The Accelerated Approval Debate

Faster FDA Drug Approvals May Mean Less Efficacy Data

BY JOHN CARROLL

Twenty years ago, Congress set up the accelerated approval pathway for HIV and cancer medications to help speed new treatments that provided some measure of hope to patients in need. In some cases, such as HIV, the initiative led the way for a whole new standard of therapies that saved lives.

Now, the drug industry, spearheaded by lobbyist groups like the Biotechnology Industry Organization (BIO), has begun a legislative offensive backing a string of proposed laws that would significantly expand that accelerated approval pathway. Bills penned by bipartisan legislators in both the Senate and House would pressure the U.S. Food and Drug Administration to extend approvals based on compelling proof-of-concept data, allowing lengthy and expensive late-stage studies to occur after the therapeutics hit the market.

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If they're successful in easing the bills through Congress, payers could be forced to reckon with a new breed of pricey therapeutics that would debut with less efficacy data — presenting payers with thorny coverage questions. And those questions would be arriving at a time when many in the biotech industry feel that payer risk — the possibility that payers will restrict access to or refuse to cover newly approved drugs — is growing into one of the most important challenges in the development process.

The heat is on the FDA

In the lead-up to the debate over wider access to accelerated approvals, there has been intense pressure on the FDA to speed up the approval process — a time-consuming and sometimes wildly expensive proposition. And no matter how hotly argued that point may be among professionals in the biotech industry, the FDA certainly has felt the heat. Earlier this year, FDA Commissioner Margaret Hamburg defended the agency's track record, noting that independent analysts found that the FDA typically acts faster than regulators in the European Union.

A number of lawmakers, though, aren't willing to accept that analysis. Their new initiatives include:

- The Advancing Breakthrough Therapies for Patients Act, a bipartisan bill sponsored by Democratic Sen. Michael Bennet (Colorado) and Republican Sens. Orrin Hatch (Utah) and Richard Burr (North Carolina), promises to expedite the review of breakthrough drugs it defines as those "intended for a serious or life-threatening disease or condition where preliminary clinical evidence indicates that they may demonstrate substantial improvement over existing therapies."
- Transforming the Regulatory Environment to Accelerate Access to Treatments Act, or simply TREAT, sponsored by Republican Sen. Kay Hagan of North Carolina, offers to accelerate the review and approval process for medications that "treat an unmet medical need, significantly advance the standard of care, or are highly targeted therapies for serious or life-threatening diseases or conditions."*
- The Faster Access to Specialized Therapies (FAST) bill from Florida Republican Cliff Stearns and New York Democrat Ed Towns is the House bill modeled on Kagan's effort to accelerate drug approvals.

Each of these bills has been cheered by investor groups, industry lobbyists, and patient advocates who all have their own reasons to support faster regulatory clearance. Venture groups, for example, complain that the FDA's go-slow approach has made the industry unappealing for investors. Patient advocates would prefer access to midstage drugs over what's currently available. And the biopharma industry has a laundry list of reasons to push for accelerated development, not the least of which is a far more appealing business model than the high-risk one they now grapple with.

Back in early March, John Maraganore, CEO of Alnylam Pharmaceuticals, took a seat in front of a House subcommittee and hammered on some familiar themes as he advocated for the FAST bill. New technology, like new and better biomarkers, make it possible to evaluate efficacy faster than before, he argued. And without some positive changes

at the FDA, he added, the venture capital stream would shrivel.

"It is critical that the FDA engender an environment that is able ... to efficiently and predictably review innovative medicines and allow for the use of modern scientific tools and methodologies that are more efficient and better enable FDA to make determinations of benefit versus risk," Maraganore said.

House veteran Jim Greenwood, who heads BIO, offered a ringing endorsement, declaring that FAST and TREAT alike would "better enable biotechnology companies to bring new, safe, and effective treatments and cures to patients in need at the earliest point in time." Joining in the applause was the National Venture Capital Association, which has been complaining for months that the FDA's slow pace is keeping investors out of biotech, and the National Organization for Rare Diseases, which called it a "top priority."

The payer perspective

Regulatory approval, a risky situation given the low percentages of phase 1 drugs that can go on to approval, is just one enormous hurdle for developers. Pharma companies have felt insurers and international healthcare agencies push back against new drugs that may not offer dramatic improvements for patients. Wider use of accelerated reviews would force drug developers to start reaching out to payers at an early stage, possibly long before they have conclusive evidence of efficacy.

"Payers adapt slowly to changing regulatory evidence requirements," notes Dan Mendelson, CEO of Avalere Health, a managed care and pharmaceuticals consultant. "It's a balancing act for drug developers that want to move into an accelerated pathway. If they can really speed time to market, they will g,enerally win, especially if they do their homework with payers and help them understand the new requirements. To help payers adapt, they will need to get out early and educate them to compensate for the absence of phase 3 data."

As of now, America's Health Insurance Plans has not weighed in. "It's on their radar," noted AHIP spokesman Robert Zirkelbach about the group's policy analysts, but no position or legislative efforts have been mapped out.

More accelerated reviews would force manufacturers to meet early with payers to make their case — and to learn what payers really want.

At the recent Pharmaceutical Care Management Association's PBM Summit in Las Vegas, Ron Cohen, chief executive officer of Acorda Therapeutics, ran an informal poll asking his colleagues what they thought about the impact of a new law expanding the accelerated approval process. The managed care perspective, he says, is that they're unhappy with the FDA, but for completely different reasons than those expressed by drug developers frustrated with the long regulatory process needed to gain approvals. Payers "feel the FDA should be doing a better job of weeding out drugs that do an inadequate job," says Cohen. "They feel [the FDA] is too lenient." Naturally, payers don't think that quicker approvals, coupled with late-stage confirmatory trials that take place after marketing begins, would change that.

Cohen, whose company markets dalfampridine (Ampyra), a well-respected drug to help control symptoms of multiple sclerosis, sees the managed care side split into two groups: Possibly about 60 percent of payers who generally cover newly approved drugs at the price that's applied and a large minority of plans that aggressively manage costs.

"There are quite a few [payers] who work very hard to narrow and restrict access and put in strict formulary payments and prior authorization and high copays. Those plans very likely would exercise the same process for drugs that come out through accelerated approvals," says Cohen. In that group, it's not uncommon to see a flat six-month moratorium on coverage of newly approved drugs. And accelerated approvals could persuade more plans to adopt the same practice.

"It's certainly not a one-size-fits-all," says Cohen. "It adds another subtle variable into the mix, but I don't think it will be dramatic."

Cohen agrees with Mendelson that the fight for accelerated approvals highlights the need for biopharma companies to start meeting with payers early and often to make sure they get their message across — especially if they deal with plans that may not have the in-house expertise to quickly size up how new therapeutics would be a fit with their populations and employer customers.

If nothing else, accelerated approvals will bring health plans and drug developers together regardless of whether they can agree on what needs to change at the FDA.

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*__Note:__ See *"Pharma defeats biotech push for rapid approval program," February 2, 2012, Mark Hollmer,* Fierce Biotech, for an update on Sen. Kagan's initiative.