

# Novel Topical Agent Eased Osteoarthritis Pain

*Strontium chloride hexahydrate, also used in toothpaste for sensitive teeth, was well tolerated.*

BY BRUCE JANCIN

FROM THE ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY

ROME — A strontium-chloride-based topical agent showed favorable efficacy and safety for the relief of moderate to severe osteoarthritic knee pain in a phase II study.

Known as 2PX for research purposes, this low-viscosity liquid contains 10% strontium chloride hexahydrate as its active ingredient.

It proved significantly more effective than placebo in the 8-week, double-blind, randomized, crossover trial involving 78 patients with moderate to severe knee pain from osteoarthritis that was not controlled by NSAIDs or weak opioids, Dr. Stuart H.R. Ratcliffe reported.

The primary efficacy end point was change from baseline through week 4 in the WOMAC (Western Ontario and McMaster Universities) Osteoarthritis In-

dex pain subscale score. The mean 3.9-point drop in the 2PX group was significantly greater than the 2.2-point reduction with placebo.

After 4 weeks, patients were crossed to the other study arm. At 8 weeks, patients on 2PX did better on several secondary end points as well.

They had a mean 2.61-point greater decrease in WOMAC total score and a 1.87-point greater reduction in the physical function subscale, as well as a 0.23-point greater decline in the stiffness subscale, which was of borderline statistical significance.

In addition, the 2PX group demonstrated significantly greater reductions in self-reported pain intensity and greater pain relief, noted Dr. Ratcliffe, director of



pain research at MAC (U.K.) Neuroscience Ltd. of Blackpool, England, which conducted the study.

Strontium chloride hexahydrate has an excellent, well-established safety profile. It is used in toothpastes for people with sensitive teeth, he said in an interview.

Indeed, 2PX was very well tolerated in the study. Mild erythema was the only side effect more common with the agent than with saline placebo.

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DR. RATCLIFFE

to be the direct cause of 100,000 hospitalizations annually in the United States. Weak opioids are sometimes ineffective, so many osteoarthritis patients rely on strong opioids for symptom relief, with their attendant increased nausea, vom-

iting, dizziness, and constipation, Dr. Ratcliffe said.

It is a topical with almost no systemic absorption, so “clearly you can add it to any oral medication because there will be no drug-drug interactions. It probably will be a very good add-on therapy, but also safe and efficacious to use by itself in an acceptable proportion of people with osteoarthritis—knee or hand,” he said.

Strontium’s mechanism of benefit stems from its antagonistic effect on calcium-driven pathways that are involved in pain and inflammation.

In preliminary studies, 2PX has shown efficacy in neuropathic as well as nociceptive pain conditions. An ongoing, multicenter, phase III clinical trial of topical 2PX in patients with osteoarthritis of the knee is underway, as well as a phase III trial of 2PX for chronic postamputation pain. The agent is applied twice daily with a roll-on applicator. ■

**Disclosures:** Dr. Ratcliffe is employed by a company funded to conduct the phase II clinical trial by SantoSolve AS of Oslo, which is developing 2PX.

## Dietary Interventions Advised When Serum Urate Levels Reach 7 mg/dL

BY RICHARD HYER

EXPERT ANALYSIS FROM A SYMPOSIUM SPONSORED BY THE AMERICAN COLLEGE OF RHEUMATOLOGY

CHICAGO — Redefining the upper limit of serum urate for a diagnosis of gout from 9-10 mg/dL to 6.8-7 mg/dL would better serve patients, said Dr. John S. Sudy of Duke Clinical Research Institute, Chapel Hill, N.C.

Although there is no indication for urate-lowering therapy in patients with asymptomatic uricemia, practice patterns need to be changed and include earlier use of diet to reduce urate levels, he said.

Many patients currently classified as normal are in fact slowly depositing urate crystals in soft tissue, he said, and are therefore at risk for developing gout. Proper diet that limits alcohol and fructose consumption is a key intervention.

Alcohol drinkers who consume more than five drinks daily have a 2.5-fold increased risk for developing gout. A weight gain of 30 pounds since high school doubles the relative risk of developing gout, whereas a weight loss of only 10 pounds actually cuts the risk almost in half, he said.

One can of fructose-sweetened soft drink per day represents a 1.4 increase in relative risk of developing gout, and two or more represent a 1.8 relative risk (BMJ 2008;336:309-12). Fruit juice and

high-fructose fruits such as oranges and apples are also significantly associated with gout. “There are clearly metabolic pathways where fructose consumption actually leads to marked elevations in serum urate values, leading to acceleration of deposition of urate crystals in soft tissues. I’ve really begun to counsel my patients about this and counsel them to reduce their intake of fructose,” said Dr. Sudy.

To manage flares or symptoms, the low-dose colchicine regimen of 1.2 mg at onset of flare followed by 0.6 mg within 1 hour was as effective as high-dose therapy (4.8 mg), but better tolerated, he said. “It shows we can do much lower doses to achieve the same outcome, with far fewer side effects.”

The most important urate-lowering drugs remain allopurinol, febuxostat, and probenecid, said Dr. Sudy, although probenecid is rarely used. He expects the approval of enzyme replacement therapy with polyethylene glycol-modified uricase (PEG-uricase) and expects this to be an IV drug, administered every 2 weeks, for the severe, end-of-spectrum, treatment-failure gout population. “This will be a rheumatologist’s drug, maybe a nephrologist’s drug, for certain populations.”

At least two new uricosuric agents are on the horizon, he said. The drugs are RDEA594, which he described as “totally experimental,” and Tranilast, a drug al-

ready approved in Asia for anti-inflammation.

Moderator Dr. Herbert Baraf, a rheumatologist in private practice in Silver Spring, Md., questioned interleukin-1 inhibition. “Do you think that’s realistic, or is that the elephant gun on the mouse?”

“For certain applications, it’s realistic,” said Dr. Sudy. “For example for patients who don’t respond well and require large doses of corticosteroids to manage a gout flare. For patients in whom there are contraindications to using the non-steroidal. For example, the brittle diabetic with moderate or severe chronic disease. This is the strategy for the short term. For people with severe disease it could be a corticosteroid-sparing drug.” ■

**Disclosures:** Dr. Sudy disclosed research support from Savient Pharmaceuticals, Genentech, Regeneron Pharmaceuticals, and Ardea Biosciences; consulting to Ardea, Anadys Pharmaceuticals, Regeneron, and Savient; and speakers bureau with Takeda Pharmaceuticals. Duke University and Mountain View Pharmaceuticals hold patent rights in pegylated urate oxidase and its use which have been licensed to Savient Pharmaceuticals. He disclosed off-label use of allopurinol and anakinra, and experimental use of pegloticase, rilonacept, canakinumab, and RDEA594. Dr. Baraf disclosed no financial relationships.

## Suicide Warning Added To Label of Tramadol

BY ELIZABETH MEHCATIE

A warning about the risks of suicide associated with use of the opioid analgesic tramadol in certain patients has been added to the drug’s prescribing information, the Food and Drug Administration has announced.

The warnings section advises clinicians against prescribing tramadol to patients who are suicidal or prone to addictions, emphasizing that patients who are addiction-prone or taking tranquilizers or antidepressant drugs are at risk of suicide if they are taking tramadol.

Tramadol-related deaths have been reported in patients with histories of emotional disturbances or suicidal ideation or attempts, and histories of misuse of tranquilizers, alcohol, and other CNS-active drugs, according to the FDA statement.

Tramadol, a centrally acting synthetic opioid analgesic approved for the management of moderate to moderately severe chronic pain, is mar-

keted as Ultram and Ultracet (tramadol with acetaminophen).

The revised warnings are summarized in “Dear Healthcare Professional” letters for Ultram and Ultracet, dated in April, from PriCara, a division of Ortho-McNeil-Janssen Pharmaceuticals Inc. that markets tramadol.

The Ultracet warning letter also points out the risks for acetaminophen overdoses.

The revised label also advises that tramadol tablets be prescribed “with caution” to patients who are treated with tranquilizers or antidepressant drugs, patients who abuse alcohol, and those who have emotional disturbances or depression. ■

The FDA statement and letters can be found at [www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm213264.htm](http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm213264.htm). Serious adverse events associated with the use of tramadol can be reported to the FDA’s MedWatch program at 800-332-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).