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Daclizumab (Zinbryta®): An Emerging Therapy for the Treatment of Relapsing-Remitting Multiple Sclerosis

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Abstract
Multiple sclerosis (MS) is an autoimmune disorder of the central nervous system characterized by the deterioration of the myelin sheath, causing axonal damage which leads to debilitating symptoms. Most therapies for the treatment of MS, including daclizumab, primarily target relapsing-remitting multiple sclerosis (RRMS), a form of MS where patients experience periods of exacerbated symptoms as well as intermittent periods of remission. Daclizumab is a humanized monoclonal antibody that is administered as a once monthly subcutaneous injection. The SELECT trilogy of trials have been instrumental in providing safety and efficacy data for daclizumab. The DECIDE study was the first randomized controlled trial to compare daclizumab to another U.S. Food and Drug Administration (FDA) approved therapy for the treatment of RRMS. There is no universal MS treatment guideline that dictates the order in which medications are used; rather, therapy is chosen based on patient-specific factors and disease severity. Daclizumab may be preferred over other agents due to its favorable injection formulation and its duration of action, but contraindications and side effects limit its use. The pharmacist can serve a critical role in ensuring proper patient education and compliance with the Risk Evaluation and Mitigation Strategies (REMS) program in addition to providing resources to assist patients with cost concerns.

Key Terms
Antibodies; Monoclonal; Humanized; Interferon-beta 1a; Interleukin-2; Interleukin-2 Receptor alpha Subunit; Multiple Sclerosis; Multiple Sclerosis, Relapsing Remitting

Introduction

Multiple sclerosis (MS) is an autoimmune disorder of the central nervous system characterized by inflammation and destruction of axons.[1] Many different medications can be used in MS, allowing prescribers to choose which one will be most effective for each patient.[2] The goal of therapy is to reduce the number of exacerbations, and treatment is not curative.[1] Daclizumab is a humanized monoclonal antibody that was recently approved for the treatment of relapsing-remitting multiple sclerosis (RRMS).[3] A series of trials known as SELECT, SELECTION and SELECTED have demonstrated the safety and efficacy of daclizumab in the treatment of RRMS. The SELECTED trial is ongoing and will continue to bring forth further results.[4-6] The DECIDE trial showed daclizumab to be more efficacious than treatment with interferon beta-1a, but daclizumab was also associated with higher rates of adverse events.[7] Due to its potential for hepatotoxicity, daclizumab is only available through a Risk Evaluation and Mitigation Strategies (REMS) program that requires monthly liver tests.[8] Daclizumab is proving to be a useful medication for patients with RRMS.

Multiple Sclerosis

Multiple sclerosis is an inflammatory disease of the central nervous system that is believed to be primarily autoimmune in nature.[1] The disease is characterized by deterioration of myelin sheaths and axonal destruction. In early MS, immune cells from the periphery, including T- and B-lymphocytes, enter the central nervous system and attack the neurons. These T- and B-lymphocytes, among other immunological factors, remove the myelin sheath from the neuronal axons and predispose the axons to damage. If the axons are severed, damage is irreversible and leads to the deteriorating symptoms of MS described below.

The exact etiology of MS is unknown. However, several factors are thought to predispose a patient to developing MS.[1] The disease appears more often in females than males in a ratio of 2-to-1, and it is more common in Caucasian individuals (especially those of Scandinavian descent). There also appear to be genetic and environmental factors. Approximately 30 percent of MS cases are due to genetic variations. Smoking, vitamin D deficiency, Epstein-Barr virus (EBV) and high levels of dietary sodium are a few of the environmental factors that have been identified.

While clinical presentation varies among cases of MS, patients may present with visual problems, spasticity, bowel or bladder dysfunction or problems with gait.[1] The majority of MS patients present with RRMS in which patients experience exacerbations of symptoms with periods of remission in between. The majority of therapies available for the treatment of MS, including daclizumab, are approved specifically for RRMS.

Daclizumab: Pharmacology and Pharmacodynamics

Daclizumab (Zinbryta®) was approved on May 27, 2016, by the U.S. Food and Drug Administration (FDA) as a once monthly subcutaneous injection for the treatment of RRMS.[3] In RRMS, it is important to treat both the neurodegenerative and inflammatory components of the disease.[9] Daclizumab 150 mg has been shown to reduce the relapse rate of patients with RRMS to a greater extent than other treatments of 30 mcg of intramuscular interferon beta-1a.[10] Daclizumab is a humanized monoclonal antibody that blocks the alpha subunit, also known as CD25, found on high-affinity interleukin-2 (IL-2) receptors.[3] This subunit, CD25, is a transmembrane glycoprotein found on regulatory T cells as well as effector T cells that have been activated. It activates signal transduction pathways that lead to the antiapoptotic and proliferative signals in T cells.[11]

Interleukin-2 is also thought to play a role in MS pathogenesis due to its regulation of immune responses. Interaction of T cells with a foreign antigen or with IL-2 can cause IL-2 receptors to be expressed on the surface of activated T cells.[12] Once these T cells are activated, CD25 is quickly upregulated and enhances the affinity of the receptors for IL-2.[3] Daclizumab saturates CD25 and increases serum IL-2 levels nearly twofold.[12] Daclizumab also decreases regulatory T cells and increases CD56 natural killer (NK) cells.[3] These cells, which can be found in lymph nodes, have immunoregulatory functions. The CD56 NK cells are associated with positive responses to treatment as well as remission of MS during pregnancy.[13] The increase in NK cells may be due to the increased bioavailability of IL-2 after the CD25 blockade. The pharmacodynamic responses that were observed after the first dose of daclizumab were sustained during treatment and were reversible during a washout period of six months. Daclizumab was also shown to have a manageable safety profile.[3] Increased risk of infection, elevated liver function tests, and cutaneous events have occurred as a result of daclizumab treatment over a two to three year period. These adverse effects were manageable with monitoring and medical treatment.[14]

Pharmacokinetics

The pharmacokinetic properties of daclizumab are outlined in Table 1.[10,15] Daclizumab tends to be slowly absorbed in patients with MS following administration as a subcutaneous injection. Due to its half-life of approximately 22 days, daclizumab is dosed once monthly. Daclizumab also has low systemic clearance, and steady state is reached by the fourth injection.[10]

Clinical Trials

Several clinical trials have been conducted to assess the efficacy and safety of daclizumab. The SELECT trilogy of trials (SELECT, SELECTION and SELECTED) has been instrumental in providing this information.[4-6] The SELECT trial was a randomized, double-blind, placebo-controlled trial that evaluated the efficacy of two doses of daclizumab.[4] This study, along with its two extension studies (SELECTION and SELECTED), have provided ongoing data on the long-term safety of daclizumab.[4-6] Another randomized controlled trial, the DECIDE study, compared daclizumab to interferon beta-1a, another treatment option for RRMS.[7]

The SELECT trial enrolled patients aged 18 to 55 years with a confirmed diagnosis of RRMS and at least two relapses in the previous three years.[4] The patients were randomly assigned to placebo, daclizumab 150 mg or daclizumab 300 mg. All three study medications were administered subcutaneously every four weeks. This study's primary endpoint looked at annual relapse rate at 52 weeks. The percent of patients who experienced a relapse in one year was statistically significantly lower in both daclizumab treatment groups compared to placebo. Of the patients who received placebo, 36 percent experienced a relapse in the first year compared to 19 percent of the patients who received daclizumab 150 mg ($p<0.0001$) and 20 percent of the patients who received daclizumab 300 mg ($p<0.00032$).

Investigators in the SELECT trial also evaluated the safety profile of daclizumab versus placebo.[4] The rates of adverse events were similar among all treatment groups. Some adverse events of note included serious infections and cutaneous events. Nine patients from the two daclizumab groups experienced a serious infection, while no patients in the placebo group had any such reaction. Five patients receiving daclizumab experienced serious cutaneous reactions compared to zero patients who received placebo. A similar number of patients among all three groups exhibited abnormal liver function tests. While overall the results were similar, patients receiving daclizumab were more likely to present with increases of greater than five times the upper limit of normal. While this is notable, patients who experienced liver test abnormalities did not see repeat occurrences after levels were corrected, and daclizumab was continued.

Table 1. Pharmacokinetics of Daclizumab.[10,15]

Pharmacokinetics of Daclizumab	
Half-life	22 days
Bioavailability	>80%
Clearance	0.274 L/day
Time to Steady-State	4 doses
Volume of Distribution	6.34 L
Metabolism	Catabolism to peptides and amino acids
Elimination	No renal elimination

While SELECT was a landmark study in evaluating the safety and efficacy of daclizumab monotherapy, its one year duration poses some limitations as RRMS is a chronic, lifelong disease.[4] Thus, an extension trial of SELECT, referred to as SELECTION, was conducted to evaluate a second year of daclizumab therapy.[5] The patients who had received placebo in SELECT were randomized to receive either daclizumab 150 mg every four weeks or daclizumab 300 mg every four weeks. The patients who had received daclizumab in SELECT were randomized to either continue their study medication or discontinue treatment for a 24-week wash out period and then reinitiate therapy for the remaining 32 weeks. In this extension study, safety became a primary clinical endpoint, while efficacy became a secondary endpoint. All treatment groups in SELECTION experienced similar rates of adverse events.[5] As with SELECT, the adverse events with the highest rates, besides relapse of MS, were infections (37 to 43 percent), cutaneous events (13 to 22 percent) and abnormal liver function tests (28 to 44 percent). The two most common infections exhibited among the treatment groups were nasopharyngitis (10 to 17 percent) and upper respiratory tract infections (5 to 10 percent). Continual efficacy of daclizumab in year two was also investigated in the SELECTION trial. In the continuous treatment group, annualized relapse rate was similar to treatment groups in year one. In the treatment initiation group (those that received placebo in SELECT), annualized relapse rate was reduced compared to year one. Finally, in the washout and reinitiation group, annualized relapse rates during the washout period were similar to the placebo group in SELECT. However, once therapy was reinitiated, overall annualized relapse rate did not differ significantly from year one.

The SELECTED trial is an ongoing open-label extension study of SELECTION intended to assess the long-term safety and efficacy of daclizumab for up to 6.5 years of treatment.[6] The three-year data points were published in July of 2016. All patients who enrolled in SELECTED from SELECTION received daclizumab 150 mg subcutaneously every four weeks. Fifty percent of patients enrolled in SELECTED experienced infection, with nasopharyngitis and upper respiratory tract infections being the most common. Only 3 percent of patients reported serious infections which included pneumonia, urinary tract infection and bronchitis. Cutaneous events were documented in 28 percent of patients, and 2 percent reported serious cutaneous events. Abnormal hepatic lab values were reported in 15 percent of patients, and serious events were reported in 1 percent. While several adverse events were reported with daclizumab therapy in SELECTED, the results were consistent with those found in SELECT and SELECTION. The efficacy of daclizumab exhibited in the first two studies was sustained in SELECTED. As this is an ongoing study, further results on long-term efficacy and safety will continue to be reported.

While the SELECT trilogy provided information on daclizumab monotherapy versus placebo, comparisons to other medications for RRMS were lacking.[4-6] The DECIDE trial was a randomized, double-blind, active-controlled, phase III study that compared daclizumab to interferon beta-1a.[7] Enrolled patients were aged 18 to 55 years and had a confirmed diagnosis of RRMS. These patients were randomized to receive either daclizumab 150 mg subcutaneously every four weeks with intramuscular placebo once weekly or interferon beta-1a 30 mcg intramuscularly every week with subcutaneous placebo every four weeks. Investigators in the DECIDE trial evaluated the annual relapse rate during a period of 144 weeks as its primary endpoint. Secondary endpoints included new or newly enlarged hyperintense lesions, or T2-weighted lesions, which are typically located on the optic nerve and appear to correlate with disability and progression of disease.[1,7]

The annual relapse rate was statistically significantly lower in the daclizumab group when compared to the interferon beta-1a group (0.22 and 0.39, respectively; $p<0.001$).[7] The daclizumab group also presented with 54 percent fewer new or newly enlarged hyperintense lesions at week 96 ($p<0.001$). However, when evaluating disability progression in the daclizumab group versus the interferon beta-1a group, results were not statistically significant (16 percent and 20 percent, respectively; $p=0.16$). Overall, the number of adverse events was similar between the two groups. Reports of serious adverse events were slightly higher in the daclizumab group compared to interferon beta-1a (15 percent and 10 percent, respectively). Daclizumab also had higher percentages of infections, cutaneous events and serious hepatobiliary disorders. The study authors concluded that daclizumab demonstrated superior efficacy to interferon beta-1a but with higher rates of notable adverse events. Thus, a risk-benefit analysis must be conducted by patients and providers when determining clinical therapy.

Daclizumab's Place in Therapy in Multiple Sclerosis

The goal of disease-modifying therapies (DMTs) is to reduce the number of MS exacerbations and to slow the progression of the disease.[1] Treatment of MS is not curative. Table 2 and Table 3 list the FDA approved disease-modifying agents along with their mechanism of action, dose, adverse reactions and monitoring parameters.[1,16] Due to patient variability and disease severity that affect clinical decisions, prescribers are not limited in their choice of medication. Thus, prescribers can use the FDA approved DMT list to choose an agent that is most effective for the patient's specific type of MS, has tolerable side effects and is cost-effective. The efficacy of DMTs varies between individuals and may even vary throughout the course of disease. For this reason, there is no universal treatment guideline that dictates the order in which medications should be used.[2] First-generation agents such as interferon beta-1a (Avonex®, Rebif®, Plegridy®) and interferon beta-1b (Betaseron®, Extavia®) are typically considered first-line options. However, the side effect profile and warnings associated with their use limits patient eligibility for this treatment. If patients present with poor prognostic factors, second-generation agents can be prescribed as initial therapy. Ocrelizumab (Ocrevus®), a second-generation agent, was recently approved in March 2017 for relapsing and primary progressive forms of MS.[17] In

contrast to the other MS medications, ocrelizumab is a humanized monoclonal antibody that targets CD20 antigen on B-lymphocytes.[18] Rituximab was the first anti-CD20 antibody to be used for the treatment of MS; however, ocrelizumab may be more effective in inducing a stronger immunogenic response. Ocrelizumab doses 300 mg, 600 mg and high-dose 1000 mg administered intravenously at day one and day 15 of the cycle were studied in clinical trials and found to be well-tolerated with a risk of serious and opportunistic infections. The future place in therapy of ocrelizumab is uncertain, as there have been no comparative studies between ocrelizumab and first-line or second-line MS therapies.

Although the FDA continuously approves new medications such as ocrelizumab, daclizumab remains a promising option among the second-generation MS therapies. Daclizumab is a subcutaneous injection that the patient administers into the thigh, abdomen or back of the upper arm.[19] The favorable formulation and duration of action make it an ideal drug for MS treatment because daclizumab is injected only once monthly. However, daclizumab's contraindications and side effect profile limit the number of MS patients that can safely use it. Contraindications for use include pre-existing hepatic impairment, autoimmune hepatitis and hypersensitivity to daclizumab. Potential adverse events include life-threatening hepatotoxicity and immune-mediated disorders such as skin reactions, lymphadenopathy or noninfectious colitis. Due to the severity of the adverse events, the initial immune-related blood tests and monthly monitoring of hepatic function tests, the FDA has restricted dispensing solely through the Zinbryta® REMS program. In summary, daclizumab should be reserved for patients with RRMS who have had an inadequate response to at least two or more DMTs.

Table 2. First-generation Agents.[1,16]

	Avonex®, Rebif®	**Plegridy®**	**Betaseron®, Extavia®**	**Copaxone®, Glatopa®**	**Novantrone®**
Generic Name	Interferon beta -1a	Pegylated interferon beta-1a	Interferon beta-1b	Glatiramer acetate	Mitoxantrone
FDA Indication	Relapsing forms of MS	Relapsing forms of MS	Relapsing forms of MS	CIS, RRMS	SPMS, PRMS, worsening RRMS
Mechanism of Action	Reduce IFN-γ MHC expression on antigen-presenting cells Induce suppressor T-lymphocyte function by activating macrophage-activating effects			Induces suppressor T-lymphocytes Displaces and inhibits MBP binding to T cells	Antineoplastic that suppresses the activity of T cells, B cells and macrophages
Dose	Avonex®: 30 mcg IM weekly Rebif®: 22 or 44 mcg SQ TID	125 mcg SQ every 14 days	Betaseron®: 250 mcg SQ every other day Extavia®: 0.25 mg SQ every other day	20 mg SQ QD or 40 mg QD three times a week	12 mg/m^2 IV every three months; lifetime dose should not exceed 140 mg/m^2
Adverse Reactions	Injection site reactions, flu-like symptoms (chills, fever, myalgia, asthenia), depression, hepatotoxicity, leukopenia/bone marrow suppression			Injection site reactions, necrosis, vasodilation, rash, dyspnea, chest pain	Nausea, alopecia, menstrual disorder, URIs, UTIs, leukemia, cardiotoxicity
Monitoring	LFTs at one, three and six months then periodically; CBC with differential; signs and symptoms of depression; pregnancy test			No routine tests recommended	CBC with differential routinely, LFTs, cardiac monitoring, pregnancy test

Abbreviations: CBC–complete blood count, CIS–clinically isolated syndrome, IFN-γ–interferon gamma, IM–intramuscular, IV–intravenous, LFT–liver function test, MHC–major histocompatibility complex, MBP–myelin basic protein, PRMS–progressive relapsing multiple sclerosis, QD–every day, RRMS–relapsing-remitting multiple sclerosis, SPMS–secondary progressive multiple sclerosis, SQ–subcutaneous, TID–three times a day, URI–upper respiratory infection, UTI–urinary tract infection

Table 3: Second-generation Agents.[1,16]

	Gilenya®	Aubagio®	Tecfidera®	Tysabri®	Lemtrada®	Zinbryta®
Generic Name	Fingolimod	Teriflunomide	Dimethyl fumarate	Natalizumab	Alemtuzumab	Daclizumab
FDA Indication	Relapsing forms of MS	Relapsing forms of MS	Relapsing forms of MS	Relapsing forms of MS	RRMS	Relapsing forms of MS
Mechanism of Action	Spingosine-1-phosphate modulator that traps lymphocytes in lymph nodes, decreases BBB permeability	Dihydro-orotate dehydrogenase inhibitor that slows T- & B-lymphocyte DNA synthesis	Monomethyl fumarate that activates nicotinic and nuclear factor-like pathways	Humanized monoclonal antibody that binds integrin, preventing lymphocytes from crossing BBB	Anti-CD52 monoclonal antibody that inhibits B- & T-lymphocyte attachment to myelin	Anti-CD25 monoclonal antibody, interleukin-2 inhibitor
Dose	0.5 mg PO QD	7 or 14 mg PO QD	240 mg PO delayed released BID	300 mg IV every 4 weeks	12 mg IV for five consecutive days (total 60 mg), followed 12 months later by 12 mg daily for three consecutive days (total 36 mg)	150 mg SQ once monthly
Adverse Reactions	AV node block, infection, hepatotoxicity, fetal toxicity CI: QTc > 500 ms, Class Ia/III antiarrhythmic, ischemia, CHF Class III/IV	Leukopenia, neuropathy, alopecia, Stevens-Johnson syndrome BBW: teratogenicity, hepatotoxicity	Angioedema, lymphopenia vasodilation, GI upset (N/V/D)	Infections, depression, GI upset BBW: PML	Bone marrow suppression, insomnia BBW: autoimmune diseases, infusion reactions, malignancy CI: HIV	Severe skin rashes, infections, depression BBW: immune-related disorders, hepatotoxicity
Monitoring	REMS CBC with differential, LFTs, cardiac monitoring hourly for six to 24 hours after first dose, ophthalmologic exam at baseline and at three months, pregnancy test	Blood pressure, CBC with differential, pregnancy test	CBC at baseline and every six to 12 months, pregnancy test	REMS Test for anti-JCV antibodies for PML	CBC, sCr, UA at baseline and monthly for 48 months after last dose; TFTs every three months until 48 months after treatment completion; annual skin exam	REMS CBC with differential, LFTs, screen for hepatitis B & C before initiation

Abbreviations: AV–atrioventricular, BBB–blood brain barrier, BBW–black box warning, BID–twice daily, CBC–complete blood count, CHF–congestive heart failure, CI–contraindications, CIS–clinically isolated syndrome, GI–gastrointestinal, HIV–human immunodeficiency virus, IV–intravenous, JCV–John Cunningham virus, LFT–liver function test, MBP–myelin binding protein, ms–milliseconds, N/V/D–nausea/vomiting/diarrhea, PML-progressive multifocal leukoencephalopathy, PO–by mouth, PRMS–progressive relapsing multiple sclerosis, QD–every day, REMS–risk evaluation and mitigation strategies, RRMS–relapsing-remitting multiple sclerosis, sCr–serum creatinine, SPMS–secondary progressive multiple sclerosis, SQ–subcutaneous, TFT–thyroid function test, UA–urine analysis, URI–upper respiratory infection, UTI–urinary tract infection

Role of the Pharmacist

The pharmacist provides a vital role in successful patient use of daclizumab in a variety of ways including ensuring REMS program compliance, delivering patient education, providing resources to help patients afford the medication and assisting with therapy monitoring and follow up.

Cost Assistance

The approximate average wholesale price of daclizumab as of this writing is $8,200 per dose.[19] For patients not covered by federal insurance, a $0 copay program is available for qualifying patients based on income or if the medication is prescribed by an out-of-network provider.[20] The manufacturer also provides a benefits investigation service and support for finding coverage from charitable organizations for patients in need. A prior authorization is needed for daclizumab and the manufacturer also provides a help line for those who need assistance getting a prior authorization. Pharmacists can have these resources available to share with patients who are unable to afford their medication.

Zinbryta® REMS Program

Daclizumab is only available through the Zinbryta® REMS program due to its potential for hepatic damage, hepatic failure, autoimmune hepatitis and other immune-mediated disorders.[8] The program contains guidelines for patient education and monitoring. Prescribers are required to obtain a one-time certification to prescribe daclizumab. After registration, the program requires monthly liver function tests (transaminase and total bilirubin) prior to each dose and for six months after the final dose is administered. Pharmacies also are required to enroll in the REMS program in order to dispense daclizumab. The pharmacy must designate a representative to become certified and then oversee the proper implementation of the REMS program in the pharmacy. Duties of the pharmacy's representative include appropriately implementing and documenting all training, policies and procedures as proof of program compliance. The REMS program requires a pharmacy to verify that a prescriber is certified by calling the REMS program before dispensing each dose. Additionally, the pharmacy may only dispense one dose of daclizumab at a time. The pharmacist can also work to ensure patient safety by speaking with the patient about their liver function labs to help ensure proper monitoring and compliance.

Due to the REMS registration requirements, daclizumab is mainly available through specialty pharmacies. This increases the likelihood that patients will be filling prescriptions at multiple pharmacies which may promote errors due to a lack of complete medication profiles at each pharmacy. Daclizumab is an immunosuppressant and has many interactions particularly when used in combination with other immunosuppressant medications.[19] Due to the potentially severe side effects and interactions of this medication, as well as the high chance for an incomplete patient medication profile, it is important that pharmacists discuss with the patient what other medications they are taking to check for interactions. On a case-by-case basis, it may be beneficial to call the other pharmacy or pharmacies that the patient uses in addition to discussing with the patient to ensure there are no serious drug interactions.

Patient Education

Pharmacists have a vital opportunity to provide patients with key pieces of information at the time of prescription pick up. Physicians are required to enroll patients in the REMS program and provide counseling on the risks associated with daclizumab and the need for monthly liver function monitoring. Physicians must also provide patients with the Zinbryta® REMS Patient Guide and the Patient Wallet Card.[21] Pharmacists can supplement the physician's counseling by having patient guides, administration technique handouts and wallet cards available at the pharmacy to offer to patients who either did not receive or who misplaced these materials. Additionally, follow up or further counseling on potential adverse effects can augment information provided by the physician to improve patient knowledge.[19]

Pharmacists can also provide patients with information about the resources available to them. The manufacturer provides all patients access to nurse educators for on-site patient education and administration training. Nurse educators can also answer questions and assist in therapy monitoring if desired.[22] The manufacturer also provides access to a peer community for those struggling to manage their RRMS.[20]

Administration of daclizumab requires alcohol wipes, gauze pads and a sharps container. Having these materials available for purchase in the pharmacy is another way to ensure medication proper use by patients.[23] The prefilled syringe must be protected from heat and must not be frozen; it should be stored in the refrigerator, but can be stored at room temperature for 30 days.[19] Once the drug has been stored at room temperature, it should not be put back into the refrigerator. Proper storage of the medication is an important counseling point for patients, as well as something pharmacists should monitor carefully within the pharmacy itself.

While there is still plenty of room for further research in MS treatment and management, some nonpharmacologic treatment options are likely to decrease the speed of disease progression. Smoking cessation may be beneficial, as research shows that smoking can hasten progression of MS.[24] Poorly controlled chronic disease states such as diabetes and hypertension can also have a negative impact on MS, so patients should work closely with their doctor to control these disease states as well. Although diet has not been shown to impact MS, experts suggest consuming a heart healthy diet and maintaining a healthy weight. Staying active can also help build muscle and improve overall well-being.

Conclusion

Treatment of MS is not curative; thus, treatment options are mainly palliative. Medication selection for MS treatment depends on the specific type and severity of MS, tolerability of

side effects and expected cost of therapy. Daclizumab, a second-generation DMT approved for relapsing forms of MS, is available as a monthly subcutaneous injection. In clinical trials, it has shown greater efficacy than treatment with intramuscular interferon beta-1a, and its side effects are generally manageable. However, daclizumab is associated with an increased risk of life-threatening hepatotoxicity and immune-related disorders. Pharmacists can provide a role in patients' successful use of daclizumab by watching for drug interactions, ensuring REMS program compliance and providing patient education about proper use of daclizumab, proper medication storage, resources available to patients through the manufacturer and available cost assistance programs.

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