CHAPTER 1
INTRODUCTION

Multiple sclerosis (or MS) is a chronic, often debilitating disease that attacks the central nervous system (CNS). Currently there is not a cure for MS. Symptoms may range from mild to severe; such as numbness in the limbs, paralysis or loss of vision. The progress, severity, and specific symptoms of MS are unpredictable and vary from one person to another. Currently in the United States there are approximately 400,000 people with MS, 200 more are diagnosed every week. Worldwide, MS is thought to affect more than 2.1 million people.

While the disease is not contagious or directly inherited, epidemiologists have identified factors in the distribution of MS around the world that may eventually help determine what causes the disease. These factors include gender, genetics, age, geography, and ethnic background. Understanding what causes MS will be an important step toward finding more effective ways to treat, and ultimately cure, or even prevent, the disease.

People with MS typically experience one of four disease courses, each of which might be mild, moderate, or severe.

Table 1. Four Disease Courses of MS

Relapsing-Remitting MS (RRMS)	People with this type of MS experience clearly defined attacks of worsening neurologic function. These attacks—which are called relapses, flare-ups, or exacerbations —are followed by partial or complete recovery periods (remissions), during which no disease progression occurs. Approximately 85% of people are initially diagnosed with relapsing-remitting MS.
Primary-Progressive MS (PPMS)	This disease course is characterized by slowly worsening neurologic function from the beginning—with no distinct relapses or remissions. The rate of progression may vary over time, with occasional plateaus and temporary minor improvements. Approximately 10% of people are diagnosed with primary-progressive MS.
Secondary-Progressive MS (SPMS)	Following an initial period of relapsing-remitting MS, many people develop a secondary-progressive disease course in which the disease worsens more steadily, with or without occasional flare-ups, minor recoveries (remissions), or plateaus. Before disease-modifying medications became available, approximately half of the people with relapsing-remitting MS developed this form of the disease within ten years. Long-term data is not yet available to determine if treatment significantly delays this transition.
Progressive-Relapsing MS (PRMS)	In this relatively rare course of MS (5%), people experience steadily worsening disease from the beginning, but with clear attacks of worsening neurologic function along the way. They may or may not experience some recovery following these relapses, but the disease continues to progress without remissions.

Table 2. Current Approved Treatments for MS

DRUG	COMPANY	CLASS	ROUTE	PATENT EXPIRATION
Avonex	Biogen Idec, Elan	Interferon beta-1a	IM – 1x per week	September_2026
Rebif	EMD Serono, Pfizer	Interferon beta-1a	SC – 3x per week	December_2013
Betaseron	Bayer	Interferon beta-1b	SC – every 48hrs	Expired
Extavia	Novartis	Interferon beta-1b	SC – every 48hrs	Expired
Tysabri	Biogen Idec	Monoclonal antibody	IV – every 4 weeks	April_2017
Copaxone	Teva	Immunomodulator	SC – 1x daily	May_2014
Novantrone	Merck Serono, OSI	Immunomodulator	IV – every 3 months	Expired
Gilenya	Novartis	S1PR modulator	Oral – 1x daily	Feb 2014
Ampyra	Biogen Idec, Acorda	Potassium channel blocker	Oral – 2x daily	Feb 2026

Drug Profiles

The following are currently approved therapies for MS. While the drugs currently used for treatment are relatively safe, they are only effective for a limited period of time. Symptom breakthroughs do occur while on all of these types of therapies. Experts agree that more effective medications are needed; however, traditionally as the effectiveness increases, so does the drug's risk profile.

Avonex

Table 3. Avonex at a Glance

Brand Name	**Avonex**
Generic	**Interferon beta-1a**
MOA	**Interferon beta-1a**
Side Affects	**Drowsiness; flu-like symptoms (eg, headache, tiredness, fever, chills, back pain, muscle aches, weakness); pain, redness, or swelling at the injection site; stomach pain.**
Clinical Use/Dose	**30mcg - 1x a week**
Line of Therapy & Level	**First line**
FDA Approval	**Treatment for Patients with Early Multiple Sclerosis**
Year of FDA Approval	**2003**
Year Patent Expires	**2026**

Cost of Current MS Drugs

Table 19. Cost of Current MS Drugs

DRUG	DOSE	TREATMENT	PRICE	QUANTITY
Ampyra *(Ampyra is only available through mail-order pharmacies and not through your local retail pharmacy.)*	10 mg - 2x daily	To improve multiple sclerosis (MS) patients' ability to walk	$1,056	30-Day Supply
WWW.NORTHDRUGSTORE.COM, CANADA				
Avonex	30mcg - 1x a week	Treatment for Patients with Early Multiple Sclerosis	$2,250.00	30mcg 4 x 1ml
Rebif	44 mcg - 3x per week	Relapsing forms of multiple sclerosis	$1,599.00	44mcg 12 x 0.5ml
Betaseron	0.25 mg every 48hrs	Treat the relapsing-remitting form of multiple sclerosis	$2,250.00	15 prefilled syringes
Extavia	0.25 mg every 48hrs	Treatment of MS patients with relapsing forms of the disease and for newly diagnosed patients	$1,750.00	0.3mg 1 x 15 kits
Copaxone	20 ml – 1x daily	Prevent relapse of multiple sclerosis	$1,175.00	20mg/mL 28 x 1ml
Tysabri	300 mg every 4 weeks	Treatment of multiple sclerosis and Crohn's disease	N/A	N/A
Gilenya	0.5 mg - 1x daily	Treat adults with relapsing forms of multiple sclerosis	$3,501.00	0.5mg 28 capsules
WWW.DRUGSTORE.COM, US AND CANADA				
Avonex	30mcg - 1x a week	Treatment for Patients with Early Multiple Sclerosis	$3,287.12	4 30mcg/vial Kit 1 Box = 4 Vials (0.5ml Per Vial)
Rebif	44 mcg - 3x per week	Relapsing forms of multiple sclerosis	N/A	N/A
Betaseron	0.25 mg every 48hrs	Treat the relapsing-remitting form of multiple sclerosis	$2,989.83	14 0.3mg Solution 1 Box Contains Fourteen .3mg Vials.
Extavia	0.25 mg every 48hrs	Treatment of MS patients with relapsing forms of the disease and for newly diagnosed patients	$3,100.00	15 x 0.3mg
Copaxone	20 ml – 1x daily	Prevent relapse of multiple sclerosis	N/A	N/A
Tysabri	300 mg every 4 weeks	Treatment of multiple sclerosis and Crohn's disease	N/A	N/A
Gilenya	0.5 mg - 1x daily	Treat adults with relapsing forms of multiple sclerosis	$3,880.04	28 0.5mg Capsules Disp Pack
WWW.RXZONE.US				
Avonex	30mcg - 1x a week	Treatment for Patients with Early Multiple Sclerosis	$2,171.44	prefilled syringe - 30 mcg, 4 syringes

CHAPTER 5
TRANSCRIPTS

Dr. Berger Interview

K- What do you think the challenges are in the MS space; the challenges with treatment? I know there is no cure, obviously, so there are probably a lot of challenges, but that is usually where I like to start.

B- Well the landscape with respect to MS is changing very dramatically and very quickly. And recall that through 1993 there were no effective therapies, and in 1993 we have the appearance of Betaseron, and then in 1996 we had Copaxone come to the market, and Avonex and subsequently Rebif a few years after that. So we were left with what we call the platform therapies through 2005 with the introduction of Tysabri. And those platform therapies have proven to be very, very safe. We now have over 16 years of experience, 17 years with Betaseron, and the risk/benefit ratio is very high or low you should say if it is risk/benefit in the sense that Betaseron is a fairly benign drug. However, and that is true of all the platform therapies, they may not be, in some individuals, well tolerated because of the flu-like symptoms that arise with the interferons and because of the skin reactions that occur with Copaxone. But they rarely harm anybody. On the other hand, they are not as effective as these newer drugs that are coming to market. We know from head to head trials in which we know the comparative drug, for the most part, has been interferon beta 1a, either Avonex or Rebif. So we now have drugs that are more effective. However, as was demonstrated with Tysabri when it came to the market in 2005, they have a different risk profile associated with them.

Now, there was a time when the community of neurologists was quite comfortable treating MS. Through 1993, the treatment of MS was, “if you haven’t relapsed, let me know and we’ll treat you.” But there was nothing else available. And from ‘93 to 2005 the community of neurologists, for the most part, felt comfortable administering these drugs because they were benign, the monitoring of them was relativity simple, and the complication rates were exceptionally low. So it was a rare individual with MS that would be referred to an MS center for the simple reason that they can manage. Now the individuals that were being sent to MS centers were, for the most part, individuals that wanted a second opinion or wanted to be managed by an expert, or, more commonly, individuals who were either more diagnostically or therapeutically challenging. That is, people who were breaking through on the drugs that were available.

And then we would end up employing drugs, for the most part, we had only antidotal evidence of their efficacy and they did have a significant risk profile with them.

But now the landscape is changing because the drugs that we have available to us have a greater complexity to them, have significant effect profile to them, and fortunately have a better efficacy of profile. But the average community neurologist is trending towards not managing these patients themselves when they require these newer drugs. So, increasingly, they will be making their diagnosis, and all the money is in making the diagnosis. It’s the initial patient visit, it’s reading the MRI and interpreting it, it is doing the lumbar puncture and the evoke potentials.

And then the issue becomes, do they need one of these drugs? If that’s the case, why do I want to deal with it, since the follow-up office visits—I hate to say this, unfortunately its for industry, not