



EXPRESS SCRIPTS®
Charting the Future of Pharmacy

Top 10 1999 Developments On The Pharmaceutical Landscape



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Dear Friends Of Express Scripts:

Every year brings remarkable change to the pharmaceutical landscape, but I'm not sure I can remember one specific period when so many areas were undergoing such a metamorphosis. In every quarter, from drug discoveries to direct-to-consumer advertising to changing demographics, innovation and evolution are clearing the path for a retooling and reorganization of the marketplace.

A multidisciplinary Express Scripts team took a critical retrospective look at 1999 and listed what they consider to have been the Top 10 developments. The criterion for inclusion on the list was really quite simple: What 10 developments have the most potential to significantly affect our clients and the management of their pharmacy benefit?

Of all that is occurring, perhaps no trend holds more profound implications for benefit design than the transformation of the American public into informed consumers of prescription drugs.

We can no longer expect plan members to passively accept decisions made exclusively by others, either their physicians or their benefit plan sponsors. Empowered by greater access to information, plan members will increasingly expect to take an active role in their own healthcare and demand access to therapies they perceive as desirable. Continuation of a managed-care approach to pharmaceuticals will require us to heed their expectations. We must make the decision-making process more participatory. We must communicate more effectively.

This is a fascinating time in healthcare, particularly as it relates to the pharmacy benefit. The combination of celebrations and challenges made this an interesting list to compile, and I hope you find it informative.

Best Regards,

Barrett Toan
President & CEO

Express 1999 Scripts

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1 **COX-2 Inhibitors Gained 21% Share Of \$2.3 Billion Musculo-Skeletal Market Within First Six Months**

Thanks in large part to a massive direct-to-consumer advertising campaign and widespread press coverage, the non-steroidal anti-inflammatory drug Celebrex™ (celecoxib) reached blockbuster status almost as soon as it hit the market at the end of 1998. In May 1999, the Food and Drug Administration (FDA) granted approval to Vioxx® (rofecoxib), a similar drug. In combination, these two drugs captured 21 percent of the total expenditure in the musculo-skeletal drug class.

Together, Celebrex and Vioxx comprise a new class of NSAID (anti-inflammatory) drugs known as cyclooxygenase (COX) 2 inhibitors. Their near-instantaneous popularity, especially among patients with rheumatoid arthritis, is attributable to the drugs' ability to reduce inflammation effectively without the adverse upper gastrointestinal (GI) tract effects that may result from prolonged use of traditional NSAIDs such as naproxen and ibuprofen.

In December 1999, the FDA approved Celebrex for yet another indication: treatment to reduce adenomatous colorectal polyps produced by familial adenomatous polyposis (FAP), a rare disease that may lead to colorectal cancer. The drug is also being studied to determine whether it may be effective in slowing the development of other cancers or Alzheimer's disease.

Four new COX-2 inhibitors are in various stages of development, including valdecoxib and parecoxib from Searle, meloxicam from Boehringer Ingelheim and MK-663 from Merck.

What is the outlook for COX-2 utilization?

Given the proven ability of the COX-2s to reduce adverse GI side-effects, the likelihood of more new drugs in the class and the possibility of new indications, plan sponsors may expect continued growth in the utilization of COX-2 inhibitors.

Can anything be done to slow this growth?

Traditional NSAIDs are as effective as COX-2s in reducing inflammation—and considerably less expensive. Furthermore, not all patients who take traditional NSAIDs experience GI distress. Given these facts, benefit plan sponsors may wish to consider implementing an NSAID step therapy program, starting patients at low risk for GI complications on traditional NSAIDs and approving use of COX-2s only if the original prescription proves ineffective or causes adverse effects.

Additionally, plans may need to review copay levels to determine whether they should be increased. A typical 30-day COX-2 prescription runs approximately \$70, and member responsibility should be 25 percent or more.

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2 Two New Drugs Join Arsenal To Fight Influenza

The first antiviral drugs to fight influenza—Glaxo Wellcome's Relenza® (zanamivir) and Roche's Tamiflu™ (oseltamivir)—made their highly promoted debut just in time for the 1999-2000 flu season. In the week ending December 24, nearly 96,000 prescriptions were written nationwide for these two drugs.

This new class of antiviral agents has been shown to reduce the duration of flu symptoms by up to 1.3 days but only if taken within 48 hours of the onset of symptoms. By the time many people contact their doctors, this window of opportunity has already passed. In addition, unlike vaccines, neither Relenza nor Tamiflu is currently indicated for prevention of influenza.

These drugs also have not been proven effective in high-risk patients—the elderly and those with chronic disease. In other words, there is no certainty that Relenza or Tamiflu will help those who would benefit most from alleviation of symptoms. This lack of affirmative evidence prompted a British institute to declare that Relenza should not be prescribed within the British National Health Service.

As the flu season was getting under way in December 1999, the U.S. Centers for Disease Control and Prevention (CDC) released a report stating that these two agents, along with amantidine and rimantidine, are valuable treatments for influenza. The report

emphasized, however, that these drugs are not a substitute for the influenza vaccination, which remains the most effective and economical way to prevent influenza and its disabling effects.

[Is prevention the best strategy?](#)

Relenza and Tamiflu cost \$44.40 and \$53(AWP) respectively for a five-day course of treatment. Balancing the cost against potential benefits, many plan sponsors will undoubtedly conclude that prevention is still the best medicine and adopt an anti-flu strategy of including a yearly vaccination in their benefit.

3 Clinton Medicare Prescription Benefit Proposal Draws Media Attention To The Challenging Pharmaceutical Landscape

In late June, President Clinton announced his administration's proposal for the addition of a prescription benefit to Medicare. A robust national dialogue ensued and gained momentum throughout the remainder of the year, propelling the issue to the forefront of the 2000 presidential campaign.

Opponents of the measure contend that it will lead to price controls on pharmaceuticals and subsequent

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curtailment of research and development of new therapies. Others debate what criteria for coverage should be and whether the pharmacy benefit per se or comprehensive Medicare reform is the real issue.

Media coverage also has focused more broadly on the rising cost of drugs, which has restricted access for many. Accounts of Americans making drug-purchasing forays into Canada and other countries to acquire drugs at lower prices and the formation of groups to negotiate with pharmaceutical companies for discounts abound.

How does heightened media coverage impact benefit plan decisions?

Media attention to pharmaceutical issues, as well as easy availability of information on the Internet, creates more knowledgeable, more sophisticated consumers. As we move into the 21st century, people are aware of advances in medical and pharmaceutical science and strongly believe they are entitled to the best treatment available.

Plan sponsors should expect growing employee demand for inclusion in discussions around the pharmacy benefit. Sponsors also should anticipate that designing the pharmacy benefit to provide maximum choice will be the single greatest factor in employee satisfaction.

4

Direct-To-Consumer Drug Ads Surpass \$1.8 Billion, With No End In Sight

The transformation of patient to consumer is in part due to increased media coverage of pharmaceutical issues. Perhaps an even greater influence, however, is the prominence of direct-to-consumer advertising of specific medications by pharmaceutical companies.

The Food and Drug Administration eased constraints upon advertising of drug products in 1997. The pharmaceutical companies wasted no time in taking advantage of the opportunity.

According to IMS Health, an industry research company, drug companies spent \$905 million on direct-to-consumer prescription drug ads in the first half of 1999 alone—a 43-percent increase over the same period in 1998. The average consumer watches nine TV commercials for prescription drugs every day, and popular magazines are filled with full-page and double-page ads for brand medications.

What is the impact of direct-to-consumer drug ads?

Today, armed with information derived from advertising, patients more frequently “shop” for drugs the same way they shop for refrigerators and toothpaste: by brand. Convinced of the potential benefits, patients are asking their doctors for specific medications in ever-greater numbers. In other words,

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for the first time in history, patients are becoming participants in the prescribing process.

This is a sea change that must inevitably affect the approach to pharmacy benefit design if a managed-care perspective is to be maintained. Members are no longer disposed to passively and unquestioningly accept decisions; thus plan sponsors must allocate greater resources to communicating the rationale for certain formulary and plan-design decisions. This is particularly true with regard to coverage of lifestyle drugs as more of these products enter the market accompanied by advertising and high consumer demand.

5 Breakthrough May Lead To Alzheimer's Treatment

The Alzheimer's Association estimates that Alzheimer's disease costs U.S. society \$100 billion a year and that the average lifetime cost of the disease per patient is \$174,000. The disease strikes one in 10 people older than 65 and nearly half of those older than 85.

Current medications for Alzheimer's have proved disappointing in their ability to stem the course of the disease. In 1999, however, researchers identified an enzyme known as BACE (beta-site APP-cleaving enzyme), thought to be responsible for the protein build-up in the brain commonly seen with Alzheimer's.

A drug that inhibits this enzyme might slow or even prevent development of this disease that brings extreme and prolonged suffering to its victims and their loved ones.

What does this new discovery mean?

More than four million people in the United States currently suffer from Alzheimer's, and most will die of conditions to which the disease predisposes them: sepsis, pneumonia, choking and aspirating, nutritional deficiencies and trauma. Some estimate that by 2050, if a cure or effective treatment is not found, the disease will afflict 15 percent of people older than 65—14 million victims.

This truly daunting prospect places in clear perspective the importance of this discovery and other advances in Alzheimer's research that shed light on the causes of the disease and hold the potential to draw us closer to effective treatment and prevention.

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6 Advancements Improve Outcomes For Patients with Congestive Heart Failure

Three separate studies in 1999 contributed to greater understanding about how to more effectively treat congestive heart failure (CHF) by using medications currently available on the United States prescription drug market.

A study released in July revealed that adding Aldactone® (spironolactone) to standard CHF therapy could reduce the risk of death by 30 percent. Spironolactone works by blocking the angiotensin receptors for a chemical called aldosterone. Aldosterone levels, when elevated, may cause abnormal growth of heart tissue, which becomes dysfunctional and accelerates heart failure. Additional research on other compounds blocking aldosterone's effects also are under way.

The Metoprolol CR/XL (Controlled Release) Randomized Intervention Trial in Heart Failure (MERIT-HF), presented at a meeting sponsored by the European Society of Cardiology, found that adding extended-release metoprolol to an existing CHF therapy reduced the incidence of sudden death by 41 percent and the rate of death from all causes by 34 percent.

Finally, the Heart Outcomes Prevention Evaluation (HOPE) study found that Altace® (ramipril), a blood-pressure medication, reduced the incidence of heart

attack, stroke and death in high-risk patients. Ischemic heart disease, characterized by narrowed arteries and restricted blood flow, is the leading cause of CHF. Ramipril, which belongs to the class of medications known as ACE (angiotensin-converting enzymes) inhibitors, blocks the formation of angiotensin II, a naturally occurring chemical in the body that raises blood pressure by narrowing arteries.

Why are these findings important to benefit sponsors?

Three to four million people in the United States have been diagnosed with CHF, and approximately 400,000 new cases are diagnosed each year. Consider as well the fact that the incidence of CHF doubles with each decade of life, and it's easy to understand why CHF needs to be near the top of every benefit sponsor's list of concerns. In an aging population, the incidence of CHF is expected to double over the next 40 years.

What can plan sponsors do?

Ultimately, education of both patients and physicians is the key to better outcomes. In this environment of information overload, a benefit plan can provide a vitally important resource for physicians by functioning as a clearinghouse, providing them with timely, clinically sound information directly relevant to treatment of their patients.

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7 Report Reveals That Medical Errors Kill Thousands Annually

According to an Institute of Medicine (IOM) study, at least 44,000 deaths each year result from medical errors. That statistic places medical errors as the eighth leading cause of death in the United States, ahead of highway accidents, breast cancer and AIDS. The release of the report attracted extensive press coverage, and many found the revelation disquieting.

The report also stated that medication errors alone result in 7,000 deaths annually.

[Why is this finding relevant to benefit plan sponsors?](#)

The report found that the large number of deaths resulted not from individual acts of recklessness or negligence but from flaws in the way the health system is organized. To correct the problems, all participants in the health system—healthcare providers, government, consumers, insurers and benefit sponsors—must be actively involved in seeking solutions.

The IOM has set a minimum goal of a 50-percent reduction in errors over the next five years. The organization is also calling upon Congress to create a national patient-safety center, which will develop new tools and systems to address persistent problems. This is an ambitious agenda but an essential one if consumers of medical services are to retain confidence in our healthcare system.

Technology is expected to aid in solutions. For example, recently introduced hand-held computer tools will enable physicians to write prescriptions that can be printed out in the office or transmitted to the pharmacy. As use of these tools becomes more widespread, they will play a significant role in reducing prescription errors that occur as the result of indecipherable handwriting.

8 Vaccines Gain Ground In The Battle Against Infectious Diseases

Thanks to the development of vaccines, common diseases continue to disappear from the pharmaceutical landscape. In 1999, the Centers for Disease Control and Prevention (CDC) announced that measles is no longer indigenous to the United States. Of cases reported over the year, all but 29 were contracted in other countries. For all practical purposes, the disease has been eliminated.

Continuing research and development of vaccines may help further control the spread of infectious diseases. For example, VaxGen is currently conducting the first Phase III North American clinical study of their HIV vaccine, AIDSVAX, the first HIV vaccine to be approved by the Food and Drug Administration for such trials. A different formulation of the vaccine is being clinically tested in Thailand with 2,500 volunteers.

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What is the economic impact of infectious-disease immunizations?

As new, effective vaccines are developed and used, treatment of infectious diseases and their complications will be less prevalent on the pharmaceutical landscape. In 1998, the drug spend for antiviral agents was estimated at \$1.8 billion, largely due to the introduction of agents used for the treatment of HIV and AIDS. If, like measles, HIV and AIDS can be eliminated by effective vaccines, these dollars can be productively redirected to meet other needs.

9 Surgeon General's Report Focuses Public Attention On Mental Health

In America's healthcare system, treatment of mental illness has historically occupied a less-than-equal position relative to treatment for physical illness. By increasing public awareness, the Surgeon General's Report on Mental Health was intended to dispel the stigma of mental illness and other barriers that have so often prevented individuals from seeking and receiving appropriate care.

Mental healthcare is both an important quality-of-life issue and an important economic issue. According to the National Institute of Mental Health, untreated mental illness costs \$300 billion annually, including

\$150 billion in lost productivity. The National Mental Health Association estimates that untreated depression alone costs the U.S. economy as much as heart disease or AIDS.

What are the implications?

If you're a benefit plan sponsor, the report raises important questions: Does your benefit program encourage or discourage access to care? Does your pharmacy benefit reflect advances in antidepressants and other drug classes to treat mental illness? Has use of your mental-health benefit been low while your general healthcare benefit costs increased?

Research indicates that untreated behavioral health disorders often lead to excessive and expensive use of general healthcare services. For example, individuals with untreated depression may seek medical help for a variety of symptomatic physical problems, such as chronic fatigue, insomnia and backaches, that general healthcare practitioners may not recognize as signs of mental illness.

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10 New Rheumatoid Arthritis Drugs Offer Relief For Patients

A number of new drugs—COX-2 inhibitors, Enbrel[®] (etanercept), Arava[™] (leflunomide) and Remicade[™] (infliximab)—offer promising options for reducing and perhaps preventing the ravages of rheumatoid arthritis. The cost of treating a patient with these new therapies, however, may run as much as \$10,000 or more per year.

For patients, the potential benefits of these drugs are impressive: reducing or preventing joint damage, and preserving joint integrity and function. The contribution to maintaining quality of life can be substantial.

Thus far, only Arava carries the indication to slow or halt the progression of the disease. Remicade and Enbrel are indicated only to reduce symptoms, although they are being studied to determine whether they might also prevent progression of the disease.

What are the implications for pharmacy benefit plan sponsors?

Direct medical care for rheumatoid arthritis patients in the United States totals \$5 billion annually. Not only do newer drugs provide important alternatives to patients for whom standard therapies have failed but their use may also mitigate medical costs for the disease. The conclusion we can draw is that, once again, step therapy may be appropriate. Such a program provides

for first attempting treatment with less expensive standard therapies. If the initial therapy proves ineffective, the patient and his or her physician have the choice of moving to one of the newer therapies. In the long run, these drugs, although expensive, may prove the most cost-effective treatment option for some patients.