

[Supplementary online-only material for Remington G, Rodriguez Y, Logan D, Williamson C, Treadaway K: Facilitating medication adherence in patients with multiple sclerosis. *Int J MS Care*. 2013;15:36–45.]

Supplementary Table 1. Disease-modifying therapies for the treatment of MS

Treatment (brand, manufacturer)	Indication	Dosage and administration	Suggested MOA	Most common or serious side effects^a
Fingolimod (Gilenya [®] , Novartis Pharmaceuticals)	Treatment of patients with relapsing forms of MS to reduce the frequency of clinical exacerbations and to delay the accumulation of physical disability	0.5 mg PO daily	Exact mechanism of action unknown; may reduce lymphocyte action by trapping them in the peripheral lymph nodes	Back pain, bradyarrhythmia and atrioventricular block , cough, decrease in pulmonary function tests , diarrhea, elevated liver function tests, fetal risk , headache, increased liver transaminases, infections , influenza, macular edema
Glatiramer acetate (Copaxone [®] , Teva Neuroscience)	Reduction of the frequency of relapses in patients with RRMS, including patients who have experienced a first clinical episode and have MRI features consistent with MS	20 mg SC injection daily	Exact MOA unknown; increases regulatory T cells, suppresses inflammatory cytokines, blocks antigen presentation	Chest pain , dyspnea, effects on immune response , injection site reaction, lipoatrophy , rash, skin necrosis, systemic (immediately after injection) reaction , vasodilatation

<p>IFNβ-1a (Avonex[®], Biogen Idec)</p>	<p>Treatment of patients with relapsing forms of MS to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations; patients with MS in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with MS</p>	<p>30 μg IM injection once a week</p>	<p>Inhibits adhesion, inhibits synthesis and transport of MMPs, blocks antigen presentation</p>	<p>Anaphylaxis, chills, decreased peripheral blood counts, depression, fatigue, fever, flu-like symptoms, headache, hepatic injury, myalgias, nausea, remote risk for transmission of viral disease/Creutzfeldt-Jakob disease, suicide, vomiting</p>
<p>IFNβ-1a (Rebif[®], EMD Serono)</p>	<p>Treatment of patients with relapsing forms of MS to decrease the frequency of clinical exacerbations and delay the accumulation of physical disability</p>	<p>22 or 44 μg SC injection three times a week</p>	<p>Inhibits adhesion, inhibits synthesis and transport of MMPs, blocks antigen presentation</p>	<p>Abdominal pain, anaphylaxis, depression, elevation of liver enzymes, hematologic abnormalities, hepatic injury, influenza-like symptoms (headache, fatigue, fever, rigors, chest pain, back pain, myalgia), injection site disorders, remote risk for transmission of viral disease/Creutzfeldt-Jakob disease, suicide</p>

<p>IFNβ-1b (Betaseron[®], Berlex Laboratories</p>	<p>Treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations; patients with MS in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with MS</p>	<p>0.25 mg SC injection every other day</p>	<p>Inhibits adhesion, inhibits synthesis and transport of MMPs, blocks antigen presentation</p>	<p>Anaphylaxis, asthenia, depression, flu-like symptom complex, headache, hepatobiliary disorders, hypertonia, increased liver enzymes, injection-site necrosis, injection-site reaction, leukopenia, lymphopenia, myasthenia, pain, remote risk for transmission of viral disease/Creutzfeldt-Jakob disease, suicide</p>
<p>IFNβ-1b (Extavia[®], Novartis Pharmaceuticals Corporation)</p>	<p>Treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations; patients with MS in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with MS</p>	<p>0.25 mg SC injection every other day</p>	<p>Inhibits adhesion, inhibits synthesis and transport of MMPs, blocks antigen presentation</p>	<p>Abdominal pain, anaphylaxis, asthenia, chest pain, chills, depression, dyspnea, fever, flu-like symptom complex, headache, hypertension, hypertonia, impotence, increased liver enzymes, injection-site necrosis, injection-site reaction, insomnia, incoordination, leukopenia, lymphadenopathy, lymphopenia, malaise, metrorrhagia, myalgia, neutropenia, pain, peripheral edema, rash, remote risk for transmission of viral disease/Creutzfeldt-Jakob disease, skin disorder, suicide, urinary urgency</p>

<p>Mitoxantrone (Novantrone[®], EMD Serono, Inc.)</p>	<p>Reducing neurologic disability and/or the frequency of clinical relapses in patients with secondary (chronic) progressive, progressive relapsing, or worsening RRMS (ie, patients whose neurologic status is significantly abnormal between relapses)</p>	<p>12 mg/m² IV every 4 months; maximum 140 mg/m² cumulative lifetime dose</p>	<p>Inhibits topoisomerase III: interferes with RNA; causes cross-linking and strand breaks at the DNA</p>	<p>Alopecia, asthenia, cardiac toxicity, fetal harm, functional cardiac changes including decreases in LVEF and irreversible congestive heart failure, menstrual disorders including amenorrhea, nausea, secondary acute myeloid leukemia and myelosuppression, severe myelosuppression with high doses, urinary tract infection</p>
<p>Natalizumab (Tysabri[®], Biogen Idec and Elan Pharmaceuticals)</p>	<p>Monotherapy for the treatment of patients with relapsing forms of MS to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations. Generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate MS therapy</p>	<p>300 mg IV every 4 weeks</p>	<p>Binds integrins on leukocyte cell walls, preventing migration into inflamed parenchymal tissue (monoclonal antibody)</p>	<p>Abdominal adhesions, abdominal discomfort, appendicitis, arthralgia, cholelithiasis, depression, diarrhea, fatigue, gastroenteritis, headache, hepatotoxicity, hypersensitivity reactions, immunosuppression/infections, intestinal obstruction or stenosis, nausea, pain in extremity, rash, upper or lower pneumonia, PML, suicidal ideation, respiratory tract infection, urinary tract infection, vaginitis</p>

^aSide effects labeled as “serious adverse events” or noted in drug label’s warning section are shown in **bold** print.

Abbreviations: IFN β , interferon beta; IM, intramuscular; LVEF, left ventricular ejection fraction; MMP, matrix metalloproteinase; MOA, mechanism of action; MRI, magnetic resonance imaging; MS, multiple sclerosis; PML, progressive multifocal leukoencephalopathy; PO, by mouth; RRMS, relapsing-remitting multiple sclerosis; SC, subcutaneous.

Sources:

Avonex (interferon beta-1a) prescribing information. Cambridge, MA: Biogen Idec Inc.; 2012.

Betaseron (interferon beta-1b) prescribing information. Montville, NJ: Bayer HealthCare Pharmaceuticals Inc.; 2010.

Copaxone (glatiramer acetate injection) prescribing information. Kansas City, MO; Teva Neuroscience Inc.; 2009.

Extavia (interferon beta-1b) prescribing information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2009.

Gilenya (fingolimod) prescribing information. East Hanover, NJ: Novartis; 2011.

Novantrone (mitoxantrone hydrochloride) prescribing information. Rockland, MA: EMD Serono, Inc.; 2010.

Rebif (interferon beta-1a) prescribing information. Rockland, MA: EMD Serono, Inc.; 2009.

Tysabri (natalizumab) prescribing information. Cambridge, MA: Biogen Idec Inc.; 2012.

Chun J, Brinkmann V. A mechanistically novel, first oral therapy for multiple sclerosis: the development of fingolimod (FTY720, Gilenya). *Discov Med.* 2011;12:213–228.

Greenberg B, Frohman EM. Defining success in multiple sclerosis: treatment failures and nonresponders. *Adv Stud Med.* 2008;8:274–283.

Supplementary Table 2. Resources to support patients with multiple sclerosis

Resource	Education	Referrals	Research	Assistance, devices, evaluation
National Multiple Sclerosis Society 800-344-4867 www.nationalmssociety.org	■	■	■	■
Multiple Sclerosis Association of America 800-532-7667 www.msassociation.org	■	■		■
Multiple Sclerosis Foundation 888-673-6287 www.msfacts.org	■	■		■
Rocky Mountain MS Center http://livingwell.mscenter.org/complementary-care.html Website on complementary and alternative medicine for people with MS	■		■	
National Institutes of Health clinical trial listing www.clinicaltrials.gov			■	
Caregivers National Family Caregivers Association www.nfcacares.org National Caregiver's Library www.caregiverslibrary.org	■			

Resource	Education	Referrals	Research	Assistance, devices, evaluation
<p>Medication assistance programs for disease-modifying agents</p> <p>MS Active Source (Avonex and Tysabri) 800-456-2255</p> <p>Shared Solutions (Copaxone) 800-887-8100</p> <p>MS Lifelines (Rebif) 877-447-3243</p> <p>Beta Plus (Betaseron) 800-788-1467</p> <p>Novartis (Gilenya) 877-408-4974</p> <p>For all other medications, contact the manufacturing company or go to:</p> <p>www.rxhope.com www.rxassist.org www.needymeds.com</p> <p>Partnership for Prescription Assistance 888-477-2669 www.pparx.org</p> <p>The National Organization for Rare Disorders 800-999-6673 www.rarediseases.org</p>	■	■		■