Patient Package Inserts

A New Tool for Patient Education

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THE FOOD AND DRUG ADMINISTRATION (FDA) is the Federal agency charged with assuring that prescription drugs are properly labeled. Unlike the consumer-directed labeling for the over-the-counter drugs, prescription drug labeling is directed toward the physicians who prescribe and administer pharmaceuticals. To comply with the requirements of the Food, Drug and Cosmetic Act, prescription drug manufacturers or repackers must include a copy of the official labeling or "package insert" with each product they deliver. Except for the brief customized label affixed to the container by the pharmacist, prescription drug information provided to patients is usually limited to the verbal explanations provided by health care professionals.

However, since the late 1960s, the FDA has occasionally departed from the usual labeling requirements and required manufacturers to include, in addition to the physician-oriented package insert, a patient-oriented label on, or around, the dispensed drug, that is, a patient package insert (PPI).

Isoproterenol inhalators were the first products to require a PPI. It was found that these inhalators, intended to increase air passage flow, paradoxically could decrease air flow. In 1970, the FDA required a PPI for oral contraceptives, following the discovery of increased risk of thromboembolic disorders associated with the use of the pill. In view of the "elective" nature of the pill and the availability of other means of contraception, it was concluded that patients should have written information concerning risks and benefits associated with the use of oral contraceptives. Thus, patients could make an informed choice, in consultation with their physicians, as to the most desirable method of contraception.

Subsequent drug classes for which patient labeling has been required include diethylstilbestrol (the "morning after pill"), and medroxyprogesterone acetate, a long-acting injectable contraceptive. For these drugs, the PPI requirement was based on the premise that the risk-to-benefit equation was such that patient labeling could affect the decision to use them as well as their proper use by patients.

Prompted by the suggestions of a National Food and Drug Advisory Committee and a petition filed in behalf of several consumer interest groups, the FDA initiated a Patient Drug Labeling Project to investigate the feasibility of expanding the adoption of PPIs to a wide variety of prescription drugs. Since the inception of this project in 1975, it has become increasingly apparent that there is wide support for the PPI concept.

Two bills were introduced in the 94th Congress to require PPIs: the Rogers Bill, HR-14289, would require PPIs for almost all drugs, whereas the Kennedy Bill, S-1282, would require PPIs for drugs that were undergoing the final phases of clinical evaluation. In November 1976, a national symposium under

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the joint sponsorship of the FDA, the American Medical Association (AMA), the Pharmaceutical Manufacturers Association (PMA), and the Drug Information Association (DIA) was held to highlight the topic of Patient Package Inserts. Attendance by more than 700 persons from many disciplines reflected the broad support and interest in increasing dialogs regarding this important issue.

At this juncture in the development of regulatory policy, it is appropriate to focus on two general themes relating to PPIs: (*a*) a general description of the societal atmosphere fostering the evolvement of PPIs and (*b*) a general overview of FDA's activities designed to solicit outside viewpoints preparatory to formulating PPI policy.

The Climate

In the PPI arena, two potent forces are pushing and pulling these inserts into being. The pull comes from the consumerism movement, and the push is the movement toward patient education. The consumers are saying that they need more information about prescription drugs, and the health educators are saying that patients must know more about their therapy.

Consumerism movement. The consumerism movement is highlighted by laws and regulations such as the Truth in Lending Act, unit pricing, and nutritional labeling. In general, the movement is predicated on the argument that people have a "right to know." In relation to PPIs, the movement is best indicated by the petitioning of the FDA in March 1975 by a consortium of consumer advocacy groups to require PPIs for all prescription drugs. The document was filed by the Center for Law and Social Policy of Washington, D.C., in its own behalf as well as in behalf of the Consumers Union, the Consumer Action for Improved Food and Drugs organization, the National Organization for Women, the Women's Equity Action League, and the Women's Legal Defense Fund.

The petition argues that not only do people have a right to know about prescription drugs, but that written statements are necessary for decision making by consumers regarding the use of these drugs. Prescription drugs are legally defined as those that, because of toxicity or abuse potential, can be used safely only under the supervision of a physician. The petitioners argue that although such drugs are inherently dangerous, oral communications about them between physicians and patients are frequently inadequate. The physician may neglect to deliver information, and the patients may not understand the information, if provided. In addition, patients may forget the information or they may transfer drugs to other persons without the required information.

The consumer petition suggests that written information be provided by means of warning stickers that can be affixed directly to the container and by supplementary sheets containing more details about instructions for use and necessary precautions to be observed. The petitioners also suggest that although such information would undoubtedly be appropriate for almost all prescription drugs, the focus should be on drugs that may constitute a serious threat to health that could prevented by consumer knowledge; for example, drugs that are frequently used without constant supervision by a physician and drugs likely to be transferred from one person to another. Drugs such as tranquilizers and hypnotics that are hazardous during pregnancy and drugs that are overprescribed are specifically mentioned as candidates for PPIs. Under the model suggested in the consumer petition, the pharmacist would be primarily responsible for distributing PPIs.

Patient education. The trend toward patient education is evident in a number of areas. The evolving literature on compliance with therapeutic regimens indicates that unless steps are taken to insure that patients actually take the drugs prescribed for them, therapeutic failures are inevitable. In a review of methodologically sound compliance studies, Sackett and Haynes noted an average of about 46 percent noncompliance with drugs used on a chronic basis (*1*).

The Federal Government's role in patient education is well delineated in HEW's "Forward Plan for Health" (*2*). This document states that "the government's function is to enable people to make sound decisions about their health, to equip them with information and skills and other resources to translate these decisions into action. . ." In general, the plan suggests that the government should ". . . provide opportunities and incentives for people to assume full responsibility for their own health." Certainly, PPIs can help provide the information necessary for the proper use of prescribed medications. This information also could provide a basis for people to seek additional information from their physician, nurse, or pharmacist. The potential for the PPI as a health education tool is demonstrated by the production and distribution of instructional materials for patients by many commercial firms, regional associations, hospital pharmacies, and private practitioners (*3*). These materials are intended to

augment, not substitute for, verbal instructions given by health professionals.

Constraints. In contrast to the consumerism and patient education movements that are fostering the implementation of PPIs, there are constraining forces; for example, the issues of cost containment and economic implications are important considerations for any new regulatory policy. Any increased cost due to PPIs will depend on the extent, form, and method of distribution of the PPIs. A cost-effective analysis and assessment of the economic impact of PPIs must be considered before any implementing system is selected.

FDA Activities

To prepare and develop a public policy regarding PPIs, the FDA initiated a Patient Prescription Drug Labeling Project entailing three areas of activity: soliciting input, research and development, and implementation.

Soliciting input. Since mid-1974, the FDA has been soliciting input on the general concept of PPIs. Between September 1974 and July 1975, FDA officials met with 10 individual physician and pharmacy organizations and the PMA and held a special meeting with representatives of 11 consumer advocacy groups. In November 1975, the FDA issued a notice in the Federal Register asking for opinions and ideas about PPIs (*4*). Minutes of the meetings and the consumer petition were made available for review and comment. In addition to requesting that people offer their general opinions, the FDA requested that responses be phrased to address specific issues related to developing a PPI program. For example, ideas were sought concerning the format and style, the method of distribution, the selection of drugs and priorities, and the method of drafting PPIs.

More than 1,000 responses were received; about 750 of these were from consumers who favored the concept of patient drug labeling. Some consumers mentioned specific adverse drug experiences that they believed could have been avoided had certain information been known. Comments from professionals and persons in health care organizations ranged from full support to strong opposition, and also many persons called for additional study, discussion, and clarification of the issues relating to PPIs.

A second series of meetings were held in May and June 1975. In four separate sessions, FDA officials and a group of consumer advocates met with representatives from the medical, pharmacy, and pharmaceutical industries and allied health professions to explore further the needs and preferences of the groups significantly involved with any PPI program.

At a symposium on PPIs in November 1976, the viewpoints of the disciplines significantly affected by PPIs were presented by knowledgeable spokesmen. Representatives of the FDA, DIA, AMA, PMA, consumer advocacy groups, American Hospital Association, American Pharmaceutical Association, and American Society of Hospital Pharmacists presented overviews for their organizations. Additionally, a spokesman from the Department of Health and Social Security in London presented an update on what European countries are doing regarding provision of information to patients, and a physician-attorney addressed the medical-legal ramifications of PPIs.

Research perspectives were presented by panels of scientists or practitioners in medicine, pharmacy, social science, nursing, health education, and law. The focus was on the following questions: What information should patient package inserts contain? What are the potential distribution problems? What are the potential effects on the patient? What are the potential effects on the health care system? (The proceedings have been published as a separate issue of the *Drug Information Association Journal.*)

The basic issues that recurred throughout the discussions concerned the nature and objective of the PPI—whether it is a product of the consumerism movement, a right-to-know document; or whether it is a patient education document intended to improve compliance with instructions for medication. The ultimate resolutions of these issues will frame the underlying philosophy of FDA's regulatory action.

In my opinion, the goal of the PPI should be to bring about more rational use of drugs. In the majority of cases, it is the patient who ultimately decides whether to take the prescribed drug. The patient makes two kinds of decisions—an explicit decision to initiate or discontinue drug therapy and an implicit decision each time he or she remembers or forgets to take the drug. PPIs should inform patients about the risks and benefits associated with drug therapy so that they can make explicit decisions based on accurate information, such as what effects to expect, what precautions to observe, and why certain side effects might occur and what to do if they occur. This information could help to maximize drug effectiveness, promote patients' responsibility for their therapy, and improve adherence to prescribed regimens.

Improved drug usage is a goal of PPIs, and its accomplishment requires flexibility, systematic planning, and the feedback of objective evaluations. However, PPIs also have the potential for negative effects on drug usage. For example, information about adverse drug reactions could frighten and confuse people, making them less likely to take the needed drugs; unresolved questions brought forth by the PPI could cause an increase in professional and product liability; patients may tend to incorrectly self-medicate without the supervision of a physician; or PPIs may be used improperly as a substitute for verbal instructions rather than as a reinforcement of directions by the physician or pharmacist. Therefore, how PPIs are prepared, distributed, used, and received will be critical to their success.

In my view, PPIs are both patient education and right-to-know documents. Only time and experience will tell if these two themes can be successfully integrated. Since every drug or class of drugs poses problems, the particular emphasis in a PPI should depend on the type of drug. PPIs for elective drugs that have serious dangers should stress the risks and benefits of drug therapy. For drugs whose risk-to-benefit ratios clearly indicate their use, PPIs should carry more detailed instructional information for proper use and a summary of their risks and benefits.

Research and Development

Oral contraceptives (OCs) represent the most widely used drugs for which PPIs have been required. FDA's first step in original research and development was to survey users and previous users of the pill to get their views about the usefulness of the OC insert and its allied brochures. The results of the survey completed in September 1975 indicated that the overwhelming majority of users stated that they received and read the OC insert (*5*). However, when asked what was the most important side effect of the pill only 54 percent of the users who said they read the insert remembered the blood clotting information. Also, only about one-third of the women who use the pill said they received the longer brochure that is distributed by physicians upon request. In response to a survey question as to whether they would like to see PPIs for additional classes of drugs, the majority of respondents stated that they would.

The oral contraceptive study provides valuable feedback for FDA's decisions regarding future policy. However, the OCs are unique drugs in that users of the pill are often young and healthy women who take the drug as a prophylactic measure. Unanswered is the question of what effect PPIs will have on patients undergoing treatment for disease. For this purpose, a study of hypertensive patients using a prototype PPI is presently underway.

In addition to original research, available information in the scientific literature is being reviewed concerning issues such as what patients need to know about their drugs, what effects PPIs will have, and what is the best method of communicating this information to patients. Some of the specific areas that have been identified include patient adherence to medication regimens, nonspecific factors in drug treatment, health education and health professional-patient interaction, and human factors and communications theory.

Implementation

The discussion thus far pertains to activities of FDA in planning a PPI program. However, when public health issues have necessitated regulatory action, FDA has required specific patient labeling on an ad hoc basis. Thus, PPIs have been recently announced for the estrogens (*6*). Revised labeling has also been proposed for oral contraceptives to reflect the finding of additional risks associated with the use of these drugs and the results of the OC survey.

The 1976 symposium brought to an end the first phase in the FDA's solicitation of general input regarding the PPI program. The FDA will continue to solicit input regarding specific recommendations for methods for implementing PPIs in the future. For example, in the near future the FDA plans to publish a proposal outlining a systematic method for preparing and distributing PPIs. The proposal will solicit comments and suggestions regarding this plan.

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