Journal of Clinical Lipidology (2017) ■, ■–■

Journal of Clinical Lipidology

Original Contribution

Barriers to PCSK9 inhibitor prescriptions for patients with high cardiovascular risk: Results of a healthcare provider survey conducted by the National Lipid Association

Jerome D. Cohen, MD*, Mark J. Cziraky, PharmD, Terry A. Jacobson, MD, Kevin C. Maki, PhD, Dean G. Karalis, MD

St Louis University, St Louis, MO, USA (Dr Cohen); Research Department, HealthCore Inc, Wilmington, DE, USA (Dr Cziraky); Department of Medicine, Emory University, Atlanta, GA, USA (Dr Jacobson); Midwest Biomedical Research, Center for Metabolic and Cardiovascular Health, Glen Ellyn, IL, USA (Dr Maki); and Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA (Dr Karalis)

KEYWORDS:
PCSK9 inhibitors;
Statins;
Dyslipidemia;
Familial hypercholesterolemia;
Practice patterns

BACKGROUND: Statin therapy is recommended for reducing atherosclerotic cardiovascular disease (ASCVD) risk. Significant risk can remain because of insufficient clinical response or statin intolerance. Proprotein convertase subtilisin/kexin type-9 (PCSK9) therapy lowers low-density lipoprotein cholesterol and has recently been shown to lower ASCVD events.

OBJECTIVE: The aim of the study was to assess the barriers and challenges experienced with the access and approval reimbursement process for PCSK9 inhibitor prescriptions.

METHODS: In 2016, the National Lipid Association conducted an online survey on PCSK9 inhibitor use and barriers to prescription among experienced healthcare workers who provide care to high-risk patients with ASCVD or familial hypercholesterolemia (FH).

RESULTS: There were 434 respondent healthcare workers with extensive experience in treating lipid disorders. PCSK9 inhibitors are considered by 71.3% of respondent providers with statin-intolerant patients. There were high rates (>85%) of initial denial. The major barriers to approvals were insurer processes, provider documentation (inadequate documentation of maximally tolerated statin dose, diagnostic criteria for FH, number of statins failed if statin intolerant and most recent low-density lipoprotein cholesterol), and administrative burden (time, staff, paperwork, and appeals). Provider approval rates for getting ≥75% patients approved were higher for FH (43%) than for ASCVD patients (36%). Among providers with good approval rates, documentation was the most critical factor. Barriers more difficult to overcome include perceived higher threshold requirements by payers, drugs not on formulary, and drug costs.

* Corresponding author. National Lipid Association, 6816 Southpoint Pkwy #1000, Jacksonville, FL 32216, USA.

E-mail address: cohenjd@swbell.net

Submitted April 26, 2017. Accepted for publication April 26, 2017.

http://dx.doi.org/10.1016/j.jacl.2017.04.120

CONCLUSIONS: Healthcare providers encounter significant barriers to PCSK9 inhibitor prescriptions; many of these are related to documentation issues and can be overcome with checklists, staff support, and experience.

Introduction

Statins have been approved in the United States since 1987 and are widely used in both secondary and primary prevention of atherosclerotic cardiovascular disease (ASCVD) because of their proven benefits.[1] However, statin therapy has some important limitations. First, even with high-intensity statin treatment, some patients can fail to attain desired low-density lipoprotein cholesterol (LDL-C) reductions, and therefore remain at high risk of a cardiovascular (CV) event.[2] Patients with untreated familial hypercholesterolemia (FH) have markedly elevated LDL-C levels,[3] and in this group, a large proportion fail to attain LDL-C goals despite therapy with maximally tolerated statins plus ezetimibe.[4] Second, some patients do not tolerate statins and are considered "statin intolerant," with statin-associated muscle symptoms being the most common.[5] The incidence of statin intolerance (SI) has been difficult to estimate because of varying clinical trial designs, lack of ability to easily identify SI in postmarket assessment, and differing agents being used.[5] An Internet survey conducted by the National Lipid Association (NLA) of 10,138 current and former statin users (Understanding Statin Use in America and Gaps in Patient Education) found that 60% of former and 25% of current statin users reported muscle symptoms while taking a statin.[6]

Therefore, it is clear that statins may not be sufficient for LDL-C control in some patients, and other options are needed to ensure that more high-risk patients (ASCVD/FH) with elevated LDL-C are able to achieve treatment goals.

Relatively, recent research in the field of clinical lipidology has led to the development of inhibitors of proprotein convertase subtilisin/kexin type 9 (PCSK9).[7] PCSK9 is a key regulator of hepatic LDL receptor (LDL-R) activity. PCSK9 binds to the LDL-R expressed on the cell surface of hepatocytes, where it prevents recycling of the LDL-R and therefore promotes its degradation.[8] The result of PSCK9 inhibition is to enable more hepatic LDL-R to bind and sequester LDL-C, and thereby reduce circulating LDL-C levels, as well as levels of other potentially atherogenic lipoproteins such as very low–density lipoproteins and lipoprotein(a).[8]

At present, 2 injectable fully human monoclonal antibody PCSK9 inhibitors have been approved by the Food and Drug Administration—alirocumab (Praluent; Sanofi/Regeneron Pharmaceuticals)[9] and evolocumab (Repatha; Amgen).[10] Both of these agents are indicated as an adjunct to diet and maximally tolerated statin therapy for treatment of adults with heterozygous FH or clinical ASCVD, who require additional lowering of LDL-C.[9,10] Recently, results from the Further cardiovascular OUtcomes Research with PCSK9 Inhibition in subjects with Elevated Risk (FOURIER) trial demonstrated that addition of evolocumab to statin therapy significantly reduced CV event rates by 15% to 20% in patients with ASCVD.[11]

Given that PCSK9 inhibitors are relatively costly monoclonal antibodies, access to the approval for the use of these drugs is often limited, which can impede optimal CV risk management. Therefore, it is important to understand what the barriers to PCSK9 inhibitor prescription approval are such that healthcare systems and processes can be structured to deliver appropriately targeted, high-quality care to patients who will benefit from additional lipid-lowering therapy with these agents.

The NLA routinely publishes recommendations and statements for healthcare professionals, payers, and policy makers with the aim of optimizing the treatment of patients with dyslipidemias. For PCSK9 inhibitors, an online survey of NLA members, and other invited participants with experience in treating patients with lipid disorders, was conducted to gather information on prescribing patterns and barriers in PCSK9 inhibitor use. The major findings of this survey are reported here.

Methods

An online survey, developed by the NLA and administered by Professional Research Consultants Inc (Omaha, NE, USA), was conducted between August 26, 2016 and October 14, 2016 (open for 6 weeks). Invitees were NLA members and selected external healthcare professionals with interest and experience in caring for patients with dyslipidemias. Reminders to complete were sent over the 6-week period of the survey and at the American Society of Preventive Cardiology Annual Meeting, September 2016. The survey was also advertised by the NLA via e-mail, web advertisements on the NLA and media partners' Web sites, postcards to NLA members, social media, and responder referrals.

The survey included 170 questions designed to query the demographic and job function of the respondents, the general profile of the patients under their care (with particular reference to those at high risk of ASCVD), statin use, and treatment decisions regarding PCSK9 inhibitors. Questions were provided by an experienced group of lipid experts. The NLA was solely responsible for the creation of