

VIMOVO Backgrounder

ABOUT VIMOVO

- VIMOVO™ (naproxen/esomeprazole magnesium) 375/20–500/20 mg delayed-release tablets, co-developed by AstraZeneca and POZEN Inc., is a fixed-dose combination of enteric-coated naproxen, a pain-relieving nonsteroidal anti-inflammatory drug (NSAID), and immediate-release esomeprazole magnesium, a proton pump inhibitor (PPI).¹
- VIMOVO is an important treatment option indicated for the relief of signs and symptoms of OA, RA, and AS, and to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID associated gastric ulcers.

REGULATORY STATUS

- On April 30, 2010, the US Food and Drug Administration (FDA) approved VIMOVO for the relief of signs and symptoms of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis and to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID-associated gastric ulcers. VIMOVO is not recommended for initial treatment of acute pain because the absorption of naproxen is delayed compared to absorption from other naproxen-containing products. Controlled studies do not extend beyond 6 months.¹

PN400-301 and PN400-302 CLINICAL TRIAL DESIGN OVERVIEW

The FDA approval is based on data from a comprehensive clinical trials program.

- PN400-301 and PN400-302 were 6-month, phase III, randomized, double-blind, controlled, multi-center clinical trials that enrolled approximately 800 *H. pylori*-negative adults with OA, RA, or any other condition requiring chronic NSAID therapy who were at risk of developing NSAID-associated ulcers.²
- Patients in each study were randomised to receive either VIMOVO 500/20 mg or enteric-coated naproxen 500 mg twice-daily, over a six-month treatment period. Patients underwent upper endoscopies at baseline and at one, three, and six months – the primary endpoint was the cumulative incidence of gastric ulcers observed at these time points.²

PN400-301 and PN400-302 PRIMARY ENDPOINT RESULTS

- Data from PN400-301 and PN400-302 showed patients at risk for developing NSAID-associated gastric ulcers taking VIMOVO 500/20 mg experienced significantly fewer endoscopically confirmed gastric ulcers (GU) compared with patients taking enteric-coated naproxen 500 mg alone.²
- Data from PN400-301 showed that gastric ulcers were detected in 4.1% of patients taking VIMOVO, compared to 23.1% among patients taking enteric-coated naproxen ($p < 0.001$). PN400-302 showed that a GU was detected in 7.1% incidence of GU among patients taking VIMOVO, compared to 24.3% with enteric-coated naproxen ($p < 0.001$). These data are published in *Alimentary Pharmacology and Therapeutics*.²

PN400-301 and PN400-302 SAFETY

- In addition to gastric ulcers, commonly reported treatment emergent adverse events (experienced by $\geq 10\%$ patients in either treatment group from either study) included erosive gastritis, gastritis, dyspepsia and erosive duodenitis.²
 - In PN400-301 (n=434), 21% of patients taking VIMOVO experienced erosive gastritis, as compared to 38% taking enteric-coated (EC) naproxen. Among patients taking VIMOVO, 18% experienced gastritis, as compared to 13% taking EC naproxen, and 17% of the patients reported dyspepsia, as compared to 30% taking EC naproxen. Two percent of patients taking VIMOVO experienced erosive duodenitis as compared to 14% taking EC naproxen.²
 - In PN400-302 (n=420), incidences of erosive gastritis were reported by 18% of patients taking VIMOVO, as compared to 39% taking EC naproxen. Sixteen percent of patients taking VIMOVO experienced gastritis, as compared to 15% taking EC naproxen; 20% patients taking VIMOVO

reported dyspepsia, as compared to 23% taking EC naproxen. Two percent of patients taking VIMOVO experienced erosive duodenitis as compared to 10% taking EC naproxen.²

ABOUT OSTEOARTHRITIS

- Osteoarthritis (OA) is the most common form of arthritis,³ affecting nearly 151 million individuals worldwide⁴ and 27 million Americans⁵.
- OA, known as the “wear-and-tear” kind of arthritis, is a chronic condition characterized by the breakdown of the joint’s cartilage.⁴ The breakdown of cartilage causes the bones to rub against each other, leading to stiffness, pain, and loss of movement in the affected joints.⁴ Most often, those are the joints in the hands, spine, hips, and knees.⁶
- A combination of factors can contribute to OA, including being overweight, aging, joint injury or stress, heredity, and muscle weakness.⁷
- Approximately 80% of OA patients have some degree of movement limitation.⁷
- In 2007, OA increased the probability of missed workdays by 14% in women and by 12% in men – a greater impact than that of other common conditions such as diabetes, asthma, or anxiety disorder.⁸
- OA increases annual per capita absenteeism costs by \$469 for women and \$520 for men – approximately three lost workdays.⁸

CURRENT TREATMENT FOR OSTEOARTHRITIS

- There is no cure for OA, so treatment programs typically focus on relieving pain and improving function. They also may include a combination of physical therapy, weight control, and medication.⁷
- While NSAIDs are commonly prescribed to relieve pain associated with OA¹⁰, gastric ulcers can occur in up to 25% of chronic NSAID users.⁹
- VIMOVO offers patients an important treatment option by delivering both the proven pain relief of enteric-coated naproxen with a built in PPI in every dose of the medication.¹

Important Safety Information

- **Like all medications that contain nonsteroidal anti-inflammatory drugs (NSAIDs), VIMOVO may increase the chance of a heart attack or stroke that can lead to death. This chance increases**
 - **With longer use of NSAID medicines**
 - **In people who have heart disease**
- **NSAID-containing medications, such as VIMOVO, should never be used before or after a type of heart surgery called coronary artery bypass graft (CABG)**
- **As with all medications that contain NSAIDs, VIMOVO may increase the chance of stomach and intestinal problems, such as bleeding or an ulcer, which can occur without warning and may cause death**
 - **Elderly patients are at greater risk for serious gastrointestinal events**

VIMOVO is not right for everyone, including patients who have had an asthma attack, hives, or other allergic reaction with aspirin or any other NSAID medicine, patients who are allergic to any of the ingredients in VIMOVO, or women in late stages of pregnancy.

Serious allergic reactions, including skin reactions, can occur without warning and can be life-threatening; discontinue use of VIMOVO at the first appearance of a skin rash, or if you develop sudden wheezing; swelling of the lips, tongue or throat; fainting; or problems swallowing.

VIMOVO should be used at the lowest dose and for the shortest amount of time as directed by your health care provider.

Tell your health care provider right away if you develop signs of active bleeding from any source.

VIMOVO can lead to onset of new hypertension or worsening of existing high blood pressure, either of which may contribute to an increased risk of a heart attack or stroke.

Speak with your health care provider before starting VIMOVO if you

- Have a history of ulcers or bleeding in the stomach or intestines
- Have heart problems, high blood pressure, or are taking high blood pressure medications
- Have kidney or liver problems

Tell your health care provider about all of the medicines you take including prescription and non-prescription drugs, vitamins, and herbal supplements before starting VIMOVO.

Talk to your health care provider about your risk for bone fractures if you take VIMOVO for a long period of time.

Talk to your health care provider about your risk for developing low levels of magnesium if you take VIMOVO for a long period of time.

The most common side effects of VIMOVO include: inflammation of the lining of the stomach, indigestion, diarrhea, stomach ulcers, abdominal pain, and nausea.

Approved Uses for VIMOVO

VIMOVO is approved to relieve the signs and symptoms of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis and to decrease the risk of stomach (gastric) ulcers in patients at risk of developing stomach ulcers from treatment with NSAIDs.

VIMOVO is not recommended as a starting treatment for relief of acute pain. Controlled studies do not extend beyond 6 months.

For further information on VIMOVO, please see the full [Prescribing Information](#), including **Boxed Warnings.**

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¹ Prescribing Information for VIMOVO. AstraZeneca LP, Wilmington, DE.

² Goldstein, et al; Clinical trial: the incidence of NSAID-associated endoscopic gastric ulcers in patients treated with PN 400 (naproxen plus esomeprazole magnesium) vs. enteric-coated naproxen alone. *Aliment Pharmacol Ther* 2010; 32: 401–413.

³ Arthritis Foundation. Osteoarthritis: What is it? http://www.arthritis.org/disease-center.php?disease_id=32 Accessed April 16, 2010.

⁴ Global Burden of Osteoarthritis in the year 2000, (Symmons, Mathers, Pflieger, 2006), *Global Burden of Disease 2004*.

⁵ Helmick, C., Felson, D., Lawrence, R., Gabriel, S., et al. Estimates of the Prevalence of Arthritis and Other Rheumatic conditions in the United States. *Arthritis & Rheumatism* 58(1), 15-25. 2008.

⁶ The Mayo Clinic. Osteoarthritis: Causes. <http://www.mayoclinic.com/health/osteoarthritis/DS00019/DSECTION=causes>. Accessed February 9, 2009.

⁷ Centers for Disease Control and Prevention. Osteoarthritis. Available at <http://www.cdc.gov/arthritis/basics/osteoarthritis.htm>. Accessed July 15, 2010

⁸ Kotlarz, et al. Osteoarthritis and Absenteeism Costs: Evidence From US National Survey Data. *JOEM*. Volume 52, Number 3, March 2010.

⁹ American College of Gastroenterology. (ACG) Guidelines for Prevention of NSAID-Related Ulcer Complications.