Step Therapy: Clinicians' Concerns and Challenges

In 2019, when CMS allowed Medicare Advantage plans to implement step therapy for Part B drugs, some plans started to require that patients be treated with bevacizumab before retina specialists could try the more expensive anti-VEGF drugs, ranibizumab and aflibercept. Since that time, much has happened, including bevacizumab supply chain problems, use (and then retraction of use) of less expensive biosimilars, and more. Through it all, the Academy has been lobbying aggressively to roll back the step therapy requirement, which it considers to be suboptimal clinical care. (See "D.C. Fighting to Reverse Step Therapy," page 28.)

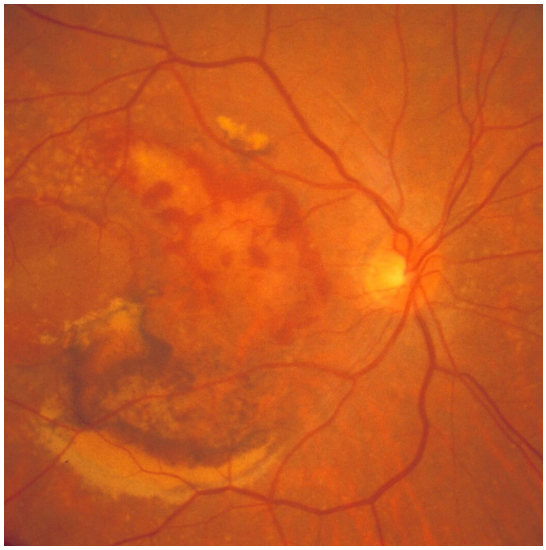
Yet the fact remains that until CMS disallows step therapy, ophthalmologists must continue to provide the best possible care for their patients under the constraints of the policy. Although the policy may save costs, it poses significant concerns and challenges for retina specialists.

What Is Step Therapy?

With step therapy, or "fail first" therapy, health plans require that patients try and fail the insurers' preferred medications before another therapy will be covered. For retina specialists, it's important to note that step therapy is most relevant for the use of anti-VEGF agents in treating proliferative diabetic retinopathy, retinal vein occlusion, and age-related macular degeneration (AMD), said Lisa S. Schocket, MD, at the University of Maryland in Baltimore.[1]

What's the policy's rationale? "The presumption with step therapy is that there's largely a comparability of a less expensive anti-VEGF with the more expensive one and that [by adhering to step therapy] you're not compromising the patient's care . . . all while achieving significant cost savings," said Paul Sternberg Jr., MD, at the Vanderbilt Eye Institute in Nashville, Tennessee.

Policy on the ground. But step therapy does raise a host of issues for physicians in terms of how to navigate the system, educate patients, and determine the best course of disease management, said John T. Thompson, MD, at Retina Specialists in Baltimore.



WET AMD. *There are several caveats when using step therapy guidelines for treatment of retina patients, such as those with wet age-related macular degeneration, said Dr. Thompson.*

What Step Therapy Does Well

The primary reason for step therapy is the potential for significant cost savings, said Dr. Sternberg. Working primarily with wet AMD patients, Dr. Sternberg's team at Vanderbilt unknowingly introduced step therapy before it became required by any of the plans he works with. In fact, his department was able to demonstrate considerable savings to some local payers, including Medicare Advantage. These payers responded, not with a mandated step therapy, but with a capitated rate that incentivized step therapy.

"Ultimately, we weren't motivated to save *us* money," said Dr. Sternberg. "We were motivated to save our patients money—especially a co-pay of several hundred dollars if they didn't have secondary insurance to cover the more expensive alternative."

He also felt an obligation to the health care system because many, if not most, of his AMD patients do just as well with the less expensive bevacizumab as their primary starting therapeutic. "Hundreds of millions of dollars are being spent each year on more expen-

BY MIKE MOTT, CONTRIBUTING WRITER, INTERVIEWING **LISA S. SCHOCKET, MD, PAUL STERNBERG JR., MD,** AND **JOHN T. THOMPSON, MD.**

sive anti-VEGF drugs for treating AMD when there are well-conducted randomized clinical trials—CATT and IVAN—showing comparability in efficacy and safety in both bevacizumab and ranibizumab," he said.[2,3]

Clinicians' Concerns

The cost savings are laudable, said Dr. Thompson, and it's true that many patients do just as well with bevacizumab for all of the three major indications—choroidal neovascularization (CNV) from macular degeneration, diabetic macular edema (DME), and venous occlusive disease. However, he outlined several caveats to be aware of when following the step therapy guidelines.

Patient intolerance. Some patients can have an immune reaction against certain anti-VEGF medication, said Dr. Thompson. This was brought to light recently with the use of brolucizumab. "Its efficacy and duration looked particularly good alongside the other three anti-VEGF medications, but there was a rare immune reaction that caused vasculitis in a very small percentage of patients." Reports of this complication triggered an extensive safety review by the drug company, he said. "That's one of the reasons why retina specialists are a bit skittish about switching drugs around."

Appropriateness of treatment. It's also known that patients with certain diseases tend to do better with the more expensive medications, said Dr. Schocket. For example, the randomized DRCR.net study Protocol T demonstrated that aflibercept is superior in patients with DME whose visual acuity is 20/50 or worse.[1] As such, she added, it is inappropriate to mandate step therapy in patients with poorer vision from DME because they may not improve as much with bevacizumab.

There are also subtypes of CNV, such as polypoidal choroidal vasculopathy, in which patients seem to be more resistant to anti-VEGF drugs, said Dr. Thompson. In these cases, retina specialists tend to use the FDA-approved drugs rather than bevacizumab.

In addition, said Dr. Schocket, some patients with persistent fluid from AMD simply do not respond to bevacizumab. "In these cases, we would need to switch them from bevacizumab to aflibercept," she said. "And the question is, if you have a mandate for step therapy, where's the turning point? What if you can tell the patient's not getting better—should you still be required to first follow through with all three [bevacizumab] injections because of protocol?"

Comorbidity: stroke. Patients with a history of stroke are also theoretically at an increased risk with bevacizumab, said Dr. Schocket. And getting around step therapy in these cases can be challenging. "One of my diabetic patients in her 40s has a clotting disorder, antiphospholipid antibody syndrome, the result of which has been dozens of strokes throughout her life," she said. "The patient does require intravitreal injections for diabetic macular edema, but I certainly wouldn't want to increase her stroke risk because of a requirement to fail first with bevacizumab."

Dr. Thompson noted that stroke is one of the complications of higher-dose anti-VEGF drugs in patients with cancer. There's evidence, he said, that ranibizumab is absorbed less into the systemic circulation than are other anti-VEGF medications. "So retina specialists will tend to favor ranibizumab for people with histories of cerebrovascular accidents."

Delays in obtaining compounded bevacizumab. Dr. Sternberg's biggest concern with step therapy is the challenge that some ophthalmologists have in accessing compounded bevacizumab. Although obtaining the drug might not be an issue at a large health care system such as Vanderbilt, where compounding is done internally, he said, "it's a very different situation for private practices or community-based practices that have less access."

And when access is a problem, it's a big problem, said Dr. Thompson. "Whether it be state regulations, compounding contaminations, or licensing issues, the use of outsourcing facilities to produce bevacizumab has resulted in intermittent shortages," he said. For example, if one particularly large outsourcing facility is cited by the FDA for contamination, the result is that many private practices have to scramble to find other sources—sources that aren't able to handle that giant uptick in demand all at once. "At that point," said Dr. Thompson, "how can you abide by step therapy?"

Considerations for Your Practice

Your day to day. How step therapy affects your day-to-day practice can largely depend on what type of practice you are operating in, said Dr. Sternberg. He said that in the academic setting at Vanderbilt, step therapy has simplified daily life. "When patients come in with wet AMD, we already have a treatment plan in place. This helps our staff know exactly what to have on hand and exactly what our treatment protocols will be."

At Dr. Thompson's three-physician private practice, however, step therapy has created a number of headaches. Many of his patients have different insurance plans, and many of these plans have different subclasses of coverage, each with different sets of rules that may or may not pertain to step therapy. "We spend too many resources figuring out when we can or cannot start a patient on a particular anti-VEGF drug," he said. "Yes, we can petition the insurance company for our preference, but that results in additional delays in treatment because the insurance company doesn't give you immediate approval in most situations."

The physician/patient relationship. Step therapy's layers of rules can interfere with the physician's treatment of the patient, as well as the patient's choice, said Dr. Thompson. "When I see a patient with new-onset CNV, for example, I tell them about all three drugs and present a balanced view of each," he said. "At least half of these patients feel strongly that they want an FDA-approved medication for their ocular problem. They don't want to have to fail another therapy first, especially if they're losing vision."

Dr. Sternberg has had similar experiences with new patients requesting certain treatments that they see offered on television or online. And if they feel strongly about it after discussion, he accedes to their wishes. "The patient is

the boss—I'm not," he said. "We always try do what is in their best interests—clinically and financially."

Regardless of step therapy protocols, there is no circumstance in which Dr. Sternberg forces an existing patient to switch to another medication. "That's not good medicine," he said. "I'm more than happy to fight the insurance company and have a peer-to-peer discussion with their medical director if they're trying to push me to move a patient off a medication that's giving them a good result."

And that is what's at the heart of the step therapy dilemma, said Dr. Schocket. "Practicing medicine is an art and not a cookbook or an algorithm prescribed by a third party. I shouldn't be making a decision based on a medication being less expensive, and I shouldn't be making a decision based on a medication being more expensive. I should be making a decision based on what's best for the patient."

1 Wells JA et al., for the Diabetic Retinopathy Clinical Research Network. *N Engl J Med.* 2015; 372(13):1193-1203.

2 Martin DM et al., for the Comparison of Age-Related Macular Degeneration Treatments Trials (CATT) Research Group. *Ophthalmology.* 2012; 119(7):1388-1398.

3 Chakravarthy U. *Lancet.* 2013;382(9900):1258-1267.

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See disclosure key, page 8. **For full disclosures,** see this article at aao.org/eyenet.

D.C. Fighting to Reverse Step Therapy

The Academy has urged CMS to "move swiftly to reinstate the step therapy prohibition in Medicare Advantage plans for Part B drugs." Although the agency seemed open to stricter guardrails in recent interactions, the Academy, as part of a broad effort, is leading another push for a full ban on the cost-cutting practice.

Nearly 60 patient and provider groups, including the American Medical Association and Medical Group Management Association, joined the call for action in a November 2021 Academy-led letter to CMS. The letter reiterated that step therapy in Medicare Advantage plans has caused "clear instances of patient harm [including] patients becoming legally blind or experiencing long-term hospitalizations, infections, increased disease activity, and disability." The letter reinforces the message from an Academy-led meeting with CMS in September, in which the Academy convened several patient and provider groups to share how step therapy harms patients. CMS requested recent examples after dozens of societies signed an Academy-led letter last April opposing the practice.

Health equity. George A. Williams, MD, Academy senior secretary for advocacy, said it's also an issue of health equity. Medicare Advantage plans disproportionately serve patients from minority groups, compared to Medicare fee-for-service. As long as Medicare Advantage plans continue to allow step therapy, patients treated under these private for-profit plans don't get the same health care as those in fee-for-service. That practice violates the law.

"If you or your mother came to me and you had already lost vision in one eye, and you had advanced disease in your other eye requiring immediate treatment, I think you would want all your treatment options available. I know I would," Dr. Williams said. Medicare Advantage patients don't have all those options, and profit-motivated insurers that require step therapy continue to interfere in the physician-patient relationship, including clinical decision-making.

Biosimilars. In early November, just weeks after the Academy and the American Society of Retina Specialists told CMS that Medicare Advantage plans are putting profits over patients, the agency put some restrictions in place to keep ophthalmic patients safe from "potentially dangerous" biosimilar drugs.

Agreeing with Academy concerns, CMS stopped its insurers from requiring off-label biosimilars Zirabev and Mvasi as substitutes for Avastin in treating eye conditions in their step therapy programs. In a letter to Medicare Advantage plans, CMS said that "Part B step therapy programs may include a drug supported only by an off-label indication if the off-label indication is supported by widely used treatment guidelines or clinical literature that CMS considers represent best practices."

Although CMS took this positive action, it reiterated that biosimilars that are FDA approved for ophthalmic use can be used in step therapy programs in Medicare Advantage. (See "A Wrench in the Works," with this article at aao.org/eyenet.) The Academy strongly believes that step therapy should not be allowed at all. CMS prohibited step therapy (for Part B drugs) from 2012 to 2018 but removed the ban in 2019. To reimpose a step-therapy ban, CMS would likely have to include the change in a formal rule.

If you observe adverse reactions or patient harm because of a step therapy requirement, email healthpolicy@aao.org to help guide the Academy's ongoing work with CMS.

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