod is a once-a-day oral option that has been known to cause bradycardia and macula edema since sphingosine receptors are found in the heart and eyes.<sup>12</sup>

When discussing DMT with patients it is important to explain the purpose of DMT is to prevent relapses and mitigate disease progression.<sup>12</sup> DMT does not improve symptom control. However, there is a plethora of pharmalogical agents that can be used for symptom management. Baclofen, tizanidine, and other muscle relaxers are prescribed to help with muscle stiffness and spasms. The use of modafinil can be used to alleviate fatigue and day-time drowsiness.

# Non-pharmacological therapy

MS can be a challenging disease for any provider. It is ever more challenging for a patient. Patients may need more help understanding their disease and therapy. Nonpharmacologic-therapies can help patients improve symptoms, disease progression, and allow patients greater autonomy.<sup>13</sup> Sleep hygiene, stress management, and eating a healthy diet are areas of focus for patients.<sup>14</sup> These areas help control risk factors like smoking and stress, but also it has been shown that individuals that maintain healthy body weight were less likely to experience episodes of relapse.<sup>14</sup>

# Conclusion

MS is an encompassing disease that impacts all aspects of a person's life. There have been pharmacological advancements that have delayed the onset of flares but none have eliminated all disease activity. Hopefully one day, new treatment will advance to the point of eliminating disease activity. Health care professionals treating MS are encouraged to take a holistic role where the patient is listened to and heard in order to maximize their quality of life.

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# The P&T Committee met for its quarterly business meeting on May 8, 2025.

Highlights of this meeting include:

Alyse Williams, MD has been selected to fill the physician vacancy on the P&T Committee.

Sublocade will be moved to the pharmacy program for billing. It will be limited to indication for adult patients over age 18, with a maximum dose of 600 mg in the first month, followed by 100 mg per month. Concurrent use of oral buprenorphine or Brixadi will not be allowed.

Dupixent will be covered for its new indication for chronic spontaneous urticaria in patients who do not respond to antihistamines.

Nicotine replacement therapy will have updated dosing limits allowing for 24 pieces of gum per day, 20 lozenges per day, and 40 mg nasal spray per day. All therapies will require prior authorization after 84 days. Any combination of patches may be used in that 84-day period.

Alhemo, Journavx, Onapgo, Zunveyl, and Sofdra were limited to indication and referred to the Department of Health for cost analysis and PDL placement. Journavx will be limited to a 14 day supply.

Intrarosa was limited to indication.

All prior authorization criteria are open for public comment. Comments should be sent by email to <u>alewis13@uwyo.edu</u>by July 15, 2025.

The next P&T Committee meeting will be held August 14, 2025 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

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> June 2025 In This Issue

Treatment of Multiple Sclerosis P&T Committee Meeting Update

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