Three Specialty Categories to Watch in 2006

Specialty pharmaceuticals are redefining the blockbuster drug. This category contains the drugs with the highest per-patient costs and highest trend in the pharmaceutical marketplace. But those same drugs represent the greatest advances in medicine of recent years. They have made the most profound difference to patients with complex health conditions, reducing pain and discomfort, improving quality of life and slowing the progression of disease.

The specialty categories discussed below represent some of the most exciting science in medicine today and, importantly, illustrate many of the reasons it is so important to consider and plan for specialty pharmaceuticals in your pharmacy benefit design.

Pulmonary Arterial Hypertension (PAH). More product choices magnify the need for greater plan management. PAH is a rare, life-threatening lung disorder, with an estimated 300 new cases per year in the United States. The disease is characterized by extremely

A Focus on Specialty Pharmaceuticals

In the first three quarters of 2005, specialty pharmacy represented 8.5 percent of our PBM Book of Business gross cost, but trend for the biotech/specialty category was over 20 percent PCPM (per cardholder per month; see page 4). With annual per patient cost of up to $250,000, hundreds of specialty drugs in development and ever-wider utilization of these innovative medications, every plan needs to consider cost and care management strategies to maximize the significant investment that specialty pharmaceuticals demand.

In this issue of TrendsRx Quarterly, you’ll learn about technological and clinical advances in the specialty area, some of the most promising drugs in the specialty pipeline, and the suite of strategies Caremark has developed to help you manage your specialty pharmacy expense, reduce overall healthcare costs and support better patient outcomes.
elevated blood pressure in the pulmonary artery and lung arteries. Difficult to diagnose and treat, patients with PAH typically lived less than three years after diagnosis as recently as the mid 1980s. Treatment advances, many involving biologically derived pharmaceuticals, now allow patients to survive as long as ten to 20 years. There has been a wave of new specialty treatments for PAH. Revatio® and Ventavis® were approved in 2005 with two others—Thelin® and ambrisentan—expected to be approved in 2006. Average annual cost of specialty therapy for PAH can range from $30,000 to more than $100,000.

**Reasons to watch the category.** There is potential for inappropriate utilization of this category. Patients with other disorders, such as congestive heart failure, are sometimes misdiagnosed and treated for PAH. Promotional activities around new product launches could increase awareness and rates of both diagnosis and misdiagnosis of the disorder. Specialty management services help to assure appropriate utilization, effective treatment and optimal outcomes for each patient.

**Multiple Sclerosis (MS).** *Clinical management makes the most of the pharmacy investment.* Multiple sclerosis is a chronic disorder in which the immune system attacks the nervous system. It affects an estimated 500,000 people in the United States. Symptoms include loss of muscle control, blurred vision and fatigue. The disease is progressive, can be disabling and can result in premature death.

MS treatment is dominated by biologic therapies costing from $12,000 to $30,000 a year. The beta interferons—Rebif®, Avonex® and Betaseron®—have been shown to be effective, but side effects, including flu-like symptoms and liver toxicity, are troublesome. Moreover, after extended treatment, some patients produce neutralizing antibodies that reduce the effectiveness of the therapy. Copaxone®, a synthetic protein, has comparable efficacy for some patients, but a more favorable side effect profile. Tysabri®, which promised to be a significant advance in MS treatment, was launched and withdrawn in the last year after two patients died of a serious neurological disorder.

---

**A Specialty Pharmaceutical Glossary**

**Specialty pharmaceuticals**—drugs which generally require close supervision and monitoring during therapy; often high-cost; many, but not all, are biologically derived; may need special storage or handling; can be oral but administration may also be by injection, infusion or inhalation

**Biotechnology drugs**—drugs derived biologically, typically proteins produced by live cells, grown in sterile, temperature-controlled containers; many biotech drugs are based on advances in genetic research and they work in a targeted fashion at the cellular level, actually altering the course of a disease; also known as biopharmaceuticals

**Orphan drug**—drug used for treating an “orphan disease,” one affecting fewer than 200,000 people; “orphan drug status”, defined by the Orphan Drug Act of 1983, is granted by the U.S. Food and Drug Administration and provides patent protection for seven years; nearly half of all drugs produced by biotechnology companies are orphan drugs

The glossary was developed using information from Medicines in Development, Biotechnology 2004, PhRMA (Pharmaceutical Research and Manufacturers of America)
Reasons to watch the category. Trend for MS specialty therapies has been close to 20 percent in 2005. There is no cure for MS, and current treatments are not entirely satisfactory. That is one reason for the speculation around the possible relaunch of Tysabri®, which would probably carry a black box warning if relaunched. Because these therapies often prove problematic for patients, specialty management services are particularly important to promote adherence and continued effectiveness and to help prevent progression of the disease.

Rheumatoid arthritis (RA). New indications lead to rapid growth in utilization. Another disease of the immune system, rheumatoid arthritis is a serious and disabling disease characterized by inflammation of connective tissues. RA patients have three times the direct medical costs, twice the hospitalization rate and 10 times the work disability rate of an age- and sex-matched population. Up to one-third of people with RA do not get sufficient response from baseline treatments including the use of analgesics, non-steroidal anti-inflammatory drugs (NSAIDs) and COX-2 inhibitors. For this population—an estimated 750,000 Americans—advanced RA therapies may be appropriate.

Tumor necrosis factor (TNF) blockers have become the standard of care for the treatment of moderate to severe RA. The anti-TNF agents Enbrel®, Humira® and Remicade®—which range in cost from $15,000 to $20,000 a year—have been shown to be effective in the treatment of other inflammatory disorders as well, and drugs in the category are adding indications for psoriatic arthritis, psoriasis, Crohn’s disease and other disorders. Filings for more indications for these drugs are expected. Orencia® (abatacept), recently approved by the FDA and expected to launch in 2006, appears to be effective for patients resistant to anti-TNF therapy.

Reasons to watch the category. Utilization of specialty drugs indicated primarily for severe to moderate RA is increasing rapidly—a major reason for a gross trend over 40 percent among anti-TNF agents. The addition of Orencia may further expand the RA population utilizing specialty pharmaceuticals. In addition, there is an increasing tendency among clinicians to initiate earlier drug treatment for RA to minimize progression of the disease. Specialty management programs can encourage the use of less expensive therapies for this purpose prior to initiating the use of biologics.

With a robust pipeline, groundbreaking science, multiplying indications and growing utilization for common, chronic illness—specialty pharmaceuticals offer remarkable benefits for patients and particular challenges for health plans and plan sponsors. Throughout this issue of TrendsRx® Quarterly, you’ll learn more about how Caremark helps plans and payors make the most of their benefit. For more information on Caremark Specialty Pharmacy Services, please contact your account representative.

1 “Medical Therapy for Pulmonary Arterial Hypertension; ACCP Evidence-Based Clinical Guidelines.” www.chestjournal.org, accessed November 8, 2005.
In the first three quarters of 2005, Caremark biotech/specialty trend in our Book of Business (BOB) reached 20.8 percent, an increase over the 2004 number but less than widely reported industry forecasts of over 22 percent. For the same period, biotech/specialty grew from 5.9 percent of gross cost in 2004 to 8.5 percent.

These increases are largely driven by expanding utilization as new biotech products are launched and existing products are used for a wider range of conditions. Increasingly, biotech drugs are expanding beyond their original “orphan drug” status and are being used to treat such common chronic conditions such as asthma and psoriasis. Every plan should have a long-term strategy in place to make sure that the considerable investment in these pharmaceuticals is used optimally.

Drivers of Growth

New drugs. There are more than 370 potential specialty drugs currently in clinical trials with possible indications for approximately 200 diseases. An estimated 20 new specialty products could be approved in the next 12 months alone.¹

Expanding indications. Many existing specialty products have applied to the FDA for additional indications. Each such expansion broadens the market of potential utilizers. For example, Remicade® is indicated to treat rheumatoid arthritis, ulcerative colitis, Crohn’s disease, psoriatic arthritis and ankylosing spondylitis. Pending indications include juvenile rheumatoid arthritis, hepatitis C and chronic obstructive pulmonary disease (COPD).

Direct-to-consumer (DTC) advertising. DTC advertising has already impacted prescribing patterns and drug spend for specialty products. Such promotion is likely to continue and expand.

Medicare Part D. The launch of Medicare Part D could result in further increases in specialty utilization, as the population of seniors with prescription benefit coverage expands. Many specialty products are indicated for conditions more common among seniors such as cancer, rheumatoid arthritis and psoriasis.

Contact your Caremark account representative for information on the specialty pipeline, and watch TrendsRx® Quarterly for updates.

¹ Ernst & Young, 2005 Global Biotechnology Report: Industry Revenues Grow by 17%. Global Markets (Emerging June 1, 2005)
Q1-Q3 2005: 7.3% PCPM

The Caremark Book of Business (BOB) gross trend continued in the single digits through third quarter. While utilization continues to be a key driver, trend has been moderated by the effective maximization of the opportunities presented by the launch of generics in key categories, especially in the antidepressant selective serotonin reuptake inhibitors (SSRIs).

Major shifts have occurred in the Caremark Top Ten Category listing, which ranks drug categories by percentage of BOB spend. The anti-inflammatory analgesics, which include the non-steroidal anti-inflammatory drugs (NSAIDs) as well as the COX-2 inhibitors, dropped to eighth place. The category has had a negative trend through most of 2005, the result of ongoing safety concerns about, and market withdrawals of, COX-2 inhibitors Vioxx® and Bextra®. On the other hand, trend for the proton pump inhibitors has been on the rise, probably due to their use in conjunction with NSAIDs prescribed in place of COX-2 inhibitors.

Anticonvulsants, ranked tenth in 2004, have now assumed fifth place. While the availability of generic versions of category leader Neurontin® has helped to moderate trend, utilization of the anticonvulsants has been growing due to widespread and acceptable off-label use for pain relief. The September 2005 launch of Lyrica® is expected to further increase trend for the anticonvulsants over time. Lyrica is the only drug in the class indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy.

While statins remain first in our Top Ten, gross trend for the specific class has moderated. Statin combinations such as Vytorin™ and Caduet® and Zetia®, which is a cholesterol absorption inhibitor, are drawing market share. The overall gross trend for cholesterol-lowering drugs measured over 12 percent PMPM; gross trend for statins hovers at just over four percent.

The antidepressant category is also showing the effects of market shifts. Trend for the third-ranked SSRIs has been negative, largely due to the availability of generics for key products such as Paxil®, Wellbutrin® SR and Celexa™, as well as safety concerns around pediatric use. In addition, utilization of the serotonin-norepinephrine reuptake inhibitors (SNRIs) is increasing. The SNRIs include Effexor® XR and Cymbalta®.

Compared to Q3 2004, spend and utilization of influenza agents increased significantly in 2005. Concerns about vaccine shortages as flu season approached as well as extensive media coverage of a potential avian influenza (bird flu) epidemic may have led to stockpiling and increased utilization of this category.

Caremark scored the highest among top competitors in 10 of the top 15 satisfaction drivers in the 2005 PBMI Customer Satisfaction Report. Caremark took top honors in overall service and performance, and in delivering savings.
It is estimated that there are more than 1,000 potential treatments currently in the pharmaceutical pipeline. Approximately one-third of these products can be classified as biotech with more than 40% of the drugs in late stage development classified as specialty pharmaceuticals.

In late 2005, the FDA approved Orencia™ (abatacept), a biologic drug for the treatment of moderate to severe rheumatoid arthritis (RA) in individuals who have failed other therapies. The first in a new class of drugs for this condition, Orencia is expected to capture sizable market share as it will be the only drug with an indication for use in RA patients who have not responded adequately to currently available biologic drugs.

Patients with movement disorders associated with Huntington’s disease may benefit if tetrabenazine receives FDA approval. Available in Europe for many years, tetrabenazine would be the first and only drug approved in the United States for the treatment of this inherited, rare, progressive and neurological disorder. Patients with other types of movement disorders such as Parkinson’s disease may also benefit from the use of tetrabenazine.

Duodopa® could provide patients with severe Parkinson’s disease relief from their tremors. This drug is a gel suspension formulation of the currently available oral tablet Sinemet® (carbidopa/levodopa). Duodopa® is administered directly into the small intestine through a tube. Once the tube is in place, the drug can be administered continuously by a small pump. Administering the drug via this route allows for a consistent blood level of the drug and better control of a patient’s symptoms. Duodopa® will likely be available late 2006.

A vaccine for the prevention of cervical cancer, Gardasil™ (quadrivalent human papillomavirus types 6, 11, 16, 18, recombinant vaccine), is likely to come to market in 2006. Short-term results from a recently released clinical trial showed this vaccine to be 100% effective in preventing pre-cancerous cervical changes and very early-stage cervical cancer in over 12,000 women between the ages of 16 and 23. Gardasil™ prevents infection with the sexually transmitted strains of human papilloma virus (HPV) that are the primary cause of genital warts and abnormal Pap tests.

Several promising cancer treatments are expected to be available in 2006. Two oral therapies, Nexavar™ (sorafenib, approved and launched late 2005) and Sutent (SU-11248, sunitinib malate), could change the standard of care for the treatment of renal cell cancer. Provenge® (sipuleucel-T), an injectable oncolytic that “attacks” only cancer cells, offers hope for the treatment of certain types of prostate cancer.

New therapies for the treatment of macular degeneration, a condition for which few therapies currently exist, are on the horizon. Retane™ (aneocortave acetate) will likely launch in early 2006, and Lucentis™ and Evizon™ (squalamine) are in late stage development with projected launches in 2007.

---

**Potential Specialty Drugs Represent Nearly Half of Drugs in Late-Stage Development In the U.S.**

<table>
<thead>
<tr>
<th>Traditional Drugs in Development</th>
<th>Specialty Drugs in Development</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Intravenous chemotherapy agents are not included as specialty drugs.

---

**Specialty Drug Pipeline Expands In Biotechnology Era**

![Image](image-url)
Long considered a potential blockbuster, Acomplia™ (rimonabant) is pending approval at the FDA, with expected approval and launch during Q1 2006. The drug is the first in a new class of medications called selective cannabinoid-1 (CB1) receptor blockers. Projected indications for the drug include the treatment of obesity and metabolic syndrome (a group of risk factors which place a person at increased risk of developing heart and kidney disease, as well as type 2 diabetes.) The drug may also have potential as an aid in smoking cessation.

If approved as an obesity medication, Acomplia could potentially have a considerable market. It is estimated that one-third of the American population—over 60 million people—is obese. While current obesity medications have a relatively small market, Acomplia will likely capture significant marketshare and will expand the overall market, according to Caremark projections. Moreover, we expect that the drug will have a longer duration of therapy and will be approximately three times more expensive that its competitors in the obesity market. Peak U.S. sales of $1 billion are expected. Contact your account or clinical manager regarding suggestions for appropriate benefit design for this drug in your plan.

Emerging generics

**Statins.** Beginning in Q2 2006, the statin market could see significant shifts. It is anticipated that a generic version of Pravachol® (pravastatin, annual brand sales $1.88B) will launch in April with a six-month period of exclusivity. In June, multiple vendors are expected to launch generic versions of Zocor® (simvastatin, annual brand sales $4.56B). Prices for simvastatin should be very competitive at launch; prices for pravastatin should drop by Q4. Cholesterol-lowering drugs have led the therapeutic categories in spend for several years; savings from the maximization of these generic launches should be significant. Talk to your Caremark account representative to make sure your plan makes the most of this opportunity.

**Cold and flu season.** Multiple vendors are expected to offer the generic version of Flonase® (fluticasone propionate, annual sales $1B+) once the pending citizens petitions are resolved. While the key patent for Flonase, a corticosteroid nasal spray used as a respiratory anti-inflammatory, has already expired, launch of the generic has been repeatedly delayed. Current projections are that generics will be available early in 2006. Azithromycin, generic for the antibiotic Zithromax® (annual brand sales $2B+, including Z Pak), launched in mid-November.
Management Services for High Cost, High Care Specialty Patients

The BioCare Solutions™ suite of services delivers a high level of personal service and care to patients with chronic conditions on specialty medications. Our comprehensive specialty management services integrate the principles and practices of disease management in order to deliver quality care, improve health and reduce overall costs.

BioCare Solutions—Caremark Specialty Pharmacy Services—designed to improve health and reduce overall cost

- **Provide superior service to patients**: Caremark has nearly 30 years of experience, expertise and commitment to high standards.
- **Administer personal, high-quality care and support**: Patient-centric approach identifies and works one-on-one with patients who can benefit from highly effective clinical programs designed to improve adherence and outcomes.
- **Gain greater control of your entire specialty spend**: Our comprehensive reporting helps identify additional opportunities for improving outcomes and lowering costs.
- **Improve patient outcomes**: Our clinically superior, results-driven services use evidence-based medicine to improve quality of life and slow disease progression.
- **Manage your specialty program more easily and effectively**: We offer customized implementation, ongoing pull-through support and dedicated account services.
- **Optimize overall healthcare costs**: Caremark offers clinical support services that minimize complications, drug interactions, hospitalizations, surgeries and other medical expenses.
- **Build greater patient satisfaction**: Excellent services, high level of care, and convenient home delivery are just some of the benefits for patients.

**Core services** include benefit management, pharmacy care management, distribution services, and patient education and support. Plan participants have access to the pharmacy and clinical staff for their support in answering questions 24 hours a day, seven days a week. Patients appreciate and benefit from the expertise of a CareTeam comprised of pharmacists, nurses and technicians who have concentrated experience with key conditions. The CareTeams reach out to patients to educate them on their medication and condition, to ensure prescription reordering and to work through any other condition-related issues that the patient may be experiencing. This personalized care leads to better outcomes, lower overall costs, and the assurance that medications are used appropriately and consistently.

**Enhanced Services** offer a higher level of support with clinical management and disease management strategies that follow evidence-based guidelines.

- Clinical Management Programs focus on best-demonstrated practices and address management of populations of patients. The enhanced clinical guideline segment of the management services helps to ensure that the right candidates get the appropriate drugs. There is a continuous evolution in understanding of these drugs and the conditions they treat. The clinical guidelines management group reviews medical literature and consults with physicians in order to verify that treatment parameters followed are meeting the current standards of medical practice. Depending upon benefit plan design, our clinical team will consult with the prescribing physician regarding any prescription that falls outside those standards.
Accordant is a disease management company, an affiliated company of Caremark, Inc., which has a special focus on individuals living with high impact, complex chronic diseases. Accordant is unique from its competitors in that the conditions which are targeted are rare, complex and progressive. Very few of these conditions have established best-practice and management guidelines available in the public domain. Many of the diseases that Accordant focuses on have average annual costs of over $20,000. Consequently, a concentration on quality improvement can result in both significant cost reductions and enhancements in patient satisfaction.

Accordant helps people with complex, chronic diseases improve their quality of life through direct interaction with them and their caregivers. The interactive health management program combines personalized content, specialized education, disease-specific assessment tools and interaction with specially trained clinicians, to effectively deliver improved quality of life to patients while reducing healthcare costs and improving outcomes.
For the last 16 months, Caremark has collaborated with the Centers for Medicare/Medicaid Services (CMS) on the Medicare Replacement Drug Demonstration (MRDD) project. As the only prescription benefit manager chosen for MRDD, Caremark has direct experience in the administration of the same benefit model as Medicare Part D prior to Part D being rolled out. Some of the challenges encountered in this pilot include:

Confusion in the marketplace—Seniors were unsure about how the Medicare discount card versus Medicare Part B versus Medicare Part D, and other supplemental coverages relate. Moreover, there are five benefit levels, including an out-of-pocket versus out-of-pocket with low-income subsidy level, which all require understanding.

Substantial out-of-pocket requirement—For most seniors in the pilot program, the out-of-pocket cost was $3,600, which must be met by the beneficiary, their family or a qualified 501(c)3 charity.

Working with charitable organizations—Because some seniors were unable to meet the co-pay and needed financial assistance, Caremark identified, qualified and coordinated with charitable organizations and foundations to provide these beneficiaries with funds so they could receive their crucial medications. Additionally, Caremark assisted some beneficiaries in transitioning from free goods programs to MRDD with co-pay assistance.

Communication—Despite efforts to educate beneficiaries about the coverage, some still experienced “sticker shock” at the pharmacy. Even with a $0 premium, some beneficiaries instead decided to obtain their specialty medications by other means or preferred to “stay with what they know.”

Operational considerations—Our call center times with MRDD beneficiaries were significantly longer because seniors had numerous questions, were perplexed by the benefit and often called several times for clarification or to ask follow-up questions. As a result, Caremark implemented extensive staff training to better prepare our representatives in explaining the offering to beneficiaries.

A Step Ahead
With this in-depth, first-hand knowledge in Medicare claims adjudication, reporting requirements, actuarial modeling and beneficiary cost-sharing strategies, Caremark has the experience and resources for a smoother roll out of Medicare Part D.

MRDD at a Glance—

- A 16-month pilot, including nearly 42,000 Medicare beneficiaries
- Caremark, the only prescription benefits manager chosen for this Medicare Part D pilot, was contracted to provide benefit administration, retail network management and mail pharmacy services through Caremark Specialty Pharmacy Services
- Provided the first actual experience with Medicare Part D provisions
- Provided coverage for 33 specialty drugs for the treatment of cancer, multiple sclerosis, hepatitis C, pulmonary arterial hypertension and rheumatoid arthritis
- Developed by the CMS to significantly improve access to self-administered medications for severely ill beneficiaries and evaluate overall medical cost savings
Medicare Part D: January 1 Roll Out

On January 1, the much-anticipated Medicare Prescription Drug Benefit (Part D) took effect with 21 million enrollees. Enrollment is ongoing. According to Health and Human Services Secretary Mike Leavitt, the goal is 28 to 30 million enrollees in 2006.

There are significant challenges in rolling out this new coverage. Its provisions will likely have far-reaching effects on healthcare delivery in the U.S. For example, it is expected that adoption of ePrescribing technology will be hastened by the requirement that drug plans participating in Medicare Part D must support electronic prescribing.

Another Medicare Modernization Act (MMA) provision likely to have broad impact is the competitive acquisition program (CAP), which was created in an attempt to limit the costs of physician-administered drugs under Medicare Part B. These drugs, often high-cost specialty medications and biologics, typically are administered at physicians’ offices to treat diseases such as cancer, rheumatoid arthritis, lupus and more. Historically, physicians have purchased these drugs, administered them to their patients, and then billed Medicare for the cost of both the drug and their services. The Centers for Medicare/Medicaid Services (CMS) developed CAP as a way to create a more competitive environment for Medicare Part B drugs and ensure that CMS was paying fair and reasonable rates for specialty drugs.

Under the proposed CAP rules, physicians will need to choose between buying and billing these drugs under an average sales price (ASP) structure or obtaining the drugs through vendors selected through a competitive bidding process. Those who choose to work with CAP vendors will obtain the drugs through the vendors, the vendors will bill Medicare for the administered drugs and then the vendors will bill beneficiaries for their co-payment and deductible. The proposed program met with widespread public and industry comment, and CMS currently has suspended the submission of vendor bids for CAP pending a more detailed review and consideration. Caremark provided comments on the CAP program to CMS and has participated in the development of comments along with the Pharmaceutical Care Management Association.

The Caremark state government relations staff in Washington, D.C., is continuously involved in efforts to educate state legislators about how pharmacy benefit strategies can aid in managing drug spend. Legislators from several states have toured Caremark mail pharmacies to learn about how these facilities support safety, convenience, efficiency, emergency preparedness and compliance with state regulations.

In many states, Caremark continues to work with legislators on bills regarding benefit design, mail pharmacy services, PBM licensure and transparency, wholesale operations and Internet pharmacy services. In 2006, Caremark looks forward to continuing to work on your behalf at both the state and national level.
Over the last ten years, new cancer therapies have been instrumental in lowering the number of cancer deaths, increasing survival times and improving quality of life for cancer patients. Many breakthrough cancer therapies reflect our increased understanding of the human genome, and research is ongoing. There are an estimated 700+ new oncology products in manufacturer pipelines; more than half are biopharmaceuticals. Some of the major approaches being investigated include:

**Targeted cancer therapies.** Traditional cancer therapies have a broad spectrum of attack and are likely to affect both healthy and cancerous cells, causing severe side effects. In contrast, targeted cancer therapies interfere selectively on a molecular level with cancer cell growth and division, promising to harm fewer normal cells and reduce the incidence of side effects. Many targeted therapies currently in use or under investigation focus on blocking or interfering with the proteins or enzymes that signal cancer cells to grow and divide uncontrollably. Eventually, cancer treatments may be individualized to “match” the molecular targets produced by an individual patient’s tumor. “Targeted therapies” is a broad designation. Avastin™ (for colorectal cancers) and Herceptin® (for breast cancers) are considered targeted therapies.

**Cancer vaccines.** Like the more familiar vaccines aimed at infectious diseases, cancer vaccines stimulate the body’s natural immune responses. Some cancer vaccines under investigation are designed to treat existing cancers. Others are preventive. A cancer vaccine may contain cancer cells, parts of cells or antigens—substances that stimulate the production of antibodies. Vaccines are targeted therapies (see above). Gardasil™, a genetically engineered vaccine against cervical cancer, is pending FDA approval.

**Gene therapy.** Gene therapy involves introducing genetic material into a person’s cells to fight disease. It is being investigated as a way to restore a missing gene function—such as tumor suppression—or make cancer cells more susceptible to chemotherapy or other treatments. Gene therapy is also being investigated as a way to stimulate the body’s immune response to attack cancer cells. For example, researchers are investigating the possibility of adding new genes to tumor cells taken from a patient, then reintroducing the altered cells to the patient. The theory is that the immune system will be better able to recognize and attack the altered cells—as well as other cancer cells that “look like” them.

**Examples of specific modalities of drug action being researched**

**Anti-angiogenesis drugs or angiogenesis inhibitors** act to inhibit the formation of blood vessels that feed tumors. Avastin™ is an example.

**Immune modulators** modify the body’s immune response.

**Interferons** interfere with the ability of a cell to reproduce.

**Monoclonal antibodies (mAB)** are laboratory-made versions of naturally occurring proteins that bind to and neutralize foreign invaders. Rituxan® (for non-Hodgkins lymphoma), Avastin, Herceptin, Erbitux™ (for colorectal cancers) are examples.