Proceedings of ICBioMed 2026 Symposium: Biomedical Engineering and Smart Medicine
DOI: 10.54254/2753-8818/2026.HZ35033

Therapeutic Strategies for Multiple Sclerosis: Approved and Investigational Treatments

Letong Chen

Westtown School, West Chester, USA
letong.chen080130@gmail.com

Abstract. Multiple sclerosis (MS) is a chronic autoimmune condition of the central nervous system that links its pathogenesis to immunological dysregulation, genetic predispositions, and environmental triggers. With significant immunology and neuroscience progress in recent years, the treatment of MS has shown remarkable advances. This study summarizes currently approved disease modifying therapies (DMTs) along with innovative therapeutic interventions reaching clinical trial testing and further development. Interferon-beta, glatiramer acetate, and dimethyl fumarate are all FDA-approved therapeutic agents; they exert their immune-regulating actions by lowering rates, inflammation, and progression, yet they also have side effects, lack patient adherence, and are ineffective in progressive MS. As the primary focus of research, the Bruton's Tyrosine Kinase (BTK) Inhibitors have also been shown in recent years to have the potential to bridge chronic neuroinflammation through B cells and myeloid immune cells. Moreover, the newly developed agents promoting myelin repair and neuroprotection will open up new therapeutic options for improved neurological impairment. Some innovative therapeutic approaches have yielded positive results; however, their long-term effectiveness and safety must further be confirmed. From a general perspective, MS treatment is gradually drifting from focusing only on immune-mediated inflammation to also include a general therapeutic approach involving neuroprotection and tissue repair, hence offering patients more favorable treatment onset and opportunities.

Keywords: Multiple sclerosis, Therapeutic strategies, Investigational treatments

1. Introduction

Multiple sclerosis (MS) stands as a persistent immune system disorder that targets the body's central nervous system, which creates harmful impacts on cerebral tissues, spinal cord structures and ocular nerve pathways throughout the human body. Patients often experience symptoms such as disrupted vision, weakness in their limbs, abnormal feelings to the touch, and impaired motor functions. MS etiology is still not fully understood today, but it is thought to be related to genetic, environmental, and immunological problems.

In the past few years, thanks to the advancements in medicine and immunology, understanding of MS have intensified dramatically. Studies have revealed that T and B cells, as well as various inflammatory cytokines, are important contributors to the development and expansion of the disease.

DOI: 10.54254/2753-8818/2026.HZ35033

During the same period, technical breakthroughs such as magnetic resonance imaging (MRI) have allowed doctors to identify and diagnose MS cases early [1].

The treatment of MS has made significant progress over the past 20 years. Many disease-modifying therapies (DMTs) have been introduced into clinical care; these drugs help in decreasing the frequencies of the relapse, the inflammation, and the progression of the disease. Still, current treatments have perceived weaknesses a few adopters of these drugs suffer adverse effects, while others are not as effective when utilized in the analysis of progressive MS. Therefore, scientists are still exploring new therapeutic approaches, including Bruton's Tyrosine Kinase (BTK) inhibitors, myelin repair promoters, and neuroprotective medications.

This article provides information about the currently approved disease-modifying therapies for MS together with a summary of treatment strategies currently under review that may establish the new pattern of MS treatment in the near future. Research of multiple sclerosis (MS) is constantly progressing with more and more disease-modifying therapies being introduced into clinical practice. Such medications help to prevent the disease progression by modifying the immune system, clearing up the inflammatory process, and protecting the nervous system. Currently, the common and approved treatment methods mainly focus on injection and oral medicine.

2. Approved therapeutic strategies

2.1. Injectable disease-modifying therapies

IFN-β ranks with the earliest pharmaceutical agents that get deployed for managing cases of MS, which shapes immune functioning and lessens harmful outcomes brought by inflamed cells toward neural tissue so that disease flare-ups drop in frequency, which reliable research reports confirm that interferon-beta cuts down the generation of pro-inflammatory cytokines and lifts the level of anti-inflammatory cytokine activity to ease widespread neural inflammation inside bodily nerve frameworks.

For the time being, IFN-β-1a, IFN-β-1b, and pegylated IFN-β-1a are the most commonly used interferon-biopharmaceuticals in clinical office practice. Some adverse effects are present in interferon beta. For instance, fever, headaches, muscle discomfort, and redness/swelling at the injection site are among the side effects of interferon beta. To encourage patients' adherence, a few novel formulations were created to prolong the drug's half-life and lower the frequency of injections.

Another commonly used injectable drug is glatiramer acetate. This medication mimics myelin proteins, thus interfering with immune system attacks on their myelin sheath. Secondly, such injection stimulates the development of anti-inflammatory T cells, which alleviates the nervous system's inflammatory process. Among some immunosuppressants coming with high efficacy, glatiramer acetate has a relatively good safety profile, so the medicine is often used by patients with mild-to-moderate MS as their long-term therapy [2, 3].

On the whole, injectable medications constitute an important class of MS management techniques; however, as injections are often required for a long time, the problem of adherence during treatments may arise in some cases.

2.2. Oral disease-modifying therapies

Compared to injectable drugs, oral medications have increased convenience of use and have consequently gained increasing popularity among patients in recent years. Dimethyl fumarate (DMF) represents a prevalent oral medical preparation which sees extensive clinical application for

DOI: 10.54254/2753-8818/2026.HZ35033

therapeutic care directed at patients diagnosed with MS across global medical institutions. Initially, DMF was used for psoriasis treatment, but later, immunomodulatory and antioxidant activities were identified, so the drug was introduced into MS therapy. Oral administration showed better patient adherence than conventional injectable drugs [4].

DMF mode of action is based on cell antioxidant pathway activation, reducing inflammation and oxidative damage. Moreover, it affects T-cell and B-cell function, allowing to decrease aberrant immune activity. Clinical evidence indicates that DMF can reduce relapses in MS patients and new lesions on MRI.

DEFINE alongside CONFIRM stand as two big late-stage clinical research programs which carry out thorough examinations on how well DMF works for disease management, which enrolls individuals who receive a formal diagnosis of relapsing-remitting multiple sclerosis (RRMS) while each research project checks treatment results from DMF against placebo and alternative medical interventions, which people who receive DMF medication gain obvious drops in yearly relapse rate alongside clear shrinkage of fresh or expanding tissue spots that MRI scanning identifies [4]. Scientists suggest that this therapeutic effect is caused not only by DMF immunomodulatory effects but also possible Nrf2 pathway activation within cells and improvement in antioxidant activity [4].

Although DMF has good efficacy, it has some side effects, such as lymphopenia, flushing, and gastrointestinal discomfort. A small percentage of patients are more likely to develop severe opportunistic infections, such as progressive multifocal leukoencephalopathy (PML). The reawakening of JC virus triggers a dangerous infectious condition that attacks the central nervous system, which people who build up intense and long-lasting low lymphocyte counts face greater vulnerability toward PML with elevated risk levels seen among elderly patient groups. Therefore, in accordance with current international guidelines, patients receiving this medicine should undergo routine blood tests and an enhanced MRI to guarantee treatment safety [5].

Oral disease-modifying therapies made medication administration more patient friendly; however, during long-term treatment, safety is still a concern [4, 5].

3. Clinical therapies under investigation

3.1. Bruton's tyrosine kinase inhibitors (BTK inhibitors)

Scientific exploration that targets care plans for multiple sclerosis (MS) puts major present attention on inhibitor compounds which act against BTK, which BTK carries out an essential function inside signal transmission pathways belonging to B lymphocytes and myeloid immune cell populations within bodily immune frameworks. It is believed that BTK inhibition may decrease aberrant immune activation and chronic CNS inflammation. BTK inhibitors differ from traditional immunosuppressive medications, as they allow for more targeted modulation of immune cell activity rather than a blanket suppression of immunity.

At present, the most prominent BTK inhibitors are evobrutinib, tolebrutinib and fenebrutinib (Table 1). Evobrutinib was among the first to reach Phase III trials. To test its efficacy, researchers performed two international, multicenter, randomized, double-blind, controlled trials evolutionRMS1 and evolutionRMS2 against the approved drug teriflunomide. It was shown that evobrutinib was efficacious in decreasing the inflammatory activity seen on MRI but was unable to reduce the relapse rate in either Phase III trial (evolutionRMS1 and evolutionRMS2) with respect to teriflunomide, underperforming expectations [6]. Tolebrutinib is a relatively new BTK inhibitor that has attracted great attention. Rather than have a predominant effect only on the peripheral immune system, tolebrutinib is better able to cross the blood-brain barrier (BBB) and therefore act upon

DOI: 10.54254/2753-8818/2026.HZ35033

microglia and B cells within the CNS. This quality has prompted researchers to speculate an improved capacity for treating chronic neuroinflammation and disease progression [7]. The GEMINI clinical investigation which aims to measure therapeutic performance from tolebrutinib for cases marked as relapsing-remitting MS (RRMS) sets tolebrutinib side by side with teriflunomide that gains official medical authorization for regular clinical use, which measurable contrasts do not emerge in key trial markers and yearly disease flare frequency metrics collected from every cohort of enrolled participants. However, secondary endpoints suggest tolebrutinib may have certain benefits in delaying disease progression. Researchers hypothesize that this effect may stem from the ability of the compound to cross the BBB and act against inflammation within the CNS. This study confirms that future MS treatments will require not only control of immune mechanisms in the periphery but a greater effort toward ameliorating the chronic inflammation within the CNS [7]. Fenebrutinib is a highly selective BTK inhibitor, and it may have a lower rate of off-target effects and potentially a safer profile than other BTK inhibitors. Though lacking Phase III validation, phase II investigations indicated its efficacy decreasing the number of new inflammatory lesions on MRI and fenebrutinib appears to still be a valuable therapeutic strategy worthy of further study [6-8]. Fenebrutinib' s novelty lies in its non-covalent mode of BTK inhibition, with higher specificity than prior BTK inhibitors, allowing it to maintain selectivity for other kinases, a lower risk for side effects. Using MRI to evaluate disease activity, fenebrutinib was compared to a placebo in the Phase II FENopta clinical trial. The number of new gadolinium-enhancing lesions was dramatically lowered for patients receiving fenebrutinib, demonstrating its efficacy in reducing inflammatory activity within the CNS. Researchers believe this compound will perform well in balancing efficacy and safety and serves as a critical candidate for future BTK inhibitor therapeutic approaches. Nevertheless, Phase III clinical trials have not yet been able to confirm efficacy, safety, and sustainability, considering the brief follow-up period in recent research [8].

The BTK inhibitors offer a promising new approach for therapeutic intervention for MS. In addition to influencing the peripheral immune system, it may also alleviate chronic inflammation within the CNS. These mechanisms are still under investigation, and additional long-term clinical data are required to support their efficacy and safety profiles.

Table 1: Comparison of investigational BTK inhibitors

Drug	Mechanism of Action	Clinical Trial Outcomes	Ref.
Evobrutinib	Inhibits BTK, modulates B cells and myeloid immune cells	No significant reduction in relapse rate vs. teriflunomide in Phase III studies; results below expectations	[6]
Tolebrutinib	Inhibits BTK, penetrates the blood-brain barrier	No significant difference in annual relapse rate in GEMINI studies; potential to slow disease progression	[7]
Fenebrutinib	Highly selective, non-covalent BTK inhibitor	Reduced new gadolinium-enhancing lesions in Phase II FENopta study; under Phase III validation	[6-8]

3.2. Other therapies

Researchers have not only explored BTK inhibition but also new myelin-repair-promoting and neuroprotective therapies. Since myelin destruction represents one of the key pathological features of MS, medication can restore myelin and therefore neurological function rather than just decrease the relapse rate.

One of the potential medications that have been tested for its ability to repair myelin is opicinumab. It aims to improve myelin repair by inhibiting LINGO-1. Opicinumab delivered stable

DOI: 10.54254/2753-8818/2026.HZ35033

safety profiles and promising therapeutic capacity within a mid-stage clinical research program which enrolls individuals living with sudden inflamed optic nerve tissue, which full-scale treatment outcomes fail to maintain steady uniform performance across monitored subjects so this pharmaceutical agent never turns into a routine medical solution for clinical practice [9].

Another medication undergoing trials is Ibudilast, which is being researched primarily for progressive MS patients who often do not have therapeutic options. The SPRINT-MS trial revealed that Ibudilast might have some neuroprotective potential as it slows brain atrophy. However, more studies are needed to ascertain whether it can improve patient long-term functional outcomes.

Thus, MS treatment will continue to develop once its therapeutic options extend beyond the control of immune-mediated inflammation to neuroprotection, myelin repair, and the treatment of progressive forms [10].

4. Conclusion

As mentioned in this article, the most recent clinical advancement in MS treatments for multiple sclerosis (MS) focuses on a number of significant problems. Interferon beta and glatiramer acetate are injectable agents that help reduce immune attacks by modifying the immune reactions and acting as myelin protein analogs. They effectively reduce the relapse rate and improve neuroinflammation. Nevertheless, because glatiramer acetate is well tolerated, it can be used for long-term treatment. Dimethyl fumarate is an oral drug that causes a clear effect on annualized relapse rates and new lesions discovered via magnetic resonance imaging (MRI) by triggering antioxidant-related mechanisms and modifying the activity of T and B cells. In addition, it contributes to the convenience of medicine intake in patients. However, these agents still have disadvantages related to side effects, low compliance with prescribed medicines, and a lack of effects on progressive MS. Tolebrutinib is a Bruton' s tyrosine kinase inhibitor that can directly cross the blood-brain barrier and target microglia and B cells in the central nervous system (CNS). The candidate drug failed to cut yearly flare-up frequencies inside a well-performed late-stage clinical study which delivers reliable trial data yet this agent displays a noticeable tendency to support stable disease relief, which Fenebrutinib acts as a strongly targeted non-covalent blocking compound which lessens inflammatory reactions inside CNS structures efficiently while carrying minimal chances of unintended bodily impacts recorded during mid-stage clinical assessments. In addition, agents that contribute to myelin remediation and neuroprotection, such as drugs targeting the LINGO-1 pathway (opicinumab) and decreasing brain atrophy (Ibudilast), go beyond simple immunosuppression and provide additional options for preventing neurological impairment.

Overall, current achievements have initially established a therapeutic framework transitioning from peripheral immune control to central immune modulation and neural repair. Looking ahead, the development of MS therapies will focus more on multi-dimensional comprehensive strategies: developing drugs with high blood-brain barrier permeability that precisely target resident innate immune cells in the CNS, so as to control chronic neuroinflammation while lowering the risks of systemic immunosuppression; advancing combination regimens integrating immune modulation, neuroprotection and myelin regeneration to achieve synergistic effects of anti-inflammation, tissue repair and functional preservation; and implementing individualized treatment based on biomarkers and disease stages, alongside optimizing drug delivery systems to enhance central targeting. These patterns collectively suggest that MS treatment will evolve from a single anti-inflammatory model into a comprehensive intervention system that integrates immune resetting, tissue repair and neurological function preservation.

DOI: 10.54254/2753-8818/2026.HZ35033

References

[1] Montague, T., Campbell, N., Kolbe, S.C., Kuhlmann, T. and Reddel, S.W. (2025) Advancements in multiple sclerosis. Internal Medicine Journal, 55(6), 895–904.
[2] Filipi, M. and Jack, S. (2020) Interferons in the treatment of multiple sclerosis: A clinical efficacy, safety, and tolerability update. International Journal of MS Care, 22(4), 165–172.
[3] Arnon, R. and Aharoni, R. (2004) Mechanism of action of glatiramer acetate in multiple sclerosis and its potential for the development of new applications. Proceedings of the National Academy of Sciences of the United States of America, 101(Suppl. 2), 14593–14598.
[4] Diaz, G.M., Hupperts, R., Fraussen, J. and Somers, V. (2018) Dimethyl fumarate treatment in multiple sclerosis: Recent advances in clinical and immunological studies. Autoimmunity Reviews, 17(12), 1240–1250.
[5] Jordan, A.L., Yang, J., Fisher, C.J., Racke, M.K. and Mao-Draayer, Y. (2022) Progressive multifocal leukoencephalopathy in dimethyl fumarate-treated multiple sclerosis patients. Multiple Sclerosis Journal, 28(1), 7–15.
[6] Montalban, X., Arnold, D.L., Fox, R.J., Gold, R., Wiendl, H. and Turner, B. (2024) Safety and efficacy of evobrutinib in relapsing multiple sclerosis (evolutionRMS1 and evolutionRMS2): Two multicentre, randomised, double-blind, active-controlled, phase 3 trials. The Lancet Neurology, 23(11), 1085–1098.
[7] Oh, J., Arnold, D.L., Cree, B.A.C., Fox, R.J., Kappos, L. and Wiendl, H. (2025) Tolebrutinib versus teriflunomide in relapsing multiple sclerosis. New England Journal of Medicine, 392(16), 1564–1576.
[8] Sriwastava, S., Elkhooly, M. and Amatya, S. (2024) Recent advances in the treatment of primary and secondary progressive Multiple Sclerosis. Journal of Neuroimmunology, 390, 578315.
[9] Cadavid, D., Balcer, L., Galetta, S., Aktas, O., Ziemssen, T. and Vanopdenbosch, L. (2017) Safety and efficacy of opicinumab in acute optic neuritis (RENEW): A randomised, placebo-controlled, phase 2 trial. The Lancet Neurology, 16(3), 189–199.
[10] Fox, R.J., Coffey, C.S., Cudkowicz, M.E., Gleason, T., Goodman, A. and Klawiter, E.C. (2021) Effects of ibudilast on MRI measures in the phase 2 SPRINT-MS study. Neurology: Neuroimmunology & Neuroinflammation, 8(2), e943.