Evaluation of Dronedarone Use in the US Patient Population Between 2009 and 2010: A Descriptive Study Using a Claims Database

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ABSTRACT

Background: The utilization pattern of dronedarone was unknown, especially regarding prescribers' compliance with the product's prescribing information (PI) following its availability and the implementation of the Food and Drug Administration–approved risk evaluation and mitigation strategy for the drug in the United States.

Objective: This study was designed to evaluate the dronedarone prescribers' adherence to PI regarding the following contraindications: (1) patients with heart failure (HF) with a recent decompensation requiring hospitalization or referral to a specialist, (2) concomitant use of potent CYP3A4 inhibitors, and (3) concomitant use of QT-prolonging drugs.

Methods: Patients prescribed dronedarone between July 2009 and August 2010 were identified through LabRx. The following rates surrounding dronedarone use were examined: (1) atrial fibrillation or atrial flutter in the past year, (2) worsening or hospitalization for HF within the month before prescription, and (3) concomitant prescription of potent CYP3A4 inhibitors and concomitant prescription of QT-prolonging drugs within the following month.

Results: A total of 4595 dronedarone prescriptions were filled by 1820 patients. More than 94% of the participants had ≥1 diagnosis of atrial fibrillation or atrial flutter in the previous year. Worsening of or hospitalization for HF was found in 61 (3.4%) patients within the month before receiving dronedarone, including 18 patients with HF as the primary cause for hospitalization. Potent CYP3A4 inhibitors were prescribed to 10 (0.6%) patients within a month following dronedarone initiation, 6 of whom received them for topical use only. QT-prolonging drugs were prescribed to 67 (3.7%) patients within a month following dronedarone initiation, among which >90% were other antiarrhythmics.

Conclusions: Dronedarone was used mostly in compliance with PI and risk evaluation and mitigation strategy in the studied population. In the LabRx database, dronedarone was commonly dispensed to patients with cardiovascular risk factors and rarely dispensed to patients with contraindications such as worsening HF or hospitalization for HF or with concomitant prescriptions of potent CYP3A4 inhibitors, QT-prolonging drugs, or both. (*Clin Ther*. 2011;33:1483–1490)

Key words: dronedarone, heart failure, potent CYP3A4 inhibitors, QT-prolonging drugs, risk evaluation and mitigation strategy.

INTRODUCTION

Dronedarone is a multichannel blocker designed to eliminate the noncardiovascular toxicities associated with amiodarone.[1] It was originally developed as an antiarrhythmic for the prevention of atrial fibrillation (AF) or atrial flutter (AFL) recurrences in patients with nonpermanent AF/AFL (ie, paroxysmal and persistent AF/AFL).[2] However, based on ATHENA (A Placebo-Controlled, Double-Blind, Parallel Arm Trial to Assess the Efficacy of Dronedarone 400 mg BID for the Prevention of Cardiovascular Hospitalization or Death From Any Cause in Patients With Atrial Fibrillation/Atrial Flutter [AF/AFL]), a large outcomes trial in patients with AF/AFL, dronedarone was approved for the

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reduction of cardiovascular hospitalizations in nonpermanent AF/AFL in the United States.[3–4] Dronedarone is specifically indicated to reduce the risk of cardiovascular hospitalization in patients who have paroxysmal or persistent AF/AFL, who have had a recent episode of AF/AFL and have associated cardiovascular risk factors (ie, age >70, hypertension, diabetes, prior cerebrovascular accident, left atrial diameter ≥50 mm or left ventricular ejection fraction <40%), who are in sinus rhythm, or who will undergo cardioversion.[4]

Before ATHENA, an evaluation of dronedarone in patients with advanced heart failure (HF) and recent decompensation (ANDROMEDA) was conducted and was terminated early because of an increased risk of mortality observed with dronedarone.[5] Although dronedarone represented the first and only antiarrhythmic treatment for AF/AFL with proven outcomes benefits, patients who should not receive the drug owing to increased risk were also defined during its development. To ensure the appropriate use of dronedarone to maximize its benefit:risk profile, a risk evaluation and mitigation strategy (REMS) was designed for dronedarone that was part of the basis of the Food and Drug Administration's approval, similar to the REMS programs used for many other drugs. The REMS program for dronedarone was specifically developed to prevent dronedarone use in patients with the New York Heart Association (NYHA) Class IV HF or NYHA Class II to III HF with a recent decompensation requiring hospitalization or referral to a specialized HF clinic—that is, patients included in the ANDROMEDA study. The REMS educates prescribers through a comprehensive communication plan about increased mortality when dronedarone is used in that patient population and informs patients through a medication guide about the serious risks of dronedarone, including increased mortality in patients with severe unstable HF. With the focus on worsening HF or hospitalization for HF, the goal of the REMS is that at least 90% of patients started on dronedarone will not have had worsening HF or have been hospitalized with HF during the month prior to their prescription.

Based on ATHENA and ANDROMEDA, among other trials,[2,3,5] dronedarone is also labeled as contraindicated in the United States in patients taking potent CYP3A4 inhibitors that significantly raise serum dronedarone levels owing to their interaction.[4] It is also contraindicated in patients taking drugs that prolong the QT interval and may induce torsades de pointes because of drug interactions.[4]

To evaluate the prescribers' adherence to prescribing information (PI) regarding the contraindications for patients with worsening HF or hospitalization for HF and concomitant use of potent CYP3A4 inhibitors and/or QT-prolonging drugs following REMS implementation for dronedarone, and to describe dronedarone's general utilization patterns among US patients, we conducted this study using the LabRx (United Healthcare) database. LabRx (InVision Data Mart, OptumInsight, Eden Prairie, Minnesota) is an integrated medical and prescription claims database. In general, LabRx is representative of the broader US population in terms of age, gender, and regional distributions. Since LabRx is an employment-based, private insurance claims database, it has a lower rate of patients aged 65+ years (6% in the LabRx vs 12% in the US population). However, because of its large size, this database may provide sufficient numbers of patients, including a subgroup aged 65+ years, and thus a reliable evaluation of the outcomes of interest.

METHODS

Study Population

In this study, the analysis was performed among all patients who were prescribed dronedarone at least once as identified in the LabRx database between July 20, 2009 (the launch date of dronedarone in the United States), and August 16, 2010 (the date of the latest data update received from the database vendor for the current analyses).

Exposure Measurement

Exposure to dronedarone was defined as 1 or more filled prescriptions for dronedarone. The National Drug Code (NDC) was used to identify dronedarone in the LabRx database. The NDC is a code set that serves as a universal product identifier for human drugs and biologics in the United States.[6]

The exposure start date (baseline of the study cohort or index date) for each patient was defined as the dispensing date of the first dronedarone prescription. The treatment duration on dronedarone begins accumulating on the first day of dronedarone prescription and continues with the subsequent dronedarone prescriptions until (1) the end of the dronedarone days supplied, (2) the enrollment end of membership, or (3) the end of the observation period, whichever occurred