Disease Modifying Therapies in the Treatment of MS

Generic	Brand	Indications	Dosing	Route of Administration	Pregnancy Rating (Cree, 2013)	Patient Support Programs	Warnings	Safety Management Strategies and Recommended Monitoring	Potential Mechanisms	Common Adverse Events
Interferon b-1a	Avonex	Relapsing forms of MS* CIS	30 mcg weekly	IM	For all: C	MS Active Source® avonex.com msactivesource.com 800-456-2255	Hepatic and hematologic abnormalities; depression; injection site reactions with SC administration	CBC, LFT q 3 mos during first year, then q 6 mos thereafter; thyroid function tests q 3-6 mos during first year, then yearly thereafter; monitoring for mood changes; education and site rotation with SC IFN	Benefits modulated primarily through an anti-inflammatory mechanism. Potential effects include down regulation of proinflammatory cytokines, reduced expression of major histocompatibility antigens and decreasing transmigration of T-lymphocytes across the BBB. (Bermel & Rudick, 2007)	Flu-like symptoms; leukopenia; elevated liver enzymes; thyroid dysfunction
	Rebif	Relapsing forms of MS* Study 1 Study 2	44 mcg tiw	SQ		MS LifeLines™ rebif.com mslifelines.com 877-447-3243				
Interferon b-1b	Betaseron	Relapsing forms of MS* CIS	250 mcg every other day	SQ		BETAPLUS® betaseron.com 800-788-1467				
	Extavia	Relapsing forms of MS* CIS Formulation identical to Betaseron; no additional studies done	250 mcg every other day	SQ		Patient Support Program extavia.com 866-925-2333				
Glatiramer acetate	Copaxone	Relapsing-remitting MS CIS	20 mg qd	SQ	B	Shared Solutions® copaxone.com sharedsolutions.com mswatch.com 800-887-8100	Lipoatrophy and skin necrosis	Site rotation is essential; monitoring	May promote an anti-inflammatory Th2 shift of T cells in the peripheral circulation, which may be mediated through an inhibitory effect on antigen-presenting cells . (Farina et al., 2005)	Injection-site reactions; lipoatrophy; post-injection vasomotor syndrome
Fingolimod	Gilenya	Relapsing forms of MS* Study 1 Study 2	0.5 mg qd	Oral	C	Patient Support Program gilenya.com 877-408-4974	Infection; macular edema; dose-dependent decreased pulmonary function; elevated serum hepatic transaminases; hypertension	Screening white blood cell count, serum transaminase determination, serum bilirubin determination, serum varicella zoster antibody testing (in patients with no history of chicken pox), baseline ECG, and ophthalmologic evaluation; baseline pulse/blood pressure prior to first dose and observation of all patients for 6 hours after the first dose for signs and symptoms of bradycardia; ophthalmologic evaluation after 3 to 4 months of treatment and in the event of new visual symptoms	Binds to a docking site (sphingosine-1-phosphate receptor, or S1P receptor) on immune cells, including T cells and B cells, sequestering some immune cells in the lymph nodes, thereby reducing their availability for cell-mediated immune responses. (Horga & Montalban, 2008)	Headache, flu, diarrhea, back pain, elevated liver enzymes, cough
Teriflunomide	Aubagio	Relapsing forms of MS* Study 1	7.0 mg and 14.0 mg; qd	Oral	X	MS One To One MSOnetoOne.com 855-676-6326	Infection; elevated serum hepatic transaminases ("black box" warning); fetal death and malformations ("black box warning); skin reactions; blood pressure increase; respiratory effects	Pre-treatment: evaluation for infection, pregnancy, renal failure, peripheral neuropathy, interstitial pulmonary disease and hypertension; white blood cell count, serum transaminase determination and serum bilirubin determination. During treatment: blood pressure monitoring; serum transaminase determinations.	Teriflunomide inhibits a mitochondrial enzyme, dihydroorotate dehydrogenase, which is involved in the de novo pathway of pyrimidine synthesis. This inhibition interferes with DNA synthesis particularly in rapidly dividing cells such as lymphocytes. Reduced lymphocyte activation my lead to the observed immunosuppression and reduced inflammation. An alternate salvage pathway allows pyrimidine synthesis to continue at a reduced rate in resting cells.	Abnormal liver function, alopecia, diarrhea, influenza, nausea and paresthesias
Dimethyl fumarate	Tecfidera	Relapsing forms of MS* Study 1 Study 2	240 mg bid	Oral	C	MS Active Source® avonex.com msactivesource.com 800-456-2255	Lymphopenia	Recent CBC (< 6 months) before starting treatment, and annually or as clinically indicated.	Mechanism is unknown. Dimethyl fumerate (DMF) and the metabolite, monomethyl fumarate (MMF), have been shown to activate the Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway in vitro and in vivo in animals and humans. The Nrf2 pathway is involved in the cellular response to oxidative stress. MMF has been identified as a nicotine acid receptor agonist in vitro.	Flushing, abdominal pain, nausea, diarrhea
Natalizumab	Tysabri	Relapsing forms of MS* As monotherapy; generally recommended for those who had an inadequate response to, or could not tolerate, a first-line therapy; no concurrent or prior use of immunosuppressant Study 1 Study 2	300 mg q 4 wks	IV	C	MS Active Source® biogenidec.com tysabri.com 800-456-2255	Progressive multifocal leukoencephalopathy; hypersensitivity reactions; hepatotoxicity; infections resulting from immunosuppression	TOUCH Safety Monitoring Program Risk factors for PML Antibody-positive for JC virus; prior treatment with immunosuppressant; > 2 yrs on Tysabri. Antibody testing should be repeated every six months. Collaborative PML Consortium PML Registry at NINDS	Binds to alpha4/beta 1 integrin on activated lymphocytes and monocytes; inhibits leukocyte migration across the BBB . (Ropper, 2006)	Hypersensitivity reactions; infusion reactions (headache, rigors)
Mitoxantrone	Novantrone	SPMS, PRMS, worsening relapsing-remitting MS	12 mg/m2 q 3 mos Lifetime max: 8-12 doses total (140 mg/m2)	IV	D	None available at this time	Cardiac toxicity; acute myelogenous leukemia (more likely to occur at cumulative doses >60 mg/m2)	Baseline LVEF and repeat LVEF prior to each dose (with treatment terminated if LVEF <50%); continued monitoring of cardiac function after completion of treatment	Inhibits DNA synthesis; reduces lymphocytes; reduces Th1 cytokines.	Blue-green urine 24 hours after administration; infections, bone marrow suppression, nausea, hair thinning, bladder infections, mouth sores

*Relapsing forms include relapsing-remitting MS (RRMS), secondary-progressive MS (SPMS), and progressive-relapsing MS (PRMS), in those patients who continue to have relapses.

Adapted from the National MS Society website.

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