

# Multiple Sclerosis (MS) Patient Adherence to Delayed-Release Dimethyl Fumarate and Patient Reported Side Effects from a Specialty Pharmacy Program.

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## Background

- Biogen Idec's delayed-release dimethyl fumarate (DMF; also known as gastro-resistant DMF; TECFIDERA®) oral medication to treat MS became available in March 2013 for relapsing forms of MS.
- Walgreens Connected Care<sup>SM</sup> for MS (CCMS) program provides enhanced management and care for patients taking DMF including assessments of patient reported side-effects and related information. CCMS incorporates discussions about disease progression, appropriate medication dosing and administration, adherence counseling, recommendations regarding supportive care, and advice about overall health and wellness. Limited real world evidence is currently available for MS patients taking DMF.

# Objective

 The main objective was to describe 6- and 12-month adherence levels, after controlling for other factors. A secondary objective was to describe the prevalence of patient reported side effects.

# Methods

 Adherence was measured using PDC (proportion of days covered)<sup>1</sup> for a 6- or 12-month follow-up period. Patient reported side effects were collected through the CCMS telephonic assessments.

## Methods cont.

5,279 patients were at least 18 years of age and initiated therapy from April 2013 to December 2013, and followed through June 2014. The demographic profile of patients was similar to the national MS population (see Table 1).

### Results

#### Study Sample:

Table 1. Patient Characteristics Utilizing DMF

Characteristic	N= 5,278	%/SD
Age Mean (SD)	46.9	(11.4)
Median (IQR)	47.0	17.0
Gender Female	4,039	76.5%
Comorbidities <sup>1</sup> 0	3,618	68.5%
1-2	1,377	26.1%
3+	284	5.4%
Adjunctive Medications <sup>2</sup> 0	4,569	86.6%
1-2	608	11.5%
3+	102	1.9%
Prior DMT within 365 Days <sup>3</sup>	1,531	29.0%
Reported Naïve to Therapy	n=3,758	
Yes	465	12.4%
No	3,210	85.4%
Unknown	83	2.2%
Reported Years Diagnosed	n=3,704	
Mean (SD)	10.5	(8.7)
Median (IQR)	9.0	11.0

<sup>1</sup>One year prior to and concurrent with Tecfidera fills, count of different categories from Medi-span's Medical Condition Master Database<sup>TM</sup>

<sup>2</sup>Concurrent with Tecfidera fills, not in prior comorbidities

<sup>2</sup>Concurrent with Tecfidera fills, not in prior comorbidities. <sup>3</sup>Based on prior year utilization of at least 2 fills for 8 DMTs

#### Adherence:

- Median PDC for the 3,319 patients with six full months of data was 92.9% (range 16.5-100).
- For the 1,216 patients with 12 months of data, the median PDC was 82.2% (range 10.1-100).

## Results cont.

- The 12-month PDC was adjusted for age, gender, index fill with starter kit, U.S. regions, comorbidities, adjunctive medication, prior utilization of another DMT, number of side effects reported, reported relapse, and managed duration in the CCMS program.
- This fixed set of variables resulted in a significant OLS regression model on 1,216 patients (p < 0.0001), accounting for about 46% of the variance in PDC (R-square=0.68).
- Patient age, prior DMT utilization and duration of CCMS participation were significantly associated with higher PDC values, whereas, beginning with a starter kit, or being from northeast were negatively associated with higher PDC values.
- Median adherence to other MS medications utilized prior to DMF was 90.1% (range 1.7-100) at 6 months
- Only 214 (4.0%) patients switched from DMF to another DMT within 12 months. Those not switching therapy had significantly fewer reported side effects (P < 0.02).

#### Side Effects:

• 4,179 patients were asked at least one side effect question (see Table 2). The most common response was none (1,830 or 43.8%), followed by reports of flushing (1,790 or 42.9%) and abdominal pain (698 or 16.7%).

#### Relapses:

 For assessed patient relapse within the last 30 days, 107 reported a relapse (2.6%) after the first 62 days of therapy through end of study (see Table 3).

Table 2. Patient Reported Side Effects Associated with DMF<sup>1</sup>

Characteristic	N	<b>%</b>		
Flushing	1,790	42.9		
Abdominal pain	698	16.7		
Other	465	11.1		
Nausea/Vomiting	238	5.7		
Diarrhea	205	4.9		
Headache	64	1.5		
Skin problems	48	1.2		
Tired (fatigue)	47	1.1		
Low occurrence (15 at < 1%)	153	<1.0		
None	1,830	43.8		
Column total	5,385	4,175		
1 The numerator is the total number of unique side offects per patient at				

 $^{1}$ The numerator is the total number of unique side effects per patient at any time during the follow-up period (n=5,538 multiple responses). The denominator is the total number of unique patients who had the side effect question asked during the follow-up period (n=4,175 patients).

Table 3. Patient Reported Relapse Associated with DMF<sup>1</sup>

Reported Relapse in last 30 days	N	%
No	3,750	90.6
Yes	390	9.4
Yes (after 31 days)	287	7.6
Yes (after 62 days)	107	2.6

 $^{1}$ The numerator is the total number patients that indicated a relapse within the last 30 days during the follow-up period (n=390). The denominator is the total number of unique patients asked about relapses (n=4,140).

### Conclusion

- In the first year post approval, the 6-month adherence rates for patients utilizing DMF were similar to those of other patients treated with a DMT prior to starting DMF. As observed with other chronic medication use, adherence was lower at 12 months. Adherence was influenced by patient characteristics (e.g., age, region, prior DMT, and initial starter kit) and length of CCMS participation.
- Rates of patient-reported side effects were comparable to those seen in clinical trials, and the percentage of patients reporting no side effects (43.8%) was higher than that reported in the clinical literature.

<sup>1</sup>Nau DP. Proportion of Days Covered (PDC) as a Preferred Method of Measuring Medication Adherence. Pharmacy Quality Alliance (PQA). 2012. http://www.pqaalliance.org/images/uploads/files/PQA%20PDC%20vs%20%20MPR.pdf. Accessed February 18, 2015.

Presented at the 2015 Annual Meeting of the Consortium of Multiple Sclerosis Centers (CMSC) in Indianapolis, Indiana from May 27 -30. For more information on this presentation, please contact: Francis.Staskon@Walgreens.com or Janeen.DuChane@Walgreens.com. Research Sponsor was Biogen, Idec.

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