Tofacitinib (Xeljanz®) Utilization Patterns and Persistency Among 4.4 Million Continuously Enrolled Commercially Insured Members Over Four Years

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Background

- Tofacitinib (Xeljanz®), an oral Janus kinase inhibitor, was approved on Nov. 6, 2012 to treat adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to methotrexate.[1]
- According to the prescribing information, tofacitinib may be used as monotherapy or in combination with methotrexate or other nonbiologic disease-modifying antirheumatic drugs (DMARDs). Tofacitinib should not be used in combination with biologic DMARDs.[1]
- There are many DMARD alternatives to tofacitinib including non-biologic DMARDs and biologic DMARDs. Biologic DMARDs are comprised of both tumor necrosis factor (TNF) inhibitors and non-TNF inhibitors.
- The American College of Rheumatology guidelines recommend non-biologic DMARDs as first line therapy for early and established RA, with methotrexate as the preferred agent. Tofacitinib is an option for second line therapy in patients with established RA.[2]
- In a retrospective cohort analysis of 455 patients with RA and at least one tofacitinib claim, therapy in the 12 months before tofacitinib therapy was: a nonbiologic DMARD for 80.0 percent of patients, a biologic DMARD for 66.8 percent, a TNF inhibitor for 42.0 percent and a non-TNF inhibitor biologic DMARD for 37.4 percent.[3]
- The wholesale acquisition cost of tofacitinib is over $42,000 per year.
- Due to limited tofacitinib long-term safety and efficacy information, it is important to understand tofacitinib real world utilization patterns and persistency in order to develop management strategies.

Objective

- To evaluate tofacitinib utilization patterns and persistency in order to optimize managed care pharmacy programs.

Methods

- Members in the analysis are from 12 Blue Cross and Blue Shield clients with a combined average commercially insured population of 13.8 million members per month.
- Prescription claims data were queried for tofacitinib claims among 4.4 million commercial members continuously enrolled and receiving pharmacy benefits from Prime Therapeutics LLC (Prime) from 2012 to 2015 and less than 70 years of age as of Dec. 31, 2015.
- The first tofacitinib claim in the data was found on Dec. 3, 2012. Members with at least one tofacitinib claim (earliest claim = index date) from Dec. 1, 2012 to Dec. 31, 2015 were included in the analysis. Tofacitinib utilizing members were followed from their index date through Dec. 31, 2015.
- The number of members with a tofacitinib claim in each month was tracked to determine the utilization trend.
- Medical claims were used to identify diagnoses of tofacitinib utilizers.
- Prior and concurrent DMARD assessment and the persistency analysis were limited to tofacitinib users with an RA diagnosis.
- Average member age was based on age as of Dec. 31, 2015.
- Prior and concurrent DMARD assessment
  - Prior DMARD use was defined as a DMARD claim in the 12 months preceding the tofacitinib index date or 11 months for the 13 members with a tofacitinib index date during Dec. 2012.
  - Concurrent DMARD therapy was defined as a DMARD claim between the tofacitinib index date and the last tofacitinib claim date plus days supply.
- Persistency analysis
  - Tofacitinib persistency was assessed via Kaplan-Meier (KM) analysis. Members were censored if they had a tofacitinib supply on Dec. 31, 2015 or had less than a 90-day gap in therapy since tofacitinib index date through Dec. 31, 2015.
  - Discontinuation was defined as a greater than 90-day gap in therapy after the end of a tofacitinib claim plus days supply. For example, if a tofacitinib claim was incurred on Jan. 1, 2015 with a 30-day supply, then discontinuation would be declared if the member had no subsequent tofacitinib claim by May 1, 2015 (Jan. 1, 2015 + 30-day supply + 90-day gap).
  - Tofacitinib duration of therapy was defined as the time between the tofacitinib index date and the last tofacitinib claim before discontinuation or censoring plus the days supply of the last tofacitinib claim.
  - The analyzable population follow-up time was calculated by averaging the numbers of days between the members' tofacitinib index date and Dec. 31, 2015.

Results

- Tofacitinib analyzable population identification **(Figure 1)**
  - 887 tofacitinib utilizers were identified from a commercially insured cohort of members continuously enrolled between Jan. 2012 and Dec. 2015 and less than 70 years of age as of Dec. 31, 2015.
  - 862 (97.2 percent) of the 887 tofacitinib utilizing, continuously enrolled, commercially insured members had an RA diagnosis.
    - Average age was 53.6 years and 78.9 percent were female
  - Of the 25 tofacitinib utilizers without an RA medical claim, these potential tofacitinib off-label indications were identified by reviewing the members' medical claims:
    - Alopecia (n = 10)
    - Vitiligo (n = 2)
    - Systemic lupus erythematosus (n = 1)
    - Ankylosing Spondylitis (n = 1)
    - Psoriasis (n = 1)
    - Unable to identify a diagnosis for which tofacitinib has a potential role in therapy (n = 10)
- Tofacitinib utilization per month among 4.4 million continuously enrolled commercially insured members from 2012 through 2015 **(Figure 2)**
  - 887 members had at least one tofacitinib claim from December 2012 through December 2015.
  - The utilization trend line equation is $y = 10.549X$, $R^2 = 0.987$, indicating the utilization growth rate was a consistent 10.5 commercially insured members per month (0.24 members per 100,000 commercially insured members per month).
  - Tofacitinib utilization increased from 13 utilizers (0.29 members per 100,000 commercially insured members) in the month of Dec. 2012 to 415 utilizers (9.34 members per 100,000 commercially insured members) in the month of December 2015.
- Prior and concurrent DMARD use in 862 tofacitinib utilizers with RA **(Table 1)**
  - In the year prior to initiating tofacitinib, 771 (89.4 percent) members had a claim for any DMARD, 432 (50.1 percent) for methotrexate, 642 (74.5 percent) for any non-biologic DMARD, 528 (61.3 percent) for any biologic DMARD, and 375 (43.5 percent) for any TNF inhibitor.
  - Of the 771 members with a DMARD claim in the year prior to initiating tofacitinib, 243 (31.5 percent) had a claim for only non-biologic DMARDs, 129 (16.7 percent) had a claim for only biologic DMARDs, and 399 (51.8 percent) had a claim for both biologic and non-biologic DMARDs.
  - During therapy with tofacitinib, 485 (56.3 percent) members had a claim for any DMARD, 299 (34.7 percent) for methotrexate, 458 (53.1 percent) for any non-biologic DMARD, and 61 (7.1 percent) for any biologic DMARD.
- Tofacitinib Kaplan-Meier (KM) derived persistency for 862 members with RA **(Figure 3)**
  - 16.6 months (497 days) mean and 15.7 months (472 days) median tofacitinib follow-up (tofacitinib initiation to Dec. 31, 2015)
  - The tofacitinib KM discontinuation rates were:
    - 30.2 percent at 6 months
    - 44.3 percent at 12 months
    - 53.2 percent at 18 months
    - 57.1 percent at 24 months
  - 25 percent of members discontinued tofacitinib at 4.9 months (147 days) and 50 percent of members discontinued at 15.6 months (469 days).

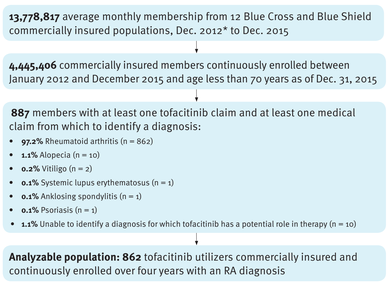
Limitations

- The data used in this study is limited to a continuously enrolled commercial population in the United States. Findings may not be generalizable to Medicare or Medicaid populations or other geographic regions.
- Administrative pharmacy and medical claims have the potential to be miscoded and include assumptions of members' drug utilization, medication taking behaviors and diagnoses.
- The study design assessed previous DMARD use for a year prior to each member's first tofacitinib claim and did not account for medications taken more than a year before the first tofacitinib claim.
- 57 percent of the members in the KM analysis were censored, which could have produced a less reliable persistency curve beyond 24 months. The actual duration of therapy in these members is unknown.
- Utilization patterns may have been influenced by tofacitinib prior authorization criteria that was active for approximately 80 percent of the analyzed population.

Conclusions

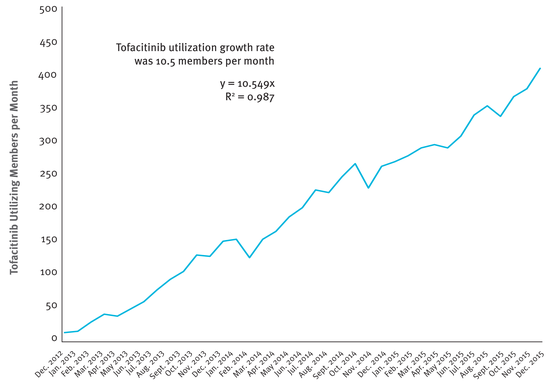
- Although tofacitinib utilization has been low, it has increased steadily since the drug's approval at a rate of 0.24 members per 100,000 commercially insured members per month.
- Despite tofacitinib being identified in the American College of Rheumatology Guidelines[2] as a second line therapy option in patients with established rheumatoid arthritis, 1 in 10 tofacitinib utilizers had no disease-modifying antirheumatic drug (DMARD) claim in the year prior to initiating therapy. About 3 of 4 tofacitinib utilizers had a non-biologic DMARD claim prior to initiating therapy, in accordance with the guidelines.[2]
- The prior DMARD use assessment results in this study were similar to those in a retrospective cohort analysis of 455 patients with RA and at least one tofacitinib claim.[3] Presence of a prior nonbiologic DMARD claim was 74 percent in this study versus 80 percent in the retrospective cohort analysis, a biologic DMARD claim was 61 percent versus 67 percent, a tumor necrosis factor (TNF) inhibitor claim was 44 percent versus 42 percent, and a non-TNF inhibitor biologic DMARD claim was 25 percent versus 37 percent.[3]
- At six months, three of 10 members discontinued tofacitinib and more than four of 10 discontinued at one year follow-up. As RA is a chronic disease, this is a high discontinuation rate after a short period of therapy. Providers and payers should look for ways to improve persistency and consider outcomes based contracts where managed care organization reimbursement from pharmaceutical manufacturers is linked to tofacitinib adherence and persistency.
- Payers should develop care and utilization management programs that encourage adherence, persistency and the most cost effective RA treatment strategies. These programs should emphasize the use of a nonbiologic DMARD, preferably methotrexate, as first line therapy in RA and prevent the use of tofacitinib with biologics.

Figure 1. Tofacitinib (Xeljanz) Analyzable Population Identification



* Tofacitinib was Food and Drug Administration (FDA) approved on Nov. 6, 2012 for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to methotrexate. The first tofacitinib claim in the data was found in December 2012.

Figure 2. Tofacitinib (Xeljanz) Utilization per Month among 4.4 Million Continuously Enrolled Commercially Insured Members from 2012 through 2015



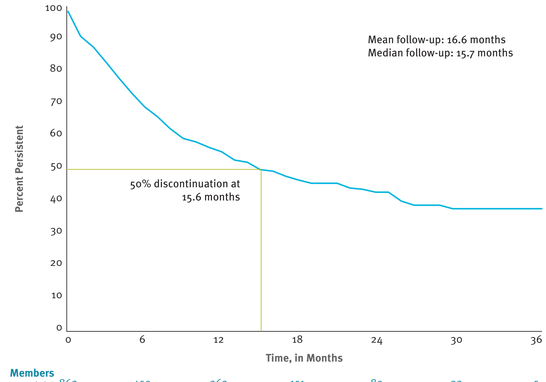
Eligibility: 887 members in this graph were commercially insured, continuously enrolled from 2012 to 2015, and less than 70 years of age as of Dec. 31, 2015 with at least one tofacitinib claim from December 2012 through December 2015.

Table 1. Prior and Concurrent Disease-Modifying Antirheumatic Drug (DMARD) Use in 862 Tofacitinib (Xeljanz) Utilizers with Rheumatoid Arthritis

DMARD Class		DMARD	Number of members with any claim in 12 months before tofacitinib (%)		Number of members with any claim during treatment with tofacitinib (%)	
Non-biologic DMARDs*		Hydroxychloroquine	202	(23.4%)	146	(16.9%)
		Sulfasalazine	79	(9.2%)	45	(5.2%)
		Methotrexate	432	(50.1%)	299	(34.7%)
		Leflunomide	167	(19.4%)	99	(11.5%)
		Any non-biologic DMARD	642	(74.5%)	458	(53.1%)
Biologic DMARDs	Tumor Necrosis Factor (TNF) Inhibitors	Infliximab	29	(3.4%)	0	(0.0%)
		Etanercept	96	(11.1%)	4	(0.5%)
		Adalimumab	222	(25.8%)	12	(1.4%)
		Golimumab	28	(3.2%)	5	(0.6%)
		Certolizumab	62	(7.2%)	6	(0.7%)
		Any TNF inhibitor	375	(43.5%)	26	(3.0%)
	Other biologic DMARDs	Abatacept	101	(11.7%)	7	(0.8%)
		Anakinra	3	(0.3%)	0	(0.0%)
		Rituximab	34	(3.9%)	9	(1.0%)
		Tocilizumab	99	(11.5%)	19	(2.2%)
		Any of the other biologic DMARDs	215	(24.9%)	35	(4.1%)
	Any of the above biologic DMARDs		528	(61.3%)	61	(7.1%)
No DMARD			91	(10.6%)	377	(43.7%)
Any DMARD			771	(89.4%)	485	(56.3%)
	Only non-biologic DMARDs		243	(31.5%)	424	(87.4%)
	Only biologic DMARDs		129	(16.7%)	27	(5.6%)
	Both biologic and non-biologic DMARDs		399	(51.8%)	34	(7.0%)

*In addition, 29 (3.4%) members had prior use of azathioprine, 2 (0.2%) had prior use of cyclosporine, and 1 (0.1%) had prior use of auranofin.

Figure 3. Tofacitinib (Xeljanz) Kaplan-Meier (KM) Derived Persistency for 862 Members with Rheumatoid Arthritis (RA)



Discontinuation was defined as a greater than 90-day gap in therapy from the end of a tofacitinib claim plus days supply and the next tofacitinib claim. For example, if a tofacitinib claim was incurred on Jan. 1, 2015 with a 30-day supply, then discontinuation would be declared if the member had no subsequent claim by May 1, 2015 (Jan. 1, 2015 + 30-day supply + 90-day gap).

Eligibility: 862 members in this graph were commercially insured, continuously enrolled from 2012 to 2015, and less than 70 years of age as of Dec. 31, 2015 with at least one tofacitinib claim from December 2012 through December 2015 and a diagnosis of RA.

Censoring occurred when a member had a tofacitinib supply on Dec. 31, 2015 or had less than a 90-day gap in therapy since tofacitinib initiation through Dec. 31, 2015.

*Members at risk: Members who did not discontinue therapy and were not censored up to and including the time point shown on the graph are at risk of discontinuing therapy or being censored in the future.

References

1. XELJANZ (tofacitinib) [package insert]. New York City, New York: Pfizer; Revised June 2015.
2. Singh JA, Saag KG, Bridges SL Jr, *et al.* Arthritis Rheumatol. 2016 Jan;68(1):1-26.
3. Harnett J, Curtis JR, Gerber R, et al. Clin Ther. 2016 Jun;38(6):1451-63.

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