Compounding Unit-of-Use Kits

White Paper

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Content:

Introduction

Compounding is defined by the USP as “the preparation, mixing, assembling, altering, packaging, and labeling of a drug, drug-delivery device, or device in accordance with a licensed practitioner's prescription, medication order, or initiative based on the practitioner/patient/pharmacist/compounder relationship in the course of professional practice.”

Compounding pharmacy is how the practice of pharmacy began and has continued for several thousand years. During the last millennium, the industrial revolution led to the development and growth of pharmaceutical manufacturers and they manufactured numerous dosage forms of almost every drug they produced. However, in the past 25-30 years, the manufacturers are minimizing the variety of dosage forms for each drug, are merging and are dropping many different products in favor of those that are more profitable. As a result, compounding pharmacy, which had declined in the 1950s, started growing again back in the 1970s with the provision of many preparations that were not commercially available, intravenous admixture programs in hospitals, etc. To this is added the shortage of many commercial products and now compounding pharmacy has grown significantly in its impact on patient care and is vitally important in healthcare today.

Many preparations that are compounded are quite time-consuming and routine. Also, there are some pharmacies that are not doing a significant amount of compounding but are still called upon to do some compounding for specific physicians and patients. To accommodate these needs, “compounding kits” were introduced a number of years ago to assist pharmacists in meeting these special needs. A kit is defined as “a set of articles used for a specific purpose; A set of parts or materials to be assembled”. These compounding kits contain all the necessary materials for the compounding of a specific preparation for a specific patient. The goal of utilizing compounding kits is “One prescriber, one patient and one kit (pharmacist)”

Background

The USPTO has issued a patent (US 8,276,757 B2) regarding a method for the preparation, storage and dispensing of compounded suppositories. The FIRST container (suppository mold) and the method for suppository-compounding is user-friendly and time saving for a pharmacy. The FIRST suppository mold is also customer friendly because the take-home molds are especially designed to not only maintain the integrity of each suppository once compounded, but also provide convenient patient dispensing.

Each individual kit is designed to enable the pharmacy to comply with USP <795> standards and to facilitate the compounding process.

Facilitate the compounding process

As mentioned, a compounding kit is designed to minimize errors, as each kit contains all the required materials, properly weighed and/or measured, as well as the dispensing container. The advantages are

that a kit is (1) user-friendly and convenient, (2) saves time, (3) contains accurately pre-weighed and/or pre-measured ingredients, (4) contains detailed instructions, (5) is disposable and eliminates cleanup required using traditional compounding methods, (6) less waste, (7) guaranteed outcome as there is no trial-and-error in developing a formulation, (8) distribution can be monitored for supply chain of custody, and (9) components are repackaged and kits assembled in cGMP facilities. They also allow for faster compounding than usual as a number of the steps described in the definition of compounding above are accomplished within the kit itself.

Regulatory Compliance

The goal of the compounding kits is “one Rx from one prescriber for one patient”. The unit-of-use kits facilitate compliance with USP Chapter <795>.

The company that owns and distributes the kits does not compound any drugs or fill prescriptions for patients. The components of each kit are packaged so that a pharmacist or physician may prepare one prescription for one patient. The supplier of compounding components in the form of a user-friendly unit-of-use compounding kit provide the compounding pharmacist with an entire compounding process that is quick and simple to encourage practitioners to dispense an on-site and on-demand compounded drug preparation for each individual valid prescription.

The repackaged active ingredients contained in the unit-of-use kits are components of FDA approved products; e.g., active pharmaceutical ingredients and excipients. The APIs are routinely used as components of pharmacy compounded products and meet USP/NF standards. None of the unit-of-use kits should involve drug products that are commercially available in the marketplace or that are essentially copies of commercially available FDA-approved drug products; nor should they involve products on the “negative” or “do not compound” list.

The first provider of the compounding kits, CutisPharma, maintains appropriate licenses from the Commonwealth of Massachusetts, Department of Public Health-Board of Registration in Pharmacy, the Food and Drug Administration, and the Drug Enforcement Administration (Controlled Substances Registration). Additionally, appropriate licenses/permits/registrations have been obtained for nationwide distribution of CutisPharma, Inc.'s controlled substance as well as non-controlled substance own-label pharmaceutical products. The company is also registered with FDA as a distributor and has been assigned a labeler code (65628). Importantly, the Company maintains all intellectual property rights and distributes only these components packaged as kits and under its own (CutisPharma) label. U.S. Patent Nos. 6,708,822 B1, 7,434,690 B2, 7,815,929, and 8,276,757 B2 have been issued and additional U.S. patents are pending. The Company has also been awarded Verified-Accredited Wholesale Distributors (VAWD) accreditation by the National Association of Boards of Pharmacy (NABP).

Reimbursable

Each kit product contains an NDC Number, which makes it easier for the third party reimbursement process; they can also reduce audit-related adjustments.

Manufacturing /Packaging /Repackaging

The kit provider has secured from its active pharmaceutical ingredient (API) suppliers letters of assurance that the manufacturer of the API(s) for incorporation as a component of the unit-of-use kits, have registered the manufacturing facility with FDA. Before incorporation into unit-of-use kits, drug components undergo compendial testing (USP/NF), as follows:

1. API: at least first three batches-full monograph testing + manufacturer's CoA.
2. Subsequent batches-assay and ID + manufacturer's CoA.
3. Inactives: at least first three batches-full monograph testing.
4. Subsequent batches-ID + manufacturer's CoA.

Example supporting documentation for a kit may include the following:

1. **Re-packaging and Assembly of a kit-**
   - A typical C of A for the active drug.
   - A typical C of A for the active drug as it is received at the contract manufacturing facility (full-monograph for the first 3-lots).
   - A typical C of A for the active drug representing 3-USP Identification tests (A,B,C) and an Assay as it is received at the contract manufacturing facility after the vendor has been qualified using 3-lots.
   - Respective USP Identification Tests are carried out for all non-active ingredients.
   - Preparation of drug formulation.
   - Re-packaging of ingredients.
   - Kit assembly.
   - Minimum fill <755> testing
   - Kit shelf-life: Determined by applying ICH testing frequencies and conditions including an additional time point of 36-months at room temperature and analyzing active drug contents using a USP or validated laboratory method. Results indicate the stability information packaging and storage requirements.

2. **Product Release-**
   - Beginning/Middle/End samples observed for Appearance and tested for active drug content using a validated method. In our hands, all of these samples met assay requirements.

3. **Uniformity of dosage unit:**
   - Top/Middle/Bottom samples from the compounded

preparations are analyzed for active drug concentrations via a USP or validated HPLC method. Contents of top, middle and bottom aliquots from the same container displayed uniformity for active drug.

4. **Beyond-use date:**
   Active drug concentrations (mg/g) in compounded preparations (stored at proper temperatures) are analyzed on appropriate days, e.g. 1, 30, 90 and 180. The active drug concentrations on days 30, 90 and 180 are compared to those found on day 1 and the results evaluated for the assignment of a beyond-use date.

Summary

As pharmaceutical compounding continues to grow and evolve, there will be many innovations that will come to enable pharmacists to compound more accurately and more efficiently. Compounding kits are one example as described in this paper. As with any innovation that is worthy, there will be growth and expansion as the value is understood, appreciated and implemented in pharmacy practice. The ultimate goal of pharmaceutical compounding and innovation is enhanced quality patient care; this goal is met as compounding kits are utilized in many pharmacy practice sites.