Drug Approval and Labeling [1]

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A primary role of the U.S Food and Drug Administration (FDA) is to make sure that all prescription and over-the-counter drugs in the United States are safe and effective. This oversight includes biological products. Also called “biologics,” these include vaccines and products that come from blood and tissues. Within the FDA, there are 2 centers that review research conducted on new drugs and biologics. They are the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research. This research helps them to decide whether a drug or biologic should be approved for use.

Improving the process

Drug development and approval is often lengthy. For many doctors and patients, the development and approval of new cancer treatments is not fast enough. The FDA is working to speed up this process in several ways:

- Meeting with drug sponsors early in the drug development process. This helps to design clinical trials in the best possible way and to review the resulting data.

- Working with European countries and Japan to streamline the approval of drugs in the United States that are approved in these countries. The International Conference on Harmonization (ICH) is an effort among the drug agencies of Europe, Japan, and the United States. It was created to make sure that the details required for drug approval are similar between countries.

- Using the Orphan Drug Act to provide incentives for sponsors to develop new drugs that treat rare diseases. This also includes many types of cancer. Orphan drugs are therapies that treat rare diseases or conditions that affect fewer than 200,000 people in the country.

FDA programs to speed up drug development and approval

The FDA has several programs to help new drugs reach patients sooner:

- **Fast track.** The FDA's fast track program helps speed up the process of drugs that treat an unmet medical need for serious or life-threatening diseases. One example of this is cancer. An unmet need exists when there is no available therapy or when a disease is not treated by an existing therapy. Based on this, drug sponsors may request fast track approval for a new drug. This process promotes talk between the drug sponsor and the FDA before the submission of a New Drug Application (NDA). This helps avoid issues in the design of the clinical trial or the data presentation that could delay FDA approval. Most drugs that are suitable for fast track approval may also apply for priority review (see below).

- **Breakthrough therapy.** This FDA designation is available for drugs that treat serious conditions. Application for the designation is based on preliminary research data showing substantial improvement over the currently available treatments on a clinically significant endpoint(s). The designation helps a company to meet with FDA earlier in the testing process to speed up the development and review. FDA may suggest that a company apply for breakthrough therapy designation after reviewing preliminary data.

- **Accelerated approval.** This FDA program is designed for drugs that treat serious, life-threatening conditions and fill an unmet medical need. It provides a way for drug sponsors to request an interim approval based on study results that are not “standard outcome measures.” These findings are “surrogate endpoints.” They are indirect measures of how well the drug treats cancer. For instance, it could be tumor shrinkage or a change in lab test results. After approval, the sponsor must conduct a clinical trial using standard outcome measures to know if the drug really works. They must also complete other clinical trials to confirm the benefits of the drug. If these studies do not confirm the benefits, the approval for that indication will be withdrawn.

- **Priority review.** This process is for drugs that offer major advances in treatment. It is also for drugs that provide a treatment for a condition that does not have an adequate existing treatment. However, the sponsor can only apply for priority review after submitting an NDA. Therefore, it does not speed the drug development and testing process. Instead, it decreases the time between when the application is submitted and the FDA approves the

drug.

Learn more about the fast track, breakthrough therapy, accelerated approval, and priority review programs from the FDA [3].

Getting drugs to patients who need them

Drugs that are not yet approved by the FDA and are undergoing research are called investigational drugs. These drugs are often only given to patients who are enrolled in a clinical trial [4].

The FDA may approve a drug after researchers complete the clinical trials and analyze the data. It is approved if the benefit of taking the drug is greater than the risk of possible side effects. The FDA recognizes that people who have tried all of the existing treatments may be willing to accept a higher level of risk. It has created programs to provide people with cancer and other serious illnesses with access to investigational drugs.

The best way to gain access to investigational drugs is to enroll in a clinical trial. Clinical trials have eligibility criteria (strict rules) that may limit some patients from enrollment. However they may still be able to receive the investigational drug under expanded access/compassionate exemption (see below).

Federal laws permit drug makers to charge a patient for the actual cost of an investigational drug they receive. Patients and their doctor should talk with the drug maker about potential costs before getting the drug. Most insurance companies will not reimburse the doctor or patient for these charges. Learn more about this regulation [5].

- **Expanded access/compassionate exemption.** Patients may be able to take the drug by enrolling in a large or mid-sized expanded access program through the drug maker. If they do not offer a program for a certain drug, the patient or doctor may submit an individual patient request. In this instance, the doctor works with the drug's manufacturer to try to get the drug. The doctor then submits a request to the FDA, which reviews requests on a case-by-case basis. Learn more about expanded access/compassionate exemption from the FDA [6].

- **Individual Patient INDs.** The FDA's Individual Patient Investigational New Drug (IND) allows doctors to request access to a new drug for a patient. In this instance, the patient is not eligible for any clinical trials and there are no other treatments. There must be enough data to show that the drug may be effective and has no unreasonable risks.

Off-label use

When the FDA approves a new drug, it only approves the drug to treat a specific condition (for example, breast cancer) when given in the manner described on the drug's label. Drug makers may still perform more research on other uses for the drug, such as treating another type of cancer. A doctor may prescribe an FDA-approved drug to treat a condition not listed on the label or use it in a different way from what is listed on the label. This is called an off-label use of the drug.

Off-label drug use in cancer treatment is common for many reasons. First, the FDA often approves drugs for treating only a certain type or stage of cancer. The label only reflects past research when the agent received FDA approval. After approval, researchers may identify effective uses in treating other types of cancer. Second, many cancer treatments involve a combination of multiple drugs. In such instances, 1 or more of the drugs is often used in an off-label way. Multiple drug therapies are also constantly changing as doctors study new mixtures to improve patient care.

Medicare and other types of health plans provide coverage for certain off-label uses if data on effectiveness is available. Learn more about off-label drug use from the NCI [7].

Approval by the FDA for new labeling information

To gain FDA approval of new uses or indications for an already-approved drug, the sponsor must submit a supplemental marketing application to the FDA. This is called a Supplemental New Drug Application (sNDA). A sNDA establishes the safety and effectiveness of the product for the new use. In some cases, a sponsor may discover that the data required to submit an additional request may not be as extensive as the one for initial approval.

Patient involvement

One of the best ways for patients to get involved in the drug process is to enroll in a clinical trial [4]. Not only does it contribute to better treatment, it also provides the patient with closely monitored care. The FDA has a program to include patients in the development and approval process, called the Patient Representative Program [8]. This program allows a person with cancer to participate in FDA’s public advisory committee meetings as a patient. Their role is to provide insight on issues, problems, and questions important to the viewpoint of patients and family members.

More Information

Drug Discovery and Development [9]

Drug Information Resources [10]

PRE-ACT: Preparatory Education About Clinical Trials [11]

How to Protect Yourself From Cancer Treatment Fraud [12]

Being a Cancer Advocate [13]

Additional Resources

NCI: Access to Investigational Drugs [14]

FDA: Drugs [15]

Links
[1] http://www.cancer.net/research-and-advocacy/introduction-cancer-research/drug-approval-and-labeling
[2] http://www.cancer.net/about-us
[3] http://www.fda.gov/forpatients/approvals/fast/ucm20041766.htm
[4] http://www.cancer.net/node/24863
[5] http://www.fda.gov/RegulatoryInformation/Guidances/ucm126427.htm
[6] http://www.fda.gov/NewsEvents/PublicHealthFocus/ExpandedAccessCompassionateUse/default.htm
[7] http://www.cancer.gov/about-cancer/treatment/drugs/off-label
[8] http://www.fda.gov/ForPatients/About/ucm412709.htm
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