



Speeding Up the Drug Approval Process—and What That Means for Patients

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Drug development is often a long and risky endeavor often taking 10-15 years of clinical trials. For patients anxiously awaiting the next generation of life-saving and sustaining therapies made possible by exciting advancements in molecular genetics, immunology

and rare disease research, that wait is too long. Fortunately, regulatory agencies across the globe are leveraging the latest science to speed up that process for exciting new therapies for areas of unmet medical need. Through innovative trial designs, novel endpoints, emerging data sources including patient-generated data and enhanced communication between regulators and sponsors, expedited pathways are breaking down barriers between drug developers and patients in need. Regulatory agencies including those the United States (US), the European Union (EU), Japan and Canada have developed several tools to enhance the efficiency of drug therapy review and approval. Read on for some examples:

Fast Track (US)

First introduced in 1988 in the wake of the AIDS epidemic, the fast track designation expedites the review of drugs that either treat a serious and potentially life-threatening condition, or fill an unmet medical need.^{5,6} It allows companies and the Federal Drug Administration (FDA) to communicate more frequently, and for the FDA to review individual parts of the drug's application as they are submitted—a rolling review process.³ In 2017, 39 percent of expedited, novel drug applications were reviewed in the fast track pathway.³

Priority Review (US)

In 1992, the FDA decided to add the priority review designation to the drug approval process. By providing a mechanism for expedited review with the same rigor used for standard review, new drugs can be made accessible, faster, for patients lacking a therapy for their condition, which must be serious as defined by the FDA.¹ Drugs in this category are intended to do one of four things in comparison with existing treatments: increase efficacy in treatment; prevent or diagnose a condition; eliminate or reduce a treatment-limiting drug reaction; increase patient compliance; or offer evidence of safety and effectiveness in a new subpopulation, like children.⁵ In 2017, 61 percent of all expedited drug approval applications were designated as priority review.³

Targeted Examples of Priority Review (US)

Throughout the years, the FDA has also added other qualifying criteria to priority review. Under the Generating Antibiotic Incentives Now (GAIN) Act of 2012, drugs that treat serious infectious diseases are assigned to this review timeline and are given the fast

track designation.^{5,13} The new antibiotic or antifungal must focus on a specific, qualifying pathogen rather than be broad-spectrum. GAIN also gives developers market exclusivity for qualifying drugs for five years.¹³

The FDA has also introduced a priority review voucher system that gives an incentive to pharmaceutical companies to develop drugs for neglected tropical diseases, rare pediatric diseases, and medical countermeasures for terrorism. The voucher can be used by companies to expedite the review of a different product, or they can be traded and sold on the open market.⁷

Accelerated Approval (US)

The accelerated approval pathway was introduced in 1992, but it was greatly expanded in 2012. Current law allows for a drug to be approved under this pathway if it treats a serious condition and fills an unmet medical need on a surrogate or intermediate clinical endpoint.⁵ Simply put, rather than having to show that patients live longer if they use a cancer drug, a company can show that from treatment, a patient has met another, surrogate endpoint—such as that their tumors have shrunk in size. The FDA also allows intermediate clinical endpoints, which show short-term benefit in chronic diseases or a benefit to a clinical endpoint that predicts an overall clinical effect.⁵

Down the line, companies still must confirm that a surrogate endpoint, such as tumor shrinkage, or intermediate endpoint, such as decreased relapse rate in multiple sclerosis patients, do actually lead to patients living longer. If this is ultimately not the case, the FDA can revoke approval status of the drug.⁵ Of the drugs approved for expedited review in 2017, 13 percent of those went through accelerated approval.³

Breakthrough Therapy (US)

The breakthrough therapy designation was created in 2012, and can be applied to drugs that offer significant improvement over existing therapies for patients with life-threatening illnesses.¹ With this designation, companies get intensive guidance from the FDA on drug development and approval, and it also offers a rolling approval process similar to the fast track designation.⁶ Companies must show evidence for a substantial clinical improvement to be able to receive breakthrough therapy status on a new drug or combination of drugs.⁶ In 2017, this status was applied to 37 percent of all approved drugs in the expedited review process.³

Regenerative Medicine Advanced Therapies (US)

In 2016, the FDA introduced the regenerative medicine advanced therapies (RMAT) designation under the 21st Century Cures Act. This designation has all the same benefits as the breakthrough therapy designation and the fast track review process, but it can only be applied to cell therapies and it does not require evidence that the treatment offers substantial improvement over available therapies.¹² These types of treatments include stem-cell, gene, chemo- and immunotherapy; chimeric antigen receptor (CAR) T-cell therapy, a new type of cancer treatment, also falls under this category.

Accelerated Assessment (EU)

In the EU, drugs are approved through the Committee for Medicinal Products for Human Use in the European Medicines Agency (EMA). Accelerated assessment is the EU parallel to priority review in the US and reduces the assessment time from the standard 210 days to 150 days. To be eligible, companies must demonstrate that the medicine would be of major interest to public health, particularly from the viewpoint of therapeutic innovation—filling a gap in the market.⁸

Priority Medicines Scheme (EU)

Introduced in early 2016, the priority medicines scheme or designation, known as PRIME, provides enhanced support for the development of medicines that target an unmet medical need. Similar to the fast track review process in the US, the scheme enhances interaction and early dialogue between regulators and developers of promising drugs. These dialogues optimize development plans and speed up evaluation so medicines can reach patients earlier. Early clinical data is required to demonstrate eligibility, and successful products will also be eligible for faster market review under accelerated assessment.⁹

Conditional Marketing Authorization (EU)

Similar to the accelerated approval program in the US, conditional marketing authorization allows for early approval of an important medicine in an area of unmet medical need. It's meant to speed patient access to treatments for serious, debilitating, or life-threatening diseases, emergency situations and orphan diseases. A positive risk-benefit balance needs to be demonstrated to gain this authorization and may be based

on phase 2 clinical trial data from or from the use of a validated surrogate endpoint. After conditional approval, a comprehensive data package must be submitted to the EMA to convert the temporary authorization to a standard one, which lasts for 5 years and can be renewed.¹⁰

Sakigake (Japan)

In 2015, the Japanese Ministry of Health, Labor and Welfare introduced sakigake, a product designation similar to the breakthrough therapy designation in the US and PRIME in the EU. Like its international counterparts, eligibility for sakigake requires potential products to be innovative treatments with substantial improvement over current therapies in treating the targeted disease; but in addition, the product's early development must take place in Japan.¹⁴ The sakigake benefits include rolling review of the drug approval application, increased government-industry communication and the promise of a full review within 6 months of submission.¹⁴

Notice of Compliance with Conditions (Canada)

Health Canada, the government agency that reviews drug approval applications, first adopted the notice of compliance with conditions (NOC/c) track in 2002, which provides an opportunity to get a medicine to market earlier. The qualifying criteria are that the disease or condition being treated must be serious, life-threatening or severely debilitating, and that there is no alternative therapy or that it demonstrates significant improvement in the benefit-risk profile compared to existing treatments. NOC/c eligibility can be determined with phase 2 or early phase 3 clinical trial data, and, when granted, allows the product to be marketed and sold immediately under the condition that the developer performs additional safety and benefit studies.¹⁵

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