

Letters

**RESEARCH LETTER**

Initial Experience Prescribing Commercial Tafamidis, the Most Expensive Cardiac Medication in History

Tafamidis is a stabilizer of the transthyretin (TTR) protein tetramer, which was recently shown to reduce all-cause mortality and cardiovascular hospitalizations. Tafamidis was approved by the US Food and Drug Administration on May 3, 2019, for the treating TTR amyloid cardiomyopathy and has a list price of $225 000 per annum. A recent study showed that tafamidis exceeds conventional cost-effectiveness thresholds. In this article, we describe our early experience in prescribing commercial tafamidis. All patients with an established diagnosis of TTR amyloid cardiomyopathy who presented to the Oregon Health & Science University Multidisciplinary Amyloidosis Program and received a prescription for commercial tafamidis were included in the analysis. We did not intentionally exclude women, but all of our consecutive cohort were men. Approval and a waiver of consent because of minimal risk for participants were obtained from the institutional review board of Oregon Health & Science University.

From May through November 2019, 50 consecutive patients (mean [SD] age, 76 [8] years) were prescribed tafamidis and 43 patients (86%) successfully obtained the drug. Only 1 patient (2%) did not have prescription insurance, while 38 patients (76%) had Medicare Part D, 6 (12%) had private insurance, 2 (4%) had Veterans Affairs insurance, and 3 (6%) had other types. Of the 7 (14%) who did not obtain tafamidis, 3 could not afford the out-of-pocket cost, 2 declined further attempts at drug procurement, 1 died before receiving tafamidis, and 1 elected to enroll in a research study. The mean (SD) cost of a 30-day supply of tafamidis was $23 485 ($2). All prescriptions required prior authorization (3 patients [6%] required a prior authorization appeal). Prior to financial assistance, the median and mean (SD) 30-day out-of-pocket costs of tafamidis were $1909 (range, $250-$3144) and $3082 ($5216), respectively ( insurers covered a mean [SD] 89% [17%] of the total tafamidis cost). Fifteen patients (30%) qualified for copayment assistance from a foundation and an additional 13 (26%) received financial assistance from the manufacturer (Table). All patients who qualified for financial assistance paid $0, while the median and mean (SD) 30-day out-of-pocket costs of tafamidis for patients without financial assistance were $250 (range, $39-$1763) and $1683 ($858), respectively (Figure). The median time from prescribing to mailing tafamidis was 26 (range, 12-78) days.

Our initial experience prescribing tafamidis demonstrates that the current system depends heavily on copayment assistance programs. Regulations instituted in 2005 by the US Office of the Inspector General and the US Department of Health and Human Services aimed to ensure compliance of the patient assistance programs with the Anti-Kickback Statute. The most pertinent regulation to patients is that the assistance should be based on reasonable and consistent measures of financial need, requiring certain thresholds to be put in place under which patients may qualify for assistance. There are many elderly individuals who do not qualify for assistance based on these thresholds but have other preexisting competing financial commitments that prohibit them from being able to afford the costly copayments. In addition to these eligibility stipulations, the funds in these nonprofit foundations are liable to run out. We have experienced periods during which programs have closed temporarily, causing tremendous uncertainty for patients. In our experience, some of the patients who were initially denied manufacturer assistance had success with an additional level of appeal. In these cases, patients directly appealed to the manufacturer with more granular explanations of unaccounted financial obligations and hardship that may not be captured on an income tax report. Finally, we have an integrated multidisciplinary amyloidosis...
program, a specialty pharmacy, and a dedicated pharmacist who spent an average of 1 hour per patient to ensure they can afford tafamidis. As such, our experience might not be easily applicable to other health care settings.

Ahmad Masri, MD, MS  
Hongya Chen, PharmD  
Catherine Wong, MD  
Katherine L. Fischer, MSN, RN  
Chafic Karam, MD  
Walid F. Gellad, MD, MPH  
Stephen B. Heitner, MD

Author Affiliations: The Knight Cardiovascular Institute, Oregon Health & Science University, Portland (Masri, Chen, Wong, Fischer, Heitner); Oregon Health & Science University Amyloidosis Center, Portland (Masri, Chen, Wong, Fischer, Karam, Heitner); Department of Neurology, Oregon Health & Science University, Portland (Karam); Center for Pharmaceutical Policy and Prescribing, Division of General Internal Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania (Gellad).

Accepted for Publication: April 2, 2020.

Corresponding Author: Ahmad Masri, MD, MS, Oregon Health and Science University, 3181 SW Sam Jackson Rd, Mail Code: UHN-62, Portland, OR 97239 (masri@ohsu.edu).

Published Online: June 17, 2020. doi:10.1001/jamacardio.2020.1738

Author Contributions: Dr Masri had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Masri, Wong, Heitner.

Acquisition, analysis, or interpretation of data: Masri, Chen, Fischer, Karam, Gellad, Heitner.

Drafting of the manuscript: Masri, Heitner.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Masri, Heitner.

Administrative, technical, or material support: Masri, Chen, Fischer, Karam, Heitner.

Supervision: Masri, Chen, Heitner.

Conflict of Interest Disclosures: Dr Masri reported grants from Pfizer and Alcece outside the submitted work. Dr Heitner reported grants and personal fees from Pfizer, Eidos, Ionis, and Alcece during the conduct of the study and grants and personal fees from Pfizer, Eidos, Ionis, and Alcece outside the submitted work. No other disclosures were reported.

Assessment of QT Intervals in a Case Series of Patients With Coronavirus Disease 2019 (COVID-19) Infection Treated With Hydroxychloroquine Alone or in Combination With Azithromycin in an Intensive Care Unit

The novel coronavirus disease 2019 (COVID-19) outbreak is an ongoing situation caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).1 Studies in patients with mild to moderate COVID-19 symptoms have suggested benefits of hydroxychloroquine alone or in combination with azithromycin against SARS-CoV-2 and raised hope for treating the disease.2 As a result, these treatments are increasingly used off-label for patients with COVID-19, including for those in intensive care units (ICUs).2,3 However, both medications are known to induce QT prolongation via a human Ether-à-go-go–related gene potassium channel blockade, which can promote life-threatening ventricular arrhythmias.4,5 Safety data for these treatments are largely lacking for patients with COVID-19. This is even more relevant for critically ill patients who are particularly exposed to electrolyte imbalance and/or drugs leading to an increased risk of QT prolongation.6 Therefore, we aimed to examine the safety of hydroxychloroquine with or without azithromycin regarding QT interval in ICU patients with COVID-19.

Methods | This study was approved by our institutional ethics committee (Comité d’Ethique du CHU de Lyon) with a waiver for informed consent because of the retrospective nature of the study. All consecutive patients with COVID-19 confirmed by positive reverse transcription–polymerase chain reaction results on respiratory samples admitted to the ICU who received hydroxychloroquine (200 mg, twice a day, for 10 days) with or without azithromycin (250 mg, daily, for 5 days) were included. Treatment began in the absence of contraindication, including corrected QT (QTc) intervals greater than 460 milliseconds (Bazett formula). All other drugs (given before or after ICU admission) listed in CredibleMeds (https://crediblemeds.org) with known or possible risk of QT prolongation/torsades de pointes were classified as drugs...