Preserving & Strengthening *FDA's Accelerated Approval Pathway*

IGT Institute for Gene Therapies

EVERYLIFE FOUNDATION FOR RARE DISEASES

Established in 1992 to address the critical public health needs created by the HIV/AIDS epidemic, the **accelerated approval (AA) pathway** today facilitates earlier patient access to drugs for severe or life-threatening illnesses with limited to no treatment options. Congress enhanced FDA's authorities and encouraged broader use of the pathway to approve drugs treating rare diseases in 2012[1] so that many more patients could benefit from this pathway.

Approval by the FDA is based on clinical trials that study the drug or treatment's effect on a surrogate endpoint, a biologic marker that is reasonably likely to predict clinical benefit (e.g., laboratory measurement, radiographic image, physical sign, or intermediate clinical endpoint).[2] Using a surrogate endpoint can save valuable years in the drug approval process for patients with rapidly progressing, devastating diseases. As a condition of FDA approval, confirmatory clinical trials are conducted to confirm the predicted clinical benefit.

FAST FACTS

As of 2021, more than **270 treatments** have been approved through the pathway

28% of drugs approved in 2021 were approved through the AA pathway.[3]

78% of AA drugs approved two years ago or earlier have been converted to traditional approval [4]

ACCELERATED APPROVAL IS IMPORTANT FOR REALIZING THE PROMISE OF GENE THERAPIES

Gene therapies are different from traditional pharmaceutical and biologic medicines in that they are delivered as one-time treatments that can offer long-lasting – sometimes lifelong – benefits for patients and the healthcare system alike. By targeting the cause of disease at the DNA level, gene therapies have the potential to fundamentally reshape the trajectory of many diseases.

The AA pathway can be an important option for certain gene therapies. The science of gene therapy development and surrogate endpoint development have the following synergies:

- For certain diseases, the DNA-level changes enabled by gene therapies serve to repair the root cause of disease and restore biological pathways. The restoration of biological pathway function in many, if not all cases, meets the threshold for a biomarker to be determined "reasonably likely to predict clinical benefit."
- Assessment of surrogate endpoints is especially important for diseases that progress over long periods of time or in diseases where functional outcome measures may be subject to a lot of variability.
- Gene therapies in development today target some of the most severe diseases, usually genetic, which often impact young children, thereby aligning with Congress' intent in expanding this pathway to include rare diseases; 95% of which have no approved therapies.

By using the AA pathway, drug developers and the FDA can make these innovative and potentially transformative therapies available to patients years in advance of the traditional FDA approval route. A study of oncology products approved via AA were available 3.4 years faster than traditionally approved oncology medicines.[5]

While not all gene therapies will be approved through the AA program, the pathway can be helpful in facilitating patient access to certain gene therapies that target either rare diseases or serious conditions with unmet medical needs such as neuromuscular conditions, sickle cell disease, hemophilia, etc.

Preserving & Strengthening

FDA's Accelerated Approval Pathway

IGT Institute for Gene Therapies

EVERYLIFE FOUNDATION FOR RARE DISEASES

MISPERCEPTIONS ARE THREATENING THE FUTURE OF THE ACCELERATED APPROVAL PATHWAY

MYTH	vs	FACT
The accelerated approval pathway is not as rigorous as traditional approval.		Treatments approved via the AA pathway are subject to the same FDA standards for proving safety and efficacy as traditional drug approvals.
Surrogate endpoints are inferior to clinical outcome measures.		Surrogate endpoints can have advantages over clinical outcomes, especially in cases where they can more accurately capture real-time disease progression or improvement.
Treatments approved via the accelerated approval pathway are responsible for big increases in state Medicaid spending.		Spending on drugs approved via the accelerated approval pathway accounted for less than one percent of annual Medicaid spending between 2007 and 2018.[6]
Treatments approved via the accelerated approval pathway should be considered experimental.		Treatments approved via the AA pathway are subject to the same FDA standards for proving safety and efficacy as traditional drug approvals. Policies that treat them differently diminish Congress' intent in creating the pathway.
The AA pathway has gone too far afield of original intent for HIV/AIDS – too many treatments are approved through this pathway.		Over the past decade, only 15% of drugs approved by the FDA were approved via this pathway. The intent remains the same – to speed up the availability of treatments for patients with life-threatening diseases.

These misperceptions and others have resulted in calls for rash changes to the pathway itself and restrictions on access to AA drugs. Some have proposed limiting the type of treatments that can be approved and setting arbitrary timelines for confirmatory trials, among other modifications that would result in significant delays in patient access to life-changing therapies. Various proposals within the Medicaid program would impose restricted coverage for drugs approved under the pathway and/or reduced reimbursement rates for these therapies. There are opportunities to strengthen the pathway and unleash its potential to transform outcomes for patients with previously untreatable diseases, but elements of some current proposals have the potential to reduce manufacturer incentives to develop innovative treatments or discourage participation in the Medicaid program. Ultimately, patients with serious illnesses would be the ones who suffer.

ACCELERATED APPROVAL CAN BE A LIFELINE FOR MILLIONS OF PATIENTS WITH SERIOUS DISEASES

We must preserve and strengthen the pathway to help ensure patients have access to safe and effective gene therapies as quickly as possible.

Learn more from our Patient Advocacy Advisory Council Member, EveryLife Foundation for Rare Diseases

1. Food and Drug Administration Safety and Innovation Act of 2012, Pub. L. No. 112-144, 126 Stat. 993-1132 (2012).
2. 21 C.F.R. § 601.41.
3. "ADVANCING HEALTH THROUGH INNOVATION: NEW DRUG THERAPY APPROVALS 2021." Available at https://www.fda.gov/media/155227/download (last accessed March 7, 2022)
4. https://www.youtube.com/watch?v=FoScXVVBVdw&list=PLDScWcpkQ5CyIJgOqkp2O88IrV2fHRdkk&index=8
5. https://friendsofcancerresearch.org/blog/optimizing-the-use-of-accelerated-approval/
6. https://www.fightchronicdisease.org/sites/default/files/FINAL%20Quantifying%20Impact%20-%20White%20Paper%20v6.pdf