Expedited Drug Approval Programs

The process for collecting evidence in support of a new drug approval involves multiple steps. Drug developers (sponsors) collect evidence during pre-clinical and clinical phases of the process and submit it to the U.S. Food and Drug Administration (FDA) for evaluation of the drug's safety and efficacy. The next step is a final review for marketing authorization which occurs when a drug sponsor submits a New Drug Application (NDA) to FDA for small molecule drugs or a Biologics Licensing Application (BLA) for biologics. FDA follows a standard review process – which typically takes up to 10 months – to determine whether to approve the drug. Throughout this process, from drug development to post-market monitoring, there are various points in which drug sponsors and FDA interact and exchange information. The time it takes for drug development and approval varies by drug and therapeutic area and FDA review is only part of this process. In most cases, most of this time is spent by drug sponsors in the data collection phases, e.g. clinical trials.

But not all approvals follow the standard review process. Drug therapies that address unmet medical needs, treat serious or life-threatening conditions, or show a significant advantage over current therapies may be eligible for one or more of FDA's four *Expedited Review Programs.* These programs are designed to accelerate the approval process and make the therapies available to patients quicker if it is determined the therapies' benefits justify their risks.[1] The four Expedited Review Programs are ***Priority Review***, ***Accelerated Approval***, ***Fast Track***, **and** ***Breakthrough Therapy.*** The programs have distinct and overlapping criteria and features and are relevant during different points of the drug development and approval process. In recent years, cancer therapies have frequently been approved through these programs.

Priority Review

For drugs with Priority Review designation, FDA's goal is to act on a drug sponsor's marketing application within six months rather than the usual 10 months for a standard review process. Eligible Priority Review drugs **must treat a serious condition and provide a significant improvement in safety or effectiveness over existing treatments.**[1] Drug sponsors can request Priority Review when they submit either an NDA or BLA. Another method for a drug sponsor to obtain Priority Review designation is through a Priority Review Voucher. If a drug sponsor develops a treatment for a neglected tropical disease, rare pediatric disease, or medical countermeasure it can be awarded a Priority Review Voucher which can be redeemed at the drug sponsor's discretion to obtain Priority Review or sold to another sponsor to use for the same purpose. A drug sponsor with a Priority Review Voucher will inform FDA of its intent to use the voucher when it submits either an NDA or BLA.

Accelerated Approval

A drug in the Accelerated Approval pathway is approved based on a surrogate endpoint or intermediate endpoint that is reasonably likely to predict a drug's clinical benefit, such as decreased morbidity and mortality. Because it can often take years to measure primary outcomes like survival, surrogate or intermediate endpoints (e.g. decreasing biomarker levels, imaging results) can serve as a proxy for clinical benefit. Eligible Accelerated Approval drugs **must treat a serious condition, provide a meaningful advantage over available therapies, and demonstrate a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity and mortality or other clinical benefit.**[1] Drug sponsors generally explore the possibility of Accelerated Approval with FDA early in the drug development process (e.g. during the design of clinical trials).

[1] U.S. Food and Drug Administration Center for Drug Administration. Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research. (2014). Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics.

Fast Track

Drugs awarded Fast Track designation give the drug sponsor additional opportunities to interact with FDA reviewers during the drug development and review process. Early and frequent communication with FDA can address questions and issues which can lead to faster approval. An additional feature of Fast Track designation is *rolling review* which allows FDA to review portions of a drug sponsor's NDA or BLA before the complete application is submitted. Eligible Fast Track drugs **must treat a serious condition and nonclinical or clinical data must demonstrate the potential to address unmet medical need.**[1] Drug sponsors can request Fast Track designation during the drug development process, generally before submitting an NDA or BLA.

Breakthrough Therapy

Drugs awarded Breakthrough Therapy designation have all features of Fast Track designation plus organizational commitment from FDA senior managers to interact and provide intensive guidance on drug development during the clinical phases. Eligible Breakthrough Therapy drugs **must treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies.**[1] Drug sponsors can request Breakthrough Therapy designation no later than the end of phase II clinical trial meetings with FDA. Alternatively, FDA may suggest the drug sponsor request Breakthrough Therapy designation if the Agency believes the drug is eligible and can benefit from the designation.

Overview of Expedited Review Programs

	Features	Eligibility	Consideration
Priority Review	NDA or BLA is reviewed within 6 months	Treat a serious condition **AND** Provide significant improvement in safety or effectiveness **OR** A drug application submitted with a Priority Review Voucher	At the time of NDA or BLA submission
Accelerated Approval	Approval is based on a surrogate or intermediate endpoint	Treat a serious condition **AND** Provide a meaningful advantage over available therapies **AND** Demonstrate a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity and mortality or other clinical benefit	Early in the drug development process
Fast Track	Early and frequent communication with FDA reviewers Rolling Review	Treat a serious condition **AND** Nonclinical or clinical data demonstrate the potential to address unmet medical need	During the drug development process, generally before submitting an NDA or BLA
Breakthrough Therapy	All features of Fast Track, organizational commitment from FDA senior managers, and intensive guidance on drug development	Treat a serious condition **AND** Preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies	No later than the end of phase II clinical trial meetings with FDA