

## ACCELERATED APPROVAL

The U.S. Food and Drug Administration's standard approval process for new drugs delivers patients the safest, most advanced medications in the world.<sup>1</sup> But it is time consuming, sometimes taking as long as 12 to 15 years.

For diseases with few or no treatment options, the FDA offers several options to expedite the approval process. One of those is accelerated approval, first implemented in 1992 and codified by Congress 20 years later via the Food and Drug Administration Safety and Innovation Act.

Today, accelerated approval is a powerful mechanism for getting novel medications to patients with serious conditions who desperately need treatment options.





## *Q: What is the drug approval process typically like for new medications?*

A new medication's path to approval through the FDA's standard process begins with testing on animals. After that, the developer submits and receives FDA approval for an investigational new drug application, which outlines how the drug's sponsor will conduct clinical trials.

Following three phases of clinical trials, conducted under FDA oversight, the sponsor submits a new drug application to attain market approval. This application contains all data collected during testing, information about the medication's reactions in the body and details about its manufacturing.

The FDA then considers the application. The agency evaluates the drug's safety, effectiveness and usage instructions. It also inspects the production location.<sup>2</sup>

This development and approval process is thorough but lengthy — years for development, and sometimes up to a year for FDA application review.<sup>3</sup> Patients with life-threatening, serious conditions and rare diseases cannot always wait this long.

## *Q: How can the FDA expedite the approval of new medications?*

The FDA offers four approaches to expedite medication approval: Fast Track, Priority Review, Breakthrough Therapy and Accelerated Approval. While all are intended to speed up a medication's time to clinic, each is a little different.

- **Fast Track** is a process designed to facilitate the development and review of new medications to treat serious medical conditions for which there is no current treatment.
- **Breakthrough Therapy** designation also expedites the development and review of new drugs but for medicines that could provide a substantial improvement over available therapies.
- **Priority Review** status goes to drugs for which the FDA decides to take action on within six months of the application being submitted.
- **Accelerated Approval** allows drugs that fill an unmet medical need for serious conditions to be approved based on a surrogate endpoint instead of clinical outcomes.<sup>4</sup>



## *Q: What is accelerated approval?*

Accelerated approval expedites market authorization for medications that treat serious conditions and fill unmet needs for patients. Approval is based on the medication's effect on what's known as a surrogate endpoint. These are predictors of the clinical benefit the medication is meant to provide. In the interest of time, surrogate endpoints serve as stand-ins for the actual clinical benefit. For example, for drugs that intend to treat cancers, an acceptable surrogate endpoint could be tumor shrinkage.

Surrogate endpoints can look to laboratory measurements, radiographic images, physical signs or other measures that are likely to predict clinical benefit.

## *Q: How does accelerated approval differ from other FDA expedited programs?*

All four FDA programs facilitate the development and review of new drugs to address unmet medical needs in treating serious conditions. Accelerated approval differs, however, in the timing of requests, qualifying criteria for proposed medications and decision factors. It has been primarily used when a disease's course is long and measuring a new drug's intended clinical benefit would require extensive time. It has also been used in acute disease settings where clinical benefit can be shown only through large studies.

Accelerated approval is also unique in that it is an approval pathway instead of a designation. An approval pathway is a means to achieve market authorization. Designations, on the other hand, speed up approval processes or provide tax credits and exclusivity, which allows developers to

have sole market access for a medication for a period of time.<sup>5</sup>

## *Q: How can accelerated approval benefit patients?*

Patients and clinicians battling serious medical conditions need effective medications without delay. Accelerated approval reduces their wait times. Medications approved through expedited programs generally reach the clinic a year before those approved through the standard approval process.<sup>6</sup>

Cancer patients in particular have benefitted from accelerated approval. Oncology treatments have been shown to reach the clinic about 3.4 years faster when going through the accelerated approval pathway.<sup>7</sup>

Rare disease patients also benefit from accelerated approval. One well known example is deferiprone, a treatment for certain types of anemia, including sickle-cell anemia. Accelerated approval allowed for a biomarker endpoint to predict effectiveness for approval in 2011.

Patients with swiftly progressing neurodegenerative conditions can also benefit from expedited drug approval. For example, patients with amyotrophic lateral sclerosis have a life expectancy of two-five years after diagnosis.<sup>8</sup> Helping them gain access to novel medications could improve outcomes and prolong life.

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*Q: How does the accelerated approval pathway balance safety with timely access?*

Accelerated approval, as well as other expedited pathways, adheres to the same rigorous standards required by the traditional FDA drug approval process.

Medications must still be tested in what are known as phase 4 confirmatory trials, which demonstrate effectiveness. If trial results show that the drug provides a clinical benefit, the FDA converts the accelerated approval to traditional approval. But if the results show no benefit or are inconclusive, the FDA may withdraw approval. It can even order the medication to be removed from the market.<sup>9</sup>



*Q: How do medications first approved through the accelerated pathway go on to attain traditional approval?*

Not every drug put forward for accelerated approval receives permission to use the pathway. As of June 30, 2022, only 282 medications had completed the accelerated approval process. Of those, about three-fourths have converted to traditional approval, according to a study of drugs reviewed by the FDA between 1992 and 2016.

To gain traditional approval, sponsors of drugs that underwent accelerated approval must conduct post-marketing confirmatory studies to verify that the endpoint used in early studies does in fact predict clinical benefit. If trials do not verify the clinical benefit of a drug or demonstrate enough benefit to justify the risks, then approval may be withdrawn or the drug's label adjusted.<sup>10</sup>

Medications that were initially approved through the accelerated approval pathway and then went on to earn traditional approval include some well known and beneficial medications. Examples include:

- **Keytruda**, which has been approved as a supplement to chemotherapy to help treat metastatic breast cancer.
- **Intence**, for combination treatment of HIV infection.
- **Ferriprox**, used to treat symptoms related to the rare inherited blood disorder thalassemia.



## CONCLUSION

Since its introduction in 1992, accelerated approval has made hundreds of medications available to patients who needed treatment options. Many of the medications have gone on to attain traditional FDA approval, having demonstrated safety and efficacy in required confirmatory studies.

As efforts to address burdensome, costly diseases continue accelerated approval offers a powerful tool to fuel innovation and provide patients timely treatment.

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