

CENTER FOR DRUG EVALUATION AND RESEARCH

**APPLICATION NUMBER:
22511Orig1s000**

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VIMOVO safely and effectively. See full prescribing information for VIMOVO.

VIMOVOTM
(naproxen and esomeprazole magnesium) DELAYED RELEASE TABLETS

Initial US Approval:

WARNING: CARDIOVASCULAR AND GASTROINTESTINAL RISKS

See full prescribing information for complete boxed warning

Cardiovascular Risk

- Naproxen, a component of VIMOVO, 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. (5.1)
- VIMOVO is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery. (4, 5.1)

Gastrointestinal Risk

- NSAIDs, including naproxen, a component of VIMOVO, 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 (GI) events. (5.4)

INDICATIONS AND USAGE

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 (1)

DOSAGE AND ADMINISTRATION

One tablet twice daily. Use the lowest effective dose. Not recommended in moderate/severe renal insufficiency or in severe hepatic insufficiency. Consider dose reduction in mild/moderate hepatic insufficiency (2)

DOSAGE FORMS AND STRENGTHS

Delayed release tablets: 375 mg/20 mg or 500 mg/20 mg of naproxen and esomeprazole magnesium (3)

CONTRAINDICATIONS

- Known hypersensitivity to any component of VIMOVO or substituted benzimidazoles (4)
- History of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs (4, 5.8, 5.9, 5.13)
- Use during the peri-operative period in the setting of coronary artery bypass graft (CABG) surgery (4, 5.1)
- Late pregnancy (4, 5.10, 8.1)

WARNINGS AND PRECAUTIONS

- Serious and potentially fatal cardiovascular (CV) thrombotic events, myocardial infarction, and stroke. Patients with known CV disease/risk factors may be at greater risk (5.1)
- Serious gastrointestinal (GI) adverse events, which can be fatal. The risk is greater in patients with a prior history of ulcer disease or GI bleeding, and in patients at high risk for GI events, especially the elderly. VIMOVO should be used with caution in these patients (5.4, 8.5)
- Treatment should be withdrawn when active and clinically significant bleeding from any source occurs (5.5)
- Elevated liver enzymes and, rarely, severe hepatic reactions. Discontinue use immediately if abnormal liver enzymes persist or worsen (5.11, 8.6, 12.3)

- New onset or worsening of pre-existing hypertension. Blood pressure should be monitored closely during treatment with VIMOVO (5.2, 7.1, 7.4)
- Congestive heart failure and edema. VIMOVO should be used with caution in patients with fluid retention or heart failure (5.3)
- Renal papillary necrosis and other renal injury with long term use. Use VIMOVO with caution in the elderly, those with impaired renal function, hypovolemia, salt depletion, heart failure, liver dysfunction, and those taking diuretics, or ACE-inhibitors. Not recommended for patients with moderate or severe renal impairment (2, 5.6, 5.7, 7.1, 7.4, 8.7)
- Anaphylactoid reactions. Do not use VIMOVO in patients with the aspirin triad (5.8)
- Serious skin adverse reactions such as exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, which can be fatal and can occur without warning. Discontinue VIMOVO at first appearance of skin rash or any other sign of hypersensitivity (5.9)
- Long-term PPI therapy is associated with an increased risk for osteoporosis-related fractures of the hip, wrist or spine (5.16)
- Symptomatic response to esomeprazole does not preclude the presence of gastric malignancy (5.4)
- Atrophic gastritis has been noted on biopsy with long-term omeprazole therapy (5.4)

ADVERSE REACTIONS

Most common adverse reactions in clinical trials (>5%): erosive gastritis, dyspepsia, gastritis, diarrhea, gastric ulcer, upper abdominal pain, nausea (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact AstraZeneca at 1-800-236-9933 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Concomitant use of NSAIDs may reduce the antihypertensive effect of ACE Inhibitors, diuretics, and beta-blockers (7.1, 7.4, 7.9)
 - Concomitant use of NSAIDs increases lithium plasma levels (7.5)
 - Concomitant use of VIMOVO with methotrexate may increase the toxicity of methotrexate (7.6)
 - Concomitant use of VIMOVO and warfarin may result in increased risk of bleeding complications. Monitor for increases in INR and prothrombin time (7.7)
 - Esomeprazole inhibits gastric acid secretion and may interfere with the absorption of drugs where gastric pH is an important determinant of bioavailability (eg, ketoconazole, iron salts and digoxin) (7.11)
- USE IN SPECIFIC POPULATIONS**
- Pregnancy Category C: VIMOVO should not be used in late pregnancy (4, 5.10, 8.1)
 - Hepatic Insufficiency: VIMOVO is not recommended in patients with severe hepatic insufficiency (2, 4, 5.11, 8.6, 12.3)
 - Renal Insufficiency: VIMOVO is not recommended in patients with moderate or severe renal insufficiency (2, 5.6, 5.7, 8.7, 12.3)

SEE 17 FOR PATIENT COUNSELING INFORMATION AND FDA APPROVED PATIENT LABELING OR MEDICATION GUIDE
REVISED MM/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

Cardiovascular Risk..... 4

1 INDICATIONS AND USAGE 4

2 DOSAGE AND ADMINISTRATION 5

3 DOSAGE FORMS AND STRENGTHS 6

4 CONTRAINDICATIONS 6

5 WARNINGS AND PRECAUTIONS 6

5.1 Cardiovascular Thrombotic Events 6

5.2 Hypertension 7

5.3 Congestive Heart Failure and Edema 7

5.4 Gastrointestinal Effects — Risk of Ulceration, Bleeding, and Perforation..... 7

5.5 Active Bleeding..... 8

5.7 Advanced Renal Disease9

5.8 Anaphylactoid Reactions.....9

5.9 Skin Reactions9

5.10 Pregnancy10

5.11 Hepatic Effects.....10

5.12 Hematological Effects11

5.13 Preexisting Asthma11

5.14 Concomitant NSAID Use11

5.15 Corticosteroid Treatment.....11

5.16 Bone Fracture12

5.17 Masking of Inflammation and Fever.....12

5.18 Laboratory Tests.....12

6 ADVERSE REACTIONS12

6.2	Postmarketing experience	16
7	DRUG INTERACTIONS	17
7.1	ACE-inhibitors.....	17
7.2	Aspirin	17
7.3	Cholestyramine.....	18
7.4	Diuretics	18
7.5	Lithium.....	18
7.6	Methotrexate	18
7.7	Anticoagulants.....	18
7.8	Selective Serotonin Reuptake Inhibitors (SSRIs).....	19
7.9	Other Information Concerning Drug Interactions.....	19
7.10	Drug/Laboratory Test Interaction.....	19
7.11	Interactions related to absorption.....	20
7.12	Antiretroviral agents.....	20
7.13	Effects on hepatic metabolism/cytochrome P-450 pathways.....	21
7.14	Other pharmacokinetic-based interactions.....	21
8	USE IN SPECIFIC POPULATIONS	22
8.1	Pregnancy	22
8.2	Labor and Delivery	23
8.3	Nursing Mothers	23
8.4	Pediatric Use	23
8.5	Geriatric Use	23
8.6	Hepatic Insufficiency.....	24
8.7	Renal Insufficiency	24
10	OVERDOSAGE	24
11	DESCRIPTION	26
12	CLINICAL PHARMACOLOGY.....	27
12.1	Mechanism of Action.....	27
12.2	Pharmacodynamics.....	27
12.3	Pharmacokinetics	28
13	NONCLINICAL TOXICOLOGY	34
13.1	Carcinogenesis, Mutagenesis, Impairment of Fertility .	34
13.2	Animal Toxicology and/or Pharmacology	35
14	CLINICAL STUDIES	36
16	HOW SUPPLIED/STORAGE AND HANDLING	38
17	PATIENT COUNSELING INFORMATION	38

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

Cardiovascular Risk

- Non-Steroidal Anti-inflammatory Drugs (NSAIDs), a component of VIMOVO, 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 [see *Warnings and Precautions (5.1)*].
- VIMOVO is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery [see *Contraindications (4)*, and *Warnings and Precautions (5.1)*].

Gastrointestinal Risk

- NSAIDs, including naproxen, a component of VIMOVO, 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 [see *Warnings and Precautions (5.4)*].

1 INDICATIONS AND USAGE

VIMOVO is a combination product that contains naproxen and esomeprazole. It is indicated 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.

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