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Update on Efficacy of Generic Finasteride

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Finasteride 5mg was approved by the U.S. Food and Drug Administration (FDA) in 1992 for the treatment of benign prostatic hyperplasia, and in 1997 for male pattern hair loss (MPHL) in the 1mg dose. For many years, because of cost and availability issues of finasteride 1mg, physicians, especially outside of North America, have suggested that patients divide brand or generic 5mg finasteride into quarters. Recently, numerous hair transplant physicians have commented on anecdotal reports by their patients of increased shedding and progressive hair loss noted after changing from brand to generic finasteride 1mg. This raises several questions about generic medications: how does the efficacy compare to brand, how are generic drugs regulated, are there variations among generic manufacturers, and is the active ingredient evenly distributed in the tablet?

Using bioequivalence as the basis for approving generic copies of drug products was established by the "Drug Price Competition and Patent Term Restoration Act of 1984," also known as the Hatch-Waxman Act. This Act expedites the availability of less costly generic drugs by permitting the FDA to approve applications to market generic versions of brand-name drugs without conducting costly and duplicative clinical trials. At the same time, the brand-name companies can apply for up to five additional years longer patent protection for the new medicines they developed to make up for time lost while their products were going through the FDA's approval process. Brand-name drugs are subject to the same bioequivalence tests as generics upon reformulation.

According to the FDA website, a generic drug is identical or bioequivalent to a brand-name drug, and must follow the same standards as the innovator drug:

- Contain the same active ingredients as the innovator drug (inactive ingredients may vary).
- Be identical in strength, dosage form, and route of administration.
- Have the same use indications.
- Be bioequivalent.
- Meet the same batch requirements for identity, strength, purity, and quality.
- Be manufactured under the same strict standards of FDA's good manufacturing practice regulations required for innovator products.

In order to obtain FDA approval to market a generic drug, companies must submit an abbreviated new drug application (ANDA). The ANDA process does not require the drug sponsored to repeat preclinical (animal) and clinical (human) research on ingredients or dosage forms already approved for safety and effectiveness. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent (i.e., performs in the same manner as the innovator drug). Bioequivalence is often demonstrated by studies measuring the time it takes the generic drug to reach the bloodstream in 24-36 healthy volunteers. This determines the rate of absorption, or bioavailability, of the generic drug, which is then compared to that of the innovator drug. The generic version must deliver the same amount of active ingredients into a patient's bloodstream in the same amount of time as the innovator drug. Bioavailability is usually assessed by measuring the area under the plasma concentration–time curve (AUC).[1]

For FDA approval, a generic manufacturer must demonstrate that the 90% confidence interval for the ratio of the mean responses (usually of AUC and the maximum concentration, C_{max}) of its product to that of the brand-name drug is within the limits of 80% to 125%. While AUC refers to the extent of bioavailability, C_{max} refers to the rate of bioavailability.[2]

The 80-125% criterion is used to compare two treatments to evaluate bioequivalence. The bioequivalence test states that we can conclude that two treatments are not different from one another if the 90% confidence interval falls completely within the range 80-125%. The 80-125% criterion cannot conclude that the drugs are the "same," only that they are not "different." For drugs with a narrow therapeutic index range, small differences in dose or serum concentration may have therapeutic failures or adverse events, and the acceptance range of 80-125% may need to be smaller.[3]

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