

## Supplemental Material

Table S1. Generic Names of Drugs Included for Analysis of Medications Used for Symptom Management

Class	Generic name
Corticosteroids	corticotropin methylprednisolone methylprednisolone ac, micro methylprednisolone acet-water methylprednisolone acetate methylprednisolone sod succ methylprednisolone sod succ/PF methylprednisolone, micronized methylprednisolone/bupivacaine prednisone prednisone micronized
Bladder dysfunction	darifenacin hydrobromide desmopressin (nonrefrigerated) desmopressin acetate fesoterodine fumarate mirabegron oxybutynin oxybutynin chloride prazosin HCl prazosin HCl/polythiazide propantheline bromide solifenacin succinate tamsulosin HCl terazosin HCl tolterodine tartrate trospium chloride
Spasticity	cyclobenzaprine/diet. supp. 11 baclofen cyclobenzaprine HCl cyclobenzaprine HCl/msm cyclobenzaprine/TENS electrode cyclobenzaprine/TENS unit/elec cyclobenzaprine/capsai/menthol cyclobenzaprine/irr cntr-irr 2 cyproheptadine HCl cyproheptadine/lys/B comp/zinc dantrolene sodium methocarbamol methocarbamol/aspirin orphenadrine citrate orphenadrine/acetaminophen orphenadrine/aspirin/caffeine tizanidine HCl tizanidine/irritant cntr-irrt2
Opioids	a.p.c. w/codeine

acetaminophen/butalbital/codeine phosphate  
acetaminophen/caffeine/dihydrocodeine bitartrate  
acetaminophen/codeine phosphate  
acetaminophen/hydrocodone bitartrate  
acetaminophen/meperidine hydrochloride  
acetaminophen/oxycodone hydrochloride  
acetaminophen/pentazocine hydrochloride  
acetaminophen/propoxyphene hydrochloride  
acetaminophen/propoxyphene napsylate  
acetaminophen/tramadol hydrochloride  
apap/butabarbitol na/codeine phos  
apap/butalbital/caff/codeine phos  
asa/oxycodone hcl/oxycodone terephthalate  
aspirin (buffered)/codeine phosphate  
aspirin/butalbital/caffeine/codeine phosphate  
aspirin/caffeine/dihydrocodeine bitartrate  
aspirin/caffeine/propoxyphene hydrochloride  
aspirin/carisoprodol/codeine phosphate  
aspirin/codeine phosphate  
aspirin/hydrocodone bitartrate  
aspirin/oxycodone hydrochloride  
aspirin/pentazocine hydrochloride  
belladonna alkaloids/opium alkaloids  
buprenorphine  
buprenorphine hydrochloride  
buprenorphine/naloxone  
butorphanol tartrate  
codeine phosphate  
codeine sulfate  
dihydrocodeine/apap/caffeine  
fentanyl  
fentanyl citrate  
hydrocodone bitartrate  
hydrocodone bitartrate/ibuprofen  
hydromorphone hydrochloride  
ibuprofen/oxycodone hydrochloride  
levomethadyl acetate hydrochloride  
levorphanol tartrate  
meperidine hydrochloride  
methadone hydrochloride  
morphine sulfate  
morphine sulfate/naltrexone hydrochloride  
naloxone hydrochloride/pentazocine hydrochloride  
oxycodone  
oxycodone hydrochloride  
oxymorphone hydrochloride  
propoxyphene hydrochloride  
propoxyphene napsylate  
tapentadol hydrochloride  
tramadol hydrochloride

Nonopioid analgesics	bromfenac sodium celecoxib diclofenac potassium diclofenac sodium diclofenac sodium/misoprostol diclofenac submicronized diflunisal etodolac fenoprofen calcium flurbiprofen ibuprofen ibuprofen/famotidine indomethacin indomethacin, submicronized ketoprofen ketorolac tromethamine lansoprazole/naproxen meclufenamate sodium mefenamic acid meloxicam meloxicam, submicronized nabumetone naproxen naproxen sodium naproxen/esomeprazole mag oxaprozin piroxicam rofecoxib salsalate sulindac tolmetin sodium
Stimulants	amphetamine amphetamine sulfate amantadine armodafinil atomoxetine HCl clonidine HCl dexmethylphenidate HCl dextroamphetamine sulfate dextroamphetamine/amphetamine guanfacine HCl lisdexamfetamine dimesylate methamphetamine HCl methoxamine HCl methylphenidate methylphenidate HCl modafinil solriamfetol HCl
Antidepressants	amitriptyline HCl amoxapine

	<p>                     brexanolone                      bupropion HBr                      bupropion HCl                      citalopram hydrobromide                      clomipramine HCl                      desipramine HCl                      desvenlafaxine                      desvenlafaxine fumarate                      desvenlafaxine succinate                      doxepin HCl                      duloxetine HCl                      escitalopram oxalate                      esketamine HCl                      fluoxetine HCl                      fluvoxamine maleate                      imipramine HCl                      imipramine pamoate                      isocarboxazid                      levomilnacipran HCl                      maprotiline HCl                      mirtazapine                      nefazodone HCl                      nortriptyline HCl                      olanzapine/fluoxetine HCl                      paroxetine HCl                      paroxetine mesylate                      phenelzine sulfate                      protriptyline HCl                      selegiline                      sertraline HCl                      tranylcypromine sulfate                      trazodone HCl                      trimipramine maleate                      venlafaxine HCl                      vilazodone HCl                      vortioxetine hydrobromide                 </p>
Anticonvulsants	<p>                     brivaracetam                      cannabidiol (CBD) extract                      carbamazepine                      clobazam                      diazepam                      divalproex sodium                      eslicarbazepine acetate                      ethosuximide                      ethotoin                      ezogabine                      felbamate                      gabapentin                      gabapentin enacarbil                      gabapentin/capsai/me-sal/menth                 </p>

	<p>gabapentin/lidocaine/menthol lacosamide lamotrigine levetiracetam mephenytoin mephobarbital methsuximide midazolam oxcarbazepine paramethadione perampanel phenacemide phenobarbital phenytoin phenytoin sodium phenytoin sodium extended pregabalin primidone rufinamide stiripentol tiagabine HCl topiramate trimethadione valproic acid valproic acid (as sodium salt) vigabatrin zonisamide</p>
Benzodiazepines	<p>chlordiazepoxide alprazolam diazepam oxazepam clonazepam estazolam flurazepam triazolam clorazepate lorazepam clobazam temazepam midazolam</p>

Table S2. Demographics and Comorbid Chronic Conditions for Medicare Beneficiaries With Multiple Sclerosis

	<b>Total</b>	<b>Nonuser</b>	<b>DMT user</b>	<b>P value</b>
	N=43,283	n=13,120	n=30,163	
<b>Age, mean (SD), y</b>	61.5 (10.5)	64.2 (11.0)	60.4 (10.1)	<.001
<b>Age, No. (%)</b>				<.001
<50 y	5549 (14.0)	1399 (10.7)	4650 (15.4)	
50-54 y	4500 (10.4)	1003 (7.6)	3497 (11.6)	
55-59 y	6094 (14.1)	1489 (11.3)	4605 (15.3)	
60-64 y	6730 (15.5)	1772 (13.5)	4958 (16.4)	
65-69 y	10,412 (24.1)	3179 (24.2)	7233 (24.0)	
>=70 y	9498 (21.9)	4278 (32.6)	5220 (17.3)	
<b>Female sex, No. (%)</b>	32,696 (75.5)	9783 (74.6)	22,913 (76.0)	<.001
<b>Race, No. (%)</b>				<.001
White	37,690 (87.1)	11,882 (90.6)	25,808 (85.6)	
Black	4018 (9.3)	839 (6.4)	3179 (10.5)	
Hispanic	416 (1.0)	79 (0.6)	337 (1.1)	
Asian	119 (0.3)	30 (0.2)	89 (0.3)	
North American Native	92 (0.2)	28 (0.2)	64 (0.2)	
Other/unknown	948 (2.2)	262 (2.0)	686 (2.3)	
<b>Region, No. (%)</b>				<.001
Northeast	9200 (21.3)	2935 (22.4)	6265 (20.8)	
Midwest	11,234 (26.0)	3633 (27.7)	7601 (25.2)	
South	14,886 (34.4)	4099 (31.2)	10,787 (35.8)	
West	7824 (18.1)	2437 (18.6)	5387 (17.9)	
Outside U.S.	139 (0.3)	16 (0.1)	123 (0.4)	
<b>Entitlement pathway, No. (%)</b>				<.001
Old age	19,913 (46.0)	7456 (56.8)	12,457 (41.3)	
DIB	>23,330 (>53.8)	>5655 (>43.0)	>17,670 (>58.5)	
ESRD	suppressed	suppressed	suppressed	
Both DIB and ESRD	27 (0.1)	suppressed	21 (0.1)	
<b>Low-income subsidy, No. (%)</b>	6836 (15.8)	1321(10.1)	5515 (18.3)	<.001
<b>Chronic conditions, No. (%)</b>				
Acquired hypothyroidism	5810 (13.4)	2368 (18.0)	3442 (11.4)	<.001
Alzheimer disease, related disorders, or senile dementia	2737 (6.3)	1355 (10.3)	1382 (4.6)	<.001
Anemia	8271 (19.1)	3553 (27.1)	4718 (15.6)	<.001
Cataract	5549 (12.8)	2207 (16.8)	3342 (11.1)	<.001
Chronic kidney disease	3478 (8.0)	1580 (12.0)	1898 (6.3)	<.001
Chronic obstructive pulmonary disease	2345 (5.4)	1125 (8.6)	1220 (4.0)	<.001
Diabetes	6202 (14.3)	2257 (17.2)	3945 (13.1)	<.001
Glaucoma	3036 (7.0)	1151 (8.8)	1885 (6.2)	<.001
Heart failure	2428 (5.6)	1213 (9.2)	1215 (4.0)	<.001
Hyperlipidemia	13,469 (31.1)	5224 (39.8)	8245 (27.3)	<.001
Hypertension	15,522 (35.9)	6187 (47.2)	9335 (30.9)	<.001
Ischemic heart disease	5491 (12.7)	2315 (17.6)	3176 (10.5)	<.001
Osteoporosis	3593 (8.3)	1658 (12.6)	1935 (6.4)	<.001
Rheumatoid arthritis/osteoarthritis	10,357 (23.9)	4310 (32.9)	6047 (20.0)	<.001
Anxiety disorders	6367 (14.7)	2622 (20.0)	3745 (12.4)	<.001
Depressive disorders	11,757 (27.2)	4666 (35.6)	7091 (23.5)	<.001
Fibromyalgia, chronic pain and fatigue	7938 (18.3)	3354 (25.6)	4584 (15.2)	<.001
Mobility impairments	4583 (10.6)	2452 (18.7)	2131 (7.1)	<.001

Obesity	3790 (8.8)	1400 (10.7)	2390 (7.9)	<.001
Peripheral vascular disease (PVO)	2892 (6.7)	1486 (11.3)	1406 (4.7)	<.001
Pressure and chronic ulcers	3171 (7.3)	1914 (14.6)	1257 (4.2)	<.001
Tobacco use	3377 (7.8)	1220 (9.3)	2157 (7.2)	<.001

DIB, disability insurance benefit; DMT, disease-modifying therapy; ESRD, end-stage renal disease.

Table S3. Median Annual Pharmaceutical Expenditures for Patients With Multiple Sclerosis (MS)

Drug	N=43,283 (%)	Median No. of distinct medications (IQR)	Total cost (IQR)	OOP cost (IQR)	Non-LIS			LIS		
					n=36,447 (%)	Total cost (IQR)	OOP costs (IQR)	n=6836 (%)	Total cost (IQR)	OOP costs (IQR)
Self-administered DMTs	29,141 (67.3)	1 (1, 1)	\$56,602 (\$44,010, \$61,981)	\$3666 (\$234, \$5163)	23,783 (65.3)	\$56,794 (\$44,837, \$62,038)	\$4566 (\$849, \$5270)	5358 (78.4)	\$55,374 (\$40,036, \$61,673)	\$13 (\$6, \$13)
Natalizumab	1199 (2.8)	1 (1, 1)	\$43,637 (\$20,975, \$52,029)	\$8727 (\$4193, \$10,523)	1012 (2.8)	\$43,937 (\$22,100, \$52,306)	\$8848 (\$4363, \$10,523)	187 (2.7)	\$34,691 (\$13,418, \$52,029)	\$6883 (\$1791, \$10,406)
Medications for MS-related symptoms	40,041 (92.5)	4 (2, 6)	\$947 (\$238, \$3128)	\$112 (\$30, \$322)	33,650 (92.3)	\$888 (\$226, \$2918)	\$149 (\$50, \$379)	6391 (93.5)	\$1367 (\$325, \$4766)	\$15 (\$5, \$48)

DMT, disease-modifying therapy; IQR, interquartile range; LIS, low-income subsidy; OOP, out-of-pocket.

\*\*Monthly OOP costs are zero for those with Medicare supplement.