Multiple Sclerosis Medication

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Medication Summary

Treatment and management of multiple sclerosis should be targeted toward relieving symptoms of the disease, treating acute exacerbations, shortening the duration of an acute relapse, reducing frequency of relapses, and preventing disease progression.

Drugs approved for use in MS that reduce the frequency of exacerbations or slow disability progression are referred to as disease-modifying drugs (DMDs). These DMDs can be further classified as immunomodulating (or receptor modulating) or immunosuppressives. Some immunosuppressants are also FDA-approved as antineoplastic agents.

Drugs that treat MS-related symptoms (eg, acute exacerbations, cognitive dysfunction, fatigue, spasticity, bowel and bladder problems, and pain) but do not modify the course of the disease are referred to as symptom-management medications.

Immunomodulators

Class Summary

Immunomodulators or receptor modulators are indicated for the treatment of patients with relapsing forms of MS. They help to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations.

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Interferon beta-1b (Betaseron, Extavia)

Interferon beta-1b was the first medication approved by the FDA for MS. It is approved for the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations. It has shown efficacy in patients who have experienced a first clinical episode and have MRI features consistent with MS.[10]

The exact mechanism by which interferon beta-1b exerts its effects is unknown. Interferon beta inhibits the expression of pro-inflammatory cytokines, including interleukin (IL)-1 beta, tumor necrosis factor (TNF)-alpha and TNF-beta, interferon gamma (IFN-γ), and IL-6. IFN-γ is believed to be a major factor responsible for triggering the autoimmune reaction leading to MS.

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Dalfampridine (Ampyra)

Dalfampridine, a broad-spectrum potassium blocker is approved as a treatment to improve walking in patients with MS. The improvement in walking was demonstrated by an increase in walking speed.[117]

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Interferon beta-1a (Avonex, Rebif)

Interferon beta-1a is approved for the treatment of patients with relapsing forms of MS. It helps to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations.

The exact mechanism by which interferon beta-1a exerts its effects is not fully defined. Interferon beta inhibits the expression of proinflammatory cytokines, including interferon

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Alemtuzumab (Lemtrada)

Alemtuzumab is a recombinant monoclonal antibody against CD52 (lymphocyte antigen). This action promotes antibody-dependent cell lysis. It is indicated for relapsing forms of multiple sclerosis. Because of the risk for severe and lasting autoimmune adverse effects, use is reserved for patients who have an inadequate response to 2 or more other drugs for MS.

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Peginterferon beta-1a (Plegridy)

Precise mechanism by which peginterferon beta-1a exerts its effects in patients with multiple sclerosis is unknown. Interferons are thought to alter response to surface antigen and may enhance immune cell activities. It is indicated for treatment of relapsing forms of multiple sclerosis.

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Natalizumab (Tysabri)

Natalizumab is indicated as monotherapy for MS to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations. Natalizumab is a recombinant humanized monoclonal antibody that binds with alpha-4 integrins and inhibits their adherence to their counterreceptors. The specific mechanism by which natalizumab exerts its effects in MS has not been defined.

Natalizumab has a black-box warning for progressive multifocal leukoencephalopathy (PML). Because of the risk of PML, natalizumab is available only through a special restricted distribution prescribing program called the Tysabri Outreach Unified Commitment to Health (TOUCH).

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Glatiramer acetate (Copaxone)

Glatiramer acetate is approved for the reduction of the frequency of relapses in patients with relapsing-remitting MS, including patients who have experienced a first clinical episode and have MRI features consistent with MS. Glatiramer acetate's mechanism of action is unknown, but this agent is thought to modify immune processes believed to be responsible for the pathogenesis of MS.[12] The recommended dosage is 20 mg/day administered subcutaneously. The sites for injection include the arms, abdomen, hips, and thighs.

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Fingolimod (Gilenya)

Fingolimod is the first oral therapy for relapsing forms of MS approved by the FDA. Like other disease-modifying drugs (DMDs) for MS, fingolimod can reduce the frequency of clinical exacerbations and delay the accumulation of physical disability. The recommended dosage for fingolimod is 0.5 mg once a day.[16]

The mechanism by which fingolimod exerts therapeutic effects in MS is unknown, but it appears to be fundamentally different from that of other MS medications. Its activity may involve a reduction of lymphocyte migration into the central nervous system.

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Teriflunomide (Aubagio)

Teriflunomide is an oral immunomodulatory agent that elicits anti-inflammatory effects by inhibiting dihydroorotate dehydrogenase, a mitochondrial enzyme involved in pyrimidine synthesis. It is indicated for relapsing forms of MS.

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Dimethyl fumarate (Tecfidera)

multiple sclerosis. DMF is metabolized rapidly by presystemic hydrolysis by esterases in the GI tract, blood, and tissues (before it reaches systemic circulation) and is converted to its active metabolite, monomethyl fumarate (MMF). MMF activates the nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway, a transcription factor encoded by the *NFE2L2* gene. The Nrf2 antioxidant response pathway is a cellular defense against oxidative stress. MMF has been identified as a nicotinic acid receptor agonist in vitro.

Corticosteroids

Class Summary

Corticosteroids are used to reduce inflammation and expedite recovery from acute relapses. The most commonly used corticosteroids in MS include methylprednisolone, dexamethasone and prednisone. Short courses of intravenous methylprednisolone with or without a short prednisone taper have been used.

View full drug information

Methylprednisolone (Solu-Medrol, Depo-Medrol

Methylprednisolone is given for acute exacerbations of MS. By reversing increased capillary permeability and suppressing polymorphonuclear neutrophil (PMN) activity, methylprednisolone may decrease inflammation. In addition, it may alter the expression of some proinflammatory cytokines.

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Dexamethasone (Baycadron, Dexamethasone Intensol)

Dexamethasone can be given for acute exacerbations of MS. It stabilizes cell and lysosomal membranes, increases surfactant synthesis, increases serum vitamin A concentration, and inhibits prostaglandin and proinflammatory cytokines. Dexamethasone is available as an injection that can be administered intravenously or intramuscularly and in various oral formulations (tablets, elixir, and solution).

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Prednisone (Sterapred)

Prednisone prevents or suppresses inflammation and immune responses when administered at pharmacological doses. Prednisone's actions include inhibition of leukocyte infiltration at the site of inflammation, interference in the function of mediators of inflammatory response, and suppression of humoral immune responses. Oral prednisone tapers are commonly administered with or without methylprednisolone.

Immunosuppressants

Class Summary

Immunosuppressants are used for their ability to suppress immune reactions. Agents such as methotrexate have shown some effectiveness in delaying progression of impairment of the upper extremities in patients with secondary progressive MS. Azathioprine has been studied in clinical trials and has shown modest effects on relapses and progression of disease. Methotrexate and azathioprine have not been approved by the US Food and Drug Administration for use in MS.

View full drug information

Azathioprine (Azasan, Imuran)

This immunosuppressive antimetabolite drug is an imidazolyl derivative of 6-mercaptopurine. It is cleaved in vivo to mercaptopurine and converted to 6-thiouric acid by xanthine oxidase. Azathioprine is generally used in the treatment of transplant rejection or severe, active, erosive rheumatoid arthritis, but it has been used off-label for MS.[128]

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Methotrexate interferes with DNA synthesis, repair, and cellular replication. It inhibits dihydrofolic acid reductase, which participates in the synthesis of thymidylate and purine nucleotides. Methotrexate has been used off-label for MS.

Antineoplastic Agents

Class Summary

Antineoplastic agents such as cyclophosphamide and mitoxantrone have been used in MS patients.

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Mitoxantrone

Mitoxantrone is an immunosuppressive agent approved for the treatment of secondary progressive or aggressive relapsing-remitting MS. It is used for reducing neurologic disability and/or the frequency of clinical relapses in patients with secondary (long-term) progressive, progressive relapsing, or worsening relapsing-remitting MS (ie, patients whose neurologic status is significantly abnormal between relapses). Mitoxantrone is not indicated in the treatment of patients with primary progressive MS.

Mitoxantrone therapy can increase the risk of developing secondary acute myeloid leukemia (AML) in MS patients and in patients with cancer.[15]

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Cyclophosphamide

Cyclophosphamide has been used for the treatment of progressive MS. Evidence of benefit is mixed. This agent has not been approved for MS but has been used off-label in MS patients. Cyclophosphamide is associated with leukemia, lymphoma, infection, and hemorrhagic cystitis.[129]

Dopamine Agonists

Class Summary

Amantadine is approved for the prophylaxis and treatment of influenza A and Parkinson disease and has been used off-label to relieve fatigue in patients with MS. It has relatively few side effects and is well tolerated .

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Amantadine (Symmetrel)

Amantadine is not FDA approved for use in MS, but dosages of 100 mg given orally twice a day have commonly been used for fatigue.[114] The mechanism by which amantadine counteracts fatigue in MS patients is unclear.

Skeletal Muscle Relaxant

Class Summary

Pharmacologic treatment of spasticity includes baclofen (Lioresal, Gablofen) as a first-line agent. Baclofen can be titrated easily in divided doses. Patients using this medication may report fatigue or weakness as an adverse effect. Dantrolene (Dantrium) acts within muscles on excitation-contraction coupling; however, it is rarely used because it can cause liver damage.

View full drug information

Baclofen (Lioresal, Gablofen)

Baclofen is a skeletal muscle relaxant used as a first-line treatment for spasticity in patients with MS. It can effectively relieve spasms and has modest effects in improving performance

constant or variable dose over a 24-hour period to increase efficacy and decrease side effects.

View full drug information

Dantrolene (Dantrium)

Dantrolene is a skeletal muscle relaxant that acts directly on skeletal muscle to decrease spasticity. Dantrolene is believed to decrease muscle contraction by directly interfering with calcium ion release from the sarcoplasmic reticulum within skeletal muscle cells. It affects all muscles of the body and is used less frequently than baclofen because of hepatotoxicity at higher doses and numerous drug interactions.

Neuromuscular Blockers, Botulinum Toxins

Class Summary

The FDA has approved the use of botulinum toxin (Botox) for the treatment of upper limb spasticity in MS. The FDA has also approved this agent for the treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition (eg, MS) in adults who have an inadequate response to, or are intolerant of, an anticholinergic medication.

View full drug information

OnabotulinumtoxinA toxin (Botox)

OnabotulinumtoxinA toxin is an injectable neurotoxin that temporarily blocks connections between the nerves and the muscles, leading to short-term relaxation of the targeted muscle. The drug can be injected again when the muscle-relaxing effects have worn off, but not more frequently than every 3 months.

It is approved for the treatment of upper limb spasticity in adults to decrease the severity of increased muscle tone in elbow flexors (biceps), wrist flexors (flexor carpi radialis and flexor carpi ulnaris), and finger flexors (flexor digitorum profundus and flexor digitorum sublimis).

Alpha2-Adrenergic Agonists

Class Summary

Tizanidine (Zanaflex) is a centrally active alpha$_2$ -adrenergic agonist that is also used to treat spasticity in patients with MS. It can be used alone or in combination with baclofen.

View full drug information

Tizanidine (Zanaflex)

This centrally acting alpha-adrenergic agonist is presumed to decrease spasticity by increasing presynaptic inhibition of motor neurons. Tizanidine has effects similar to those of baclofen, but it produces less weakness and more sedation. This drug can be titrated starting with 2 mg, with maximum doses of 36 mg/day.

Benzodiazepines

Class Summary

Benzodiazepines are used as second-line agents for the treatment of spasticity in patients with MS. Agents in the benzodiazepine class that are commonly used include diazepam and clonazepam. While these compounds can be useful adjunct medications, they can be sedating and habit-forming and are not FDA approved for use in MS.

For patients who also experience sleep disorders, the provider may take advantage of the sedating effects of the benzodiazepines to manage the spasticity and sleep problem with a single medication. For patients with cognitive impairment, benzodiazepines may be contraindicated due to their adverse CNS effects.

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