



November 17, 2008

The Honorable Andrew C. von Eschenbach, M.D.
Commissioner
Food and Drug Administration
Parklawn Building
5600 Fishers Lane
Rockville, MD 20857

RE: October 2008 FDA Correspondence with Compounding Pharmacies

Dear Commissioner von Eschenbach:

The American Pharmacists Association (APhA), the International Academy of Compounding Pharmacists (IACP), the National Community Pharmacists Association (NCPA), the National Alliance of State Pharmacy Associations (NASPA), and the American College of Apothecaries (ACA) are writing in response to the Food and Drug Administration's (FDA) recent correspondence with nine pharmacies that dispense pharmacist compounded preparations containing the drug ingredient, estriol, in response to valid prescriptions. Combined, these organizations represent more than 125,000 pharmacists and others interested in advancing patient care, as well as millions of patients who rely on their services each day.

We have been supportive of the Agency's action to address what has been described as false and misleading marketing of bio-identical hormone replacement therapy (BHRT) preparations; however, we remain concerned with FDA's continued actions and threats of action against the use of estriol as an ingredient in pharmacist compounding. For reasons outlined below, we ask the Agency to refrain from taking enforcement action against those pharmacies that, pursuant to valid prescriptions, dispense preparations compounded by pharmacists with estriol or any other ingredient compounded in accordance with the 1997 Food and Drug Administration Modernization Act (FDAMA) Section 503A.

CPG Lacks Public Input Creating Inappropriate Basis for Actions Against Pharmacies

FDA has stated that its actions against pharmacist compounded preparations containing estriol are based in its compounding CPG (CPG 460.200) – specifically in Factor 3 of the policy, which outlines

ingredients permissible for use in pharmacy compounding. The factor is significantly more restrictive than FDAMA, which contained a section on pharmacy compounding that listed three sources of bulk drug ingredients that could be used in compounding. Those sources included drug substances that comply with the standards of an applicable U.S. Pharmacopoeia or National Formulary monograph.

In response to the significant concerns expressed by pharmacy organizations and the public, FDA subsequently acknowledged that the CPG should be revised. We believe that receiving input from healthcare organizations and the public is critical to achieving an optimal FDA policy for ensuring the patients receive the medications they need. We ask for this to be undertaken, and for a formal public comment period on the CPG to be conducted, before initiating an enforcement action against a pharmacy that is dispensing pharmacist compounded preparations containing estriol pursuant to a valid prescription based solely on the contents of the CPG.

Furthermore, CPGs by their very nature do not have the force of law. As stated in its preamble, it is only the “current thinking” of the Agency and “does not operate to bind FDA or the public” (see, CPG 460.200, p.1). We are concerned that the Agency may be overextending the authority of this CPG in using it alone to justify enforcement actions.

IND Proposal Remains Unworkable

Moreover, FDA states that pharmacies may not compound drugs containing estriol unless a doctor prescribing the drug obtains a valid investigational new drug application (IND). However, it has become clear that the Agency IND process creates an impossible and undue burden on medical doctors treating individual patients in a community clinical setting.

One of the barriers for prescribers with the IND process is the institutional review board (IRB) approval and review process. The process is prohibitively costly and burdensome for treating individual patients in a clinical setting. This requirement alone, in effect eliminates pharmacist compounded preparations containing estriol as a treatment option. Furthermore, new information provided to us by doctors investigating the IND process has revealed that IRBs may not be able to accept protocols and studies that include existing patients. If this is true, it would mean that IND patients currently taking pharmacist compounded preparations containing estriol could not be part of any IND that is supposed to be set up for this very purpose.

In addition, we understand that at least one application by a physician who followed the Agency’s instructions and guidance on completing INDs for pharmacist compounded preparations containing estriol has been denied.

Pending Litigation Changes Legal Landscape

Finally, a recent court decision reaffirmed FDAMA 503A minus faulty advertising provisions and gives additional credence to arguments for allowing access to pharmacist compounded preparations containing estriol. In the wake of this recent decision by the U.S. Court of Appeals (*Medical Center Pharmacy v. Mukasey*), the Agency has communicated that it intends to apply “the non-advertising provisions of [FDCA] section 503A to entities that are covered by this provision that are located within the jurisdiction of the Fifth Circuit (i.e., Texas, Louisiana, and Mississippi) as well as to the plaintiffs that brought the *Medical Ctr. Pharm.* Case. Elsewhere, FDA will continue to apply the

enforcement policy articulated in Compounding Policy Guide section 460.200 [“Pharmacy Compounding”], issued by FDA on May 20, 2002.”

FDA’s bifurcated policy creates confusion, inconsistent national policies and unnecessary inequalities to access. The plaintiff pharmacies and all pharmacies in Louisiana, Texas, and Mississippi are allowed to dispense pharmacist compounded preparations containing estriol while all other pharmacies are not. Thus, we ask that the Agency refrain from taking enforcement action against those pharmacies that are dispensing valid prescriptions for pharmacist compounded preparations containing estriol in accordance with 503A until this pending litigation is ultimately resolved.

In closing, we reiterate our concerns with continued Agency actions against compounding pharmacies that provide pharmacist compounded preparations containing estriol pursuant to a valid prescription. Estriol as an ingredient in pharmacist compounded preparations continues to be allowed by state boards of pharmacy, United States Pharmacopeia (USP) and the Pharmacy Compounding Accreditation Board (PCAB) standards, and federal legislation recognized by federal courts. Only FDA’s non-binding CPG would restrict its use. There doesn’t appear to be justification for selective restriction of the drug ingredient and current application of standards creates great inconsistency and confusion.

In light of pending litigation, an unrevised CPG and an unworkable IND process, we ask that the Agency withhold taking enforcement action against pharmacies dispensing pharmacist compounded preparations containing estriol pursuant to a valid prescription. Thank you for your consideration of the views of the nation’s pharmacists. We would appreciate the opportunity to further discuss these issues with you.

Sincerely,

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