

PAIN MANAGEMENT REVIEW AND OUTLOOK

Higher demand for more efficient pain drug and device treatments is helping drive the pain-management market.

The United States is the world's leading pain-management market. Roughly 50 million Americans live with chronic pain, which is more than the combined amount of people with diabetes, heart disease, and cancer. A serious, undertreated public-health problem, uncontrolled pain costs an estimated \$100 billion in the United States every year when considering healthcare expenses, lost income, and lost productivity.

An estimated 76.5 million Americans 20 years of age and older have had a problem with pain of any type that persisted for more than 24 hours (excluding acute pain).

About 42 million Americans have reported that pain or physical discomfort disrupts their sleep at least a few nights per week.

According to an industry survey, the four most common types of pain are low back pain, severe headache or migraine pain, neck pain, and facial ache or pain.

Back pain is the No. 1 cause of disability in Americans younger than 45 years old. More than 26 million Americans between the ages of 20-64 years old experience frequent back pain.

An estimated 70% of patients with cancer experience significant pain during their illness, however, fewer than half receive adequate treatment for their pain.

An estimated 46 million U.S. adults have reportedly been told by a physician that they have some form of arthritis, rheumatoid arthritis, gout, lupus, or fibromyalgia.

Burden of Pain

According to findings reported by Pfizer from the National Health and Nutrition Examination Survey, the National Health Care Surveys, and the National Health Interview Survey, more than 100 million adults (51% of the population) aged 20 years and older have reported pain at one or more body sites or experienced dental pain or headaches/migraines. The body sites included joints, low back, neck, and face/jaw. More than one-quarter of adults older than 40 years reported low back pain within a three-month period. One-quarter of women ages 20 years to 39 years old had severe headaches or migraines during the three-month term.

Numerous diseases and conditions are associated with pain, including arthritis, peripheral neuropathy, fibromyalgia, and shingles. Each year, there are about 5.4 million ambulatory and inpatient healthcare visits with a diagnosis of fibromyalgia, 1.9 million diabetic neuropathy visits, and 1.5 million shingles visits. Half of adults with diabetes who have peripheral neuropathy have reported symptoms of pain/tingling in their feet or numbness/loss of feeling within a three-month period. Forty-four percent of adults with arthritis experienced limitations in their usual activities because of arthritis or joint pain.

Pain may be caused by bodily injury or harm. During 2006, there were about 34 million injury-related physician office visits. Analgesic drug therapy was reported at 40% of these injury-related visits.

Adults with pain have worse health status and experience more disability in terms of lost work days, activity limitations, reduced sleep, and increased psychological distress than adults without pain. According to the Pfizer report, 1 in 3 adults with face or jaw pain report fair or poor health status, nearly 1 in 5 adults with neck pain are unable to work, and 1 in 9 adults with severe

headaches/migraines experience psychological distress.

Since Merck & Co.'s pain and arthritis medicine Vioxx was recalled from the market in September 2004, FDA has been fixated on the safety of previously approved products and ensuring that additional blockbuster products do not cause such a public commotion. The popular COX-2 selective, non-steroidal anti-inflammatory drug was withdrawn from the market due to concerns of its increased risk for heart attack, thrombosis and stroke by a relative increase in thromboxane.

"Having Bextra and Vioxx withdrawn from the market has resulted in only one new NSAID becoming available in the last 7 years and that is Vimovo," stated Robin K. Dore, M.D. Dr. Dore is a rheumatologist, a clinical professor of medicine at the David Geffen School of Medicine at UCLA, and works in a private practice in Tustin, Calif.

Vimovo (naproxen/esomeprazole magnesium) 500/20-mg modified-release tablets is a fixed-dose combo of entericcoated naproxen (an NSAID) and immediate-release esomeprazole (a stomach acid-reducing PPI). Marketed by London pharma giant AstraZeneca Plc., Vimovo is indicated for the symptomatic treatment of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis in patients at risk for developing NSAID-associated gastric and/or duodenal ulcers and where treatment with lower doses of naproxen or of other NSAIDs is considered insufficient. Vimovo was jointly developed by the pharma company Pozen Inc. of Chapel Hill, N.C.

Most pharma companies have not developed new NSAIDs, or such drugs have not been approved for U.S. marketing, according to Dr. Dore. Examples include Arcoxia

(etoricoxib) and an arthritis compound from the French pharma company NicOx SA. Despite the METAL clinical trial that included more than 30,000 patients, Merck's COX-2 inhibitor Arcoxia was not approved in the United States despite being cleared for marketing in the European Union. "This has certainly discouraged other companies from entering this market in the United States," she says.

The Vioxx recall has made many patients reluctant to take pain medicine, observes Ira Fox, M.D., co-founder of Anesthesia Pain Care Consultants. "Vioxx and other drugs that have been either recalled or have developed a reputation for complications make patients hesitant to take perfectly safe and effective medication," he says.

Some of the industry has been up in arms over cardiovascular toxicity concerns regarding COX-2 inhibitors. As a result, the treatment paradigm has shifted back to the use of traditional NSAIDs.

Victory Pharma Inc.'s lead pain product Naprelan, for example, aims to minimize side effects in two ways. The product contains naproxen, which has the lowest NSAID-associated cardiovascular risk. Also, the product uses a patent-protected delivery system that may minimize the GI irritation experienced with other NSAID drugs among particular patients.

"The failure of certain drugs, such as COX-2 inhibitors, has not had much of an impact on this sector as we have so many other products in the pharmaceutical sector and in the complementary and alternative medication sector to help our patients with choices," shares Sahar Swidan, Pharm.D., CEO and president of Pharmacy Solutions Inc. and clinical associate professor of pharmacy at the University of Michigan College of Pharmacy.