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KEEP THEM COMING BACK FOR MORE

Awareness advertising has given way to targeted patient-education and patient-compliance initiatives, opening up a new avenue for improving sales. BY STEVE NILES

Money spent to research and market a product is wasted if the patient decides not to take the drug. By educating patients on the importance of complying with their prescriptions, pharmaceutical companies can improve their reputations and boost the bottom line. There are many reasons why patients do not adhere to a prescribed drug regimen. Increasingly, pharmaceutical companies are developing patient-education initiatives designed to address those issues. Although a variety of media channels are used to reach patients, the Internet has become most important.

In the past, a pharmaceutical company's equation for success involved adding sales representatives, raising prices, and launching direct-to-consumer marketing. The equation has changed. Pipelines for most pharmaceutical companies are not as strong as they were five years ago, companies are finding diminishing returns in adding to their sales forces, price increases are under more scrutiny, and direct-to-consumer advertising is showing questionable return-on-investment.

Educational programs are becoming one of the first choices of marketing tools because of their cost effectiveness. "What we're seeing now is that most brand managers are trying to do more with less," says Kerr Holbrook, VP, marketing, McKesson Specialty (mckesson specialty.com). "By that I mean trying to recognize the full lifetime value of the patient, and they do that through these educational adherence-type programs."

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SIXTH ANNUAL REPORT

FUTURE BLOCKBUSTERS

The diabetes drug Exubera is expected to gain FDA marketing clearance in 2006 after years of industry anticipation. BY ANDREW HUMPHREYS AND REBECCA MAYER

Regarded as the most important advance in insulin administration in 80 years, Exubera is on track to reach the U.S. and EU marketplaces this year. This innovative drug initially was expected to be submitted for U.S. marketing clearance in 2001, but more long-term safety studies became necessary. Upon approval, Exubera would offer diabetes patients, for the first time, the ability to aggressively treat their disease with insulin in a non-invasive manner. For type 2 patients, this could mean earlier adoption of insulin, better compliance, and overall better disease management. For type 1 patients, Exubera could reduce the number of injections and allow for improved meal-time blood glucose management.

Pfizer Inc. and the Sanofi-Aventis Group are expected to promote and manufacture Exubera in Europe and the United States to adult patients with type 1 and type 2 diabetes. Nektar Therapeutics, as the developer of the inhalation device and inhalation for-

mulation for Exubera, will manufacture a portion of the dry-powder insulin and provide the devices.

There are 20.8 million people in the United States, or 7% of the population, who have diabetes. Although an estimated 14.6 million people have been diagnosed with diabetes, 6.2 million people are unaware that they have the disease. Diabetes affects almost 180 million people worldwide and that figure is expected to grow to 300 million during the next 20 years.

Med Ad News has identified 10 products that are expected to be approved for U.S. marketing for the first time this year and generate eventual peak sales of at least \$1 billion. In addition to Exubera, the other products anticipated to receive clearance from U.S. regulators in 2006 are the asthma drug **Alvesco**, developed by Altana Pharma Inc. and Sanofi-Aventis; Merck & Co.'s human papillomavirus vaccine **Gardasil**; the anticancer compound **Nexavar**, which is being jointly developed by Bayer Pharmaceuticals Corp. and Onyx Pharma-

ceuticals Inc.; J&J's **paliperidone** extended-release drug for schizophrenia; **panitumumab**, a metastatic colorectal cancer drug from Amgen Inc.; **Revlimid**, developed by Celgene Corp. to treat fatal blood disorders and cancer; Pfizer's **Sutent** for treating stomach and kidney cancers; **Trexima**, developed by Pozen Inc. and to be marketed by GlaxoSmithKline for treating migraine; and Pfizer's smoking-cessation product **varenicline**.

In addition to profiling the 10 aforementioned products, this special report contains an update regarding four medicines that were featured in Med Ad News' January 2005 Future Blockbusters report that now are expected to receive approval from the U.S. Food and Drug Administration in 2006. These products are Sanofi-Aventis' **Acomplia**, a smoking-cessation and obesity-management drug; **Entereg**, to be jointly promoted by Adolor Corp. and GlaxoSmithKline for the management of postoperative ileus; **indiplon** for

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OVERGROWN PLANTS CHOKER PROFITABILITY

Faced with a need to find more savings, companies are weeding out manufacturing facilities as the industry has more capacity than is needed. BY ERIC LADLEY

Manufacturing has emerged as a popular target for cost cutters. Research and development largely has escaped downsizing because companies need new products to drive long-term growth. Executives like to avoid cutting sales and marketing, which boost short-term growth and quarterly results. Instead, the supply chain is being tightened. Some companies have closed smaller, nonstrategic plants, and others have outsourced production or explored moving production to less expensive

locations. These trends have been especially pronounced with facilities used to manufacture small-molecule medicines.

Cost cutting has been going on in pharmaceutical companies for years, but typically focused on shared services, infrastructure, finance, information technology, and help desks. Manufacturing had been ignored. The focus on production has increased in the past two years as executives facing economic pressure realize how much money can be saved by closing or streamlining facilities. Estimates from some large

pharmaceutical companies say restructuring manufacturing operations could add up to savings of as much as \$4 billion, according to Pete Mooney, practice director, U.S. life sciences, and principal, Deloitte Consulting LLP (deloitte.com).

"I talked to one client who said he can roughly take at least \$2 billion out of their supply chain," Mr. Mooney told Med Ad News. "That equates to what they would invest in a blockbuster."

Analysts say pharmaceutical companies are only in the beginning stages of scaling back facilities, although almost all of the major companies are following plans for consolidating their operations. Many of

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Coming back

from cover

Patient-education programs are necessary because most patients forget most of what their doctor tells them less than six minutes after walking out the door, according to the patient-education company **HealthEd**. About 33% of adults frequently fail to follow the treatment regimens for medications they were prescribed. About 50% of all patients do not take medications as directed, resulting in billions of dollars in lost revenue. Patients need more comprehensible education materials. According to HealthEd, about 90 million adults read at or below the eighth-grade level.

"We are at the forefront of a sea change in health marketing," says Roy Broadfoot, president and founder, HealthEd (healthed.com). "The industry has recognized the strong need for a shift from communication of information to patient-centered education."

The good news is, pharmaceutical companies are getting better at offering effective compliance programs, according to Elizabeth Boehm, senior analyst, **Forrester Research Inc.** (forrester.com). The pharmaceutical industry is moving away from the awareness-driven focus that relied on television DTC advertising, to embracing the idea of compliance/adherence/persistence and targeting a much smaller audience. "Compliance/adherence/persistence programs have been around for a long time, but there hasn't been a solid platform ... to deliver it on a broad scale inexpensively," she says.

The use of the Internet is allowing companies to target their audiences, according to Eve M. Stern, senior VP, business de-

velopment and marketing, **NexCura Inc.** (nexcure.com), a health-care information and communications company. These Internet-based, patient-centered education programs arm consumers with evidence-based information and tools they need to make informed choices about their treatment options and side effects. The result is greater compliance and a higher level of patient satisfaction. Adherence programs that are supported by an ongoing relationship with patients are more successful than one-time or even periodic outreach messages.

"The message of such campaigns must be relevant, appropriate, and targeted to patient needs on the continuum of the disease course," Ms. Stern says. "The patient-education information needs to be tailored to the patient's information needs at each critical decision point as the patient navigates through his or her treatment regimen."

To create a successful adherence program, Ms. Stern recommends that companies first mount an evidence-based educational e-mail campaign to a targeted, permission-based patient database of registered users. This process builds a trusted relationship.

"Follow that with an invitation to order educational materials, and patients will appreciate and value the information and act on messages that support compliance and follow-up care," Ms. Stern says.

In another example of effectively using the Internet in compliance programs, physicians can provide patients with an information prescription to log on to a particular Website at the time of diagnosis. After viewing the educational materials specific to their conditions in a relaxed, unbiased environment, patients are much more likely to order additional educational materials, Ms. Stern says. Patients can access information

on demand at their own level of readiness. Patients can be given an incentive, such as a rebate or coupon for a product discount, to increase the response rates.

Patients want personalized, individual attention and education, according to Georgianna Donadio, Ph.D., founder and director of the **National Institute of Whole Health** (wholehealtheducation.com). "We must return to relationship-centered medicine and treat our patients the way we would want to be treated if we suddenly found ourselves in a disease or pathology state," Dr. Donadio says.

The National Institute of Whole Health educates medical professionals and works with insurance and pharmaceutical companies to put Whole Health educators into health and medical practices so that they may educate patients about their health and empower them to change behavior to meet compliance, improve outcomes, and reduce costs.

Ms. Stern believes that some pharmaceutical companies are making great strides in the area of patient education, but the industry can do far more. Many pharmaceutical companies continue to invest in physician-education and awareness programs and underinvest in targeted consumer-education strategies.

"It is ironic that at a time that pharmaceutical companies are investing in and developing ever more targeted therapies, they seem to be allocating more dollars to broadcast, 'systemic' marketing strategies," Ms. Stern says. "With the continued growth in the consumer movement and consumer-driven health plans forcing patients to become more accountable health-care purchasers, pharma companies would be wise to bolster their patient-education programs to targeted patients in concert with the programs they are doing for health-care providers."

Good for the bottom line

Consumer Health Information Corp. estimates that 30% to 85% of patients disregard refills and that 10% to 20% of initial prescriptions go unfilled. This means drug brands are losing out on millions of dollars in revenue.

"If the pharmaceutical company does not provide the patient with the information they need, that pharmaceutical company is never going to reap the benefits of long-term sales for chronic disease medications," says Dorothy L. Smith, president and CEO of Consumer Health Information (consumer-health.com).

Patient-education programs increase sales by emphasizing the importance of compliance with a complete course of treatment, which includes taking correct dosages at the right intervals for the optimal period of time. Patients are more apt to go back for refills, complete their full prescriptions, and even just fill their prescriptions in the first place when they understand the implications of noncompliance, according to Eric Boles, research team leader, **Cutting Edge Information** (cuttingedgeinfo.com).

"Sales increase with earlier patient participation in the identification of treatment options, adverse effects, and patient-initiated conversations about alternative treatment options and compliance with treatment guidelines," Ms. Stern says. The ultimate benefit is to the bottom line for product brand teams.

According to Dr. Donadio, in the U.S. statin market alone, one year of noncompliance costs pharmaceutical companies al-

most \$3.9 billion in revenue. As little as a 5% increase in compliance rates can translate to \$30 million to \$40 million in revenue. "It makes good and profitable business sense to provide support and endowments to health-education organizations who produce models of patient-health education that are proven to affect the compliance statistics, even marginally, as this results in significant revenue increase for the drug companies," Dr. Donadio says.

Causes of noncompliance

Compliance issues do not spring up gradually. The first prescription to be filled is usually where the initial problem with compliance begins, according to Gene Guselli, CEO and co-founder, **InfoMedics** (infomedics.com). If the patient has any difficulties in understanding why, when, and how to take the medicine, noncompliance will occur, most often by the patient refusing to fill the prescription in the first place.

"If you allow that to continue to occur without a spontaneous type of feedback captured from the patient to the doctor, then it is very difficult to ultimately get those patients to comply," Mr. Guselli told *Med Ad News*. "It's almost like practicing prevention for compliance. The best time to catch noncompliance and to do something about it is before it occurs."

InfoMedics provides information to doctors as to whether the first prescription has been filled. When the doctor receives feedback from the data collected by InfoMedics that the patient did not fill the prescription, the situation can be corrected before there is an exacerbation from a health-care expenditure standpoint or before the patient is too far down the road of noncompliance.

Mr. Boles believes that there are five primary reasons for patient noncompliance. Patients may stop taking their medication too soon, forget to take one or more doses, take medications at the wrong times, fail to fill the initial prescription, or take the incorrect dose.

To address these issues, drug companies already do many things. From a drug-development standpoint, they try to develop products in convenient formulations, Mr. Boles says. A daily dose is better than a twice-daily dose, and a weekly dose is better than a daily dose, for example. If there is a delivery device, such as a syringe, companies try to make the device easy to use. Mr. Boles cites **Abbott Laboratories'** (abbott.com) arthritis drug **Humira**, which comes in a prefilled injection device with large, easy-to-grip wings, so arthritis sufferers can administer the drug more easily.

Analysts with **Datamonitor Plc.** note that in the area of osteoporosis management and treatment, there is a low level of patient compliance with prescribed drugs. Difficulties here are due to the chronic nature of osteoporosis, requiring long-term treatment that can be costly — particularly to elderly patients who have to pay for their own medications. Many patients fail to take the drugs correctly or stick to the strict dosing requirements associated with some commonly used products, leaving them at greater risk.

"The chronic nature of the disease and the lack of major external warning signs until the disease is advanced and a fracture occurs means that patients cannot appreciate the long-term benefit of the drugs they are taking," says Victoria Williams, women's health analyst, **Datamonitor** (datamonitor.com).

To deal with this particular patient-

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HealthEd developed this ad to promote the importance of patient education.

compliance issue, more osteoporosis products are being developed with long-interval, intermittent-dosing regimens. Leading bisphosphonates on the market, including Merck & Co.'s **Fosamax** and Procter & Gamble Co.'s (pg.com) and **Sanofi-Aventis'** (sanofi-aventis.com) **Actonel**, can be taken weekly, but newer drugs will offer an even longer gap between doses. For example, **Roche** and **GlaxoSmithKline's** (gsk.com) **Boniva** is available in a once-monthly pill formulation. **Amgen Inc.'s** (amgen.com) monoclonal antibody **denosumab** could be offered in a once-every-six-months injection, and **Novartis** (novartis.com) is developing **Aclasta** as an annual I.V. push.

Although the new products may offer only small increases in terms of efficacy, in real terms the increase in patient compliance may see them improve actual outcomes for patients significantly. "Less-frequent dosing is one the biggest opportunities for effectively treating sufferers of osteoporosis," Ms. Williams says. "If one takes into account the increase in patient compliance these new drugs may confer, they may ultimately punch well above their weight in terms of efficacy in real-life situations."

Cost is another factor that marketers can address by distributing coupons, for example. "If you look at health-plan data, one of the fastest ways to influence drug consumption is to change co-pays," Ms. Boehm says. "By offering coupon programs, companies can measure and often influence behavior. But the challenge with couponing is if it's overly broad, you're simply discounting your product."

The programs that McKesson Specialty runs with its clients are multidimensional. They involve the Internet, paper mailers, nurse calls, and personal contact with a patient. Another element the programs involve, which Mr. Holbrook says is distinct and unique from previous programs, is an element of cost offset to help the patient overcome the financial barriers. McKesson Specialty has developed a product called **LoyaltyScript**, a card-based product that patients can bring to the pharmacy to get discounts off their co-pay.

"That is just the foundation of a more holistic relationship-marketing program," Mr. Holbrook told *Med Ad News*. "Because once you get the patient going into the pharmacy and using the card to get the discount, you then can get data from the patient in terms of when they filled their prescription. You can engage in more dialogue with them as they enroll in the card, so you can then meet the patient where they are. If they like

to be talked to via the Web or by mail or by phone, you can make a more-specific intervention with the patient using the channel — Web, paper, phone — that's most impactful to them."

Another compliance issue is related to drug safety, particularly in the light of the media hype following Merck's withdrawal of **Vioxx**, according to Destry Sulkes, M.D., managing director, **MedsiteCME** (medsitecme.com), a provider of free online continuing medical education. "Patients are getting very concerned about safety in ways they've never been before," Dr. Sulkes says.

Miscommunication is a common cause of noncompliance. According to Ms. Smith, patient comprehension is different from readability. "Many companies just quit at the readability stage and don't go to the next step, which is to make sure the information is understandable to the average person," she says. "A good example is the instruction 'Do not eat red meat.' This passes the readability level and is at grade 4, however this instruction is not understood by patients because they think that once they cook the meat it is no longer red and is OK to eat."

Ms. Smith believes that the only way a company is going to produce materials that patients are going to understand is to ensure that the authors not only know how to translate the materials into appropriate wording but also know how to apply patient-counseling techniques to the language so that the patients are motivated to take the medication.

"This takes experience in clinical practice, actually counseling patients and knowing what types of answers are needed for common patient questions," Ms. Smith says. "It also takes expertise in understanding how to develop creative behavior modification strategies that will work at the right stage of the therapy. It depends on whether it is the initial prescription, the first refill, the third or sixth refill, or the 1-year refill."

Noncompliance is most often a conscious decision, according to Charlene Prounis, CEO of **Flashpoint Medica LLC** (flashpointmedica.com). She believes that the primary reason why patients fall off a drug regimen is because they do not feel like they need the drug.

"The issue is that the therapeutic alliance was not achieved in that doctor/patient encounter," Ms. Prounis says. "To me, that's the real crux of it."

Flashpoint Medica designs programs intended to strengthen that therapeutic alliance. According to Ms. Prounis, there are

three things that must happen to make sure the patient goes out and buys the drug and stays on the drug. First, the patient needs to understand and accept the diagnosis, so the doctor must communicate the diagnosis effectively. Second, the patient must agree with the treatment that the doctor is proposing. Third, the patient's concerns about the medicine and the side effects must be well addressed.

Flashpoint Medica developed a patient program for a client's anti-anxiety drug with a role for patients and doctors. "If you think of the encounter as two people, the patient has to come in and be a little bit more prepared," Ms. Prounis says. "That means maybe they've done a little research that today's patient should. Or maybe they at least understand what it is they want to bring up to the doctor. Maybe they haven't done the Internet research, but they've prepared in their mind the questions that they want to ask. Most people don't do that. They get in and they wait for the doctor to question them."

The patient must also know how to talk to the doctor in language that the doctor will appreciate. The patient must be more objective in describing symptoms. The doctor, meanwhile, needs to understand and appreciate the patient's perspective.

"The last thing patients need when they leave the doctor's office to get to this better therapeutic alliance are more instructions and a rationale why they have chosen this drug," Ms. Prounis says.

When writing patient-education materials, the developer must try to predict all the problems that a patient can encounter with a specific sentence. "One thing I have learned after counseling patients and writing patient-education materials for the past 20 years is, if anything can be misinterpreted by a patient, it will be," Ms. Smith told *Med Ad News*.

The simplest cause of noncompliance with a medication regimen to address is forgetfulness. Marketers need to create a reminder that people will accept. This could be done using a variety of different channels and requires a relatively short message.

Roche (roche.com) established a call center for its obesity drug, **Xenical**, and staffed the center with nurses who were specially trained in metabolism-based conditions. Apart from answering questions, the call center provides dosage and refill reminder calls to subscribers.

Many companies deliver dosage and refill reminders to subscribing patients, Mr. Bolesh says. Some companies provide desktop-reminder tools for download. **Forest Laboratories Inc.** (frx.com) did this with the depression drug **Celexa**. Merck (merck.com) has an e-mail reminder program for **Fosamax**, **Pfizer Inc.** for **Lipitor**, and **AstraZeneca** (astrazeneca.com) for the cholesterol drug **Crestor**. Some high-tech drug packaging — such as blister packs for pills — may emit beeps or blinking lights when the time comes for a dose.

Of the many ways the patient-adherence challenge can be addressed, integrating well-designed pharmaceutical packaging is an essential component, according to Steven Palmisano, senior VP/management supervisor, **Interlink Healthcare Communications** (interlinkhcc.com).

"Although packaging is only part of what is required, we believe that it is a key element toward improved patient adherence that has received less focus than other alternatives," Mr. Palmisano told *Med Ad News*. "Pharma companies must research what the core issue is for nonadherence related to their specific brand and then determine how they can resolve it. In

most instances, they'll be able to translate what they learn into a better-designed package to address an important element of this adherence challenge."

According to Mr. Palmisano, packaging should add value to the brand, not just communicate FDA-required information. To that end, pharmaceutical companies should concentrate on consumer-friendly packaging that offers simple instructions and reminders for patients to properly take their medicine. Unit-of-use packaging with adherence-related reminders should be used wherever possible to control the medication-administration instructions a patient receives from the pharmacy.

"Based on their own marketing research and expertise, ad agencies specializing in pharmaceuticals should understand these challenges and be capable of working with their clients — and sometimes directly with packaging experts — to implement packaging that supports the primary issue that impacts patient adherence with that specific product, to overcome patient compliance hurdles," Mr. Palmisano says.

Beyond the simple causes of noncompliance, marketers must examine the condition. In support of **Lipitor**, **Pfizer** (pfizer.com) is a partner in the Taking Health to Heart program. The Taking Health to Heart Program is a collaboration between the Atlanta Regional Commission, which is the Atlanta area's agency on aging, and the Fulton County Office of Aging. Pfizer and the agencies focused on heart health after holding many discussions on coronary artery disease data, treatment guidelines, and increases in risk associated with age. The program is designed to improve education around the importance of cholesterol management in the elder population and to evaluate the effect of lifestyle interventions on the level of coronary risk among the participants in the program.

Pfizer mails its "Close to the Heart" cholesterol-management materials to the participants each month. The program augments these educational materials with existing exercise activities and nutritional classes offered at senior centers, as well as with a series of creative, monthly educational programs designed to reinforce the importance of continued participation.

"If you look at the heart-disease market, it's an accepted if not fully proven fact that if you can get somebody involved with their overall lifestyle changes, drug adherence tends to come along with it and not the other way around," Ms. Boehm told *Med Ad News*. "Getting them motivated around fitness and nutrition, etc., often creates more adherent patients."

The physician's role

Patients are savvy, educated, and have access to medical information in books and on the Internet. Educational programs that preach compliance without solid data will be viewed with skepticism, according to Nan Andrews Amish, consultant, **Big Picture Healthcare** (bigpicturehealthcare.com). This will hurt the effectiveness of regimens where completing a program is truly important, for example, with a course of an antibiotic.

"Patients today are seeking partners in their health, and they are becoming more and more frustrated with drug regimens that have side effects and that do not cure a condition," Ms. Amish told *Med Ad News*.

Smart doctors are seeking their own education to improve their relationship-building skills, according to Ms. Amish. "When

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