



Pharmacy Compounding

Introduction

Pharmacy Compounding is an ancient practice in which pharmacists combine, mix or alter ingredients to create unique medications that meet specific needs of individual patients. Compounding is a practice that continues to attract the scrutiny of the U.S Food and Drug Administration (FDA) – mainly because of instances where compounded drugs have endangered public health.

The FDA considers virtually all compounded drugs as unapproved new drugs for which safety and efficacy have not been demonstrated with the type of data the FDA requires to approve a new drug. However, the FDA also considers “traditional compounding” to be a valuable service and does not take enforcement action against these practices. The FDA defines traditional compounding as customizing a drug for someone who is allergic to a dye or preservative in an FDA approved medicine, or compounding a liquid dosage form specifically for a younger patient, etc. Compounding does not generally include mixing or reconstituting commercial products in accordance with the manufacturer’s instructions or the product’s approved labeling.

Red Flags and Enforcement Activities by the FDA

The emergence over the past 10 - 15 years of firms with pharmacy licenses making and distributing unapproved new drugs in a way that is clearly outside the bounds of traditional pharmacy practice is of great concern to the FDA. FDA enforcement has been directed to those pharmacies whose activities raise the kinds of concerns normally associated with a drug manufacturer and whose compounding practices result in significant violations of the new drug, adulteration, or misbranding provisions of the federal Food, Drug, and Cosmetic Act (FDCA). In addition, unlike commercial drug manufacturers, pharmacies are not required to report adverse events associated with compounded drugs. In a May 2007 consumer newsletter, the FDA reported knowing of more than 200 adverse events involving 71 compounded products since 1990.

Examples of some of these adverse events included: Three deaths due to contaminated compounded intravenous solutions, and blinding of two patients as well as damaged eyesight to others from a bacterially contaminated compounded product used in cataract surgery. In a 2001 FDA survey of compounded drug products, the agency found 34 percent of the products tested failed standard quality tests (usually failing potency analyses) as opposed to a less than 2 percent failure rate for commercially produced drug samples. Examples of medications included in the testing sample included sterile injectables (e.g., dipyrindamole, papaverine, phentolamine, etc.), pellet implants (e.g., estradiol), ophthalmic solutions/ointments (e.g., ciprofloxacin, dexamethasone, timolol, etc.), inhalation (e.g., tobramycin), and oral products (e.g., progesterone, estradiol, etc.). As a consequence, the FDA has issued a number of warning letters to pharmacies that specialize in female hormone products (e.g., “Bioidentical hormone replacement therapies”), anti-infective inhalation products, sustained-release/delayed-release/extended-release products, and local anesthetic pain products. FDA Warning Letters have also been sent in cases where the FDA believes pharmacy communications (e.g., advertisements, Web site information, etc.) contain false and misleading claims about product safety, effectiveness, and superiority to FDA approved and commercially available products. When contemplating further action against compounding pharmacies the FDA considers whether the pharmacy engages in the following acts:

- Compounding drugs in anticipation of receiving prescriptions, except in very limited quantities in relation to the amounts of drugs compounded after receiving valid prescriptions.
- Compounding drugs that were withdrawn or removed from the market for safety reasons.
- Compounding finished drugs from bulk active ingredients that are not components of FDA approved drugs (e.g., estriol) without an FDA sanctioned investigational new drug application (IND).
- Receiving, storing, or using drug substances without first obtaining written assurance from the supplier that each lot of the drug substance has been made in an FDA registered facility.
- Receiving, storing, or using drug components not guaranteed or otherwise determined to meet official compendia requirements.
- Using commercial scale manufacturing or testing equipment for compounded drug products.
- Compounding drugs for third parties who resell to individual patients or offering compounded drug products at wholesale to other state licensed persons or commercial entities for resale.

- Compounding drug products that are commercially available in the marketplace or that are essentially copies of commercially available FDA-approved drug products. In certain circumstances, it may be appropriate for a pharmacist to compound a small quantity of a drug that is only slightly different than an FDA approved drug that is commercially available. In these circumstances, the FDA will consider whether there is documentation of the medical need for the particular variation of the compound for the particular patient.
- Failing to operate in compliance with applicable state law regulating the practice of pharmacy.

What are we experiencing?

PrimeTherapeutics, Inc. (Prime), a separate company providing pharmacy benefit manager (PBM) services for Blue Cross and Blue Shield of Illinois, has identified the billing practices of non-traditional compounding pharmacies as one of the most common reasons network pharmacies are placed on Corrective Action Plans (CAPs) or other related actions. As a result of ongoing claims auditing activities, Prime has been able to identify a number of pharmacies with questionable compounding practices. Examples of inappropriate practices include: Submitting pharmacy claims with incorrect or invalid National Drug Codes (NDCs) according to the compounding log, claims for compounds which contain medications that are not covered by Medicare Part D based on their intended route of Administration, marketing of compounded drugs utilizing a non-FDA approved aerosolizing device, and compounding copies or near copies of FDA approved commercially available drugs. In two instances, further research following an on-site pharmacy audit, Prime discovered that both pharmacies had received warning letters from the FDA detailing a number of issues such as the misbranding of drugs, unsubstantiated efficacy claims, and marketing of unapproved medical devices. Another pharmacy was discovered to be dispensing an excessive quantity (i.e., 540 - 5ml bottles) of antimicrobial ophthalmic drops to be diluted with saline and administered intranasally three times daily for the treatment of recurrent upper respiratory infections. *The total cost of one 30 day prescription of this unproven therapy was \$10,000.*

What do the CMS regulations say?

Chapter 6 of the Medicare Prescription Drug Benefit Manual provides the following guidance on the coverage of "Extemporaneous Compounds":

- Compounded prescription drug products can contain: (1) all Part D drug product components; (2) some Part D drug product components; or (3) no Part D drug product components.
- Only costs associated with those components that satisfy the definition of a Part D drug are allowable costs under Part D because the compounded products as a whole do not satisfy the definition of a Part D drug. As a consequence, claims for compounded prescriptions can consist only of NDCs for FDA approved prescription drug products. Traditional compounding powders are typically not FDA-approved drug products.
- The labor costs associated with mixing a compounded product that contains at least one Part D drug component can be included in the dispensing fee.

What are we asking providers to do?

Providers should discuss with their patients in detail whether the use of compounded medications in lieu of FDA approved and clinically tested products is indeed the best option for their specific medical needs. Patients or practitioners who encounter problems (e.g., adverse drug events, etc.) with compounded products are asked to file a MedWatch report with the FDA via telephone at (800) 332-1088; via fax at (800) FDA-0178; via mail at MedWatch, 5600 Fishers Lane, Rockville, MD 20852-9787; or online at www.fda.gov/medwatch.

References:

1. U.S. Food and Drug Administration. "Limited FDA Survey of Compounded Drug products," Feb. 13, 2003. Accessed online on Jan. 12, 2010 at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm155725.htm>.
2. U.S. Food and Drug Administration. "The Special Risk of Pharmacy Compounding," May 31, 2007. Accessed online on Jan. 12, 2010 at <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm107836.htm>.
3. U.S. Food and Drug Administration. "FDA Takes Action Against Compounded Menopause Hormone Therapy Drugs," Jan. 8, 2008. Accessed online Jan. 12, 2010 at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ucm116832.htm>.
4. Anon. "FDA Takes Action Against Compounded Bioidentical Hormones." *Pharmacist's Letter/Prescriber's Letter*. 2008; 24(2): 240209.