

Factors Predicting Patient Compliance With Specialty Drug Therapy for Multiple Sclerosis, Inflammatory Conditions and Hepatitis C



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Patients taking specialty medications face many challenges in managing their treatments, including complex dosing regimens, coordination with physicians' offices or involvement of a home-health service when administration requires medical supervision. In addition, patients often have to cope with unpleasant side effects that can make them feel worse than before beginning therapy. Taken together, these complexities work against patients' efforts to remain compliant with their therapy, pointing to the need for an enhanced level of patient support to encourage adherence to therapy. This enhanced level of support is provided by a team of experienced healthcare professionals specifically trained in specialty medicine. This higher level of care includes disease-specific and drug-specific patient counseling, including information on proper drug administration, how to identify and treat drug side effects, and assistance with administrative issues including payment processes and financial assistance.

To better understand the dynamics affecting compliance with specialty medications, the objectives of this study were to:

- Profile patients using key specialty-pharmacy medications and the cost-sharing arrangements they face in obtaining their specialty medications
- Evaluate predictors of compliance, including patient demographics, distribution channel (i.e., the pharmacy that dispenses the patient's medication) and patient copayment



**This study has been peer-reviewed and approved by the
Saint Louis University Center for Outcomes Research.**

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Data represented paid-prescription claims from Jan. 1, 2004, through Dec. 31, 2005, and eligibility data for a select group of Express Scripts plan sponsors. Plan sponsors selected for the study sample were private- and public-sector employer groups, managed-care organizations, third-party administrators and unions. Plan sponsors included in the analysis offered integrated (Home Delivery and retail) prescription-drug benefits within an employer-based market (i.e., no Medicare or Medicaid) and offered a subsidized prescription benefit (i.e., no 100% copayments).

Patients taking a specialty medication for multiple sclerosis (MS), inflammatory conditions (IC) or hepatitis C within an index period of July 1, 2004, through Dec. 31, 2004, were selected for the study. In retrospective claims analysis, an index period is a fixed time period over which patients are identified for study inclusion and is typically chosen to ensure sufficient follow-up for all patients. Inflammatory conditions included conditions such as rheumatoid arthritis, psoriasis and Crohn's disease. Only those patients eligible for pharmacy benefits throughout the entire study period of Jan. 1, 2004, through Dec. 31, 2005, were included in the analysis.

The drugs evaluated under each disease area were¹:

- MS: Avonex[®], Betaseron[®], Rebif[®] and Copaxone[®]
- IC: Enbrel[®] and Humira[®]
- Hepatitis C: Copegus[®], Pegasys[®], Intron A[®], Rebetol[®] and Peg-Intron[®]

Analysis

The Cox proportional hazards model was used to analyze the relationship between time to nonpersistence and copayment category and distribution channel, controlling for age, gender and whether the patient was a new user (MS and IC). Patients were identified as new to therapy if they had no specialty prescription in the respective disease category in the 180 days prior to the first claim in the index period. Patients' ages were calculated as of Jan. 1, 2005.

A unique medication was defined using the first eight digits of the generic product indicator (GPI) code. The average copayment per prescription was calculated by dividing the total copayment by the number of 30-day-equivalent prescriptions. For example, a prescription with a 90-day supply is adjusted to three 30-day prescriptions. This value was categorized into five groups: ≤ \$20, \$21 to \$50, \$51 to \$75, \$76 to \$150 and > \$150.

¹Due to inadequate sample size, Infergen[®], Kineret[®], Novantrone[®], Remicaide[®], Roferon-A[®] and Tysabri[®] were excluded from the analysis.

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Patients were categorized into a distribution channel based upon where 70% or more of their prescriptions were dispensed. Using this criteria, patients were categorized into one of four channels: retail, Home Delivery, CuraScript Specialty Pharmacy and other specialty pharmacy. Patients with less than 70% of prescriptions filled in any one distribution channel were categorized as mixed users.

In order to mitigate the effect of distribution channel bias, only those patients enrolled with a plan sponsor that had a CuraScript exclusive pharmacy network program were assigned to the CuraScript channel. This program uses the CuraScript pharmacy exclusively to reimburse specialty medications, with up to two fills allowed in other distribution channels prior to exclusive reimbursement under CuraScript.

Compliance with medication was measured at a fixed point in time using a measure of persistency. Persistency was measured by determining whether the member had medication available at a fixed point in time. Under this method, patients taking medication to treat IC and MS were followed for 365 days from the date of the first claim within the index period. Patients whose last prescription claim in the follow-up period, plus the days' supply of the last claim, was within 60 days of the 365-day follow-up period were classified as persistent. Persistency was measured at the therapy-class level to accurately reflect use by patients who receive multiple medications for a disease.

A similar method was used to measure persistency for hepatitis C. However, given that the length of therapy may vary based upon patient response or genotype, a shorter follow-up period of 168 days was evaluated. There are six major strains or genotypes of the hepatitis C virus that respond differently to treatment and require different minimum lengths of therapy. The recommended minimum length of therapy with perinterferons plus ribavirins for genotypes 1a and 1b, the most common in the U.S., are 48 weeks with genotypes 2 and 3; the next most common, requiring a minimum of 24 weeks. Since genotypes cannot be distinguished from pharmacy claims data, a follow-up of 24 weeks or 168 days was chosen to determine persistency for hepatitis C specialty medications. Therefore, to limit any potential bias resulting from a different proportion of genotype across channel, and because it is not possible to determine genotype from the pharmacy-claims data, this time period was chosen. Patients whose last prescription claim, plus the days' supply of the last prescription claim, for their hepatitis C medication was within 28 days of their 168-day follow-up period were classified as persistent.

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Demographic and Cost Sharing

Multiple Sclerosis

Of the 7,985 MS patients between July 1, 2004, and Dec. 31, 2004, 77% were female, with an average age of 47 years (standard deviation [SD]=10.1) (Table 1). Eighteen percent of members had no MS medication in the 180 days preceding their index medication. The average copayment was approximately \$30 (SD=\$59). Table 2 indicates that 61% of MS patients paid \$20 or less per specialty prescription, and 3% were paying more than \$150 per prescription.

Inflammatory Condition

Of the 10,734 members selected as having a specialty medication to treat an inflammatory condition between July 1, 2004, and Dec. 31, 2004, 64% were female, with an average age of 51 (SD=13.6) (Table 1). Thirty percent of members had no inflammatory-condition medication in the 180 days preceding their index medication. The average copayment was approximately \$30 (SD=\$60). Table 2 indicates that 62% of IC patients paid \$20 or less for their specialty medication, and 3% paid more than \$150 per prescription.

Hepatitis C

Of the 1,245 patients filling a hepatitis-medication prescription during the index period, 35% were female, and the average age was 49 (SD=8.2). While the average copayment was \$31 (SD=\$52), 64% of patients paid \$20 or less for their hepatitis C medication (Tables 1 & 2).

Table 1

Demographic and Utilization Profile of All Users by Disease Area

Therapeutic Class	N	Percent Female	Average Age (Standard Deviation)	Percent New User	Average Copayment per Prescription (Standard Deviation)
Multiple Sclerosis	7,985	77	47(10.1)	18%	\$30.09 (58.79)
Inflammatory Condition	10,734	64	51(13.6)	30%	\$29.65 (59.76)
Hepatitis C	1,245	35	49(8.2)	100%	\$30.97 (52.00)

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Table 2

Average Copayment per Prescription by Disease Area and Copayment Category*

DISEASE	Copayment Category	N (%)
Multiple Sclerosis	≤\$20	5,031 (61)
	\$21-\$50	2,303 (30)
	\$51-\$75	212 (3)
	\$76-\$150	198 (3)
	>\$150	238 (3)
Inflammatory Condition	≤\$20	6,694 (62)
	\$21-\$50	3,217 (30)
	\$51-\$75	341 (3)
	\$76-\$150	207 (2)
	>\$150	275 (3)
Hepatitis C	≤\$20	791 (64)
	\$21-\$50	334 (27)
	\$51-\$75	38 (3)
	\$76-\$150	36 (3)
	> \$150	45 (4)

* Numbers may not sum to 100 due to rounding.

Persistency

To evaluate the relationship between persistency and key independent variables, Cox regressions were tested, controlling for age, gender, channel type, copayment amount and whether the patient was new to therapy.

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Cox Regression

Table 3

Odds Ratio (Confidence Interval) of Discontinuing Therapy by Model Predictor Variables

Predictor Variables	Multiple Sclerosis (n=7,985)	Inflammatory Conditions (n=10,734)	Hepatitis C 168-Day Follow Up (n=1,245)
Age	0.98 (0.98-0.99)	0.99 (0.989-0.996)	ns
New User			
No	Reference	Reference	na
Yes	1.49 (1.39-1.59)	1.43 (1.37-1.50)	na
Female	ns	1.14 (1.09-1.20)	ns
Distribution Channel			
CuraScript	Reference	Reference	Reference
Retail	1.43 (1.27-1.61)	1.33 (1.23-1.45)	1.25 (1.01-1.56)
Traditional Home Delivery	1.40 (1.23-1.59)	1.22 (1.11-1.35)	1.37 (1.03-1.82)
Other Specialty	1.34 (1.18-1.52)	1.38 (1.23-1.54)	ns
Copayment Amount			
≤ \$20	Reference	Reference	Reference
\$21-50	0.92 (0.85-0.99)	0.94 (0.90-0.99)	ns
\$51-75	ns	ns	ns
\$76-150	ns	1.17 (1.01-1.35)	ns
>\$150	1.19 (1.03-1.37)	1.14 (1.00-1.28)	1.46 (1.15-1.85)

ns= not significant; na=not applicable; multiple sclerosis and inflammatory condition persistency measured at 1 year

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Multiple Sclerosis

- Older age and those who were continuous users were less likely to be nonpersistent with their MS medication.
- Compared to those filling their MS specialty medication with CuraScript, those filling with a retail pharmacy, Home Delivery or another specialty-pharmacy provider had 43%, 40% and 34% increases, respectively, in the odds of nonpersistence.
- Patients paying over \$150 per prescription had 19% greater odds of being nonpersistent than those paying less than \$20.

Inflammatory Condition

- Older age and those who were continuous users were less likely to be nonpersistent with their IC medication.
- Compared to those paying less than \$20 per prescription, patients paying from \$76 to \$150 and more than \$150 per prescription had a relatively modest increase in the odds of nonpersistence; 17% and 14% respectively.
- Compared to those receiving their medications through CuraScript, those receiving their medications through the retail pharmacy, Home Delivery or other specialty provider had, respectively, 33%, 22% and 38% greater odds of nonpersistence.

Hepatitis C (at 168 days of follow-up)

- Compared to those receiving their medications through CuraScript, those receiving their medication through the retail pharmacy and Home Delivery had 25% and 37% greater odds of nonpersistence, respectively.
- Compared to patients paying less than \$20 per prescription, those paying greater than \$150 had 46% greater odds of nonpersistence.

Conclusion



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- Results suggest that a higher-level of care, as provided under CuraScript, may positively impact patient compliance. We recognize that other factors uncontrolled for in this analysis may have contributed toward higher rates of persistency in CuraScript. However, we believe that the ability of specialty pharmacies to provide experienced and knowledgeable clinical-support teams to be an important factor in greater compliance. The ability of specialty pharmacies to provide experienced and knowledgeable clinical-support teams and coordination of home-care services to its patients would influence adherence.
- For two of the three disease areas, those in CuraScript had significantly lower rates of nonpersistence compared to those in other specialty pharmacies, suggesting possible differences between CuraScript and other specialty pharmacy providers in how they encourage patients to remain compliant with their specialty medications.
- Only at the highest copayment levels (> \$150 per prescription) were patients more likely to become nonpersistent with their specialty medications. Together with the fact that these medications are designed for more severe conditions that impact activities of daily living, patients appear to be more willing to pay higher copayments, possibly forgoing expenditures for other items in order to pay for their specialty medications. Whether nonpersistence at the highest copayment level represents “true” discontinuation or members seeking coverage under their medical benefit should be explored further.

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For aid in interpretation of actual mean persistency rates, adjusted and unadjusted means are presented in the Table below. For the MS and IC conditions, these findings were generated from analysis of variance models, controlling for average age, copayment amount, continuous users and gender. Means for the hepatitis C patients are unadjusted.

Appendix A

Persistency Rates by Distribution Channel

Distribution Channel	Multiple Sclerosis*	Inflammatory Conditions*	Hepatitis C 168-Day Follow-Up**	Hepatitis C 90-Day Follow-Up**
CuraScript	91.7	87.0	81.7	91.3
Retail	82.3	79.3	73.4	84.4
Home Delivery Traditional	84.4	81.6	65.8	92.7
Other Specialty	85.8	77.3	74.2	82.8

*Estimated marginal means, controlling for average age, copayment amount, continuous users and gender

**Unadjusted means