Dinovo®

Naproxen and Esomeprazole
Delayed Release Tablet

Description

The active ingredients of Dinovo® are naproxen which is a NSAID and esomeprazole magnesium which is a Proton Pump Inhibitor (PPI). Dinovo® is available as a round biconvex, multi-layer, delayed release tablet combining an enteric coated naproxen core and an immediate release esomeprazole magnesium layer surrounding the core.

Indications

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. Dinovo® 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.

Dosage and Administration

Rheumatoid Arthritis, Osteoarthritis and Ankylosing Spondylitis

The dosage is one tablet twice daily of Dinovo® 375 mg naproxen and 20 mg of esomeprazole or 500 mg naproxen and 20 mg of esomeprazole.

The tablets are to be swallowed whole with liquid. Do not split, chew, crush or dissolve the tablet. Dinovo® is to be taken at least 30 minutes before meals.

Geriatric Patients

Studies indicate that although total plasma concentration of naproxen is unchanged, the unbound plasma fraction of naproxen is increased in the elderly. Use caution when high doses are required and some adjustment of dosage may be required in elderly patients.

Patients With Moderate to Severe Renal Impairment

Naproxen-containing products are not recommended for use in patients with moderate to severe or severe renal impairment (creatinine clearance < 30 mL/min).

Hepatic Insufficiency

Monitor patients with mild to moderate hepatic impairment closely and consider a possible dose reduction based on the naproxen component of Dinovo®.

Dinovo® is not recommended in patients with severe hepatic impairment because esomeprazole doses should not exceed 20 mg daily in these patients.

Pediatric Patients

The safety and efficacy of Dinovo® in children younger than 18 years have not been established. Dinovo® is therefore not recommended for use in children.

Contraindication

Dinovo® is contraindicated in patients with known hypersensitivity to naproxen, esomeprazole magnesium, substituted benzimidazoles, or to any of the excipients.

Dinovo® is contraindicated in patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Dinovo® is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery. Dinovo® is also contraindicated in patients in the late stages of pregnancy.

Adverse Reactions

Naproxen

The following adverse reactions have been identified during post-approval use of naproxen. *Body as a Whole:* anaphylactoid reactions, angioneurotic edema, menstrual disorders, pyrexia (chills and fever); *Cardiovascular:* congestive heart failure, vasculitis, hypertension, pulmonary edema; *Gastrointestinal:* gastrointestinal bleeding and/or perforation, hematemesis, pancreatitis, vomiting, colitis, exacerbation of inflammatory bowel disease (ulcerative colitis, Crohn's disease), nonpeptic gastrointestinal ulceration, ulcerative stomatitis, esophagitis, peptic ulceration; *Hepatobiliary:* jaundice, abnormal liver function tests, hepatitis (some cases have been fatal); *Hemic and Lymphatic:* eosinophilia, leucopenia, melena, thrombocytopenia, agranulocytosis, granulocytopenia, hemolytic anemia, aplastic anemia; *Metabolism and Nutritional Disorders:* hyperglycemia, hypoglycemia; Nervous System: inability to concentrate, depression, dream abnormalities, insomnia, malaise, myalgia, muscle weakness, aseptic meningitis, cognitive dysfunction, convulsions; *Respiratory:* eosinophilic pneumonitis, asthma.

Esomeprazole

The following adverse reactions have been identified during post-approval use of esomeprazole. *Blood and Lymphatic:* agranulocytosis, pancytopenia; *Eye:* blurred vision; *Gastrointestinal:* pancreatitis; stomatitis; *Hepatobiliary:* hepatic failure, hepatitis with or without jaundice; *Immune System:* anaphylactic reaction/shock; *Infections and Infestations:* GI candidiasis; *Metabolism and Nutritional Disorders:* hypomagnesemia; *Musculoskeletal and Connective Tissue:* muscular weakness, myalgia; *Nervous System:* hepatic encephalopathy, taste disturbance; *Psychiatric:* aggression, agitation, depression, hallucination; *Renal and Urinary:* interstitial nephritis; *Reproductive System and Breast:* gynecomastia; Respiratory, *Thoracic, and Mediastinal:* bronchospasm; *Skin and Subcutaneous Tissue:* alopecia, erythema multiforme, hyperhidrosis, photosensitivity, Stevens-Johnson syndrome, toxic epidermal necrolysis (some fatal).

Precaution

Cardiovascular Thrombotic Events: Clinical trials of several COX-2 selective and nonselective NSAIDs of up to three years duration have shown an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs, both COX-2 selective and nonselective, may have a similar risk. *Hypertension:* NSAIDs, including naproxen, a component of Dinovo®, can lead to onset of new hypertension or worsening of preexisting hypertension, either of which may contribute to the increased incidence of CV events. *Congestive Heart Failure and Edema:* Fluid retention, edema, and peripheral edema have been observed in some patients taking NSAIDs and should be used with caution in patients with fluid retention or heart failure. *Gastrointestinal Effects - Risk of Ulceration, Bleeding, and Perforation:* NSAIDs, including naproxen, a component of Dinovo®, can cause serious gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration, and perforation of the stomach, small intestine, or large intestine, which can be fatal. While naproxen and esomeprazole combination has been shown to significantly decrease the occurrence of gastric ulcers compared to naproxen alone, ulceration and associated complications can still occur. *Renal Effects:* Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. *Pregnancy - Pregnancy Category C:* In late pregnancy, as with other NSAIDs, naproxen, a component of Dinovo®, should be avoided because it may cause premature closure of the ductus arteriosus.

Drug Interactions

Several studies conducted with naproxen and esomeprazole combination have shown no interaction between the two components.

Commercial Pack

Dinovo® 375/20 Tablet: Box containing 50 delayed release tablets in 5X10's blister strips. Each delayed release tablet contains Naproxen USP 375 mg and Esomeprazole Magnesium USP equivalent to Esomeprazole 20 mg.

Dinovo® 500/20 Tablet: Box containing 50 delayed release tablets in 5X10's blister strips. Each delayed release tablet contains Naproxen USP 500 mg and Esomeprazole Magnesium USP equivalent to Esomeprazole 20 mg.

BEXIMCO PHARMA

Manufactured by

BEXIMCO PHARMACEUTICALS LTD.

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148 x 210 mm