Access to PCSK9 Inhibitors

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Recent news about Aetna prior authorization (PA) processes[1] has highlighted one reason why appropriate patients have such difficulties in accessing therapies prescribed by their physicians and advanced healthcare professionals. Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors are a class of therapies that has been exceptionally difficult to access through payers' utilization management processes. One such process is PA, a set of clinical criteria that can be quite restrictive. News reports have revealed that an Aetna medical director for Southern California said in an October 2016 deposition that although he was responsible for overseeing the preauthorization of care, he never examined patients' medical records during his tenure.[1] Instead, he relied on nonphysicians employed by Aetna to review the medical records and provide him with pertinent information, such as laboratory values. Though the medical director was purportedly acting as a "peer" to other doctors, he inappropriately delegated responsibility to nonphysicians, perhaps partially explaining the lack of consistency in the payers' decisions.

This supplement to *Reviews in Cardiovascular Medicine* focuses on PCSK9 inhibitors to educate physicians on their mechanism of action, safety, and efficacy. We take a responsible and data-driven approach to identify the appropriate patient types who would benefit most from this relatively expensive but effective therapy. Prescribing a PCSK9 inhibitor to an appropriate patient, who remains at extreme and very high risk with persistently elevated low-density lipoprotein cholesterol (LDL-C) levels, should lead to their having access to the treatment. But the news report mentioned above contributes to widespread physician cynicism regarding the validity of the current PA process. Finally, the Aetna revelation has led to action by many states to review insurance company practices, including complex PA requirements and burdensome step therapy demands, that have been shown to result in whimsical final decisions regarding approval or denial of doctors' prescriptions.

The finding that final approval rates for PCSK9 inhibitors have been reported to be around 30% in commercial insurance and 58% in Medicare recipients is only the tip of the iceberg.[2] This high denial rate occurs even in the highest risk patients, such as those with familial hypercholesterolemia (FH) and persistently elevated LDL-C. Of the 237 presumptive FH patients who had an LDL-C value >190 mg/dL despite statin-based lipid-lowering therapy, 63% of prescriptions for PCSK9 inhibitors were rejected. Many prescriptions are probably never written, as physicians are frustrated by the burdensome process to access PCSK9 inhibitors, at times leaving our patients at unnecessary risk for myocardial infarction and stroke. Baum and colleagues have reported that PAs require that healthcare practitioners complete complex paperwork, up to 17 pages in the case of the PCSK9 inhibitors.[3] In 2006, it was estimated that healthcare practitioners spent 1.1 hours per week, nurses spent 13.1 hours per week, and clerical staff spent 5.6 hours per week on PAs. In 2009, total healthcare system costs for PAs were estimated to be $23 to $31 billion per year. More recent national surveys confirm that the cost per year to healthcare practitioners has risen to between $83,000 and $85,000 per practitioner.[4]

Table 1 shows the complexity of the authorization process for both alirocumab and evolocumab.

TABLE 1

Administrative Prior Authorization Requirements for PCSK9 Inhibitors in 2016, by Type of Insurance Coverage*

	Alirocumab				Evolocumab			
	Commercial	HIX	Medicare	Medicaid	Commercial	HIX	Medicare	Medicaid
No. of covered lives subject to PA requirements, in millions	116.5	6.5	32.4	65.1	119.7	7.3	15.5	65.3
Prescriber specialty %								
Medication must be prescribed by or in consultation with a specialist	66%	48	42	32	65	46	71	36
Cardiologist†	98	100	100	100	100	98	100	100
Lipid specialist†	83	56	90	88	85	59	87	92
Endocrinologist†	94	88	98	69	95	87	97	69
Specialist (not specified)†	38	35	10	6	37	35	14	6
No. of PA criteria or fields required on form								
HeFH, mean (min, max)‡	17 (6, 72)	27 (10, 44)	11 (1, 37)	19 (3, 53)	18 (6, 73)	33 (10, 39)	13 (1, 37)	16 (3, 32)
HoFH, mean (min, max)‡	N/A	N/A	N/A	N/A	19 (6, 73)	26 (7, 35)	11 (1, 47)	16 (4, 32)
ASCVD, mean (min, max)‡	21 (6, 72)	32 (10, 50)	9 (1, 39)	19 (3, 53)	20 (6, 73)	27 (9, 38)	11 (1, 39)	16 (3, 32)
Submission of medical records required for approval, %	75	58	69	40	73	55	64	43
Reauthorization required, %	64	58	98	46	61	46	100	47
Initial coverage duration specified, %§	40	33	43	35	50	40	77	36
Median duration, mo (min, max)	3 (2, 6)	3 (2, 6)	3 (2, 6)	3 (2, 6)	3 (2, 6)	3 (2, 6)	3 (2, 6)	3 (2, 6)

ASCVD, cardiovascular disease; HeFH, heterozygous familial hypercholesterolemia; HIX, health insurance exchange; HoFH, homozygous familial hypercholesterolemia; N/A, not applicable; PA, prior authorization; and PCSK9, proprotein convertase subtilisin/kexin type 9.
*Percentages may not add to 100 because of rounding.
†Denominator for these estimates is the percentage of enrollees subject to the prescriber specialty requirement.
‡All mean estimates are weighted by the number of enrollees in each plan.
§Denominator for this estimate is the percentage of enrollees subject to reauthorization.

Knowles and colleagues demonstrated similar findings of frequent PCSK9 inhibitor denials in high-risk and appropriate patients with either FH or atherosclerotic cardiovascular disease.[5]

Clinicians may appeal an insurance company's decision regarding a prescribed therapeutic such as a PCSK9 inhibitor. Reports from the FH Foundation found that greater than 80% of initial prescriptions for PCSK9 inhibitors are denied. Of these initial denials, only 46.6% of Medicare and 26.7% of privately insured patients ultimately gained approval after extensive appeals (unpublished data, FH Foundation, Pasadena, CA).

Optimizing the Approval Process

Transparency in approval requirements would assist the clinician and patient in determining whether a drug is appropriate for that patient. This could ensure the patients with the most to benefit from a therapy receive it and reduce unnecessary efforts by clinical staff and patients. Of course, payers would also have to create transparent internal processes for approval or denial, enabling clinicians and patients to communicate more easily with payers. The National Forum for Heart Disease and Stroke Prevention is leading a multi-stakeholder initiative to identify best practices to guide payers in developing appropriate and responsible prior authorization processes.[6]

Optimizing the In-office Authorization Process

A successful approach to the authorization process is to develop a protocol to identify the key historical information in the medical record needed to support authorization and to transfer that information to the authorization forms in an accurate way. A PA form is available online,[3] and can aid in collating necessary information to gain access to PCSK9 inhibitors. It is recommended that one staff member be assigned this responsibility. Oftentimes this duty is relegated to untrained and medically unsophisticated medical assistants who may not be capable of accurately identifying the key information in the medical record to populate the authorization forms, which can lead to a denial.

Key clinical information can include

1. Specific documentation of previous history of a clinical atherosclerotic coronary vascular event such as acute coronary syndrome, myocardial infarction, stroke, transient ischemic attack, peripheral vascular disease, or revascularization.
2. For patients who are presumed to be a heterozygote for familial hypercholesterolemia, documentation of untreated LDL-C levels, family history of hyperlipidemia and accelerated coronary artery disease, and FH probability scoring using the Dutch Lipid Clinic, Simon Broome, American Heart Association, or World Health Organiztion criteria.[7]
3. Specific documentation of statin intolerance including name and dose of statins not tolerated and manifestation of intolerance (myalgia, liver function abnormalities, allergy, etc).

What Happens to the Patients Who Are Rejected for a PCSK9 Inhibitor?

With so many high-risk patients being rejected or having their access delayed through the PA process, can we estimate what their outcomes are like?

A retrospective cohort study using data from January 2016 to January 2017 in commercially insured and Medicare patients requesting access to evolocumab and/or alirocumab in the IQVIA Formulary Impact Analyzer (FIA) database was presented in abstract form by Baum and colleagues.[8] They compared the cardiovascular event rate in all patients requesting a PCSK9 inhibitor at 3 months and 6 months after the index request. The cardiovascular event rate was numerically higher for patients rejected for PCSK9 inhibitor therapy compared with the overall population of patients requesting PCSK9 inhibitor therapy:

- 3-month rate of acute cardiovascular events: 9.07 vs 8.33 per 100 patient-years
- 6-month rate of acute cardiovascular risk: 7.29 vs. 6.73 per 100 patient-years

This is consistent with the failure of the PA process to accurately identify the highest risk patients who would benefit from treatment with a PCSK9 inhibitor. In this analysis, it is estimated that 110,000 cardiovascular events will occur annually in high-risk individuals who are prescribed and denied a PCSK9 inhibitor.

Conclusions

It is the responsibility of physicians, health systems, and payers to provide patients with the best treatments in a trustworthy way. By understanding the published safety and efficacy data for PCSK9 inhibitors, clinicians can make informed decisions about this therapy. One can question the intent of the PA process itself: Was it designed as a

tool to lead to appropriate use, or a barrier to prevent it? What is clear is that PAs have indeed become a barrier, and our patients are paying the price through co-pays and adverse health outcomes. ■

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