

POLICY & PRACTICE

Arthritis Spending Reaches \$32B

Nearly 10% of adults in the United States sought treatment for arthritis in 2005, according to figures from the Agency for Healthcare Research and Quality. More women than men reported experiencing arthritis—12% versus 7%. The disease was also more common among non-Hispanic white adults (11%) and black non-Hispanic adults (10%), compared with Hispanics (6%) and non-Hispanic Asian adults (4%). The cost of treating arthritis was \$32 billion in 2005, with most of the dollars being spent in ambulatory care (36%). About 31% was spent on inpatient care and 21% was spent on prescriptions. Home health costs made up 12% of the costs and less than 1% was spent on visits to the emergency room.

Prior Authorization for DMARDs

Most state Medicaid programs require prior authorization for at least one biologic disease-modifying antirheumatic drug (DMARD), according to an analysis published in the November issue of *Arthritis Care & Research*. In 2006, 32 states had implemented or were planning to implement policies for prior authorization, but the drugs included and the specific criteria varied widely. For example, 20 states asked for detailed clinical criteria such as the number of swollen or painful joints, rheumatoid factor levels, and radiologic findings. Six states required that a rheumatologist prescribe the biologic DMARD and two states required that a purified protein derivative be checked before starting treatment. After a later further analysis of the utilization of adalimumab and etanercept, the researchers found that prior authorization seems to control growth in utilization at first but utilization appears to rise again over time.

Pfizer Settles Bextra Claims

Pfizer Inc. has struck a multimillion-dollar agreement to resolve most of the pending claims involving its drug Bextra (valdecoxib), which was withdrawn from the market in 2005. The company agreed to pay \$60 million to attorneys general in 33 states as well as in the District of Columbia and also to adopt certain compliance practices in response to suits alleging that the company violated state laws in its promotion and marketing of Bextra. Pfizer also announced that it was setting aside \$745 million in anticipation of a final settlement of pending personal injury claims involving the company's other cyclooxygenase-2 inhibitor, Celebrex (celecoxib). That amount should resolve more than 90% of the suits alleging that Celebrex caused heart attack, stroke, or other injury in those who took the drug. Several courts have ruled that the plaintiffs had failed to prove that the drug led to these effects. Pfizer settled to remove the cloud over the drug, the pharmaceutical company said in a statement.

Lupus Foundation Awards \$1.1 Million

The Lupus Foundation of America spent more than \$1.1 million in 2008 to fund research grants and fellowships. The grants will support research in pediatric and adolescent lupus, lupus in men, the use of adult stem cells in lupus, and mid- to late-stage translational studies. Other areas of research funded this year include studies of cutaneous lupus, kidney disease and lupus, and the cognitive effects of lupus. But the grants awarded were far short of the requests received by the organization, according to the Lupus Foundation. The organization received more than 77 grant applications totaling about \$7.8 billion in requests for lupus research funding.

HIPAA Enforcement 'Limited'

The Centers for Medicare and Medicaid Services has not provided effective oversight and has taken only "limited actions" to ensure that covered entities adequately implement patient privacy regulations contained in the Health Insurance Portability and Accountability Act of 1996, according to a report from the Health and Human Services Department's Office of Inspector General. The OIG found that the CMS had not conducted any compliance reviews of covered entities, and instead relied on complaints to target investigations. However, the CMS has received very few complaints about violations, the report said. "As a result, the CMS had no effective mechanism to ensure that covered entities were complying with the HIPAA security rule" or that electronic health information was being adequately protected, the report concluded. CMS has taken steps to begin conducting compliance reviews in an effort to identify security problems and vulnerabilities under HIPAA, the OIG said.

Mass. Blues Require E-Prescribing

Blue Cross Blue Shield of Massachusetts said it will require all physicians to prescribe electronically beginning in 2011 in order to qualify for any of the health plan's physician incentive programs. Currently, 99% of primary care physicians and 78% of specialists participate in the insurer's incentive programs, which reward physicians for meeting nationally recognized quality standards and patient safety goals. Currently, e-prescribing is an optional measure in the plan's incentive programs. The insurer said it realized that start-up costs involved with implementing an e-prescribing system continue to be a barrier to adoption for physicians, and said it would provide some financial assistance for doctors in 2009 to offset those start-up costs. A 2006 study by the plan showed that physicians who used an e-prescribing device were able to choose more cost-efficient drugs, and therefore saved 5% on their drug costs relative to physicians who did not use the technology.

—Mary Ellen Schneider

Table 10:
Percent of RA Patients Reporting Adverse Events
in Controlled Clinical Trials*

Event	Placebo Controlled		Active Controlled (Study III)	
	Placebo [†] (N = 152)	ENBREL (N = 349)	MTX (N = 217)	ENBREL (N = 415)
Injection site reaction	10	37	7	34
Infection (total)**	32	35	72	64
Non-upper respiratory infection (non-URI)**	32	38	60	51
Upper respiratory infection (URI)**	16	29	39	31
Headache	13	17	27	24
Nausea	10	9	29	15
Rhinitis	8	12	14	16
Dizziness	5	7	11	8
Pharyngitis	5	7	9	6
Cough	3	6	6	5
Asthenia	3	5	12	11
Abdominal pain	3	5	10	10
Rash	3	5	23	14
Peripheral edema	3	2	4	8
Respiratory disorder	1	5	NA	NA
Dyspepsia	1	4	10	11
Sinusitis	2	3	3	5
Vomiting	-	3	8	5
Mouth ulcer	1	2	14	6
Alopecia	1	1	12	6
Pneumonitis ("MTX lung")	-	-	2	0

* Includes data from the 6-month study in which patients received concurrent MTX therapy.

[†] The duration of exposure for patients receiving placebo was less than the ENBREL-treated patients.

** Infection (total) includes data from all three placebo-controlled trials. Non-URI and URI include data only from the two placebo-controlled trials where infections were collected separately from adverse events (placebo N = 110, ENBREL N = 213).

In controlled trials of RA and psoriatic arthritis, rates of serious adverse events were seen at a frequency of approximately 5% among ENBREL- and control-treated patients. In controlled trials of plaque psoriasis, rates of serious adverse events were seen at a frequency of < 1.5% among ENBREL- and placebo-treated patients in the first 3 months of treatment. Among patients with RA in placebo-controlled, active-controlled, and open-label trials of ENBREL, malignancies (see **WARNINGS: Malignancies**), **ADVERSE REACTIONS: Malignancies** and infections (see **ADVERSE REACTIONS: Infections**) were the most common serious adverse events observed. Other infrequent serious adverse events observed in RA, psoriatic arthritis, ankylosing spondylitis, or plaque psoriasis clinical trials are listed by body system below:

Cardiovascular: heart failure, myocardial infarction, myocardial ischemia, hypertension, hypotension, deep vein thrombosis, thrombophlebitis

Digestive: cholecystitis, pancreatitis, gastrointestinal hemorrhage, appendicitis

Hematologic/Lymphatic: lymphadenopathy

Musculoskeletal: bursitis, polymyositis

Nervous: cerebral ischemia, depression, multiple sclerosis (see **WARNINGS: Neurologic Events**)

Respiratory: dyspnea, pulmonary embolism, sarcoidosis

Skin: worsening psoriasis

Urogenital: membranous glomerulonephropathy, kidney calculus

In a randomized controlled trial in which 51 patients with RA received ENBREL 50 mg twice weekly and 25 patients received ENBREL 25 mg twice weekly, the following serious adverse events were observed in the 50 mg twice weekly arm: gastrointestinal bleeding, normal pressure hydrocephalus, seizure, and stroke. No serious adverse events were observed in the 25 mg arm.

Adverse Reactions in Patients with JIA

In general, the adverse events in pediatric patients were similar in frequency and type as those seen in adult patients (see **WARNINGS** and other sections under **ADVERSE REACTIONS**). Differences from adults and other special considerations are discussed in the following paragraphs.

Severe adverse reactions reported in 69 JIA patients ages 4 to 17 years included varicella (see also **PRECAUTIONS: Immunizations**), gastroenteritis, depression/personality disorder, cutaneous ulcer, esophagitis/gastritis, group A streptococcal septic shock, Type 1 diabetes mellitus, and soft tissue and post-operative wound infection.

Forty-three of 69 (62%) children with JIA experienced an infection while receiving ENBREL during three months of study (part 1 open-label), and the frequency and severity of infections was similar in 58 patients completing 12 months of open-label extension therapy. The types of infections reported in JIA patients were generally mild and consistent with those commonly seen in outpatient pediatric populations. Two JIA patients developed varicella infection and signs and symptoms of aseptic meningitis which resolved without sequelae.

The following adverse events were reported more commonly in 69 JIA patients receiving 3 months of ENBREL compared to the 349 adult RA patients in placebo-controlled trials. These included headache (19% of patients, 1.7 events per patient-year), nausea (9%, 1.0 events per patient-year), abdominal pain (19%, 0.74 events per patient-year), and vomiting (13%, 0.74 events per patient-year).

In open-label clinical studies of children with JIA, adverse events reported in those aged 2 to 4 years were similar to adverse events reported in older children.

In post-marketing experience, the following additional serious adverse events have been reported in pediatric patients: abscess with bacteremia, optic neuritis, pancytopenia, seizures, tuberculous arthritis, urinary tract infection (see **WARNINGS**), coagulopathy, cutaneous vasculitis, and transaminase elevations. The frequency of these events and their causal relationship to ENBREL therapy are unknown.

Patients with Heart Failure

Two randomized placebo-controlled studies have been performed in patients with CHF. In one study, patients received either ENBREL 25 mg twice weekly, 25 mg three times weekly, or placebo. In a second study, patients received either ENBREL 25 mg once weekly, 25 mg twice weekly, or placebo. Results of the first study suggested higher mortality in patients treated with ENBREL at either schedule compared to placebo. Results of the second study did not corroborate these observations. Analyses did not identify specific factors associated with increased risk of adverse outcomes in heart failure patients treated with ENBREL (see **PRECAUTIONS: Patients with Heart Failure**).

Adverse Reaction Information from Spontaneous Reports

Adverse events have been reported during post-approval use of ENBREL. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to ENBREL exposure.

Additional adverse events are listed by body system below:

Body as a whole: angioedema, fatigue, fever, flu syndrome, generalized pain, weight gain

Cardiovascular: chest pain, vasodilation (flushing), new-onset congestive heart failure (see **PRECAUTIONS: Patients with Heart Failure**)

Digestive: altered sense of taste, anorexia, diarrhea, dry mouth, intestinal perforation

Hematologic/Lymphatic: adenopathy, anemia, aplastic anemia, leukopenia, neutropenia, pancytopenia, thrombocytopenia (see **WARNINGS**)

Hepatobiliary: autoimmune hepatitis

Musculoskeletal: joint pain, lupus-like syndrome with manifestations including rash consistent with subacute or discoid lupus

Nervous: paresthesias, stroke, seizures, and central nervous system events suggestive of multiple sclerosis or isolated demyelinating conditions such as transverse myelitis or optic neuritis (see **WARNINGS**)

Ocular: dry eyes, ocular inflammation

Respiratory: dyspnea, interstitial lung disease, pulmonary disease, worsening of prior lung disorder

Skin: cutaneous vasculitis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, pruritus, subcutaneous nodules, urticaria

Rx Only. This brief summary is based on ENBREL prescribing information v. 33: 03/2008

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