

# Vertebroplasty No More Beneficial Than Placebo

BY MARY ANN MOON

Vertebroplasty was no more beneficial than a sham procedure for painful osteoporotic vertebral fractures in the first two blinded, randomized, controlled trials ever to assess the technique, according to two separate reports.

These findings are likely to transform percutaneous vertebroplasty—a widely

accepted method of pain relief that has become routine therapy—from “a procedure that is virtually always considered to be successful” into one “considered no better than placebo,” James N. Weinstein, D.O., of Dartmouth-Hitchcock Medical Center, Hanover, N.H., said in an editorial.

Public institutions such as the Centers for Medicare and Medicaid Services, as well as radiologic and neurologic surgery

societies, have recommended reimbursement of vertebroplasty—endorsements that have boosted a dramatic rise in its popularity. The number of vertebroplasties performed in the United States has more than doubled in the past 6 years, Dr. Weinstein noted (*N. Engl. J. Med.* 2009;361:619-21).

The procedure involves injecting medical cement directly into a vertebral fracture to stabilize it and immediately re-

lieve pain. Many case series and small, unblinded, nonrandomized, noncontrolled studies have suggested that it is effective, though the precise mechanism of action has never been delineated.

In one of the reports, Rachele Buchbinder, Ph.D., of Monash University, Malvern, Australia, and her associates randomly assigned 38 patients with one or two recent vertebral fractures to vertebroplasty and 40 to a sham procedure.

The primary outcome measure, overall pain score, was no different between the two groups at 1-week, 1-month, 3-month, or 6-month assessments. Pain at rest, pain during the night, physical functioning, and quality of life measures also did not differ significantly, nor did the use of opioid analgesics, the researchers said (*N. Engl. J. Med.* 2009;361:557-68).

These results were consistent regardless of patients' duration of symptoms and history of previous fractures.

One subject who underwent vertebroplasty and could not receive prophylactic cephalothin because of drug allergies developed an adjacent new fracture and osteomyelitis requiring surgery. Some studies have suggested that vertebroplasty raises the risk of subsequent fractures, particularly in vertebrae adjacent to treated areas, sometimes after the medical cement has leaked into those areas, they added.

“Our results show ... the hazards of relying on the results of uncontrolled or poorly controlled studies to assess treatment efficacy,” Dr. Buchbinder and her colleagues noted.

Earlier studies may have overestimated the benefit of vertebroplasty “by failing to take into account the favorable natural history of the condition, the tendency of regression to the mean, and the placebo response to treatment, which may be amplified when the treatment is invasive,” they added.

In the other study, Dr. David F. Kallmes of the Mayo Clinic, Rochester, Minn., and his associates enrolled patients at 11 medical centers in the United States, the United Kingdom, and Australia. A total of 68 were randomly assigned to vertebroplasty and 63 to a sham procedure.

At 1 month, the two groups did not differ significantly on the two primary outcomes, which were separate measures of pain and disability. Secondary outcomes of pain intensity, disability, and quality of life also were not significantly different, Dr. Kallmes and colleagues said (*N. Engl. J. Med.* 2009;361:569-79).

One patient who underwent vertebroplasty sustained an injury to the thecal sac during the procedure and required hospitalization, they added.

Dr. Buchbinder reports receiving grant support for the trial from Cook Australia, a manufacturer of medical products and devices. Dr. Kallmes reports receiving consulting fees from Zelos Therapeutics and grant support from ArthroCare, Stryker, Cardinal, and Cook and serving as an unpaid consultant to Bone Support. Dr. Weinstein reported no disclosures. ■

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Delayed-Release Capsules

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**Brief Summary** (for Full Prescribing Information and Medication Guide, refer to package insert.)

#### INDICATIONS AND USAGE

CREON Capsules is a pancrelipase which is a combination of porcine-derived lipases, proteases, and amylases indicated for the treatment of exocrine pancreatic insufficiency due to cystic fibrosis or other conditions.

#### DOSAGE AND ADMINISTRATION

##### Dosage

CREON is not interchangeable with any other pancrelipase product.

##### Infants (up to 12 months)

- Infants may be given 2,000 to 4,000 lipase units per 120 mL of formula or per breast-feeding.
- Do not mix CREON capsule contents directly into formula or breast milk prior to administration.

##### Children Older than 12 Months and Younger than 4 Years

- Enzyme dosing should begin with 1,000 lipase units/kg of body weight per meal for children less than age 4 years to a maximum of 2,500 lipase units/kg of body weight per meal (or less than or equal to 10,000 lipase units/kg of body weight per day), or less than 4,000 lipase units/g fat ingested per day.

##### Children 4 Years and Older and Adults

- Enzyme dosing should begin with 500 lipase units/kg of body weight per meal for those older than age 4 years to a maximum of 2,500 lipase units/kg of body weight per meal (or less than or equal to 10,000 lipase units/kg of body weight per day), or less than 4,000 lipase units/g fat ingested per day.

##### Limitations on Dosing

- Dosing should not exceed the recommended maximum dosage set forth by the Cystic Fibrosis Foundation Consensus Conferences Guidelines.

#### Administration

CREON should be swallowed whole. For infants or patients unable to swallow intact capsules, the contents may be administered without crushing or chewing, followed by fluid to ensure complete ingestion.

#### DOSAGE FORMS AND STRENGTHS

- 6,000 USP units of lipase; 19,000 USP units of protease; 30,000 USP units of amylase capsules have an orange opaque cap with imprint “CREON 1206” and a blue opaque body.
- 12,000 USP units of lipase; 38,000 USP units of protease; 60,000 USP units of amylase capsules have a brown opaque cap with imprint “CREON 1212” and a colorless transparent body.
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#### CONTRAINDICATIONS

None.

#### WARNINGS AND PRECAUTIONS

- Fibrosing colonopathy, a rare, serious adverse reaction has been described in association with high-dose use of pancreatic enzyme replacement in the treatment of cystic fibrosis patients. Caution should be exercised when doses of CREON exceed 2,500 lipase units/kg of body weight per meal (or greater than 10,000 lipase units/kg of body weight per day).
- Care should be taken to ensure that CREON is not chewed or retained in the mouth to avoid irritation of oral mucosa.
- Caution should be exercised when prescribing CREON to patients with gout, renal impairment, or hyperuricemia.
- There is theoretical risk of viral transmission with all pancreatic enzyme products including CREON.
- Caution should be exercised when administering pancrelipase to a patient with a known allergy to proteins of porcine origin.

#### ADVERSE REACTIONS

- Treatment-emergent adverse events occurring in at least 2 patients (greater than or equal to 6%) receiving CREON or placebo are abdominal pain, abdominal pain upper, abnormal feces, cough, dizziness, flatulence, headache, and weight decreased.
- There is no postmarketing experience.

To report SUSPECTED ADVERSE REACTIONS, contact Solvay Pharmaceuticals, Inc. at 1-800-241-1643 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

#### DRUG INTERACTIONS

None known.

#### USE IN SPECIFIC POPULATIONS

##### Pediatric Patients

- The safety and effectiveness of CREON have been demonstrated in pediatric patients 12 years and older.
- The safety and efficacy of pancreatic enzyme products with different formulations of pancrelipase in pediatric patients have been described in the medical literature and through clinical experience.

See PATIENT COUNSELING INFORMATION and FDA-approved Medication Guide

#### Marketed by:

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