Setting the Record Straight on the Accelerated Approval Pathway

What is the Accelerated Approval Pathway?

The accelerated approval pathway, formally established by the U.S. Food and Drug Administration (FDA) in 1992, enables earlier approval of medicines that address an unmet medical need for serious or life-threatening diseases or conditions based on a surrogate or an intermediate clinical endpoint - such as a laboratory measurement (like blood glucose level for diabetes), radiographic image (like tumor size reduction), physical sign (like blood pressure for cardiovascular disease) or other measure.

The FDA also requires sponsors to conduct confirmatory studies or Phase IV clinical trials after accelerated approval to verify the anticipated clinical benefit. Moreover, the agency can use expedited procedures to withdraw a product or indication approved under the accelerated approval pathway in a number of circumstances, including if the post-approval studies fail to verify the predicted benefit.

The accelerated approval pathway has provided earlier access to treatments for HIV/AIDS, cancers and rare diseases, leading to better health outcomes for millions of patients.

MYTH: The accelerated approval pathway was driven by industry to benefit industry.

FACT: The accelerated approval pathway was developed by the FDA in 1992 in response to the growing HIV/AIDS epidemic and calls by patient advocates for the agency to expedite access to promising medicines in development.[i] Congress later codified the pathway.

Developing an innovative medicine is a lengthy and complex process, taking an average of 10-15 years. The accelerated approval pathway was designed to provide FDA with greater regulatory flexibility and allow earlier patient access to potentially lifesaving treatments.

Patients fighting rare and serious conditions – including hard-to-treat cancers – rely on the pathway to improve or even extend their lives.

MYTH: Medicines approved under the accelerated approval pathway are less scrutinized and fail to provide high therapeutic value.

FACT: Medicines granted accelerated approval must adhere to the same statutory standards for safety and effectiveness as medicines receiving a traditional FDA approval,[ii] including substantial evidence of effectiveness based on 'adequate and well-controlled clinical investigations.'[iii]

For example, accelerated approval awarded to two therapies for treatment of patients with non-small cell lung cancer (NSCLC) that had progressed or did not respond to prior therapy resulted in earlier access for over 500,000 patients and nearly 200,000 additional years lived compared with expected survival had the drugs not been available.[iii]

Ensuring that patients have access to these treatments is critical.

MYTH: Medicines approved using a surrogate endpoint are unproven.

FACT: A surrogate endpoint is a marker that is expected to predict clinical benefit but can be measured earlier. For example, in oncology, reduction in tumor size may be a surrogate for overall survival which might take a very long time to study. This saves valuable time in the drug development process, making critical treatment options available to patients sooner.

The FDA bases its decision on whether to accept a proposed surrogate endpoint on the available scientific evidence and requires sponsors to conduct confirmatory clinical studies after accelerated approval.

MYTH: The majority of confirmatory trials of medicines approved via the accelerated approval pathway are never completed or are significantly delayed by companies.

FACT: Medicines approved via the accelerated approval pathway that convert to traditional approval do so in a median time of 3.2 years.[iv]

Companies are required to conduct confirmatory studies of medicines granted accelerated approval and are subject to specific reporting requirements. The FDA is required to track, and make publicly available, progress of confirmatory trials.

At the same time, it is important to understand the challenges to conducting confirmatory trials. There are a number of reasons that a confirmatory trial may take longer than originally planned, including the inability to enroll patients as quickly as anticipated for example due to patients enrolling in other studies aimed at the same population, patients being less willing to volunteer for studies of FDA-approved medicines or small patient populations.

The FDA has implicitly recognized these complexities by showing flexibility in revising and extending enrollment milestones for pending confirmatory trials when necessary. Additionally, in 2022, Congress passed the Food and Drug Omnibus Reform Act (FDORA) to give the FDA additional authority regarding initiation and completion of confirmatory trials.

MYTH: While the FDA does have the authority to withdraw accelerated approvals, the process to do so is slow and ineffective.

FACT: Congress directed the FDA to establish "expedited procedures" to withdraw accelerated approval of products in certain circumstances.

For example, if the confirmatory studies fail to verify the predicted benefit or the company fails to conduct required confirmatory trials with due diligence, the FDA can withdraw accelerated approval after a public hearing. This helps ensure there is an appropriate level of transparency and patient input in the FDA's decision-making. In 2022, FDORA refined the expedited withdrawal procedure for medicines with accelerated approval.

MYTH: Accelerated approval medicines are draining Medicaid program budgets and policies are needed to rein in costs.

FACT: Medicaid spending data illustrate that the patient benefits of accelerated approval drugs far outweigh their cost and support preserving access to these drugs for patients on Medicaid with serious or life-threatening diseases or conditions.

An analysis of Medicaid spending from 2007 to 2018 shows that accelerated approval drugs accounted for less than 1% of Medicaid spending each year, and Medicaid spending on accelerated approval drugs remained between 0.6% to 0.8% a year after the 2012 passage of the Food and Drug Safety and Innovation Act, which encouraged accelerated approval for rare conditions, oncology and HIV/AIDS.[v]

An analysis on drivers of Medicaid and Medicare spending demonstrates that accelerated approval drugs have a minimal impact on spending while also addressing a significant unmet medical need.[vi]

i https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/accelerated-approval
ii https://www.fda.gov/media/86377/download
iii https://www.pharllc.com/wp-content/uploads/2022/07/Clinical-Benefits-of-Accelerated-Approval-Brief.pdf
iv https://link.springer.com/article/10.1007/s43441-022-00430-z
v https://www.ajmc.com/view/limiting-medicaid-access-to-accelerated-approval-drugs-costs-and-consequences
vi https://www.healthaffairs.org/do/10.1377/forefront.20220602.630543/