

## POLICY & PRACTICE

### Fall-Related Injury Legislation

President Bush recently signed legislation to prevent falls among the elderly. The Safety of Seniors Act of 2008 (H.R. 3701) directs the Secretary of Health and Human Services to conduct and support research to improve the identification of older adults who may be at risk for falling, develop and evaluate effective fall prevention interventions, and improve the diagnosis and treatment of fall victims. The legislation, introduced by Rep. Frank Pallone Jr. (D-N.J.), also calls on HHS to report to Congress on the potential for reducing falls and the most effective strategies for reducing the health care costs associated with falls. The legislation also includes a national public education campaign aimed at older adults and health care providers that would focus on reducing falls and preventing repeat falls. "Effective demonstration tests, comprehensive public information and education campaigns can help reduce and mitigate these avoidable and frequently disabling injuries," Rep. Pallone said in a statement. "This new law launches a comprehensive preventative care program to reduce the number and severity of falls to the elderly."

### Feds Develop Lupus Campaign

The federal government is developing a National Lupus Awareness campaign to increase the public's understanding of lupus symptoms, its health effects, and who is at risk for the condition. The marketing campaign also aims to raise awareness that lupus disproportionately affects young women of color. The project is being spearheaded by the Office of Women's Health, part of the Department of Health and Human Services, with support from the Advertising Council. Officials in the Office of Women's Health are also seeking lupus and women's health organizations to partner with on the project. The campaign will target the low public recognition of lupus that was documented by the Lupus Foundation of America in a recent survey. The group found that among 1,000 U.S. adults, 39% knew nothing about the disease and 22% had never even heard of it.

### Arthritis Creates Exercise Barrier

Comorbid arthritis is a significant barrier to exercise for people with diabetes, the Centers for Disease Control and Prevention reported in the Morbidity and Mortality Weekly Report. The agency's national survey found that 30% of people who have both disorders are physically inactive, compared with 21% of

those who have only diabetes and 17% of those who have only arthritis. "These findings suggest that more needs to be done to help people with diabetes and arthritis get physically active to improve their health," Dr. Chad Helmick, coauthor of the study and a CDC medical epidemiologist, said in a statement. "Engaging in regular physical activity and maintaining a healthy weight can help alleviate the pain and disability that often accompany arthritis." The CDC based its report on 2005 and 2007 data from the Behavioral Risk Factor Surveillance System. This state-based random telephone survey has been tracking health conditions and risk behaviors in the United States yearly since 1984. The data from 2005 and 2007 were combined to increase statistical power.

### FDA Pushes for Adverse Event Reports

The Food and Drug Administration is working with a medical software firm to get more physicians to submit adverse event reports to the agency. Doctors who use Epocrates products received a message on their personal digital assistant explaining how adverse event reporting works. "Physicians are on the frontline when it comes to patient care, and working with Epocrates helps us remind them of safety and error reporting directly at the point of patient contact," said Dr. Norman Marks, medical director of the FDA's MedWatch program. "We want physicians to understand that by taking a few minutes to submit a report, that action may be the necessary first step that triggers an evaluation and action by the FDA."

### Low Postmarket Compliance

The FDA has issued its annual summary report on whether pharmaceutical and biologic manufacturers are meeting their commitments to conduct post-marketing studies. According to the agency, 76% of drug makers and 81% of biologic makers had met their commitment as of Sept. 30, 2007. There were 136 drug makers and 54 biologic manufacturers with open postmarketing commitments as of that date. A closer look shows that only 12% of drug studies were completed or terminated with a final report submitted to the FDA that year. In all, 20% of biologics met that goal. Manufacturers must report annually on the status of safety, efficacy, pharmacology, and nonclinical toxicology studies required by the FDA, or report that they have committed to conduct at the time of approval or after approval.

—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**)

**Hepato-biliary:** 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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