Wyoming Drug Utilization Review

Priority Review and Breakthrough Therapy

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FDA Drug Approval Process Part II

In the last newsletter issue, we gave a general overview of the drug approval process set out by the Food and Drug Administration (FDA), as well as a couple of the expedited processes the FDA offers, including Accelerated Approval, Fast Track, and Emergency Use Authorizations (EUA). In this issue, we will discuss two additional accelerated processes, including Priority Review, and Breakthrough Therapy.

Priority Review FDA Approval Process

In 1992, the FDA created a two-tiered system of drug review under the Prescription Drug User Act (PDUFA) intended to meet goals of improving the time it took to get new drugs approved (1). The system consists of Standard Review, which has a goal review time of 10 months, and Priority Review, which has a goal review time of 6 months. The FDA's priority review process is used when the drug has the potential to represent a significant improvement in safety or effectiveness of a condition's diagnosis, treatment, or prevention. Per the FDA, significant improvement may be demonstrated by (1):

- Evidence of increased effectiveness in prevention, treatment, or diagnosis of a condition
- Substantial reduction or elimination of a drug reaction that limits treatment
- Enhanced patient adherence leading to an improvement in significant outcomes, or
- Evidence of effectiveness and safety in a new subpopulation

Similar to other expedited processes, while the Priority Review process takes a shorter amount of time than Standard Approval, the medical standards are not lowered, and the quality of evidence is still expected to be the same. Designation as Priority Review does not affect the duration of clinical trials. Logistically, the manufacturer is not required to apply for this designation, as the FDA reviews every application that it receives for priority review eligibility. After the original new drug application (NDA), biologics license application (BLA), or efficacy supplement is received, drug companies can expect this designation to occur within 60 days if the drug is eligible (1).

In 2007, the FDA implemented the Priority Review Voucher (PRV) program (2). This program operates by granting a voucher for the Priority Review process to any sponsor that meets certain criteria (2,3). Of note, these vouchers can be sold between product developers (3). Originally intended to address tropical diseases such as Cholera and Zika Virus, this program has since been expanded to include rare pediatric diseases, medical countermeasures, and diseases related to public health emergencies (2-4).

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The Government Accountability Office (GAO) published a report in 2020 assessing the program (3). Since the program's implementation, only 31 PRVs have been awarded. Seventeen of the vouchers were sold to other companies for revenue of between 67 and 350 million dollars, and a total of 16 vouchers have been redeemed (3). One commentary criticized the PRV program for low numbers of vouchers submitted, and described it as "tantamount to putting the FDA service up for sale to the highest bidder" (2).

Breakthrough Therapy FDA Designation

In contrast to the Priority Review process, the Breakthrough Therapy designation targets the drug development process (5). The intent behind this designation is to allow for faster development of drugs intended to treat serious conditions, and which may represent significant improvement over currently available therapies (6). The FDA accomplishes this by assisting the drug companies to "develop evidence needed to support approval as efficiently as possible" (5).

To qualify for this process, the drug must demonstrate substantial improvement in a significant endpoint with preliminary clinical evidence (5). The evidence from the preliminary clinical trials should generally show a clear advantage in a clinically significant endpoint over currently available therapies. For the purposes of Breakthrough Therapy, the definition of a clinically significant endpoint means one that measures an effect on irreversible morbidity or mortality (IMM), or suggests an effect on IMM or other serious symptoms, including (5):

- An established surrogate endpoint
- A surrogate or intermediate clinical endpoint that is reasonably likely to predict clinical benefit
- Effects on pharmacodynamic biomarkers not meeting criteria for an acceptable surrogate endpoint, but which strongly suggests the potential for a clinically significant effect on the underlying disease state, or
- A safety profile significantly improved compared to currently available therapies, with similar efficacy.

There are a few advantages of a Breakthrough Therapy designation as well, including:

- All features associated with Fast Track Designation (5), including:
    - More frequent meetings with the FDA to discuss the plan for drug development and appropriateness of data collection methods (7)
    - Increased frequency of communication from the FDA
    - Eligibility for Accelerated Approval and Priority Review pathways, if the relevant criteria are met, and
    - Rolling review, where the drug company submits sections of the NDA as they are completed, rather than the entire completed NDA at once (7).
- As early as phase 1, intensive guidance from the FDA on an efficient drug development program (5), and
- Organizational commitment with the involvement of senior managers (5)

Breakthrough Therapy is a designation that the drug company is required to request, and ideally, this would happen before the end-of-phase-2 meetings to provide the most benefit for the company (5). Additionally, the FDA has the ability to suggest that a drug company apply for this designation if it believes that the drug may meet criteria, and if the remaining development processes would benefit from designation as Breakthrough Therapy. After the drug company has submitted the request, the FDA will respond within 60 days. Finally, the FDA does not expect that requests for Breakthrough Therapy designation will be made after an NDA, BLA, or efficacy supplement is submitted, as there would be no benefit for doing so (5).

In summary, Priority Review and Breakthrough Therapy are two options for accelerating the drug development and review process. Priority Review focuses on the review process, and is targeted at drugs that may represent significant advances in treatment of diseases over what is currently marketed. Breakthrough Therapy focuses on the development process, and focuses on drugs that show promising results in earlier phases of clinical trials.

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The P&T Committee met for its quarterly business meeting on November 10, 2022.

Highlights of this meeting include:

After 16 years of serving the State of Wyoming, Dr. James Bush has announced his retirement. We thank him for all he has done for the P&T Committee and Wyoming Medicaid.

Xcopri will require a trial of two preferred agents for 30 days prior to approval. Dupixent will be approved for use in prurigo nodularis and eosinophilic esophagitis. Vivjoa, botulinum toxins, Skysona, Zynteglo and Spevigo will all be limited to indication. The Committee recommended that Sotyktu be available after trial of Humira for moderate to severe plaque psoriasis.

Weight loss agents were reviewed. The Department of Health is currently determining the feasibility for coverage of this class of drugs based on a change in Federal policy. The Committee recommended that, if the Department chooses to change policy to cover them, weight loss medications should be limited to indication with an initial approval of 3 months. This is expected to be an ongoing discussion with no current estimate for implementation.

The Committee reviewed Olumiant for alopecia areata and Opzelura for depigmentation associated with vitiligo. The Committee determined that alopecia areata and the depigmentation associated with vitiligo are considered to be cosmetic conditions and, therefore, drug therapy used to treat these conditions is cosmetic and will be excluded from coverage.

The draft 2023 Preferred Drug List was reviewed and will be posted for public comment at www.uwyo.edu/DUR. Comments can be sent by email to alewis13@uwyo.edu. All comments should be received by December 15, 2022. The next P&T Committee meeting will be held February 9, 2023 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

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