



Contents lists available at ScienceDirect

Journal of the American Pharmacists Association

journal homepage: [www.japha.org](http://www.japha.org)

## COMMENTARY

Pharmacist-administered long-acting injectable PCSK9 service:  
A solution to improve patient access and adherenceDave L. Dixon<sup>\*</sup>, Joseph J. Saseen

## ARTICLE INFO

## Article history:

Received 17 October 2020

Accepted 6 December 2020

## ABSTRACT

In 2015, 2 proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, alirocumab and evolocumab, were approved by the Food and Drug Administration (FDA). Both therapies reduce low-density lipoprotein cholesterol (LDL-C) by approximately 60% and reduce atherosclerotic cardiovascular disease (ASCVD) risk in patients with established ASCVD when added to background statin therapy. The initial cost of these medications was approximately \$15,000 per year, which made them largely cost-prohibitive for many patients and the overall health care system. In recent years, the cost of both agents has been reduced by 60%, and they are no longer only available through specialty pharmacies. In addition, a third PCSK9-modulating therapy, inclisiran, is nearing FDA approval. Ongoing inclisiran therapy only requires biannual subcutaneous administration and achieves LDL-C reductions of approximately 50%. As the use of PCSK9-modulating therapies increases, models that improve adherence and persistence over time will be critical to ensure patient access and maximize their value. Community pharmacists can play an important role helping patients not only obtain access to these therapies by navigating previous authorization requests but also adhere to therapy by offering administration. Community pharmacists can also provide therapeutic monitoring using point-of-care lipid testing to ensure efficacy over time. Such a service could potentially be sustained through reimbursement for administration and point-of-care lipid testing. Given the cost of these therapies, innovative models involving community pharmacists will be necessary to ensure patient access to these preventive therapies and minimize overall costs to the health care system.

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Since their approval in 2015, the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, alirocumab and evolocumab, have paved the way for novel, long-acting, subcutaneous injectable medications to reduce low-density lipoprotein cholesterol (LDL-C) levels and atherosclerotic cardiovascular disease (ASCVD) risk.<sup>1</sup> Inclisiran is a small interfering RNA agent that reduces PCSK9 synthesis and reduces LDL-C by approximately 50% with an initial subcutaneous injection, followed by

one at 3 months and then semiannually thereafter.<sup>2</sup> Thus, this therapeutic option can greatly reduce LDL-C without the need for biweekly or monthly self-administration or daily oral medication, opening the door for a “vaccine-like” option for patients with a very high risk of ASCVD who are unable to achieve desired LDL-C levels on maximally tolerated statin with or without ezetimibe.

The cost value considerations with PCSK9-modulating therapies have been extensively debated since the approvals of alirocumab and evolocumab in 2015. Given their initial wholesale price of nearly \$15,000 per year, the 2018 Guideline on the Management of Blood Cholesterol stated that “At mid-2018 list prices, PCSK9 inhibitors have a low cost value,” affirming affordability as a major barrier to their use.<sup>3,4</sup> Since approval, insurance providers have enforced strict prior authorization processes and both alirocumab and evolocumab. Moreover, access was initially restricted to specialty pharmacies. These barriers resulted in harm to patients who were denied access. In a cohort study of health care claims for nearly 140,000 individuals

**Disclosure:** The authors declare no relevant conflicts of interest or financial relationships.

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<https://doi.org/10.1016/j.japh.2020.12.009>

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**Key Points****Background:**

- Proprotein convertase subtilisin/kexin type 9 (PCSK9)-modulating therapies are very effective at lowering low-density lipoprotein cholesterol and reduce atherosclerotic cardiovascular disease risk.
- The available PCSK9-modulating therapies require subcutaneous administration.

**Findings:**

- A pharmacist-administered long-acting injective PCSK9 service may help improve patient access and adherence.
- Clinical services within the community pharmacy setting to provide long-acting PCSK9-modulating therapy should be implemented.

prescribed alirocumab or evolocumab between 2015 and 2017, those who had their claims rejected or abandoned had a statistically significant higher risk of cardiovascular events than those whose claims were paid.<sup>5</sup> Women, racial minorities, and lower-income groups were more likely to have a claim rejected, although the authors were unable to examine explanations for this observation. These data support the need for additional efforts to ensure patients have equitable access to evidence-based preventive therapies.

Despite notable price reductions in recent years, the debate about the value of alirocumab and evolocumab continues. Cost-effectiveness analyses using the current pricing structure, however, have concluded that both therapies are cost-effective if used in many very high-risk ASCVD risk groups.<sup>4</sup> Another critical factor in determining the cost-effectiveness of these therapies is primary adherence and persistence with therapy. These considerations are crucial as a reduction in ASCVD events can only be achieved with chronic, sustained use and lowering of LDL-C over several years. Although data from clinical trials<sup>6</sup> have suggested a high adherence rate to PCSK9 inhibitors, this has not necessarily been the case in real-world clinical practice largely owing to burdensome prior authorization processes and medication costs.<sup>7</sup> The question we raise here is how can community pharmacists assist the health care system to ensure patient access to these therapies as well as ensure adherence and persistence to maximize their value?

Some institutions have used specialty pharmacy services and pharmacists to successfully facilitate the prior authorization process to expand patient access.<sup>8</sup> Many specialty pharmacy services provide in-person training on self-injectable medications, such as PCSK9 inhibitors. However, specialty pharmacies and pharmacists are not available resources at every institution or for every prescriber. Furthermore, both alirocumab and evolocumab can now be obtained at any community pharmacy in comparison with their access being exclusively through a specialty pharmacy after first being approved in 2015. Therein lies an opportunity to improve patient care. Community pharmacists are uniquely positioned to greatly improve access to PCSK9-modulating therapies and

ensure adherence and persistence over time—the community pharmacist-led long-acting injectable lipid clinic.

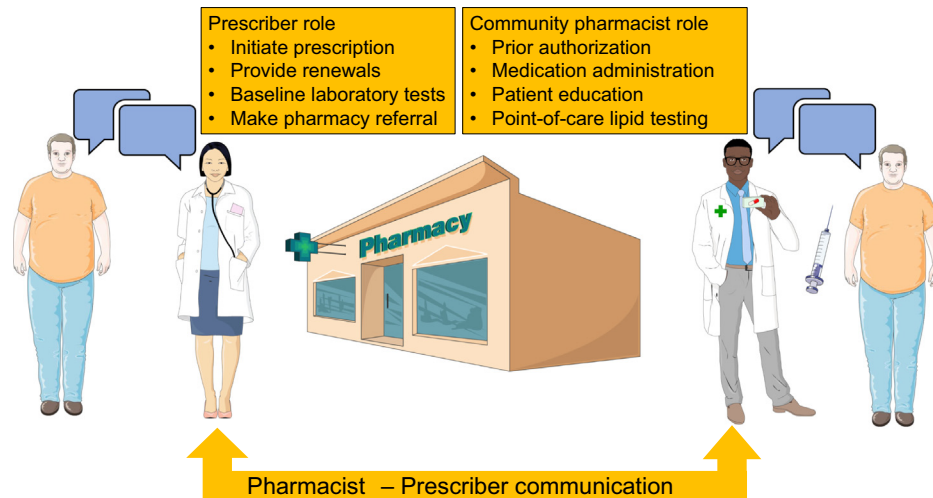
Community pharmacists are the most widely available health professionals with more than 90% of Americans living within 5 miles of a community pharmacy.<sup>9</sup> Over the past 2 decades, pharmacists have rapidly been granted authority to administer injectable therapies, including immunizations, biological agents (e.g., adalimumab), long-acting injectable antipsychotics, and injectable contraception.<sup>9</sup> These pharmacist-led services in community pharmacies have been well received by patients and shown to improve patient adherence to therapy.<sup>10</sup> Furthermore, some payers are reimbursing pharmacists who administer long-acting injectable therapies, similar to immunizations. Thus, a clear precedent exists for pharmacists to provide a similar clinical service for long-acting PCSK9-modulating therapies. This could remove an immense burden off of prescribers struggling with prior authorizations and help ensure patients adhere and persist with treatment. What would such a model look like?

Pharmacy services that provide care to patients on long-acting injectable lipid-lowering therapies could be implemented in a variety of ways. In many lipid clinics, pharmacists are already involved in the management of patients with lipid disorders.<sup>11</sup> The administration of injectable medications during follow-up clinic visits is possible, but an easier approach with fewer barriers might be to have patients receive administration at community pharmacies because of their wide availability and accessibility (Figure 1). Once prescribed, the community pharmacy could facilitate the prior authorization processes, provide patient education, and administer the medication. This type of personalized patient-care coordination could increase access and ensure adherence and persistence with therapy over time. Subsequent administrations could be performed at scheduled follow-up visits at the community pharmacy. Pharmacies could also perform point-of-care lipid testing to ensure efficacy. Community pharmacies would need to communicate with the prescriber and provide updates regarding when injections were administered, report adverse effects, and report other issues that might arise. Such bilateral communication could occur through traditional methods, such as facsimile, but would ideally be done through a shared electronic medical record or other secure platform. This would help to ensure continuity of care and reduce the overall burden on prescribers.

Another important aspect for implementation would be for community pharmacies to partner with local health systems or medical practices. PCSK9-modulating therapies are primarily indicated in patients with a very high-risk of ASCVD. Therefore, initial collaborations specifically with cardiology or endocrinology may be most fruitful. Community pharmacies could collaborate with local payers with a larger proportion of members receiving PCSK9-modulating therapies, who would benefit from ensuring their members are persistent with therapy.

The implementation of any new service will be met with challenges and barriers. First, although community pharmacists are well accustomed to managing prior authorizations, this is yet another class of medications requiring additional time and resources that could require modifications in workflow. Second, whereas alirocumab and evolocumab may be administered by the patient themselves, inclisiran will likely

## Pharmacist PCSK9 service



**Figure 1.** Pharmacist-administered long-acting injectable PCSK9 service. Abbreviation used: PCSK9, proprotein convertase subtilisin/kexin type 9.

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require administration by a health professional. There are uncertainties, however, regarding who will have the authority to administer it and how reimbursement will work. Third, community pharmacies that are not already offering point-of-care lipid testing would need to purchase the necessary equipment and supplies, train staff, and meet state and federal regulations. Finally, sufficient measures would need to be put in place to ensure adequate communication among the pharmacist, the prescriber, and the patient. All of these challenges and barriers can be overcome within the community pharmacy setting.

It is one thing to have effective LDL-C lowering medications available, but it is perhaps more important to ensure patients have equitable access. As previously mentioned, inequitable access to such therapies can lead to worse clinical outcomes and potentially cost lives. In addition, the long-term benefits of preventive medications, such as PCSK9-modulating therapies, can only be achieved with persistent adherence to the prescribed treatment regimen. We already know that poor adherence and persistence to statin therapy is associated with a higher risk of recurrent cardiovascular events and mortality.<sup>12</sup> Let us not allow the same to happen to patients prescribed PCSK9-modulating therapies.

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