Comparative Effectiveness of Allopurinol and Febuxostat in Lowering Serum Uric Acid in a Large US Commercially Insured Population

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  - Bhavik J. Pandya
    - Employee of Takeda Pharmaceuticals International, Inc., at time of study
  - Gabriel Gomez Rey
    - Employee of OptumInsight
  - Brett W. Pinsky
    - Employee of OptumInsight

BACKGROUND

- Gout affects an estimated 8.3 million Americans (4% of the US population).(1)
- Allopurinol is the most commonly used treatment for hyperuricemia, defined as serum uric acid (sUA) >7.0 mg/dL for men and >6.0 mg/dL for women.
- Nonadherence and intolerance to allopurinol can lead to treatment failure.(2)
- Febuxostat was approved by the FDA in February 2009 for the chronic management of hyperuricemia in gout patients.(3)
- A target for improving gout care is to lower sUA to ≤6.0 mg/dL.(4)


OBJECTIVE

- To assess the comparative effectiveness of allopurinol (at a dose of 300 mg) and febuxostat (at doses of 40 mg and 80 mg) in lowering sUA in real-world managed care settings in the United States.

METHODS: Study Sample

- Retrospective claims database analysis utilizing 2009-2010 medical and pharmacy claims and outpatient laboratory data from a large US health plan affiliated with OptumInsight (formerly Innovus) for commercial and Medicare Advantage health plan members with gout
- Index dose of allopurinol and febuxostat within the recommended dose range

Inclusion criteria for final patient sample:
- Adults with ≥1 medical claim with gout diagnosis (ICD-9-CM 274.xx in any position)
- ≥1 fill for either allopurinol or febuxostat between 2/1/2009 and 3/31/2010 (identification period)
- Date of first febuxostat or allopurinol fill was defined as the index date.
- Continuous enrollment for 6 months prior to the index date (pre-index period) and 23 months after and including index date (post-index period)
- No evidence of cancer during study period
- ≥1 sUA lab test (CPT codes 84550, 84560) result available 14 days after index date
METHODS: Cohort Assignment

- Febuxostat cohort: Patients who initiated on febuxostat during the identification period
- Regardless of prior allopurinol use
  - As further analyses, categorized as new febuxostat users versus those who switched to febuxostat
- Allopurinol cohort: Patients who initiated on allopurinol during the identification period

METHODS: Outcomes

sUA Measurement

- sUA test values were captured during the pre- and post-index periods.
- Pre-index sUA was calculated as both the average sUA value and the final sUA value during the pre-index period.

Outcomes Measures

- Effectiveness of lowering sUA was examined as:
  - Change in sUA from baseline period to first available sUA at least 14 days into the post-index period; and
  - Percentage of patients achieving sUA goal of <6.0 mg/dL
  - Sensitivity analysis using sUA goal of <5.0 mg/dL
- Demographic and clinical characteristics, including Quan-Charlson Comorbidity Index score, were assessed for the two cohorts during the pre-index period.

RESULTS

- 6,331 patients were identified
  - allopurinol (N=5,880)
  - febuxostat (N=451)
- Compared to allopurinol, the febuxostat cohort had differed significantly with regard to:
  - lower mean age (55.4 vs. 57.0)
  - lower % of patients residing in the Midwest (5.8 vs. 9.8) and higher % of patients residing in the South (75.7 vs. 70.6)
  - higher % of patients commercially insured (85.1 vs. 79.5) and lower % of patients enrolled in Medicare Advantage plans (14.9 vs. 20.5)
  - higher mean Quan-Charlson Comorbidity Index score (1.4 vs. 1.0)

RESULTS: Serum Uric Acid (sUA)

<table>
<thead>
<tr>
<th>sUA Laboratory Results</th>
<th>Febuxostat (N=451)</th>
<th>Allopurinol (N=5,880)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre index sUA results</td>
<td>N (%)</td>
<td>N (%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pre-index: patients with sUA results</td>
<td>312 (69.2%)</td>
<td>2445 (41.6%)</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>1.47 (0.82)</td>
<td>1.25 (0.54)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Final sUA (mg/dL)</td>
<td>8.53 (2.02)</td>
<td>7.80 (2.16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Average sUA (mg/dL)</td>
<td>8.70 (1.73)</td>
<td>7.84 (2.19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-index sUA results</td>
<td>Mean number of sUA results</td>
<td>1.67 (1.09)</td>
<td>1.61 (1.11)</td>
</tr>
<tr>
<td>Average sUA result (mg/dL)</td>
<td>6.44 (2.12)</td>
<td>6.48 (1.71)</td>
<td>0.713</td>
</tr>
</tbody>
</table>

1 All patients were required to have at least 1 post-index sUA result.

Multivariable-adjusted Change in sUA

<table>
<thead>
<tr>
<th>Outcome *</th>
<th>Parameter Estimate</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in sUA†</td>
<td>0.50</td>
<td>1.71</td>
<td>(1.39 - 2.11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Goal attainment (sUA &lt;6.0 mg/dL)‡</td>
<td>2.06</td>
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<td>(1.65 - 2.57)</td>
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*Reference group: Allopurinol
†Calculated by ordinary least squares regression
‡Calculated by logistic regression
**Limitations**

- Degree to which claims data can accurately capture an individual’s medical history is limited.
- Claims data provide excellent insight into real-world treatment patterns, but they are subject to possible coding errors.
- Presence of a prescription claim does not necessarily mean the drug was consumed, or taken as prescribed.
- Results of this analysis are primarily applicable to the patterns of febuxostat and allopurinol use in gout patients in stable managed care settings, and may not be generalizable to other populations such as non-insured or Medicaid-insured patients.

**CONCLUSION**

- Compared to allopurinol patients, febuxostat patients had higher likelihood of achieving target SUA levels <6.0 mg/dL and <5.0 mg/dL.
- Likelihood of achieving target SUA levels <6.0 mg/dL and <5.0 mg/dL was similar for febuxostat new users as well those who switched to febuxostat.

**Acknowledgements**

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- OptumInsight was hired by Takeda to conduct this study.