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Division of Documents Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket 2005N-0410

The Academy of Managed Care Pharmacy (AMCP) is pleased to provide comments to the Food and Drug Administration (FDA) on the Prescription Drug User Fee Act (PDUFA). This letter supplements the Academy's comments presented at the FDA public meeting on November 14, 2005.

AMCP is a national professional association of pharmacists and other health care practitioners who serve society by the application of sound medication management principles and strategies to achieve positive patient outcomes. The Academy's 4,800 members develop and provide a diversified range of clinical, educational and business management services and strategies on behalf of the more than 200 million Americans covered by a managed care pharmacy benefit.

The fundamental goal of the FDA is to promote and protect public health both by determining in a timely manner a drug or biologic's safety and efficacy based on clinical research, and, by taking appropriate action on the marketing of these products.

FDA approval does not mean that medications are risk-free. First, approved medications are generally safe and efficacious only when used appropriately. Second, even when used appropriately, prescription medications have potential side effects. Third, problems associated with drugs may only become apparent after a drug has been on the market and has been used by a broader population for a longer period of time than was tested during the approval process.

In order to help fund FDA activities, Congress passed PDUFA in 1992 authorizing the agency for a five year period to collect user fees from drug manufacturers seeking FDA approval of their drugs for marketing. PDUFA was subsequently renewed in 1997 and 2002. Congress must decide whether or not to pass a fourth renewal by September 2007. We understand user fees currently amount to just over one-half of total funding for drug reviews. If further legislative authority to collect user fees is not extended to the agency, Congress must establish an alternative source(s) of funding for necessary agency activities.

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AMCP believes that funding to allow the FDA to fulfill its obligation to ensure medication safety is absolutely necessary. We believe funding is imperative for not only the prescription drug review program but also for effective *postmarket risk management* and the *managing and monitoring of direct-to-consumer (DTC) advertising of prescription products*. Our rationale for this position follows.

Postmarket Risk Management

Although FDA is responsible for evaluating not only drug's efficacy but its safety as well, the reality is that the drug review process emphasizes "approval" so that patients are able to have access to new drugs as soon as possible. The process imposes limitations because of the comparatively limited timeframes and parameters of clinical trials and the relatively small population of subjects tested. Only after a drug has been on the market and available to a broader population can a determination be made as to whether a drug is effective in treating medical conditions and whether there are any safety problems associated with its use. This is the reason postmarket surveillance constitutes a patient safety imperative.

PDUFA III gave FDA authority to spend user fee funds on certain aspects of postmarket risk management. The rationale was to preserve an appropriate balance between drug efficacy and drug safety by funding safety-related activities for the first two years of product marketing for most drugs, and the first three years for potentially dangerous drugs. The authority applied only to drugs and biologics approved on or after October 1, 2002. The agency itself points out that the timing restriction has meant that user fee funds could not be used to support investigation of safety issues related to potentially harmful products such as COX-2 and SSRI medications because they were approved prior to October 2002.

The Academy applauds this step, but believes it is insufficient to adequately address the postmarket risk management task. Postmarket surveillance is an essential programmatic function for the FDA if the agency is to fulfill its mission of promoting and protecting public health. To fulfill its responsibilities, the FDA's postmarket surveillance program must provide a vehicle for the ongoing collection and review of data related to problems associated with a drug's use. This data can be used to determine if a drug should continue to be marketed to the public (1) under the original approval, (2) under modified marketing requirements (labeling, restricted distribution, etc.) or (3) be withdrawn either permanently or until further studies are conducted.

The agency's current limited authority to monitor a medication after its approval has significant shortcomings. The only course of action available to the FDA is withdrawal of a drug's approval; it cannot issue fines, restrict advertising or administer other penalties.¹ The FDA often asks manufacturers to conduct follow-up studies as a condition of approval, but the completion rate for Phase IV studies is quite poor. According to a recent *Health Affairs* article, data suggest that of the 1,191 Phase IV postmarketing commitments that had been made by manufacturers as of September 30, 2004, 68 percent had yet to be commenced,

¹ Daniel Carpenter, A Proposal for Financing Postmarketing Drug Safety Studies by Augmenting FDA User Fees, *Health Affairs* – Web Exclusive, October 18, 2005, p. W5-475.
<http://content.healthaffairs.org/cgi/content/abstract/hlthaff.w5.469v1>, accessed November 21, 2005.

compared with 18 percent that were ongoing and 12 percent that were completed.² The Academy believes Congress should give the FDA the authority to mandate follow-up Phase IV studies as a condition of approval.

Along with giving the agency the authority to require Phase IV studies of any FDA approved drug, the Academy believes Congress should assure that sufficient funding is made available through either PDUFA legislation or other funding sources to allow the agency to enforce this new activity in a robust manner.

Recommendations

The Academy recommends the following actions with regard to postmarket surveillance:

1. The FDA's authority to monitor a drug after approval must be expanded. The FDA must have authority to enforce requests for a Phase IV study short of withdrawing the drug's approval.
2. Even with the staff increases allowed by PDUFA III, the FDA's current postmarket surveillance system for identifying previously unknown adverse effects of drugs suffers from a lack of resources. FDA funding must be of an amount sufficient to recognize that postmarket surveillance is as important as the drug approval process and a part of the primary mission of the Agency.

Managing and monitoring of direct-to-consumer (DTC) advertising of prescription product

The Academy discourages the use of direct-to-consumer advertising that promotes specific prescription drug products, but supports ads that educate the public about disease symptoms and available treatment options.

AMCP recognizes that the public has a personal interest in health care. Advertising that increases public awareness about disease symptoms, informs consumers about available treatment options and diagnostic procedures that may be of benefit, stimulates discussions between prescribers and patients, and encourages individuals to pursue healthier lifestyles can improve the health status of patients. It does this by encouraging consumers to become more proactive about their health in general, and by fostering constructive dialogue between patients and their providers regarding their care.

AMCP strongly discourages advertising aimed at consumers that promotes the use of specific prescription drug products. In general, such ads aim to increase a product's market share or create a new market for the product. Whether or not a prescription item is medically indicated for a given patient, direct-to-consumer advertising of the product can create unwarranted patient demand. The ads can often be misleading, failing to sufficiently warn consumers about the potential risks of using the product and about alternative treatment options.

² Carpenter, p. W5-474.

The impact that direct-to-consumer print and electronic advertising have had on the demand for prescription drugs and the pricing of these drugs has been the subject of considerable debate -- even more so now because of the substantial increase in the amount of such advertising, growing from \$791 million in 1996 to an estimated \$3 billion in 2004.

The promotion and advertising of prescription drugs is regulated by the Food and Drug Administration (FDA) under its statutory authority. FDA's implementing regulations and its 1997 guidance contain specific requirements and explanations regarding the content of advertisements that promote prescription drugs.

The Academy believes the approach taken by the FDA's 1997 guidance, which for the first time permitted broadcast DTC advertising that specifically identifies a drug product by name, is largely responsible for the explosion in DTC advertising of prescription drugs. The guidance resulted in a shift from advertising, which until then was primarily informational, to advertising that is now primarily aimed at increasing a product's market share or creating a new market for the product. Further, the type of advertising that followed issuance of the 1997 guidance has often been misleading, because it has frequently failed to sufficiently warn consumers about the potential risks of using the product, typically does not inform them about alternative treatment options, and fails to provide information about cost issues.

The problem noted above is exacerbated by the limited authority the agency has to ensure compliance with its regulations and the 1997 guidance: When current requirements are not met, FDA's only available option is to issue a regulatory letter requesting that the advertisement be withdrawn or revised. Under current statutory authority, FDA is limited in its ability to expand its oversight of direct-to-consumer advertising. The Academy has encouraged Congress to enact legislation requiring FDA to pre-approve direct-to-consumer advertising of specific products to ensure that promotions are fair, not misleading and provide balanced information as to benefits and risks, granting enforcement authority to ensure compliance and authorizing the financial resources to support this activity.

Concern about DTC advertising has been raised as part of the drug safety debate with those calling for greater scrutiny focusing on what they argue are inappropriate prescriptions being written because of consumer response to what are characterized as a constant barrage of advertisements. While DTC advertising does not have a direct causal effect as to the safety of prescription drugs, it is of concern when looking at the overall picture of medication safety, especially if DTC advertising prompts patients to insist on taking a drug with a high risk side effect profile or for an off label condition.

Recommendations

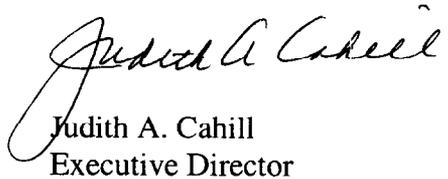
The Academy of Managed Care Pharmacy supports changes that would result in a significantly improved and comprehensive program for FDA oversight of DTC advertising. Specifically, we support the idea that the Agency should have:

1. the express authority to mandate prior approval of DTC advertising

2. sufficient funding to enforce review of DTC advertising and pursuit of remedial actions determined to be necessary
3. oversee content of DTC advertising to assure that it
 - focuses on raising awareness of disease and symptoms
 - addresses alternative treatment options
 - reasonably describes both benefits and potential risks
 - stimulates patient/provider dialogue, and
 - encourages healthier lifestyles.

AMCP appreciates the opportunity to comment on these extremely important issues. If you have any questions, please contact me at (703) 683-8416 or at jcahill@amcp.org.

Sincerely,



Judith A. Cahill
Executive Director