

## POLICY & PRACTICE

### OA Hospitalizations Skyrocket

Hospitalizations for osteoarthritis more than doubled between 1993 and 2006, according to data from the Agency for Healthcare Research and Quality. In 2006, there were about 735,000 hospitalizations for osteoarthritis in the United States, up from about 322,000 in 1993. But most of the increase occurred between 2000 and 2006, when hospitalizations for the condition rose from about 443,000 to 735,000. AHRQ officials attribute most of the increase in osteoarthritis hospitalizations to the rising number of knee replacement surgeries. In 2006, osteoarthritis was the principal diagnosis in about 90% of knee surgery hospitalizations and 50% of hip replacement hospitalizations, according to the agency. While osteoarthritis hospitalizations were on the rise, hospital stays for rheumatoid arthritis were actually on the decline. Rheumatoid arthritis stays dropped from about 30,400 in 1993 to about 18,900 in 2006. The AHRQ data are based on the 2006 Nationwide Inpatient Sample, which includes all-payer discharge data from 1,045 hospitals located in 38 states.

### Osteoporosis: Women's Disease?

Women aged 30 years and older are more likely to report being at risk for osteoporosis than are men and young adults, according to a study published in the October issue of *Health Education & Behavior*. In a study of 300 men and women across a range of age groups (18-25, 30-50, and 50-plus), the researchers used the Osteoporosis Health Belief Scale to gauge participants' perceptions about their susceptibility to osteoporosis, the seriousness of the condition, and their motivation to make changes to their health behaviors. The 35-item, self-report questionnaire grades responses on a 5-point scale. The responses revealed that women aged 30-50 years and women aged 50 and older had the highest susceptibility scores. Men aged 18-25 years had the lowest susceptibility scores, according to the study. However, the scores related to the seriousness of the condition and the motivation to change health behaviors were not significantly different among the various groups. The finding suggests that men and women of all ages may be unaware of the serious consequences of osteoporosis, the researchers wrote.

### Few MDs Targeted for Pain Med Misuse

Few physicians have been charged or sanctioned for prescribing pain medications improperly, according to a study. From 1998 to 2006, only 725 individual physicians, or about 0.1% of practicing physicians, in the United States had been criminally charged or administratively reviewed for offenses involving the prescribing of opioid analgesics. Nearly 40% of the cases involved family medicine or general practice physicians and 23.7% involved internists. In contrast, only 3.5% of cases involved pain medicine specialists. The high number of investigations of primary care physicians is not surprising given that shortage of pain specialists,

the researchers wrote. "Practicing physicians, including pain medicine specialists, have little objective cause for concern about being prosecuted by law enforcement or disciplined by state medical boards in connection with the prescribing of [controlled substance] pain medications," the researchers wrote (*Pain Med.* 2008;9:737-47 [Epub doi:10.1111/j.1526-4637.2008.00482.x]). The study was conducted by researchers from the National Association of Attorneys General, the Federation of State Medical Boards, and the Center for Practical Bioethics.

### Grants to Doctors in Hurricanes

The AMA Foundation's Health Care Recovery Fund will provide grants of up to \$2,500 to physicians in places that have been declared disaster areas by the Federal Emergency Management Agency, and the foundation currently is accepting donations to help physicians who have been directly affected by Hurricane Gustav, which affected Louisiana, Mississippi, and Texas. The foundation provides the grants to physicians in FEMA-declared disaster areas to help them rebuild or restore their damaged medical practices in those locations, said the AMA. Donations may be at [www.ama-assn.org/ama/pub/category/7611.html](http://www.ama-assn.org/ama/pub/category/7611.html).

### CMS Alters Overpayment Policy

Centers for Medicare and Medicaid Services officials are changing the procedures for recovering certain overpayments made to physicians. The CMS will no longer seek payment from a physician for an overpayment while the physician is seeking a reconsideration of the overpayment determination by a qualified independent contractor. Under the new policy, which was mandated by the 2003 Medicare Modernization Act, the CMS can only seek to recoup the payment after a decision has been made on the reconsideration. The changes, which went into effect Sept. 29, will apply to all Part A and Part B claims for which a demand letter has been issued.

—Mary Ellen Schneider

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

Event	Placebo Controlled		Active Controlled (Study III)	
	Placebo <sup>†</sup> (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.

<sup>†</sup> 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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