[redacted] ABSTRACT

Title

Drug Utilization Study to Describe the Pattern of Febuxostat Use in Relationship to Allopurinol Following Addition of the Boxed Warning and Modification of the Indication Based on the Results of the CARES Trial

Keywords

Drug Utilization, Febuxostat, Gout, Cardiovascular Disease, Urate Lowering Therapy

Rationale and Background

Following the Cardiovascular Safety of Febuxostat and Allopurinol in Patients with Gout and Cardiovascular Morbidities (CARES) trial, the United States (US) Food and Drug Administration (FDA) approved updates to the febuxostat prescribing information and added a boxed warning for cardiovascular death. In addition, the indication for febuxostat was revised to focus on patients who are allopurinol intolerant. FDA required Takeda (post-marketing commitment [PMC] 3579-1) to conduct this drug utilization study to describe the impact of these labeling changes on the dispensing patterns for febuxostat.

Research Question and Objectives

The research questions were to evaluate the impact of the 2019 labeling changes (boxed warning and modified indication) on febuxostat utilization. The objectives of the study were:

1. To describe the number and proportion of patients initiating febuxostat as new versus prevalent new users of urate lowering therapy (ULT).
2. To describe the number and proportion of febuxostat users with established cardiovascular disease (CVD).

Study Design

This was a descriptive non-interventional cross-sectional study.

Setting

The study setting was 2 large national administrative claims databases in the US.

Subjects and Study Size

The study population included patients with gout initiating febuxostat therapy on or after 01 June 2016. The date of the first febuxostat prescription was defined as the index date. The feasibility assessment identified 11,683 and 8389 patients who initiated febuxostat between June 2016 and September 2019 in the PharMetrics Plus database and the Optum's Clinformatics Data Mart, respectively.

Variables and Data Sources

Data were collected on febuxostat and allopurinol use, established CVD, morbidities of interest, concomitant medication use, and patient demographic characteristics in the IQVIA PharMetrics Plus database and the Optum Research Database (ORD).

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Results

Of 13,848 patients in the PharMetrics Plus cohort, 5913 (42.7%) were new users of febuxostat and 7935 (57.3%) were prevalent new users. In the ORD cohort, 4127 (40.5%) of the 10,198 patients were new users and 6071 (59.5%) were prevalent new users. Across the three study periods, the most common established CVD morbidity in the 12 months prior to initiation of febuxostat was diabetes mellitus (28% [PharMetrics Plus] and 47% [ORD]), followed by ischemic heart disease (17% [PharMetrics Plus] and 33% [ORD]), and heart failure/cardiomyopathy (13% [PharMetrics Plus] and 28% [ORD]). There was a higher proportion of new users with pre-existing heart failure/cardiomyopathy in the post-labeling change period (14.2% [PharMetrics Plus] and 32.9% [ORD]) compared to the baseline period (10.4% [PharMetrics Plus] and 26.0% [ORD]).

Discussion

The number of febuxostat users decreased across the three study periods, presumably due to the label change. Although an increase in the proportion of new users with pre-existing heart failure/cardiomyopathy was observed, the number of new users with pre-existing heart failure/cardiomyopathy decreased over the course of the study; this was because the denominator (the number of new users) decreased more steeply than the number of new users with heart failure/cardiomyopathy. The decrease in number of new users was also supported by the three most recent Periodic Benefit-Risk Evaluation Reports for febuxostat. The information presented in this study does not change the benefit-risk-profile of febuxostat.

Marketing Authorization Holder(s)

Takeda Pharmaceuticals U.S.A. Inc.

Names and Affiliations of Principal Investigators

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