Real-World Outcomes of Tepezza in Thyroid Eye Disease: Analyzing Treatment Persistence, Relapse, and Cost of Care

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Background

- Thyroid eye disease (TED) is a rare autoimmune inflammatory condition characterized by orbital inflammation and tissue expansion, leading to clinical manifestations such as proptosis, diplopia, eyelid retraction, and periorbital edema.[1]
- TED pathophysiology is driven by autoantibodies targeting the thyrotropin receptor and insulin-like growth factor-1 receptor (IGF-1R), resulting in downstream activation of orbital fibroblasts and progressive orbital tissue remodeling.[1]
- Teprotumumab-trbw (Tepezza), a monoclonal antibody targeting IGF-1R, became the first FDA-approved therapy for TED, demonstrating clinically meaningful reductions in proptosis and disease activity.[2] It is administered as 10 mg/kg dosing for the first infusion, followed by 20 mg/kg every 3 weeks for 7 additional infusions.[2] The cost per full treatment has increased since its approval; based on an 80-kg patient, the average sales price (ASP) has increased by $75,000 since 2022 (2025 ASP: $431,712 vs. 2022 ASP: $357,600).[3] This is drastically more expensive than off-label treatments and surgeries.[4] Prior to teprotumumab, TED initial management relied on oral and intravenous (IV) corticosteroids, immunomodulators (e.g., cyclosporine, methotrexate), monoclonal antibodies (e.g., rituximab, adalimumab), and surgical interventions (e.g., eyelid repair, orbital decompression).[1]
- IV corticosteroids are a validated, frequently used therapy for active TED and remain part of real-world practice after teprotumumab, especially when retreatment is not selected.[5]
- Despite 5 years of clinical use, real-world persistence to the full 8-dose teprotumumab regimen—and its implications for retreatment, relapse, and total medical cost of care—remains poorly understood, creating uncertainty for payers and benefit-design decision-making.
- Emerging literature suggests that TED relapses after teprotumumab use, teprotumumab retreatment, and early discontinuation of teprotumumab are occurring in real-world practice, contributing to variability in payer coverage and inconsistent reimbursement policies across health plans.[6,10]

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Objective

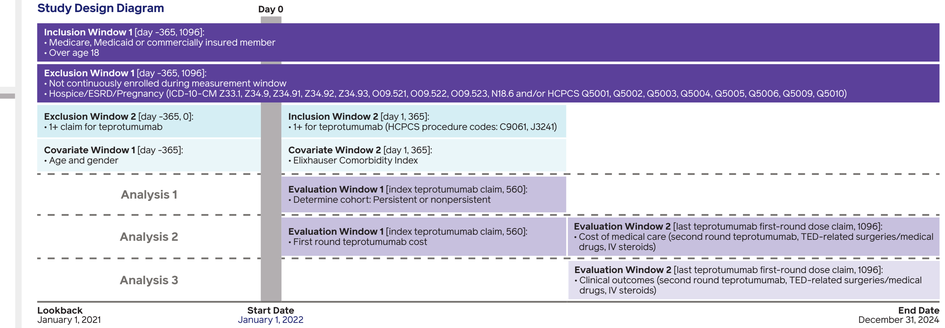
Our objective is to analyze commercial-, Medicare-, and Medicaid-insured members' persistence to teprotumumab infusions, clinical outcomes, and cost of care using medical claims.

Methods

- Figure 1 displays the study methods as outlined.
- An observational retrospective analysis of paid medical claims from a nationally representative sample of ~15 million continuously enrolled members aged ≥18 was completed using claims data from January 1, 2022, to December 31, 2024.
- Outcomes:
  - Members were classified as persistent if they completed all 8 teprotumumab doses within the allowable dosing interval. Teprotumumab retreatment was defined as members who received at least 1 dose of teprotumumab during Evaluation Window 2.
  - Teprotumumab cost was defined as the total paid amount identified through medical claims, separated into Evaluation Window 1 and Evaluation Window 2.
  - TED relapses were defined as members using post-cycle IV steroid use as a claims-based proxy following completion or discontinuation of the initial teprotumumab regimen during Evaluation Window 2.
  - TED-related medication costs were defined as the total paid amounts for medical drugs billed with a TED-related diagnosis code on the claim line during Evaluation Window 2.[7] This did not include the cost of teprotumumab.
  - TED-related surgery costs were calculated using paid amounts from claims containing a TED-related HCPCS, DRG, or ICD-10-PCS code during Evaluation Window 2.[7]
  - Demographic characteristics were assessed and compared between persistent and nonpersistent groups (age, gender, line of business; Evaluation Window 1) and the Elixhauser Comorbidity Index (ECI; Evaluation Window 1).[8]
  - Reuse of teprotumumab, TED relapses, TED-related surgery costs, and TED-related drug costs were compared between persistent and nonpersistent groups using t-tests and chi-square tests. A statistical significance threshold of 0.05 was used for all analyses, α=0.05. Cohen's *h* and *d*, a standardized effect size, was calculated between persistent and nonpersistent groups. Effect sizes ranging from 0.20 to 0.49 were considered small, from 0.50 to 0.79 were considered medium, and 0.80 or greater were considered large.[9]

Figure 1

Study Design Diagram



TED = thyroid eye disease; IV = intravenous
Persistent: Completed all 8 doses with ≤28 days between infusions
Nonpersistent: Did not complete all 8 doses or had >28 days between any 2 consecutive doses

Table 1

Persistency Between Groups

Persistence Status	Intervals >28 Days	Completed 8 Doses of Tepezza	Member Count	
Persistent		✓	120	
Nonpersistent	✓	✓	70	
Nonpersistent	✓		44	158
Nonpersistent			44	

Persistent: Completed all 8 doses with ≤28 days between infusions
Nonpersistent: Did not complete all 8 doses or had >28 days between any 2 consecutive doses

Table 2

Comparison of Demographic Characteristics Between Persistent and Nonpersistent Groups

	Total TED Sample (n=278)		Persistent (n=120, 43.2%)		Nonpersistent (n=158, 56.8%)		Significance
	Mean/%	SD/Count	Mean/%	SD/Count	Mean/%	SD/Count	*P* value
Age	50.34	12.90	50.76	11.28	50.00	14.03	0.62
Elixhauser Comorbidity Index	3.49	2.59	3.57	2.72	3.44	2.49	0.29
% female	75.18%	209	78.33%	94	72.78%	115	0.68
Line of business							
Commercial	92.45%	257	92.5%	111	92.41%	146	0.67
Medicaid	1.08%	3	1.67%	2	0.63%	1	
Medicare	6.47%	18	5.83%	7	5.06 %	8	

TED = thyroid eye disease; SD = standard deviation
Age and Elixhauser Comorbidity Index: Reported as mean and SD
Persistent: Completed all 8 doses with ≤28 days between infusions
Nonpersistent: Did not complete all 8 doses or had >28 days between any 2 consecutive doses

Table 3

Comparison of Patient Outcomes Between Persistent and Nonpersistent Groups

	Persistent (n=120, 43.2%)		Nonpersistent (n=158, 56.8%)		Significance	Effect Size
Clinical Outcomes	%	n	%	n	*P* value	Cohen's *h*
>8 teprotumumab infusions	5.00%	6	7.59%	12	0.38	-0.11
TED-related surgeries	21.66%	26	15.19%	24	0.16	0.16
TED-related medical drugs	9.17%	11	7.59%	12	0.64	0.06
IV steroids	35.83%	43	23.42%	37	0.51	0.27
Total Payment Amount	**Mean ($)**	**SD ($)**	**Mean ($)**	**SD ($)**	***P* value**	**Cohen's *d***
First round of teprotumumab*	$492,694	$205,921	$363,548	$167,733	**<0.01**	**0.70**
Second round of teprotumumab**	$20,805	$94,044	$20,208	$83,656	0.96	0.01
TED-related surgeries	$166.10	$710.50	$163.90	$653.40	0.98	0.003
TED-related medical drugs	$2.10	$10.12	$2.33	$14.94	0.88	-0.02
IV steroids	$6.75	$22.19	$8.29	$32.70	0.66	-0.05

TED = thyroid eye disease; IV = intravenous; SD = standard deviation
*The data reflects teprotumumab during Evaluation Window 1.
**The data reflects teprotumumab during Evaluation Window 2.
Persistent: Completed all 8 doses with ≤28 days between infusions
Nonpersistent: Did not complete all 8 doses or had >28 days between any 2 consecutive doses

Results

- A total of 278 members who newly initiated teprotumumab between January 1, 2022, and December 31, 2022—with a mean age of 50.3 years (SD=12.9); a mean ECI of 3.5 (SD=2.6); and within the commercial line of business (92.5%) and within Medicare and Medicaid lines of business, 6.5% and 1.0%, respectively—were included in the analysis. Of the 278 members, 120 members (43.2%) were classified as persistent, which was defined as completing all 8 doses with ≤28 days between infusions, and 158 members (56.8%) were nonpersistent, which was defined as not completing all 8 doses and/or having >28 days between any 2 consecutive doses. (Table 1)
- There were no statistically significant differences in demographic characteristics between the persistent and nonpersistent cohorts. (Table 2)
- The cost of first-round teprotumumab differed significantly between persistent and nonpersistent cohorts during Evaluation Window 1. The persistent cohort had a mean cost of $492,694 (SD=$205,921), while the nonpersistent cohort had a mean cost of $363,548 (SD=$167,733; *P*<0.001; Cohen's *d*=0.70). (Table 3)
- Clinical outcomes (member's second round of teprotumumab, utilization of TED-related surgeries or medical benefit medications, and use of IV steroids) and cost outcomes (cost associated with member's second round of teprotumumab, TED-related surgery or medical benefit medication costs, and IV steroid costs) did not differ significantly between the 2 cohorts during Evaluation Window 2. (Table 3)
- A Cohen's *h* or Cohen's *d* <0.10 indicates that group outcomes can be considered equivalent and effect sizes of 0.20–0.49 are considered small.[9] Across all nonsignificant outcomes in this study, 5 effect sizes were <0.10 and 2 were <0.20.

Limitations

- Limited follow-up time after teprotumumab treatment may not fully reflect barriers or delays in obtaining TED-related surgeries.
- Health-plan policy restrictions on teprotumumab retreatment may influence observed treatment patterns.
- Variability and lack of specificity in ICD-10-CM codes and TED-related surgeries may misidentify the study population. Claims cannot distinguish between moderate and severe TED, relapse severity, or time since diagnosis.
- Weight fluctuations during the evaluation window may have led to intra-member variability in dose. This variability was observed in the analysis, but further investigation into weight-related dose adjustment was not performed due to lack of infusion-day weight data. Future study could assess how use of fixed-baseline weight-based dosing strategies compare in terms of treatment costs and outcomes to day-of-infusion weight-based dosing strategies.
- System-level factors, including capacity limits, scheduling concerns, etc., may have been potential reasons, extending beyond clinical reasons, for nonpersistence.
- IV steroids as a claim proxy may capture utilization for conditions other than TED (e.g., unrelated autoimmune disease flare).
- Some claims documented drug waste using the "JW" procedure modifier, but others did not. After consulting with a key opinion leader, this was identified as an operational issue in which certain electronic health-record systems do not successfully transmit procedure modifier codes, inflating the teprotumumab spend.

Conclusions

- Approximately 40% of the 278 members completed the full 8-dose teprotumumab regimen with less than 28 days between infusions. Nearly 60% were nonpersistent because they did not complete all doses, took more than 28 days between at least 1 infusion, or met both criteria. These findings suggest that care coordination programs within medical pharmacy benefit management may help improve adherence and identify the reasons for nonpersistence.
- Cost analyses were consistent with prior literature that identifies teprotumumab as substantially more expensive than off-label therapies and surgical approaches. In this study, the average cost of an initial teprotumumab treatment round was significantly higher than TED-related medical drug and surgical costs.
- Across outcomes, Cohen effect sizes suggested equivalence or only small differences between the persistent and nonpersistent groups. These findings support the possibility that some nonpersistent patients may have milder disease or may reach clinical benefit before completing all 8 doses. Future studies with larger cohorts or partnerships with clinical sites could improve data robustness and enhance understanding of treatment patterns, adherence factors, and real-world patient outcomes.

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