The Significance of Information Posted on the U.S. Food and Drug Administration’s Website

We commend Marchand et al. from the U.S. Food and Drug Administration (FDA) on their article entitled “The U.S. Food and Drug Administration: Drug Information Resource for Formulary Recommendations.” We have found that the article provides a thorough summary of FDA available resources for the managed care pharmacist. We also commend Navarro for his editorial “Rediscovering FDA Websites,” since the significance of this information for comparative effectiveness research analysis cannot be more important. Given the importance of the article and the subsequent commentary, we would like to further comment on the significance of information within FDA approval packages on Drugs@FDA and FDA briefing documents from FDA advisory committee meetings.

Regulatory agencies such as the FDA provide unpublished information not readily available within the medical literature. This information is considered grey literature. Grey literature “is produced on all levels of government, academics, business and industry in print and electronic formats, but which is not controlled by commercial publishers.” Grey literature allows pharmacists, charged with making formulary recommendations, to mitigate publication bias and provide a more accurate representation of a drug’s safety and efficacy.

Research has shown that unpublished comparative effectiveness research is interspersed in FDA approval packages and FDA briefing documents, albeit not easily found. For example, a study assessing FDA approval packages for 12 antidepressants approved between 1987 and 2004 found that 31% of the clinical trials submitted to the FDA were unpublished, with the majority of the unpublished trials having a negative result. An important conclusion of the analysis was that the trials that were published in the medical literature reported a positive result 94% of the time. Subsequent analysis of the same published trials indicated that only 51% of the trials were positive. The phenomenon of selective publication and publication bias does not appear to be limited to antidepressants. A study assessing FDA approval packages for 8 second-generation antipsychotics found that 17% of trials were unpublished. Further, another study documented that over half of the clinical trials submitted to the FDA remained unpublished after 5 years for the 90 new molecular entities approved for sale in the United States between 1998 and 2000. These unpublished comparative efficacy trials are freely available and may be found through FDA approval packages found on Drugs@FDA. Health care providers, as Marchand et al. indicate, may find medical reviews and statistical reviews within the approval packages to be of utmost importance.

Studies in FDA advisory committee briefing documents from both the FDA and the sponsor may also yield important unpublished comparative effectiveness research. An example of the utility of committee briefing documents is illustrated by the DIONYSOS study. The results of the DIONYSOS study (a study comparing the efficacy and safety of dronedarone versus amiodarone for the maintenance of sinus rhythm in patients with atrial fibrillation) was readily available in the sponsor’s FDA advisory committee briefing document an entire year before the trial was published in the medical literature, likely after many formulary decisions were made.

We recognize that pharmacists will struggle with the sheer amount of information, since many of the FDA approval packages and FDA briefing documents are hundreds to thousands of pages in length. We also recognize that pharmacists will have difficulty locating studies within FDA approval packages and FDA briefing documents. These limitations should not be a deterrent for a quality review and formulary decision. It may be argued that there is no need to assess these documents, since drug approval information may be found in the FDA’s latest professional product labels (Section 14). Results from a multitude of examples have demonstrated that information is lost in transmission from FDA approval packages and FDA briefing documents to professional product labels.

Accessing and evaluating the studies within FDA approval packages and FDA briefing documents have large policy and drug coverage implications. These documents, if given their due consideration, will greatly influence the way drug benefit designs are built and managed. We encourage Medicare, Medicaid, and private insurers to include FDA briefing documents and approval packages for discussion at Pharmacy and Therapeutics Committee meetings because evidence dossier requests directly from pharmaceutical companies may not contain this information. We also encourage the Academy of Managed Care Pharmacy to include these documents within its “Format for Formulary Submission” and adopt similar search methods for grey literature as found in the Cochrane Handbook or the Agency for Healthcare Research and Quality Methods Guide for Effectiveness and Comparative Effectiveness Reviews. We thank Drs. Marchand, Rose, Fine, Kremzner, and Navarro for their contributing articles to JMCP highlighting the FDA because we feel that its website is a treasure of information.

G. Elliott Cook, PharmD, BCPS
Pharmacist
Provider Resources Inc.
ecook@provider-resources.com

Michael M. Madden, PhD
Assistant Professor of Pharmaceutical Sciences
Lake Erie College of Osteopathic Medicine School of Pharmacy
mmadden@lcom.edu
DISCLOSURES

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REFERENCES


To the Editor:

We read with interest the recent article in JMCP by Marchand et al., “The U.S. Food and Drug Administration: Drug Information Resource for Formulary Recommendations,” which provided an excellent review of information on the U.S. Food and Drug Administration’s (FDA) website.1 While targeted to managed care pharmacists, this information is also valuable to any individual involved in formulary management. Indeed, we reference the FDA’s website routinely in our drug evaluations for a system of hospitals in the Northeast region. The subsequent editorial by Navarro, “Rediscovering the FDA Website,” lists various drug information resources referenced by medical and pharmacy directors.2

We would like to recommend an additional source: the European Medicines Agency’s (EMEA) website.3 As with the FDA’s website, extensive pre-approval and postmarketing data are available. We have found this resource to be of particular value for agents that have been approved by the EMEA before receiving FDA approval (e.g., rivaroxaban). Another example is biosimilars. The EMEA has had considerable postmarketing experience with biosimilars, since they became available in Europe in 2006. The latter is typically documented in the section “Procedural steps taken and scientific information after the authorisation” for each product. Thus, we expect the EMEA’s database to be of increasing value to U.S. formulary decision makers in their respective settings since biosimilars are commercially available in this country.3

Prabashni Reddy, PharmD, MMedSc, RPh
Director
Center for Drug Policy, Partners Healthcare
preddy2@partners.org

Yu-Chen Yeh, MS, RPh
Senior Pharmacist
Center for Drug Policy, Partners Healthcare
yyeh@partners.org

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Both authors are employed by Partners Healthcare. The authors’ declare no conflicts of interest.

REFERENCES


