Analysis Shows Topical NSAID Has Potentially Better Gastrointestinal Safety Profile Than Oral NSAIDs in Treatment of Knee Osteoarthritis

Covidien

ATLANTA, Nov 08, 2010 (BUSINESS WIRE) --

Covidien (NYSE: COV), a leading global provider of healthcare products, announced the results of an analysis that will be presented at the American College of Rheumatology's Annual Scientific Meeting. A pooled analysis of safety data suggests that patients with knee osteoarthritis (OA) receiving the topical PENNSAID(R) (diclofenac sodium topical solution) 1.5% w/w had significantly fewer gastrointestinal (GI)-related adverse events than those receiving an oral non-steroidal anti-inflammatory drug (NSAID).

The study assessed the safety and tolerability profiles of topical versus oral diclofenac by analyzing two randomized, double-blind, multi-center, 12-week clinical trials of 1,397 patients with chronic knee OA pain. The most common adverse events occurring with topical diclofenac were application-site reactions, primarily skin dryness.[1,2]

"NSAID pain relievers are critical in managing debilitating osteoarthritis pain, but they have been associated with serious GI risks," said Sanford Roth, M.D., Lead Study Investigator and CEO and Medical Director, Arizona Research and Education. "The pooled analysis results suggest topical NSAIDs may have a superior GI safety profile, which is encouraging news for patients with OA of the knee."

Knee OA affects more than 10 million Americans.[3,4] It is a chronic condition in which joint cartilage, the smooth tissue that cushions the bone and allows easy joint movement, breaks down, leading to pain, stiffness and loss of movement in the joint.[5]

"Knee osteoarthritis is one of the top five causes of disability, so balancing safety and efficacy when deciding on treatment options is crucial," said Herbert Neuman, M.D., Vice President, Medical Affairs and Chief Medical Officer, Pharmaceuticals, Covidien. "These results are positive because some knee OA patients may find effective pain relief with the potential for fewer GI-related safety risks."

This analysis, funded by Covidien, is consistent with prior findings showing a lower incidence of GI adverse events with topical NSAIDs versus oral. Study results also showed that topical NSAIDs carry higher rates of GI adverse events than placebo. For more information on PENNSAID, including Important Risk Information and boxed warning, see below.

About Covidien

Covidien is a leading global healthcare products company that creates innovative medical solutions for better patient outcomes and delivers value through clinical leadership and excellence. Covidien manufactures, distributes and services a diverse range of industry-leading product lines in three segments: Medical Devices, Pharmaceuticals and Medical Supplies. With 2009 revenue of $10.3 billion, Covidien has 42,000 employees worldwide in more than 60 countries, and its products are sold in over 140 countries. To learn more about our business, please visit www.covidien.com [1].

About Osteoarthritis

Osteoarthritis is a chronic condition characterized by the breakdown of cartilage in the joint. Cartilage cushions the ends of the bones in joints - such as knees, hands, elbows, wrists, ankles and feet - which allows for easy movement. When this cartilage erodes, bones can rub together, resulting in pain and loss of free movement in the joint. Today, an estimated 27 million Americans live with osteoarthritis.[5]

The most common symptoms include pain, joint soreness, stiffness and deterioration of overall coordination, posture and walking. Despite the high prevalence of osteoarthritis, there is no cure for this disease, which tends to progressively reduce mobility and the overall health state in affected patients.

About PENNSAID

PENNSAID (diclofenac sodium topical solution) 1.5% w/w is a NSAID in a vehicle solution containing the penetrating agent DMSO.[1,2] PENNSAID was developed to help increase the effective, local delivery of pain relief to patients suffering from knee osteoarthritis, a disorder impacting an estimated 10 million patients in the United States.[6] PENNSAID is the only FDA-approved topical NSAID for the treatment of knee osteoarthritis which demonstrated statistically significant differences in all three primary efficacy endpoints: pain and physical function (WOMAC), patient overall health assessment (POHA) and patient global assessment of knee osteoarthritis.[1,2,3,7]

IMPORTANT RISK INFORMATION ABOUT PENNSAID

INDICATION

PENNSAID is indicatedfor treatment of the signs and symptoms of osteoarthritis of the knee(s).

Cardiovascular Risk

-Nonsteroidal anti-inflammatory drugs (NSAIDs) may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular

disease may be at greater risk.

-PENNSAID is contraindicated in the perioperative setting of coronary artery bypass graft (CABG) surgery.

Gastrointestinal Risk

- NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events.

PENNSAID is contraindicated in patients:

- with a known hypersensitivity to diclofenac sodium or any other component of PENNSAID
- who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal anaphylactic-like reactions to NSAIDs have been reported in such patients.

Elevation of one or more liver tests may occur during therapy with NSAIDs. PENNSAID should be discontinued immediately if abnormal liver tests persist or worsen.

Use with caution in patients with fluid retention or heart failure. Hypertension can occur with NSAID treatment. Monitor blood pressure closely with PENNSAID treatment.

Long-term administration of NSAIDs can result in renal papillary necrosis and other renal injury. Use PENNSAID with caution in patients at greatest risk of this reaction, including the elderly, those with impaired renal function, heart failure, liver dysfunction, and those taking diuretics and ACE-inhibitors.

Should not be used in pregnant or lactating women and is not approved for use in pediatric patients.

Anaphylactoid reactions may occur in patients without prior exposure to PENNSAID. NSAIDs can cause serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal.

The most common treatment-related adverse events in patients receiving PENNSAID were application site skin reactions including dry skin (32%), contact dermatitis characterized by skin erythema and induration (9%), contact dermatitis with vesicles (2%) and pruritus (4%). In a long term safety study, contact dermatitis

occurred in 13% and contact dermatitis with vesicles in 10% of patients, generally within the first 6 months of exposure, leading to a withdrawal rate for an application site event of 14%. Other common adverse events greater than placebo include: dyspepsia (9%), abdominal pain (6%), flatulence (4%), diarrhea (4%) and nausea (4%).

Do not apply to open wounds. Protect treated knee(s) from natural or artificial sunlight. Topicals such as sunscreen and bug repellant may be applied after PENNSAID treated knee(s) are completely dry. Avoid contact of PENNSAID with eyes and mucous membranes. Wash and dry hands after use.

Concurrent use with oral NSAIDs should be avoided unless benefit outweighs risk and periodic laboratory evaluations are conducted.

See Full Prescribing Information [2]**for additional Important Risk Information.**

PENNSAID is a registered trademark of Nuvo Research Inc.

[1] Roth SH, Shainhouse JZ. Efficacy and safety of a topical diclofenac solution (Pennsaid) in the treatment of primary osteoarthritis of the knee: a randomized, double-blind, vehicle-controlled clinical trial. *Arch Intern Med*. 2004;164:2017-2023.

[2] Simon LS, Grierson LM, Naseer Z, Bookman AAM, Shainhouse JZ. Efficacy and safety of topical diclofenac containing dimethyl sulfoxide (DMSO) compared with those of topical placebo, DMSO vehicle and oral diclofenac for knee osteoarthritis. *Pain*. 2009;143:238-245.

[3] Parmet S, Lynm C, Glass RM. Osteoarthritis of the knee. *JAMA*. 2003; 289:1068.

[4] Guccione AA, Felson DT, Anderson JJ, et al. The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. *Am J Public Health*. 1994;84:351-358.

[5] Arthritis Foundation. Osteoarthritis Fact Sheet. http://www.arthritis.org/media/newsroom/media-kits/Osteoarthritis_fact_sheet.pdf [3] [Last Accessed April 2010]

[6] Parmet, S., Lynm, C., & Glass, R. M. (2003). Osteoarthritis of the Knee. *JAMA*, 289(8), 1068.

[7] Tugwell, P. S., Wells, G. A., & Shainhouse, J. Z. Equivalence study of a topical diclofenac solution (PENNSAID) compared with oral diclofenac in symptomatic treatment of osteoarthritis of the knee: a randomized controlled trial. *Journal of Rheumatology*, 2004;31(10), 2002-12.

SOURCE [4]

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