Assessment of Dronedarone Utilization Using US Claims Databases

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ABSTRACT

Background: A dronedarone utilization study using US MarketScan and InVision Data Mart databases was conducted to estimate the prevalence of the following: (1) dronedarone use in contraindicated patients with worsening heart failure (HF) or hospitalization for HF within 1 month before dronedarone prescription; (2) concomitant prescribing of contraindicated drugs; and (3) recommended creatinine testing after dronedarone initiation among dronedarone users.

Methods: In this retrospective cohort study, data in the MarketScan database between July 20, 2009, and December 31, 2011, and in the InVision Data Mart database between July 20, 2009, and March 31, 2012, were analyzed. The study population included patients who received ≥1 dronedarone prescription during the study period. The following variables were reported: worsening of or hospitalization for HF, concomitant prescribing of potent cytochrome P450 CYP 3A4 inhibitors or QT-prolonging drugs, and creatinine testing.

Results: There were 31,408 and 7025 dronedarone users identified in the MarketScan and InVision Data Mart databases, respectively. Approximately 86% to 90% of patients had a diagnosis of atrial fibrillation in each database. In the MarketScan database, 40% were women and 54% were aged ≥65 years. In the InVision Data Mart database, 31% were women and 32% were aged ≥65 years. The corresponding prevalence of worsening or hospitalization for HF was 6.4% (95% CI, 6.2–6.7) and 4.7% (95% CI, 4.2–5.2) in each database, respectively. The corresponding estimates of concomitant prescribing of potent cytochrome P450 CYP 3A4 inhibitors and QT-prolonging drugs within 30 days before initiation or refilling of dronedarone were 2.0% (95% CI, 1.8–2.1) and 10.0% (95% CI, 9.7–10.4), respectively, in the MarketScan database, and 2.3% (95% CI, 2.0–2.7) and 11.2% (95% CI, 10.5–12.0) in the InVision Data Mart database. More than 50% of patients in each database had serum creatinine tests conducted after dronedarone initiation.

Conclusions: The results of the present analysis based on a long-term follow-up (nearly 3 years) were consistent with the previous findings that dronedarone has mostly been used appropriately in compliance with US prescribing in the target populations. (*Clin Ther*. 2014;36:264–272)

Key words: dronedarone, drug utilization, Risk Evaluation and Mitigation Strategy.

INTRODUCTION

Dronedarone, a multichannel blocker displaying antiarrhythmic properties, has been shown to be effective for reducing the risk of cardiovascular hospitalization or death in patients with atrial fibrillation (AF) and atrial flutter (AFL).[1,2] In the United States, dronedarone was approved as "an antiarrhythmic drug indicated to reduce the risk of cardiovascular hospitalization in patients with paroxysmal or persistent AF or AFL, with a recent episode of AF/AFL and associated cardiovascular risk factors (ie, age >70, hypertension, diabetes, prior cerebrovascular accident, left atrial diameter ≥50 mm or left ventricular ejection fraction [LVEF] <40%), who are in sinus rhythm or who will be cardioverted."[1] Based on the

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nonclinical and clinical safety information collected throughout an extensive development program, dronedarone is contraindicated in the United States in patients taking potent cytochrome P450 (CYP) 3A4 inhibitors that significantly raise serum levels of dronedarone. It is also contraindicated in patients taking drugs that prolong the QT interval and may induce torsade de pointes. In addition, dronedarone is contraindicated in patients with symptomatic heart failure (HF) with recent decompensation requiring hospitalization or New York Heart Association (NYHA) class IV HF. It is also contraindicated in patients in permanent AF who will not or cannot be cardioverted into normal sinus rhythm. In patients with permanent AF, dronedarone doubles the risk of death, stroke, and hospitalization for HF.[3]

In clinical trials, an increase in serum creatinine level was observed in patients treated with dronedarone 400 mg BID.[1] This increase occurs early after treatment initiation and reaches a plateau after 7 days. The US prescribing information for dronedarone states that renal function should be monitored periodically in patients treated with dronedarone because increases in creatinine and blood urea nitrogen have been reported in the postmarketing setting and seem to be reversible after discontinuation of dronedarone.[1]

In the United States, in addition to labeling and other pharmacovigilance action plan, a Risk Evaluation and Mitigation Strategy (REMS) program has been developed to prevent dronedarone use in: (1) patients with symptomatic HF with recent decompensation requiring hospitalization or with NYHA class IV HF; and (2) patients with permanent AF who will not or cannot be cardioverted into normal sinus rhythm. The REMS educates prescribers through a comprehensive communication plan about increased mortality when dronedarone is used in these patient populations and informs patients about the serious risks of dronedarone, including increased mortality in patients with severe unstable HF or permanent AF, through a medication guide.

To characterize dronedarone utilization patterns in the US population and to assess labeling compliance and the effectiveness of the REMS, a drug utilization study using the InVision Data Mart database has been conducted since 2009.[4] The first publication based on data between July 2009 and August 2010 demonstrated labeling compliance and effectiveness of the REMS regarding worsening HF. However, because InVision Data Mart is an employment-based private insurance claims database, it has a lower proportion of patients aged $\geq$65 years (9% in the InVision Data Mart vs 13% in the US population[5]), whereas AF and AFL are more prevalent in elderly patients than in the general population.[2,6] Thus, the MarketScan database, which is composed of MarketScan Commercial Claims and Encounters database, the Medicare Supplemental database, and the Medicaid database, was added in the study to improve the representation of elderly patients. The MarketScan Medicare Supplemental database captures Medicare-eligible retirees with employer-sponsored Medicare supplemental plans. The age and gender distribution in the MarketScan Medicare Supplemental database is compatible to the overall Medicare population (MarketScan vs Medicare: age 65–74 years, 55% vs 45%; age 75–84 years, 29% vs 26%; age $\geq$85 years, 12% vs 12%; male sex, 45% vs 45%).[7] The MarketScan database has been used in a number of studies of patients with AF.[8–11]

The current article presents results from a long-term follow-up (nearly 3 years) for evaluation of dronedarone utilization patterns in the US population by using both the MarketScan and the InVision Data Mart databases.

MATERIALS AND METHODS

Data Source

The study used the US MarketScan Commercial Claims and Encounters database, the Medicare Supplemental database, and the Medicaid database from Thomson Reuters Corporation (New York, New York). The databases are composed of de-identified patient-level records from >170 million patients since 1995. The MarketScan Commercial Claims and Encounters database includes private sector health data from 150 employers and 21 health plans. The Medicare Supplemental database captures Medicare-eligible retirees with employer-sponsored Medicare supplemental plans. On average, nearly 3.8 million lives (active patients) are covered per year. The Medicaid database contains the pooled health care experience of ~7 million Medicaid enrollees from 12 states. On average, nearly 6.8 million lives (active patients) are covered per year. The MarketScan databases are in compliance with the Health Information Portability and Accountability Act of 1996.[12]