

POLICY & PRACTICE

Musculoskeletal Disease Legislation

With an eye to the aging population, members of Congress are seeking to raise awareness of musculoskeletal diseases. Rep. Hilda L. Solis (D-Calif.) and Rep. Michael C. Burgess (R-Tex.), both members of the House Energy and Commerce Committee's subcommittee on health, recently introduced the "Access to America's Orthopedic Services Act of 2008." The bill (H.R. 6478) would direct the U.S. Department of Health and Human Services to conduct public education campaigns on musculoskeletal health and require data collection on the level of musculoskeletal research funding and the number of new investigators entering the musculoskeletal research field. The bill also would direct the Agency for Healthcare Research and Quality to issue recommendations for a cost-effective method to measure bone density. "The burden of musculoskeletal diseases and conditions has a much deeper impact on the nation's health care system than many realize," Dr. David A. Halsey, chair of the council on advocacy for the American Association of Orthopaedic Surgeons, said in a statement. "In order to fully address this impact and ensure America's access to orthopedic services, we must first identify and address gaps in musculoskeletal health services and raise awareness about the importance of educating the public on these debilitating diseases."

Follow-On Biologics May Be a Deal

Establishing an abbreviated regulatory pathway for approval of follow-on biologic drugs could reduce total national spending on biologics by \$25 billion or 0.5% over the next 10 years, according to a Congressional Budget Office (CBO) estimate based on provisions proposed as part of the "Biologics Price Competition and Innovation Act of 2007" (S. 1695), which is currently pending in Congress. The legislation would authorize the Food and Drug Administration to create a special process for approval of biologic drugs that are highly similar to or interchangeable with already licensed products. Under the bill, a follow-on biologic would be awarded 1 year of market exclusivity and 12 years of exclusivity for the original biologic product. While the estimate shows savings from the establishment of a follow-on biologic approval process, it is essential

to ensure incentives for continued biomedical innovation, according to the Biotechnology Industry Organization. Without incentives for innovation, the follow-on initiative could produce relatively minor savings as a percentage of overall health care spending.

CMS Issues PQRI Payments

Physicians who successfully reported quality measures to Medicare in 2007 as part of the Physician Quality Reporting Initiative should have received their bonus payments in August. Officials at the Centers for Medicare and Medicaid Services recently announced that they had paid out more than \$36 million in bonuses to physicians and other health professionals as part of PQRI. Of the approximately 109,000 health professionals who reported data on Medicare services provided during July-December 2007, more than 56,700 met the reporting requirements and will be receiving bonus checks. The average bonus paid to an individual provider was more than \$600, and the average bonus for a physician group practice was more than \$4,700. The largest payment to a physician group practice was more than \$205,700, according to the CMS. "These payments to physicians for participating in the PQRI are a first step toward improving how Medicare pays for health care services," Kerry N. Weems, acting administrator, said in a statement. Under PQRI, physicians can earn bonus payments of up to 1.5% of their total allowed Medicare charges by successfully reporting quality data for Medicare services provided from July to December 2007. In addition to the bonus payments, physicians and other health professionals can also start accessing confidential feedback reports on their performance. More information on the program is available at www.cms.hhs.gov/PQRI.

Pharmacies, PBMs Merge Networks

RxHub, founded in 2001 by the nation's three largest pharmacy benefit managers, and SureScripts, formed the same year by the National Association of Chain Drug Stores and the National Community Pharmacists Association, announced that they will consolidate their operations, forming a single, secure, nationwide network for e-prescriptions and the exchange of health information.

—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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