COMBINATION UPDATE

Combination Products Revolutionize the Global Healthcare Industry

By: Christine M. Ford, MBA

In recent years, the combination products market has developed into a revolutionary industry. Initially, the FDA handled most products that crossed jurisdictional lines on a case-by-case basis. With two or more agencies responsible for reviewing each product, there were issues in clarifying which policies were applicable. In 2002, under the *Medical Device User Fee and Modernization Act* (MDUFMA), the FDA established the Office of Combination Products (OCP) to oversee the regulatory process for combination products. The OCP is responsible for assigning the product to the appropriate FDA center for jurisdiction. Since the establishment of the OCP, the FDA has reported a steady increase in the number of requests from cutting-edge combination product developers for presubmission meetings to seek advice on the best approaches for scientific and clinical testing and evaluation.

The definition of a combination product according to the FDA is as follows: two or more regulated components — drugs, medical devices, or biologics combined through physical or chemical means. These include drug-coated devices, drugs packaged with delivery devices in medical kits, and drugs and devices packaged separately but intended to be used together. Some examples of combination products include drug-eluting stents, surgical mesh with antibiotic coatings, spinal fusion putties, protein-coated implants to encourage bone regeneration, and single-device-integrated glucose meter/insulin pumps for diabetics. Many such products bring together the power of advanced therapeutics with the precision dosing made possible by sophisticated delivery technologies. Already valued at $5.4 billion in 2004, the global market for combination products is achieving annual growth of 10% to 14% percent a year.[1]

In the past year, numerous combination products have received a great deal of attention. One groundbreaking combination product is Pfizer's Exubera, an inhaled powder form of recombinant human insulin (rDNA) for the treatment of adult patients with type 1 and type 2 diabetes. Approved by the FDA in January 2006, Exubera is inhaled into the lungs through the patient's mouth using a specially designed inhaler. For the some 5 million Americans who take insulin injections, this product may allow for improved insulin management. It is the first new insulin delivery option introduced since the discovery of insulin in the 1920s. This new capability has revolutionized the drug delivery industry and provided the healthcare industry with the potential for unlimited possibilities for providing safe drug delivery via the systemic pulmonary route. This technology will benefit various areas of medicine, including pain management, oncology, osteoporosis, migraines, immunosuppression, and neurologic disorders.[2]

Another product of interest is Orthovita Inc's combination product Vitagel, which received pre-market approval (PMA) from the FDA in June 2006. Vitagel is a composite liquid hemostat used in surgical procedures as an adjunct to hemostasis. This technology offers an advantageous alternative when control of bleeding by ligature or conventional procedures is inefficient or impractical. Vitagel works by combining a thrombin/collagen suspension with the patient's own plasma. The resultant fibrin/collagen clot stems bleeding and provides a robust three-dimensional matrix for soft tissue healing. Vitagel is approved for use only in conjunction with the Cellpaker plasma collection system.[3]

Lastly, approved by the FDA in April 2006, Shire plc's Daytrana is the first and only transdermal methylphenidate medication approved to treat the symptoms of ADHD. This treatment provides physicians and parents with a new, practical way to individualize treatment for children with ADHD. The patch treatment provides an option for parents whose children have a resistance to oral medication and eliminates the need for children to take additional doses of medication during their school day. In addition, because the effect of the medication in Daytrana starts to decrease upon patch removal, the ADHD patch allows parents, at the direction of the physician, to vary the duration of effect of the medication up to the recommended 9-hour wear time.[4]

The aforementioned products represent only a handful of the innovative new products on the medical industry frontier. As the evolution of medical technology continues to progress globally, many experts predict that combination products will play a crucial role in the future because they hold great promise for advancing patient care. However, continued development of these technologies is not without challenges. Manufacturing, packaging, and regulatory considerations all present potential obstacles on the path to commercialization. Combination product manufacturers should bear in mind that the assessment process of the safety and effectiveness of these products may not yet be as timely and efficient in relation to the growth of the combination products industry. However, such concerns are only a telltale sign of rapid progression and exciting new advancements. ◆

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BIOGRAPHY

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