Drug Approval and Labeling

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Key Messages:

- The U.S. Food and Drug Administration (FDA) is responsible for making sure all prescription and nonprescription drugs given to people in the United States are safe and effective.
- Because the drug development and approval process can take many years, the FDA has created a number of programs to get new drugs to people with cancer faster.
- The FDA has also developed three programs to make new, promising drugs that haven?t been approved yet available to people with cancer and other serious illnesses.
- Patients play an essential role in the development and approval of new drugs and the expanded use of existing drugs.

A primary role of the FDA is to make sure that all drugs and biological products (called ?biologics,? such as vaccines and products that come from blood and tissues) available in the United States are safe and effective for treating or preventing the conditions for which they are prescribed. Within the FDA, the Center for Drug Evaluation and Research or the Center for Biologics Evaluation and Research is responsible for reviewing research conducted on investigational drugs and biologics and using this information 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 to make sure clinical trials are designed in the best possible way and to review the resulting data.
- Cooperating with European countries and Japan to streamline the approval of drugs in the United States that have already been approved in these countries. The International Conference on Harmonization (ICH) is a cooperative effort among the drug regulatory agencies of Europe, Japan, and the United States to make sure that the information required for drug approval decisions is similar between countries.
- Using the provisions of the Orphan Drug Act to provide incentives for sponsors to develop new drugs that treat rare diseases, including many types of cancer. Orphan drugs are therapies that treat rare diseases or conditions that affect fewer than 200,000 Americans.

FDA programs to speed up drug development and approval

Fast track. The FDA's fast track program helps speed up the development and availability of drugs that have the potential to address an unmet medical need for serious or life-threatening diseases, such as cancer. An unmet medical need exists when there is no available therapy or when a disease or condition is not adequately treated by an existing therapy. Based on these criteria, drug sponsors may request fast track designation for a new drug. The fast track designation encourages discussions between the drug sponsor and the FDA about drug development plans early in the process, before the formal submission of a New Drug Application (NDA). This frequent communication helps prevent issues in the design of the clinical trial or presentation of the resulting data that could delay FDA approval. Most drugs eligible for fast track designation may also be considered for priority review (see below).

Accelerated approval. For drugs designed to treat serious, life-threatening conditions and fill an unmet medical need, the FDA's accelerated approval program provides a way for sponsors to request a provisional approval based on study results other than what are considered ?standard outcome measures,? such as overall survival. These findings are called surrogate endpoints, which are indirect measures of how well the drug treats cancer, such as an improvement in disease-related symptoms or a change in laboratory test results. After approval, the sponsor must conduct a clinical trial using standard outcome measures to confirm that the drug really is effective.

Priority review. This process is for drugs that offer major advances in treatment or provide a treatment for a condition that does not have an adequate existing treatment. However, unlike fast track and accelerated approval, the drug sponsor can only apply for priority review after submitting an NDA. Therefore, priority review does not speed the drug development and testing process. Instead, it decreases the amount of time between the application submission and FDA approval.

Learn more about the fast track, accelerated approval, and priority review programs from the FDA [2]. (Please note that this link will take you outside of Cancer.Net.)

Getting drugs to patients who need them

Drugs that are being studied and have not been approved by the FDA are considered investigational drugs. These drugs are usually only available to

patients who are participating in a clinical trial [3].

After clinical trials have been completed and the data have been analyzed, the FDA may approve a drug if the benefit of taking the drug is determined to be greater than the risk of possible side effects. Recognizing that people who have tried all of the available treatments may be willing to accept a higher level of risk, the FDA has developed three programs to make investigational drugs available to people with cancer and other serious illnesses.

Federal regulations permit drug manufacturers to charge a patient for the actual cost of an investigational drug they obtain. Patients and their physician should talk with the manufacturer about potential costs before getting the drug because most insurance companies will not reimburse the doctor and/or patient for these charges. Learn more about this regulation [4].

Expanded access/compassionate exemption. The best way to gain access to investigational drugs is to participate in a clinical trial, but clinical trials have eligibility criteria (strict rules) that may limit some patients? participation. If the trial is not appropriate, then a patient may be eligible to receive the investigational drug under expanded access/compassionate exemption. Someone wishing to pursue expanded access may be able to take the drug by enrolling in a large or intermediate-sized expanded access program offered through the drug manufacturer. If no such program is offered for a particular drug, the patient and his/her doctor may submit an individual patient request. In this situation, the doctor works with the drug's sponsor to try to get the investigational drug. The physician then submits a request to the FDA, which reviews applications on a case-by-case basis.

Individual Patient INDs. The FDA's Individual Patient Investigational New Drug (IND) allows doctors to request access to an investigational drug for a patient who is not eligible for any clinical trials and for whom there are no satisfactory alternative treatments. There must be sufficient data available to show that the drug may be effective and has not been found to have unreasonable risks.

Group C/Treatment INDs. The Group C program is an agreement between the FDA and the National Cancer Institute (NCI) that permits properly trained oncologists (doctors who specialize in treating people with cancer) to access certain investigational drugs that would otherwise only be available by participating in an NCI study. The drugs are usually being studied in a phase III clinical trial and have shown evidence of effectively treating a specific type of cancer. A patient must provide informed consent [5] before receiving an investigational drug through this mechanism. The program also enables the NCI to collect additional data regarding the safety and effectiveness of these drugs.

Off-label use

When the FDA approves a new drug, the drug is approved to treat a specific condition when given in the manner indicated on the drug's label. Additional clinical research studies may be performed to study other uses for the drug, such as treating another type of cancer. If a doctor prescribes an FDA-approved drug to treat a condition not listed on the label or instructs it to be taken differently from what is indicated on the label, it is referred to as an off-label use of the drug.

Off-label drug use in cancer treatment is common for many reasons. First, drugs are generally approved for treating only a particular type or stage of cancer. The label can only reflect the research that was conducted when the agent was granted FDA approval. After approval, a drug that is effective in treating one type of cancer is often found to be effective in treating other types of cancer. Second, many cancer treatments involve a combination of multiple drugs. In such instances, one or more of the drugs is often being used off label. Multiple drug therapies are also constantly changing as doctors study new combinations to improve patient care.

Learn more about off-label drug use from the NCI [6], including a list of states with laws requiring insurance coverage of off-label drugs.

Approval by the FDA for new labeling information

To gain FDA approval of new labeling information for an already-approved drug, the sponsor must submit a supplemental marketing application, called a New Drug Application (NDA), to the FDA to establish the safety and effectiveness of the product for the proposed new use. In some cases, a sponsor may discover that the data required to submit a supplemental application may not be as extensive as what was needed for initial approval.

The FDA has developed many initiatives to encourage supplemental applications for products used in cancer treatment. For example, the FDA has surveyed private, academic, and professional groups involved in cancer research and treatment to get their opinions of off-label drug use and has then met with drug sponsors to facilitate submission of a supplemental application.

Patient involvement

One of the best ways for patients to get involved in the drug development and approval process is to participate in a clinical trial [7]. Not only does participation in a clinical trial contribute to the advancement of cancer treatment, patients enrolled in cancer clinical trials receive closely monitored care. The FDA has two programs to include patients in the development and approval process.

The Cancer Drug Development Patient Consultant Program is designed to include the perspective of patient advocates in the drug development process. Patient advocates selected for the program participate in meetings (via phone) with the FDA and drug companies to discuss various aspects of the drug development process. Learn more about this program. [8]

The Patient Representative Program allows a person with cancer to be considered for participation in advisory committee meetings as a patient representative. The role of the patient representative is to provide insight on issues, problems, and/or questions important to the viewpoint of patients and family members. The patient representative must meet several qualifications, and voting members must be appointed as special government employees. Find out more about this program [9].

More Information

Drug Discovery and Development [10]

Drug Information Resources [11]

How to Protect Yourself Against Cancer Treatment Fraud [12]

Being a Patient Advocate [13]

Additional Resources

NCI: Access to Investigational Drugs ? Questions and Answers [14]

NCI: Approval Process for New Cancer Treatments [15]

FDA: Drugs [16]

Links:
[1] http://www.cancer.net/about-us
[2] http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/SpeedingAccesstoImportantNewTherapies/ucm128291.htm
[3] http://www.cancer.net/node/24863
[4] http://www.fda.gov/RegulatoryInformation/Guidances/ucm126427.htm
[5] http://www.cancer.net/node/24879
[6] http://www.cancer.gov/clinicaltrials/learningabout/approval-process-for-cancer-drugs/page5
[7] http://www.cancer.net/all-about-cancer/clinical-trials
[8] http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/PAtientInvolvement/ucm123859.htm
[9] http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/CancerLiaisonProgram/ucm127681.htm
[10] http://www.cancer.net/node/24505
[11] http://www.cancer.net/node/25369
[12] http://www.cancer.net/node/24559
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[15] http://www.cancer.gov/clinicaltrials/learningabout/approval-process-for-cancer-drugs/page1
[16] http://www.fda.gov/AboutFDA/Transparency/Basics/ucm192696.htm