

Etotio

Etotio 400 mg/8 mg Film Tablet



COMPOSITION: Each film-coated tablet contains as **Active Ingredients:** 400 mg etodolac and 8 mg thicolchicoside; and as **Inactive Ingredients:** In the core tablet: lactose monohydrate, microcrystalline cellulose, sodium starch, glycolate, colloidal siliconedioxide, polyvinylpyrrolidone, magnesium stearate and in film-coating: hydroxypropylmethylcellulose¹, titaniumdioxide¹, polyethylene glycol400¹. (It is obtained as a mixture.)

PHARMACOLOGICAL PROPERTIES: **Pharmacodynamic properties:** **Pharmacotherapeutic group:** Non-Selective COX Inhibitors-Musculo-Skeletal system drugs combination. ATC code: M01BX. **Mechanism of Action:** Etodolac is a non-steroid anti-inflammatory (NSAI) drug that has anti-inflammatory, anti-pyretic and analgesic activities in animal models. As with other NSAID drugs, the mechanism of action of etodolac is not clearly known; however, it is considered to be related to inhibition of prostaglandin biosynthesis. Thiocolchicoside, in-vitro, binds only to GABA-A and strychnine-sensitive glycine receptors. Thiocolchicoside, that shows its effect as a GABA-A receptor agonist, can be considered to show its muscle relaxing effects by regulator complex mechanisms at supra-spinal level; however, glycinergic mechanism of action can not be ruled out. **Pharmacokinetic properties:** Co-administration of etodolac and thiocolchicoside does not alter the pharmacokinetic properties of these drugs compared to when given alone. Etodolac is well absorbed and compared to the solution formulation, the relative bio-availability of the 200 mg capsule is 100%. Rate of absorption of etodolac does not change when given after a meal. However, ingestion of food decreases the peak concentration reached approximately to half and increases the time to peak concentration to 1.4-3.8 hours. Etodolac, within the therapeutic dose limits, is bound to plasma proteins at a rate of >99%. The free fraction is <1% and this rate is independent of the total etodolac concentration in the dose ranges studied. Etodolac is extensively metabolized in the liver. The terminal metabolism half-life is 7.3 (± 4.0) hours. Following oral administration, there is no trace of thiocolchicoside in the plasma; only its two metabolites are found: the pharmacologically active metabolite SL18.0740 and inactive metabolite SL59.0955. In humans, thiocolchicoside is bound to serum proteins at a low level (13%) and this binding is independent of therapeutic thiocolchicoside concentration. Following oral administration, thiocolchicoside is initially metabolized to aglycon 3-dimethyl thiocolchicoside (SL59.0955). Then the SL59.0955 is metabolized to SL18.0740 which has the same pharmacological activity as thiocolchicoside. Following oral administration of radio-labeled thiocolchicoside, 72% of the administered dose is found in feces and 16% is found in urine. Following oral administration of thiocolchicoside, the SL18.0740 metabolite is eliminated with a half-life of 3.2-7 hours. The half-life of the SL59.0955 metabolite is about 0.8 hours.

INDICATIONS: It is indicated in adults and adolescents aged over 16 years for treatment of osteoarthritis, painful syndromes of vertebral column, rheumatism not related to joint, painful muscle spasms in acute spinal pathologies and in pains following trauma and surgical interventions.

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CONTRAINDICATIONS: It is contraindicated in patients hypersensitive to etodolac and/or to compounds containing thicolchicoside and to any of the ingredients contained in the drug; in patients developing allergic reactions during treatment with aspirin or other NSAID drugs due to possible cross drug reactions or in patients with a history of acute asthma, rhinitis or urticaria; patients with a history of gastrointestinal bleeding or perforation related to previous treatment with NSAID drugs; patients with cardiac failure, immediately before or after by-pass and cardiac surgery; patients with active peptic ulcers or those with a history of peptic ulcers (including gastrointestinal hemorrhage due to other NSAID drugs); in relaxed paralysis?; in muscle hypotonia; during pregnancy and lactation; in pediatric patients aged 16 and below and in women of child bearing age and do not use an effective contraception method.

WARNINGS AND PRECAUTIONS: Particularly due to its etodolac content, ETOTIO, like other NSAID drugs, should be used with caution in patients with cardiac, renal or hepatic function. Dosage should be low and renal function should be monitored. In cases where clinical symptoms or findings consistent with liver failure develop or systemic signs are observed (like rash, eosinophilia), etodolac treatment should be stopped. Since development of bronchospasm with the use of NSAID drugs in patients with (or with a history of) bronchial asthma is reported, ETOTIO should be used with caution in these patients. ETOTIO should also be used with caution in patients with fluid retention, hypertension or cardiac failure. Gastrointestinal ulceration and hemorrhage signs and symptoms should be closely monitored during therapy with NSAID drugs like Etodolac and the lowest effective dosage should be administered for the shortest optimum period to minimize the potential risk for gastrointestinal adverse effects. Alternative therapies not containing NSAID drugs should be considered for high-risk patients. Patients should be informed of the signs and symptoms of serious skin reactions that can be fatal in some cases and should be advised to stop treatment in case of rash or any other signs of hypersensitivity. Thicolchicoside that is included in the contents of ETOTIO can accelerate the attacks especially in epileptic patients or in those with a risk for attacks. If diarrhea is observed following oral administration, ETOTIO treatment should be discontinued. Unwanted effects can be decreased by using the lowest effective dose for the shortest time.

This drug is under additive monitoring. This triangle will enable specifying the new safety information faster. Health care providers are expected to report suspected adverse reactions to TUFAM (www.titck.gov.tr; e-posta: tufam@titck.gov.tr; tel: 0 800 314 00 08; faks: 0 312 218 35 99).

SIDE EFFECTS/ADVERSE EFFECTS: Those related to Etodolac commonly are: asthenia/fatigue, dizziness, depression, nervousness; blurred vision; tinnitus; dyspepsia, abdominal pain, diarrhea, flatulence, nausea, constipation, gastritis, melena, vomiting; itching, rash; dysuria, frequent urination, trembling, fever. Those related to thicolchicoside commonly are: somnolence, diarrhea and gastralgia.

DRUG INTERACTIONS: Interactions associated with Etodolac: As with the other NSAID drugs, co-administration of etodolac with aspirin is not generally recommended due to the potential increase in side effects. Effectivity and side effects should be carefully observed when it is co-administered with ADE-inhibitors, furosemide, lithium, methotrexate, warfarin, cardiac glycosides, cyclosporins, phenylbutazone and probenecid, anti-thrombocyte agents and selective serotonin uptake-inhibitors, corticosteroids, tacrolimus, zidovudin, mifepristone and quinolone antibiotics.

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Interactions associated with: Co-administration of thiocolchicoside with other muscle relaxant drugs is not recommended because of the potential for increasing each other's effect. In case it is co-administered with another drug that is effective on smooth muscles, due the possibility of an increase in unwanted effects for the same reason, the patient should be closely monitored. **Pregnancy and Lactation:** Pregnancy category is X. **Pregnancy:** It is contraindicated during pregnancy and in women at child-bearing age not using effective contraceptive methods. **Lactation:** Since thiocolchicoside passes into mother's milk, ETOTIO should not be used during lactation period. **Effects on driving and machine use:** ETOTIO can cause dizziness, lightheadedness, fatigue and abnormal vision. Patients should be warned against the effects of this drug prior to driving and machine use.

DOSAGE AND ADMINISTRATION: Posology and Administration Method: It is used in adults 1 film tablet maximum 2 times a day (every 12 hours). The total period of therapy is limited by 7 consecutive days. It is only for oral use. The film tablet should be taken after a meal with water. **Additional Information for Special Populations:** Renal Failure: In studies performed in patients with mild-moderate renal failure (creatinine clearance 37-88 mL/min), no significant differences were observed in total and free etodolak metabolism. Liver failure: In patients with compensated liver cirrhosis, total and free etodolak metabolism was not altered. Although generally no dosage adjustment is required in this group of patients, etodolak clearance is dependent on liver function and dose can be decreased in patients with severe liver failure. Pediatric population: It is not used in patients younger than 16 years of age due to safety reasons. Geriatric population: The risk for adverse reactions is high in elderly patients. It should be considered that renal and hepatic functions decrease with age.

OVERDOSAGE: Symptoms following acute NSAID drug over- dosage are generally limited with lethargy, sleepiness, nausea, vomiting and epigastric pain and mostly they recover with supportive treatment. Since Etodolak is highly bound to protein, forced diuresis, alkalization of urine, hemodialysis or hemoperfusion will probably be ineffective. No specific symptom of over dosage in patients treated with thiocolchicoside was reported. In case of over dosage, medical observation and symptomatic precautions are recommended.

STORAGE CONDITIONS: Keep at room temperature below 25°C in its original package. Shelf-life is 36 months.

HOW SUPPLIED AND PACKAGE CONTENTS: Etotio 400 mg/8 mg Film Tablet, is presented in blister packages containing 14 film tablets. Sold under prescription. Please contact our firm for further details. <http://www.mn.com.tr>.

LICENCE HOLDER AND ADDRESS: Mustafa Nevzat İlaç Sanayii A.Ş. Pak İş Merkezi, Prof. Dr. Bülent Tarcan Sok. No:5/1 34349 Gayrettepe/İstanbul

PRODUCER FIRM AND ADDRESS: Mustafa Nevzat İlaç San. A.Ş. Sanayi Cad. No:13 34196 Yenibosna/İstanbul