Nonmedical switching of anticoagulants: The patient impact when formulary exclusions limit drug choice

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The letter arrived in my mailbox just before Thanksgiving.

Dear Beth,

CVS Caremark manages the pharmacy benefit for the State Health Plan. We are working with the State Health Plan to help make sure the medications covered by your pharmacy benefit are used safely and appropriately.

We are writing to inform you that starting January 1, 2022, certain prescriptions that you may have filled will no longer be covered by your pharmacy benefit plan. We’re here to help your provider choose a new covered medication.

The letter was from the largest pharmacy benefit manager (PBM) in the United States, CVS Caremark, who manages the prescription benefits for 1 in 3 Americans—nearly 110 million lives. The medication it dropped from its 2022 commercial formulary is one of the most frequently prescribed oral anticoagulants—Eliquis (apixaban), a factor Xa inhibitor approved by the US Food and Drug Administration (FDA) for the prevention and/or treatment of venous thromboembolism (VTE) and to reduce the risk of stroke in patients with nonvalvular atrial fibrillation.

Over 3 million Americans like me take Eliquis, including President Joe Biden. To have the largest PBM drop a widely prescribed anticoagulant as a therapeutic option is certain to present some headaches for both patients and clinicians in the months ahead. The move was seen as so potentially disruptive that 16 cardiovascular nonprofits spoke out against it and asked CVS Caremark to reconsider, citing concerns with limiting patient-physician medication choice, dangers of switching stable patients, its impact on historically disadvantaged patients, clinical bleed-risk data, increased administrative burden, and potential for treatment delays.1-3

Yet such decisions, born not of clinical reasons but strictly out of the revenue-maximizing contract negotiations between pharmaceutical companies and PBMs, has tangible human impact. I am one of those impacted.

I began taking an anticoagulant 18 years ago following VTE—deep vein thrombosis and bilateral pulmonary embolism, which was life threatening and resulted in an intensive care unit admit. I am at high risk for recurrence, so I fear another clotting event. But I know first-hand my potentially lifesaving treatment also comes with its own inherent risks—my father died from a massive internal bleed while anticoagulated. Anticoagulation is not a light decision. I place a premium upon optimal anticoagulation management.

When I began anticoagulation 18 years ago, I had no drug choice; warfarin was the only game in town. Warfarin is a finicky medication, and it was always a challenge to remain in a therapeutic zone. I required an office visit every 2 to 4 weeks for nearly 10 years—a royal pain in the neck to take so much time off work.

I had frequent dosage changes based upon lab results. I took a different dose on different days of the week and, as a result, dosing mistakes were not unusual. Because warfarin had many dietary and drug interactions, I had to be constantly hypervigilant about what I ate and took over the counter. And do I dare mention the perioperative management burden of coming off warfarin and having to bridge with an injectable low-molecular-weight heparin? Egad.

When the factor Xa inhibitors—the direct oral anticoagulants (DOACs)—received FDA approval, it was a godsend. To finally be...
able to take a one-dose anticoagulant that had no dietary restrictions, fewer medication interactions, and easier perioperative management and that required only an annual office visit was liberating! If one can be in love with a pill, then I fell in love with the DOACs.

With new drug choices came an enviable challenge: which drug to take? Between 2010 and 2014, four DOACs received FDA approval: Pradaxa (dabigatran), 2010; Xarelto (rivaroxaban), 2011; Eliquis (apixaban), 2012; and Savaysa (endoxaban), 2014. Generics for these drugs are not available. To receive FDA approval, the DOACs only had to demonstrate they were as safe and effective as the standard of care, warfarin. They were not compared to each other, leaving patients like myself with scant data on which to make brand selection decisions. Only now, with years of real-world use, are we finally getting useful comparative data on side effects, risks of major bleeding, and adherence factors, which show there are valid reasons why a patient and clinician together may wish to choose one drug over another. Randomized controlled trial (RCT) comparison data among the DOACs is still lacking, but meta-analysis comparing drugs directly short of head-to-head RCT does exist, and the results are consistent with previous observational studies.4

For my own care, I consulted multiple hematologists and read numerous clinical trials before deciding—with my doctor—which drug was best for my unique clotting and bleeding profile as well as personal preferences and tolerance for risk. It was a model in how shared decision making and individualized care should work: patient and clinician working together to make informed treatment choices. As a result, I have been stable for years with no new clotting or bleeding events.

But now, with the arrival of this simple form letter in the mail, which provided not even a phone number if I had a question, it seems the thoughtful shared decision making between my doctor and I means nothing. I and approximately 150,000 other patients stable on Eliquis were forced to suddenly switch anticoagulants on January 1, despite our wishes and those of our clinicians, who wrote our prescriptions. The only covered oral anticoagulant choices on formulary are warfarin and Xarelto.

What did I do? After contacting my insurance plan and CVS Caremark, I learned I could ask my doctor to file an exemption request. However, the stated approval criteria required that I first take and fail Xarelto or have another clinical indication, which was undefined. Failure of warfarin was not required. And if the exemption was approved, it would be at a higher coverage tier, making it subject to coinsurance and deductible. For me, this would mean an additional US$2400 a year.

I have no desire to return to my not so good ol’ days on warfarin, so after consulting with my hematologist, I am transitioning to Xarelto. While I trust my doctor, who has reassured me as best as he can, do I truly feel good about this change? No. Especially considering recent publications such as the January 2022 study published in the Annals of Internal Medicine showing that patients with VTE on Eliquis had lower rates for recurrent VTE and bleeding than users of Xarelto.5 Patients like me keep up with the literature, and we are finding a steady diet of favorable results for Eliquis being shared online among both atrial fibrillation and VTE patient groups. The anxiety among patients being forced to switch—many of them with years of stability on Eliquis—is downright palpalable.

For me, having instability suddenly introduced into my treatment regime has reignited the anxiety surrounding my clotting episode. The psychological impact of VTE is underappreciated. Years of stability allowed my anxiety and depression to recede quietly into the background. This sudden, unexpected change in treatment has awakened those feelings once again. Recently, I have found myself not sleeping as my mind relives both my clotting event and those final moments of my dad’s life watching him bleed to death and the doctors unable to stop it. As a patient, how am I supposed to feel good about the nonmedical switching of my anticoagulant knowing the covered drug choices I am being offered are not ones my doctor initially prescribed or the ones that the clinical evidence suggests are best for my specific goals to reduce both my clot and bleed risk? All these complex emotions over a simple little pill—it is at the same time remarkable and cruel.

My nagging fear is that one day I will receive another letter taking even this last DOAC option away—that this initial action of reducing anticoagulant choice may be a first step of moving in the direction whereby all nongeneric options are off the table due to their cost, which would mean a return to warfarin. Generic apixaban, while FDA approved, has been delayed from the US market until April 1, 2028, due to patent litigation, and there are no FDA applications pending for generics for the other DOACs.

To be clear, I am not advocating one brand of drug over another, but rather that all FDA-approved anticoagulants should remain available and affordable to patients. The reasons why we clot are varied. Our bleeding risks, potential medication interactions, and adherence challenges are so diverse that only an individualized approach to anticoagulation management can lead to the most optimal health outcomes.

For 50 years, there was only one anticoagulant, which was challenging for both patients and clinicians to use. Now, thanks to research and science, patients have five FDA-approved oral anticoagulant choices. Greater anticoagulant choice means care can be better tailored to the individual patient.

Yet that choice is being taken away by largely unregulated PBMs who are injecting themselves into the shared decisions made by patients and clinicians. This is wrong. We cannot backslide to the days when only one anticoagulant was available. Nor should we create inequities where only patients with the financial means to pay full retail price are able to receive the anticoagulant of their choice.

Patients and their clinicians deserve the full range of FDA-approved anticoagulant choices. True shared decision making necessitates that no one stand between a patient and clinician making decisions based upon the clinical evidence, while taking into consideration expected outcomes and patient preferences.
What do I want now? Of course, I’d like for CVS Caremark to reverse their decision limiting anticoagulant choice and put Eliquis back on formulary, but beyond that I think this exemplifies a serious flaw within our system that can no longer be ignored because it imperils patient safety. What good are the advances made in research and clinical trials if the new therapeutics that emerge from them are not accessible due to cost or coverage constraints? If clinical evidence cannot be acted upon at the point of care at the dictates of a profit-motivated third party, can clinicians really be said to be practicing evidenced-based medicine? Clinical decisions must be between a patient and physician only.

Federal regulatory action is needed to ensure that patients in the future will retain all FDA-approved anticoagulant choices. If as a patient I am also a health care consumer, then I am a captive customer—I have no choice of the PBM contracted by my employer-provided insurance plan. I, like most Americans, cannot simply pick another plan if I do not like the drug formulary list. It is under just such conditions where regulatory protections are most needed to safeguard consumers.

Anticoagulants are the number one class of drugs for adverse events. They require careful clinical management. I trust my doctor of 18 years to manage my anticoagulant therapy, not my insurance PBM, who is motivated by nontransparent profit motives.

That a corporation with whom I did not contract can essentially practice medicine without a license or my consent, and against the direct medical advice of my doctor, has come as quite a shock. Its legality and the lack of consumer protections to prevent patient harm is astonishing.

Letter author received from CVS Caremark
Since article acceptance, my insurance plan, the North Carolina State Health Plan, has reinstated apixaban to its formulary. As a result, I once again have covered access to apixaban. CVS Caremark’s exclusion of apixaban remains in place on its national commercial formulary.

AUTHOR CONTRIBUTIONS
None.

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