Disease Modifying Therapy Chart for Patients

	Avonex (interferon beta-1a)	Betaseron/Extavia (interferon beta-1b)	Rebif 44 µg (interferon beta-1a)	Copaxone (glatiramer acetate)
MODE OF ADMINISTRATION:				
	intramuscular [in the muscle] weekly	subcutaneous [under the skin] every other day	subcutaneous [under the skin] three times per week	subcutaneous [under the skin] daily
EFFICACY*:				
reduction in annualized relapse rate compared to placebo (typically over 2 years)	18%	34%	32%	29%
relapse free patients, DMT vs placebo	38% vs. 26%	31% vs. 16%	32% vs. 16%	34% vs. 27%
reduction in sustained disability progression on EDSS compared to placebo	37%	29%	30%	12% (not statistically significant)
reduction in new or enlarging T2 hyperintense (total acquired) lesions on MRI	33%	83%	78%	30%
reduction in MRI Gadolinium-enhancing [actively inflamed and taking up contrast] lesions	52%	not reported	84%	29%
	***The relative benefits of the Disease Modifying Therapies (DMTs) above cannot be directly compared to each other in terms of effects on MS relapses and disability because each placebo-controlled study was performed at a different time, with a different patient population, using different methodologies to enroll patients and evaluate data.**			

	Avonex (interferon beta-1a)	Betaseron/Extavia (interferon beta-1b)	Rebif 44 µg (interferon beta-1a)	Copaxone (glatiramer acetate)
SAFETY:				
	Relatively safe. Small risk of the increase of liver enzymes and abnormal hematopoietic [blood cell line] changes. Decreased white blood counts.	Relatively safe. Small risk of elevation of liver enzymes and abnormal hematopoietic [blood cell line] changes.	Relatively safe. Small risk of elevation of liver enzymes and abnormal hematopoietic [blood cell line] changes.	Relatively safe.
TOLERABILITY:				
	injection-site reactions, flu-like symptoms, fever, fatigue, myalgia [muscular pain], possible depression	injection-site reactions, flu-like symptoms, fever, fatigue, myalgia [muscular pain], possible depression	injection-site reactions, flu-like symptoms, fever, fatigue, myalgia [muscular pain], possible depression	injection-site reaction (erythema, induration [hard spot]), lipoatrophy [loss of subcutaneous fat], injection site necrosis, Copaxone immediate post-injection hypersensitivity reaction, which is a short-lived reaction of flushing, chest tightness, shortness of breath, sweating, and/or panic that infrequently follows Copaxone injection, allergic reaction

	Avonex (interferon beta-1a)	Betaseron/Extavia (interferon beta-1b)	Rebif 44 µg (interferon beta-1a)	Copaxone (glatiramer acetate)
STABILITY:				
	Prefilled syringe or pen: Store at 2°C to 8°C (36°F to 46°F); do not freeze. Protect from light. Allow to warm to room temperature prior to use (do not use external heat source). If refrigeration is not available, product may be stored at ≤25°C (77°F) for up to 7 days. Vial: Store unreconstituted vial at 2°C to 8°C (36°F to 46°F). If refrigeration is not available, may be stored at 25°C (77°F) for up to 30 days; do not freeze. Protect from light. Reconstitute with 1.1 mL of diluent and swirl gently to dissolve. Do not shake. The reconstituted product contains no preservative and is for single-use only; discard unused portion. Following reconstitution, use immediately, but may be stored up to 6 hours at 2°C to 8°C (36°F to 46°F); do not freeze.	Store at room temperature of 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F). To reconstitute solution, inject 1.2 mL of diluent (provided); gently swirl to dissolve, do not shake. Reconstituted solution provides 0.25 mg/mL (8 million units). If not used immediately following reconstitution, refrigerate solution at 2°C to 8°C (36°F to 46°F) and use within 3 hours; do not freeze or shake solution. Discard unused portion of vial.	Store at 2°C to 8°C (36°F to 46°F); do not freeze. Protect from light. May also be stored ≤25°C (77°F) for up to 30 days if protected from heat and light.	Store in refrigerator at 2°C to 8°C (36°F to 46°F); excursions to room temperature for up to 1 month do not have a negative impact on potency. Avoid heat; protect from intense light.
KAISER PERMANENTE NORTHERN CA FORMULARY STATUS (as of May 2013):				
Commercial Members	Formulary: Avonex®: For use only by, or in consultation with, a neurologist	Extavia is Formulary - For use only by or in consultation with a TPMG Neurologist. Betaseron brand is Non-Formulary	Non-Formulary	Formulary - For use only by, or in consultation with, a TPMG Neurologist
Medicare Part D Members	Specialty Tier 5	Extavia®: 0.3 mg - Brand Tier 3 Betaseron®: 0.3 mg - Specialty Tier 5	Specialty Tier 5	Specialty Tier 5

	Tysabri (natalizumab)	Gilenya 0.5 mg (fingolimod)	Aubagio (14 mg unless otherwise specified) (teriflunomide)	Tecfidera 240 mg BID (dimethyl fumarate)	Rituxan (Rituximab)
MODE OF ADMINISTRATION:					
	intravenous (infusion center) every 4 weeks	oral daily May be administered with or without food.	oral daily May be administered with or without food. Available at both 7 mg and 14 mg once daily dose - 14 mg has higher efficacy, but 7 mg may be used for individuals with poor tolerance for the higher dose.	oral twice daily Administer orally with or without food. Administering with food may decrease the incidence of flushing. Swallow capsules whole (delayed release); do not crush, chew, open the capsule, or sprinkle contents on food.	intravenous (infusion center) every 6, 9, or 12 months This is not FDA-approved and thus used off label for MS and neuromyelitis optica (NMO). FDA-approved indications include B-cell lymphomas, chronic lymphocytic leukemia, refractory rheumatoid arthritis, microscopic polyarteritis nodosa, and Wegener's granulomatosis
EFFICACY*:					
reduction in annualized relapse rate compared to placebo (typically over 2 years)	68%	54% in one trial; 48% in a second trial	32% for 14 mg and 31% for 7 mg dose in one trial; 36% for 14 mg dose and 22% for 7 mg dose in a second trial	53% in one trial; 44% in a second trial ; 49% in pooled data	56% in Hauser 2008, 87% in Bar-Or 2008
relapse free patients, DMT vs placebo	72% vs. 46%	70% vs. 46% in one trial	57% vs 46% in one trial	73% vs 54% in one trial; 71% vs 59% in a second trial	79.7% vs 60% at 48 weeks
reduction in sustained disability progression on EDSS compared to placebo	42%	30% in one trial; sustained for 3 months; 17% in a second trial	30% 12 wk sustained risk of disability reduction in one trial; 31.5% in a second trial (not significant in 7 mg group in either of the two trials)	the 12 wk sustained risk of disability reduction was 38% in one trial; 21% in a second trial; 32% in pooled data	n/a in RRMS trials
reduction in new or enlarging T2 hyperintense (total acquired) lesions on MRI	83%	74% in two trials	77% in one trial for 14 mg; 44% in one trial for 7 mg	85% in one trial; 71% in a second trial; 78% in pooled data	
reduction in MRI Gadolinium-enhancing [actively inflamed and taking up contrast] lesions	92%	82% in one trial and 67% in a second trial	80% in one trial for 14 mg; 57% in one trial for 7 mg	90% in one trial; 74% in a second trial; 83% in pooled data	91% in phase 2 trial; 88% or greater in systematic review of 4 trials done to date
	***The relative benefits of the Disease Modifying Therapies (DMTs) above cannot be directly compared to each other in terms of effects on MS relapses and disability because each placebo-controlled study was performed at a different time, with a different patient population, using different methodologies to enroll patients and evaluate data.**				

	Tysabri (natalizumab)	Gilenya 0.5 mg (fingolimod)	Aubagio (14 mg unless otherwise specified) (teriflunomide)	Tecfidera 240 mg BID (dimethyl fumarate)	Rituxan (Rituximab)
SAFETY:					
	Risk of progressive multifocal leukoencephalopathy (PML), a potentially fatal brain infection. To stratify the risk of PML infection in each patient, need to consider (1) whether the patient has a positive or negative antibody to the JC virus (2) past history of immunosuppressant therapies (3) duration of therapy. Also may be associated with liver enzyme abnormalities or liver toxicity, anaphylaxis [extreme, often life-threatening, allergic reaction], infections.	Abnormal heart changes, (for example, bradycardia [slow heart rate], heart block, possible related sudden death), increase in liver enzymes, changes in breathing, herpes viral and respiratory infections, macular edema of the eye (especially, but not limited to, history of uveitis [inflammation of a part of the eye], diabetes, old age). Long-term risk not fully defined.	Abnormal liver enzymes. Neutropenia [decrease in a type of white blood cell]. Potential for infections. Harm to unborn baby/birth defects (pregnancy category X; not to be used in women or men of childbearing age without contraception). The drug can take 2 years to be fully metabolized out of the body. Long-term risk not fully defined.	May cause lymphopenia [decrease in a type of white blood cell]. There were also a smaller number of cases of protein in the urine. Long-term risk not fully defined.	New or reactivated infections, leukopenia [decrease in a type of white blood cell], increase in liver enzymes; cases of progressive multifocal leukoencephalopathy (PML), a potentially fatal brain infection. Rituximab has been associated with PML in other rheumatological disorders, and risk in rheumatoid arthritis is 1/25,000. Risk of PML with Rituximab for MS is unknown.
	PML usually shows up as cognitive changes [change in the mental processes, like thinking, reasoning, remembering], weakness, numbness, loss of half of the visual field, headache, and/or word-finding difficulties developing over weeks (vs. MS flare over days)	*Contraindicated in patients with drugs to treat abnormal heart rhythms, medications: beta blockers, calcium channel blockers; low heart rate, heart rhythm disorders, congestive heart failure, fainting, stroke, transient ischemic attack (TIA), possibly diabetes*			
TOLERABILITY:					
	infections, post-infusion reactions, fatigue	generally well tolerated on a day to day basis; may cause headache or activated feeling, increased upper respiratory infections, fatigue, nausea, diarrhea, back pain, cough	hair loss or thinning (15%), diarrhea (20%), nausea (15%), flu-like symptoms, back pain, increased blood pressure, possible increased potential for infections, paresthesias [sensation of tickling, tingling, burning, pricking, or numbness of a person's skin]	flushing (40%), stomach pain, diarrhea, nausea, nasopharyngitis [inflammation of the nasal passages and of the upper part of the pharynx/throat] - Can take aspirin 325 mg daily that may help with flushing, using Pepto bismol and taking with fatty food may help with stomach side effects	infusion-related reactions (usually within 24 hours of initial infusion), urinary tract infections, inflammation of the sinus

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STABILITY:					
		Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F).	Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F).	Store at 15°C to 30°C (50°F to 86°F). Protect capsules from light and store in the original container. Once opened, discard after 90 days.	
KAISER PERMANENT					
Commercial Members	Formulary -Prescribing restricted to TPMG Neurologists and Gastroenterologists with guidelines and monitoring.	Non-Formulary	Non-Formulary	Non-Formulary	Formulary - Prescribing restricted to TPMG Hematologists/Oncologists and Rheumatologists
Medicare Part D Members	Specialty Tier 5	Specialty Tier 5	Specialty Tier 5	Specialty Tier 5	Brand Tier 3