Wyoming Drug Utilization Review

Summary of drug approval process: Accelerated, fast track, and emergency use authorization

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Drug approval process

In the standard drug approval process, the FDA follows procedures to evaluate the safety and efficacy of drug products before they can enter the market.

Drug approval process[1]	
Step 1	*In vivo* animal studies evaluate the initial pharmacology and potential toxicities of the test drug in animals. Once this step is complete, the drug manufacturer would submit an investigational new drug application (IND).
Step 2	Submission of the IND, a proposed plan to begin studies in humans and includes preclinical data, proposed use, and safety data. FDA reviews the data and decides on whether to allow the manufacturer to begin human trials.
Step 3	Clinical trials typically following three phases.
	Phase 1: Comprised of a small group of healthy individuals. They receive the medication, which will be evaluated based on properties of toxicology, pharmacokinetics, pharmacology, and safety.
	Phase 2: Begin evaluation in a larger group of patients, which can include 100 or more patients with the disease or have symptoms of the condition in which the investigational drug claims to treat. Phase 2 evaluates the effectiveness based on dosing, relative safety, and adverse effects.
	Phase 3: Number of participants increases, sometimes into the thousands, and in several geographical regions as part of clinical trials. Studies are usually double blind, compared to placebo, and randomized.
Step 4	Studies are called post marketing surveillance. Although the drug is approved for marketing, there is continued evaluation for safety and efficacy. Manufacturers are required to monitor for safety and efficacy throughout this phase by submitting annual reports to the FDA based on the data collected. Additionally, providers can report adverse effects through MedWatch. All adverse events reported to the manufacturer must be reported to the FDA, even if the manufacturer disagrees with the submitted report.

The drug approval process deviates slightly when it comes to generic drugs. Once a brand drug patent expires, generics can enter the process by submission of an abbreviated new drug application (ANDA) (1). ANDA reports must show proof that the generic product is similar to the innovator product based on the generic's pharmacokinetics, bioavailability, and clinical activity.

Expedited programs

The drug approval process allows the FDA to regulate safety and efficacy of drugs before medications can be marketed. The drawback to this process is that it can take several years to reach

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approval. To speed up the availability of drugs, especially for serious diseases, the FDA has developed four approaches, priority review, breakthrough therapy, accelerated approval, and fast track (2). This summary will cover the latter two.

The following definitions assist in understanding the accelerated programs.

Immediate life-threatening disease or condition	"A stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment."[3]
Serious disease or condition	"A disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one."[3]
Unmet medical need	"A condition whose treatment or diagnosis is not addressed adequately by available therapy. An unmet medical need includes an immediate need for a defined population (i.e., to treat a serious condition with no or limited treatment) or a longer-term need for society (e.g., to address the development of resistance to antibacterial drugs)."[4]

Fast Track

Fast track is a method to expedite drug approval. The justification for fast track is for serious conditions and can fill an unmet medical need (6). Fast track hosts its own conditions that must be followed. FDA will require more frequent meetings to discuss the drug's development plan to ensure appropriate collection of data to support drug approval (6).This applies to written communication over design of clinical trials as well. Should criteria be met, the fast track drug may become eligible for accelerated approval and priority review.

Accelerated approval

The accelerated approval regulations pathway was established in 1992 (5). This allowed drugs for serious conditions that would qualify for an unmet medical need to be approved (5). In 2012, Congress passed an amendment called the Food and Drug Administration Safety Innovations Act (FDASIA), allowing the FDA to accelerate approval of drugs for serious conditions that fill an unmet medical need and have an effect on a surrogate or an intermediate clinical endpoint (5).

A surrogate endpoint is a marker that predicts clinical benefit, but in of itself is not a measure of clinical benefit. Surrogate markers may include a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit. Similarly, an intermediate clinical endpoint is a measure of therapeutic effect that is likely to predict clinical benefit. By utilizing a surrogate endpoint or intermediate endpoint, the accelerated drug approval process saves important and valuable time towards providing benefit towards serious diseases.

Emergency Use Authorization (EUA)

Under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act), the FDA may authorize unapproved products or use of approved products in an emergency to diagnose, treat, or prevent serious or life-threatening diseases caused by chemical, biological, radiological, or nuclear (CBRN) threat agents (7). However, this process can only be approved when the Secretary of HHS declares that an EUA is appropriate. An example of this occurred on February 4, 2020 when Secretary of HHS identified COVID-19 as a public emergency that has significant potential to affect national security or the health and security of the US citizens (7). The same rigorous approval process applies to EUA as standard approval process. Data is reviewed and analyzed by independent experts and not scientist employed by the drug manufacturer (8-9).

References:
1. Federal law. In: Feinberg WJ Ed. Pharmacy Law – Examination and Board Review. New York (NY): McGraw Hill; 2015. Available from: http://accesspharmacy.mhmedical.com. Accessed: March 7, 2022.
2. U.S. Food and Drug Administration. Fast track, breakthrough therapy, accelerated approval, priority review. Washington (DC); 2018. Available from: https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review. Accessed: March 7, 2022.
3. U.S. Food and Drug Administration. Title 21 - - food and drugs. Chapter I – Food and Drug Administration Department of Health and Human Services subchapter D – drugs for human use. 21 CFR 312.300(b). Washington (DC); 2018. Available from: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.300. Accessed on: March 7, 2022.
4. U.S. Food and Drug Administration. Expedited programs for serious conditions – drugs and biologics. Washington (DC); 2020. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/expedited-programs-serious-conditions-drugs-and-biologics. Accessed: March 7, 2022.
5. U.S. Food and Drug Administration. Development & approval process | drugs. Washington (DC); 2019. Available from: https://www.fda.gov/drugs/development-approval-process-drugs. Accessed: March 7, 2022.
6. U.S. Food and Drug Administration. Fast track. Washington (DC); 2018. Available from: https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/fast-track. Accessed: March 7, 2022.
7. U.S. Food and Drug Administration. Emergency use authorization. Washington (DC); 2022. Available from: https://www.da.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization. Accessed: March 7, 2022.
8. Communicating about COVID-19 vaccination. Pharmacist's Letter/Prescriber's Letter. 2021; 371201. Stockton (CA): Therapeutic Research Center; 2021. Available from: https://pharmacist.therapeuticresearch.com. Accessed: March 9, 2022.
9. U.S. Food and Drug Administration. Emergency use authorization for vaccines explained. Washington (DC); 2022. Available from: https://www.fda.gov/vaccines-blood-biologics/vaccines/emergency-use-authorization-vaccines-explained. Accessed: March 7, 2022.

The P&T Committee met for its quarterly business meeting on August 11, 2022.

Highlights of this meeting include:

Tlando, Vtamo, Camzyos, Voquezna, Ztalmy, and Radicava will be limited to indication. Tlando, Quiviviq, Vtamo, Mounjaro, and Voquezna were referred to the Department of Health for cost analysis and PDL placement.

Lyvispah will require prior authorization.

The prior authorization requirement for Paxlovid will be removed to provide pharmacies easier access to the associated dispensing fee.

Proposed criteria is open for public comment. Comments can be sent by email to alewis13@uwyo.edu. All comments should be received by October 1, 2022. The next P&T Committee meeting will be held November 10, 2022 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

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