Designing in Adherence

Pharma can use a product development process for improving patient adherence.

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Advances in technology are accelerating medical discoveries at an unprecedented rate. Individualized medicines are becoming more of a reality with extraordinary developments in genetic and biopharmaceutical engineering. There is even considerable progress being made in smart medicines that are able to track when and how medications are delivered inside the body by incorporating a microchip into the medication that transmits data.1

However, all these advances are for naught if the medication is not taken.

IMPACT OF PATIENT NON-ADHERENCE

According to a report issued by the Center for Health Transformation, roughly 120,000 people die every year in America from not taking their medications as prescribed.2

In addition, it is estimated that in the United States, medication nonadherence costs approximately $290 billion per year. These costs are associated with expenditures for unnecessary hospitalizations, medical procedures, and physician treatments.3 Despite this staggering number, this is just a starting point, as the numbers do not capture such costs as lost productivity and the deterioration in quality of life caused by medication nonadherence.

These numbers are corroborated by a report issued by the World Health Organization that only 50% of patients in developed countries adhere to their medications as prescribed.4 Another study found that up to 31.4% of patients with chronic diseases do not fill their initial prescription.5 Such studies support the argument that non-adherence presents a major issue for the U.S. healthcare system.

WHY PATIENTS FAIL TO COMPLY

For many years, patient adherence has been viewed as the “Holy Grail” of the medical field—an area that can improve lives and drastically reduce healthcare costs, but remains an ongoing challenge.

On the surface, taking medication as prescribed seems a simple, logical course of action for an ill person. However, numerous reasons for noncompliance have been documented, with variability across individual patient behavioral, demographic, and therapeutic categories.

Chronic disease states, such as certain cardiovascular illnesses, offer a unique challenge. The majority of such conditions may be asymptomatic, and patients may exhibit limited physical signs of the conditions. In asymptomatic conditions, patients may believe they do not need the medication and may not even fill their prescription.6

Understanding the root causes and underlying drivers of patient non-adherence is critical to discovering solutions. For example, in a survey to help identify patterns that are typical for patients who do not adhere to medication regimens, 30% responded forgetfulness, while 27% could not provide a reason.7

In another survey of 10,000 patients conducted by Harris Interactive and BCG, they, too, cited a high level of forgetfulness to using or refilling the medication as a main reason for nonadherence.8

Additional studies show dosing regimens have dramatic effects on adherence. In a study conducted by Claxton and Cramer, the rate of adherence varied inversely with the number of doses needed throughout the day.9 For example, in the study, once-daily dosing had a higher adherence rate than three-times daily dosing. These results suggest that a reduction in the number of the dosages can have positive effects on adherence.

Given the rapid acceleration in healthcare costs, patient adherence continues to garner attention. Taking medications as prescribed is increasingly seen as a quantifiable, controllable activity that may be successfully addressed or influenced. Additionally, there appears to be a paradigm shift in the healthcare industry fueled by U.S. healthcare reform, leading to a shift from treating sickness to a focus on preventing it through wellness programs. Improved medication adherence is now being reframed as an area that can improve overall health.

There are many different approaches to improving medication adherence. These include in-home care, nursing outreach programs, incentive programs, support groups, hotlines, and electronic reminders. Some of these methods are expensive and difficult to measure, but many studies have proven successful.

Another approach is to build patient adherence into the drug development and product lifecycle, from the dose form to the delivery. This approach can create drugs that are intrinsically designed to help enhance patient adherence.

ADHERENCE BY DESIGN™

Catalent’s new program, called Adherence by Design™ (AbD), is derived from the Quality by Design (QbD) concept, an approach being embraced by pharma-
ectical companies in their manufacturing processes. The philosophy behind QbD is to start with the desired outcome, and then work backward in the process to control the critical parameters. This approach creates a model that promotes continuous improvement and enhances process controls in the areas that matter the most.

AhD programs are designed much in the same manner as QbD. Key stakeholders look at multiple parameters early in drug development and then build in features that will help promote adherence for the specific therapeutic class. This unique approach throughout the product development lifecycle can create a tailored solution designed to drive increased patient medication adherence.

Table 1 describes the potential adherence design and corresponding technologies. The packaging format can be revisited at multiple points in the product life cycle and may ultimately play a key role in enhancing patient medication adherence.

**THE ROLE OF PACKAGING**

Packaging is one area of the patient medication adherence puzzle that appears to have a significant impact on patient persistency and patient outcomes. Two studies in particular show the correlation between packaging and improved patient medication adherence. The first is “The Impact of Innovative Packaging on Adherence and Treatment Outcomes in Elderly Patients with Hypertension,” often referred to as the Ohio State University study, which was conducted by Philip Schneider. This study was one of the first studies that demonstrated a correlation between unit-dose calendar packaging and increased patient medication adherence with improved adherence and therapeutic results. The study monitored elderly patients on hypertension medication (lisinopril) packaged in Catalent’s PillCalender™ package. At the 12-month mark, the group receiving the specialized packaging had increased its refill rate by 13.7% and achieved a significant improvement in blood pressure compared with the control group.

Another study linking packaging to improved adherence was the Federal Study of Adherence to Medications in the Elderly (FAME), which observed the impact of a comprehensive pharmacy care program on medication adherence and control of blood pressure and low-density lipoprotein cholesterol (LDL-C). This study focused on 200 patients 65 years or older at the Walter Reed Army Medical Center. The program consisted of individualized medication education, specialty blister packaging combining daily medication dosages, and regular pharmacist follow-up. This study revealed a significant improvement in adherence and a clinically significant improvement to systolic blood pressure and LDL-C. The specialty blister pack was noted to be a pivotal component to ensure proper medication delivery and adherence.

**RECENT STUDY**

In the studies identified above, it has been difficult to demonstrate a clear correlation between the effects of the packaging format and patient adherence. Additionally, the sample sizes of each study were relatively small. However, in a study conducted by Catalent and SDI in January 2011, patient persistency to a medication was measured comparing a unit-dose patient adherence package with a conventional 30-count bottle package for the same drug. The study utilized patient prescription data from SDI, a provider of anonymous patient-based prescription data. The data set are from claims from more than 50% of the retail pharmacies in the United States and account for one-half of dispensed claims across all pay types. The study looked at patient persistency rates over a 12-month period by analyzing a cohort of ~200,000 qualified patients who filled their prescriptions in either a traditional bottle or a patient adherence package. Persistency rates were defined as the percentage of patients who remained compliant or restarted therapy over the 12-month tracking cycle.

The study strongly correlated improved adherence rates with the packaging format. The patient adherence packaging led to a 17-point increase in patient persistency to a drug over 12 months, as compared with the 30-count bottle.

**EFFECTIVE SOLUTIONS**

To most effectively enhance patient medication adherence, the package must incorporate multiple adherence drivers customized to the needs of the specific therapeutic area. Different packaging features can be used to improve patient engagement and drive improved adherence.

### Table 1: Technology options under the Adherence by Design™ program.

<table>
<thead>
<tr>
<th>Potential Design</th>
<th>Technologies</th>
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<tbody>
<tr>
<td>Optimizing the number of dosages.</td>
<td>Modified Release</td>
</tr>
<tr>
<td>Optimizing of size and color of dose.</td>
<td>Oral solid development.</td>
</tr>
<tr>
<td>Injectable safety devices and patient</td>
<td>Sterile Fill/finish and Injectable.</td>
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<tr>
<td>convenience with prefilled syringes.</td>
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<tr>
<td>Improving bioavailability.</td>
<td>Softgel</td>
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<tr>
<td>Adherence Packaging.</td>
<td>Packaging.</td>
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of the patient and provide a unique opportunity to communicate with the patient at the point of use. This can include such features as discrete and portable packages, or extra blank space on a package as a “billboard.” The additional billboard space can then be leveraged as a communication tool, which can provide the patient with additional confidence and comfort in managing conditions.

With the new enhancements of mobile technology, packages can also serve as a portal to the Internet. There are several different technologies that can accomplish this. Some are based on visible markings with a two-dimensional Data Matrix, such as a bar code or QR code. Other options, such as Catalent’s Media Enhanced Packaging technology, leverage imperceptible watermarks embedded in the package to connect a smart phone application with online resources without taking up packaging space. These types of technologies enable real-time content management, product-specific messaging, and instructional videos in multiple languages, or deliver special offers and coupons directly to the customer.

**CONCLUSION**

Medication nonadherence is a major issue for the United States healthcare system. To improve medication adherence, comprehensive programs and solutions need to be designed to enhance patient engagement through a variety of vehicles, platform and vectors. Solutions will need to be tailored to specific therapeutic areas and specific demographics.

Packaging can be a key driver in positively affecting patient adherence by delivering a tailored solution that increases a patient’s engagement and enhances his/her experience, ultimately helping to improve treatment outcomes.

**REFERENCES**