

Titration and Persistence with Tamsulosin Among Men with Benign Prostatic Hyperplasia in a Large Managed Care Population

Davis KL,¹ Mauskopf JA,¹ Chow W,² Chao J,² Seal B²
¹RTI Health Solutions, Research Triangle Park, NC; ²Sanofi-Aventis, Bridgewater, NJ

BACKGROUND

Benign prostatic hyperplasia (BPH) is a non-cancerous condition resulting in enlargement of the prostate gland and constriction of the urethra. Symptoms include difficult or delayed initiation of urine flow, urge of urination, frequent urination with short intervals, and feeling of incomplete bladder emptying. BPH is common among males, with the majority expected to experience symptoms by the age of 65 (Platz et al., 2002). Recent research indicates that BPH carries a substantial economic burden, with estimated annual medical costs in the US exceeding \$3 billion (Saigal and Joyce, 2005). Given the high prevalence of BPH, its impact on quality of life, and its cost implications, it is important to document current treatment patterns among men with the condition.

OBJECTIVES

- Document patterns of dose titration and persistence with tamsulosin (Flomax[®]), a commonly prescribed BPH medication
- Estimate utilization rates of other BPH therapies among men treated with tamsulosin
- Estimate monthly and annual per patient costs of tamsulosin use, stratified by patients with and without dose escalation

METHODS

Study Design:

This retrospective analysis evaluated patterns of prescription drug and medical services utilization from insurance claims of men in a large managed care population with a BPH diagnosis and treatment with tamsulosin between 10/8/99 and 1/31/05.

Data Source:

Data for this analysis were taken from the PharMetrics Integrated Outcomes Database, which includes enrollment, medical, and prescription information from 75 health plans covering more than 40 million unique patients and 2 billion healthcare transactions in the US. The PharMetrics database comprises insurance claims from managed care organizations in all four US Census regions and has a nationally representative age and gender distribution.

Inclusion Criteria:

Patients meeting all of the following criteria were included in this analysis:

- Male
- ≥ 1 BPH diagnosis (ICD-9 codes 600.xx) between 10/8/99 and 1/31/05
- ≥ 1 pharmacy claim for tamsulosin between 10/8/99 and 1/31/05
- Continuous health plan enrollment for ≥ 6 months prior to and ≥ 12 months following the first (index) tamsulosin pharmacy claim

Outcome Measures:

- Dose titration: Change in daily tamsulosin dose (ratio of quantity dispensed to days supplied) relative to index prescription
- Persistence with tamsulosin, assessed via:
 - Medication possession ratio (MPR): Following Steiner and Prochazka (1997), defined as total days supplied for tamsulosin within specific post-index periods of interest (6 and 12 months respectively) divided by the number of days in the post-index periods of interest (185 and 365 days respectively).
 - Rate of discontinuation: Defined as percentage of patients with no evidence of tamsulosin use within 60 days following the end of the days supplied of the preceding tamsulosin prescription.
- Utilization of other BPH medications subsequent to index tamsulosin prescription
- Utilization of BPH-related surgical and non-surgical procedures subsequent to index tamsulosin prescription
- Monthly and annual per patient costs of tamsulosin use, stratified by patients with and without dose escalation

RESULTS

Patient Characteristics:

- 33,671 patients qualified for study inclusion.
- Study sample comprised almost exclusively of patients ≥ 45 years of age, a substantial proportion (43.1%) of whom were elderly.
- Mean length of post-index follow-up per patient was 24.10 months.
- Among all patients, 27,440 (81.5%) had ≥ 2 valid tamsulosin doses (non-missing data on quantity dispensed and days supplied) and were thus eligible for titration assessment.

Table 1. Patient Characteristics

	N	%
Age category		
≤15	1	0.00
16-29	39	0.12
30-44	1,087	3.23
45-64	18,032	53.55
65+	14,512	43.10
Total	33,671	100.00
Geographic region		
East	9,912	29.44
South	7,941	23.58
Midwest	12,250	36.38
West	3,568	10.60
Insurance type		
Commercial	20,549	61.03
Medicaid	237	0.70
Medicare	5,795	17.21
Self	2,907	8.63
Medicare Gap	527	1.57
Mixed	1,056	3.14
Unknown	2,600	7.72
Had ≥ 2 valid tamsulosin doses ¹		
Yes	27,440	81.50
No	6,231	18.50
Avg. length of follow-up post-index Rx ²	24.01 months	

¹Valid tamsulosin dose defined by non-missing values for quantity dispensed and days supplied
²Length of follow-up calculated as number of months between index prescription and end of health plan enrollment or end of the database (Jan. 31, 2005) if there was no evidence of health insurance cessation.

Utilization of Other BPH Medications:

- Among all patients, 6,492 (19.3%) utilized ≥ 1 other BPH medication (either concurrently or in isolation) following their index tamsulosin prescription
- Tamazepam (Hytrin[®]) and finasteride (Proscar[®]) were the most commonly utilized other BPH medications.

Table 5. Utilization of Other BPH Medications Following Initial Tamsulosin Prescription

	N ¹	%
Other alpha blockers		
Alfuzosin (Uroxatral [®])	413	1.23
Prazosin (Hypovase [®])	78	0.23
Terazosin (Hytrin [®])	2,255	6.70
Total (all alpha blockers listed above)	2,746	8.16
5-ARI		
Finasteride (Proscar [®])	3,834	11.39
Dutasteride (Avodart [®])	536	1.59
Total (all 5-ARI's listed above)	4,370	12.98
Any BPH medication listed above	6,492	19.28

¹Number of patients (among all tamsulosin users [N = 33,671]) with at least one pharmacy claim for the noted BPH medications.

Titration:

- Among patients with ≥ 2 valid doses, 3,522 (12.5%) had ≥ 1 upward titration following index prescription; 946 (3.45%) had ≥ 1 downward titration.
- < 1% of all patients had multiple titrations.

Table 2. Patterns of Titration with Tamsulosin

	N	%
Titration Prevalence ¹		
Upward Titrations		
Had ≥ 1 upward titration	3,522	12.50
Had ≥ 2 upward titrations	116	0.42
Had ≥ 3 upward titrations	6	0.02
Downward Titrations		
Had ≥ 1 downward titration	946	3.45
Had ≥ 2 downward titrations	30	0.11
Had ≥ 3 downward titrations	3	0.01
Magnitude of Upward Titrations ²		
Had ≥ 1 doubling of dose	3,330	94.55
Had ≥ 1 tripling of dose	283	8.04
Had ≥ 1 quadrupling of dose	144	4.09
Avg. Index Dose and Daily Rx Cost Among ³ :	Avg. Index Dose (mg/day)	Avg. Daily Rx Cost
All tamsulosin users	0.44	\$1.27
Tamsulosin users w/ ≥ 1 upward titration	0.41	\$1.19
Tamsulosin users w/ ≥ 1 downward titration	0.92	\$2.70
Tamsulosin users w/ no titrations	0.43	\$1.22
Avg. Titration Dose and Daily Rx Cost at:	Avg. Dose at Titration (mg/day)	Avg. Daily Rx Cost ⁴
1st upward titration	0.90	\$3.05
2nd upward titration	1.63	\$5.58
3rd upward titration	1.24	\$4.56
1st downward titration	0.39	\$1.20
2nd downward titration	0.38	\$1.37
3rd downward titration	0.28	\$1.18

¹Titrations defined as a change (upward or downward) in tamsulosin dose relative to the index dose. Patients with an upward titration followed by a subsequent reduction in dose that does not fall below the original index dose are not classified as having a downward titration. Likewise, patients with a downward titration followed by a subsequent increase in dose are not classified as having an upward titration unless the subsequent dose exceeds the original index dose.

²Among patients with ≥ 2 valid tamsulosin doses (N = 27,440)

³Among patients with ≥ 1 upward titration (N = 3,522)

⁴Calculated as unit cost of the prescription divided by days supply of the prescription

Utilization of Surgical and Non-Surgical Procedures:

- Among all patients, 2,618 (7.8%) required ≥ 1 prostate surgery following their index tamsulosin prescription, while 1,248 (3.7%) required ≥ 1 non-surgical procedure.
- Transurethral resection of the prostate (TURP) was the most common surgical procedure.
- Transurethral microwave therapy (TUMT) was the most common non-surgical procedure.

Table 6. Utilization of BPH-Related Surgical and Non-Surgical Procedures Following Initial Tamsulosin Prescription

	N ¹	%
Surgical Procedures		
Transurethral Resection of the Prostate (TURP)	2,031	6.03
Transurethral Incision of the Prostate (TUIP)	122	0.36
Open Prostatectomy	89	0.26
Extensive Prostate Surgery Not Otherwise Specified	461	1.37
Any prostate surgery listed above	2,618	7.78
Non-Surgical Procedures		
Transurethral Microwave Therapy (TUMT)	566	1.68
Transurethral Needle Ablation (TUNA)	259	0.77
Transurethral Electrovaporisation (TUEVP)	148	0.44
Lesser Surgery	310	0.92
Prostatic Stent	13	0.04
Any non-surgical procedure listed above	1,248	3.71

¹Number of patients (among all tamsulosin users [N = 33,671]) with at least one claim for the noted procedures

- On average, patients with ≥ 1 downward titration initiated tamsulosin use at more than twice the labeled dose of 0.4 mg/day.
- The average titration dose and daily prescription cost at 1st upward titration was 0.90 mg/day and \$3.05, compared to 0.44 mg/day and \$1.27 at index dose.
- > 55% of all patients with ≥ 1 upward titration had their 1st upward titration within 6 months following the index prescription (Figure 1).
- Among patients with ≥ 1 downward titration, less than 45% had their first downward titration within 6 months following the index prescription (Figure 2).

Figure 1. Time to 1st Upward Titration

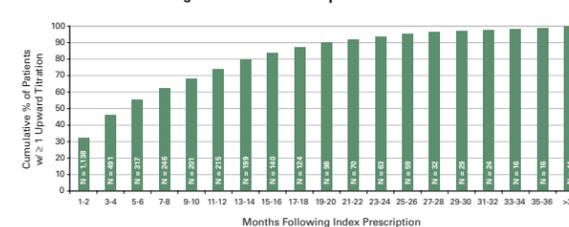
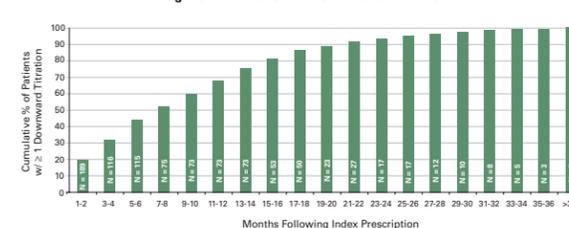


Figure 2. Time to 1st Downward Titration



Persistence:

- MPR: Following previous drug adherence studies (Grosset et al., 2005; Rosen et al., 2004; and George et al., 2000), patients with MPR < 80% were classified as non-adherent. Based on an 80% MPR threshold, less than half of all patients were adherent with tamsulosin during both a 6- and 12-month period following the index prescription (Table 3). The mean MPR for the 6- and 12-month post-index periods was 64.0% and 51.7% respectively.

Table 3. Summary of 6- and 12-Month Adherence with Tamsulosin

	N ¹	%
6 Months Post-Index Rx Adherence Category ²		
MPR 0-19%	8,579	25.48
MPR 20-39%	3,859	11.46
MPR 40-59%	3,566	10.59
MPR 60-79%	2,771	8.23
Non-adherent Total	18,775	55.76
MPR ≥ 80% (Adherent Total)	14,896	44.24
Mean MPR		64.03%
12 Months Post-Index Rx Adherence Category		
MPR 0-19%	11,122	33.03
MPR 20-39%	4,606	13.68
MPR 40-59%	4,226	12.55
MPR 60-79%	2,815	8.36
Non-adherent Total	22,769	67.62
MPR ≥ 80% (Adherent Total)	10,903	32.38
Mean MPR		51.71%

¹Among entire patient sample (N = 33,671)

- Discontinuation: Among all patients, 17,158 (50.9%) discontinued tamsulosin at some point following their index prescription. More than two-thirds of patients who discontinued tamsulosin (11,671 [68.0%]) did so within 6 months following the index prescription. Among those who discontinued, more than one-third (6,807 [39.7%]) reintiated tamsulosin use following the initial discontinuation.

Table 4. Patterns of Tamsulosin Discontinuation

	N	%
Discontinued tamsulosin following index Rx ¹	17,158	50.96
No evidence of discontinuation following index Rx ²	16,513	49.04
Time to discontinuation following index Rx ³		
1-2 months	6,854	39.95
3-4 months	3,036	17.69
5-6 months	1,781	10.38
7-8 months	1,265	7.37
9-10 months	954	5.56
11-12 months	806	4.70
> 12 months	2,462	14.35
Re-initiated tamsulosin ⁴ :		
Within 1 year following initial discontinuation	5,740	33.45
At point > 1 year following initial discontinuation	1,067	6.22
Total (any point following initial discontinuation)	6,807	39.67

¹Among entire patient sample (N = 33,671)

²Among patients with initial discontinuation (N = 17,158)

Monthly and Annual per Patient Costs of Tamsulosin Use:

- Average monthly and annual cost of tamsulosin use per patient was \$18.92 and \$227.08, respectively.
- Monthly and annual costs per patient were highest among patients with ≥ 1 upward titration (\$38.82 and \$465.81 respectively).

Table 7. Average per Patient Monthly and Annual Costs¹ of Tamsulosin Use by Titration Status²

	Avg. per Patient Cost of Tamsulosin	
	Per Month	Per Year
All Tamsulosin Users (N = 27,440)	\$18.92	\$227.08
Tamsulosin Users with ≥ 1 Upward Titration (N = 3,522)	\$38.82	\$465.81
Tamsulosin Users with ≥ 1 Downward Titration (N = 946)	\$32.08	\$384.96
Tamsulosin Users with no Titrations (N = 23,098)	\$15.47	\$185.76

¹For each patient, cost estimates represent total amounts paid for tamsulosin across their entire follow-up period divided by their total follow-up length (in months or years, as appropriate) even if a patient discontinued use mid-way through the follow-up period.

²Titration groups are not mutually exclusive. 126 patients had both an upward titration and a downward titration. Sample sizes for the respective groups therefore will not sum to the overall total for all tamsulosin users.

DISCUSSION

- The labeled dose for tamsulosin appears to be insufficient for some BPH patients, as more than 12% of those initiating treatment with the drug require a dose escalation.
- Upward titrations appear to occur somewhat faster than downward titrations.
- Persistence with tamsulosin is problematic, as more than two-thirds of all users are non-adherent with the drug over a 12-month post-index period and more than half of all tamsulosin users take a drug holiday or discontinue the treatment permanently.
- The increased monthly and annual cost burden of tamsulosin for patients with ≥ 1 upward titration is substantial.
- The increased cost among those with ≥ 1 downward titration may be driven by the substantially higher average index dose at which these patients initiate treatment.

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CONTACT INFORMATION

Keith L. Davis, MA
 Director, Health Economics
 RTI Health Solutions
 RTI International
 3040 Cornwallis Road
 PO Box 12194
 Research Triangle Park, NC 27709-2194
 Phone: 919.541.1273
 Fax: 919.541.7222
 E-mail: kldavis@rti.org
 www.rtihs.org

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