



PRIOR AUTHORIZATION CRITERIA

Brand Name: **Zylfo**
Generic: **(zileuton)**

DESCRIPTION:

Zileuton is an orally-active leukotriene modifier, specifically an inhibitor of leukotriene synthesis. Zileuton inhibits the first enzyme in the lipoxygenase pathway, 5-lipoxygenase, and thereby limits the formation of potent leukotrienes (LTB₄, LTC₄, LTD₄, and LTE₄) which are implicated in the complicated inflammatory response that occurs in asthma.

INDICATIONS:

Zyflo is indicated for the prophylaxis and chronic treatment of asthma in adults and children 12 years of age and older.

DOSAGE:

The recommended dosage of Zyflo for the symptomatic treatment of patients with asthma is one 600-mg tablet four times a day for a total daily dose of 2400mg. For the ease of administration, ZYFLO may be taken with meals and at bedtime. Hepatic transaminases should be evaluated prior to the initiation of Zyflo and periodically during treatment.

CLINICAL SIDE EFFECTS:

Commonly ZYFLO-treated patients side effects include: arthralgia, chest pain, conjunctivitis, constipation, dizziness, fever, flatulence, hypertonia, insomnia, lymphadenopathy, malaise, neck pain/rigidity, nervousness, pruritus, somnolence, urinary tract infection, vaginitis, and vomiting.

WARNING:

Zileuton undergoes hepatic metabolism. Patients with hepatic disease may not metabolize zileuton to the same extent as those with normal liver function. Zileuton is contraindicated in patients with active liver disease or with transaminase elevations ≥ 3 times the upper limit of normal.

Concomitant administration of zileuton and propranolol results in a significant increase (2-fold) in propranolol serum concentrations. Bradycardia is also potentiated by the drug combination.

Zileuton, can interact with theophylline by inhibiting theophylline metabolism and clearance. On average, a doubling of previous theophylline concentrations occurs when zileuton is added to an existing theophylline regimen. Theophylline-related adverse effects occur more frequently in patients receiving concomitant zileuton.

Concomitant administration of zileuton and warfarin resulted in a 15% decrease in the clearance of R-warfarin but no change in the clearance of the more potent S-isomer. These pharmacokinetic changes were accompanied by a significant prolongation of prothrombin time. Prothrombin times or INRs should be monitored very carefully if zileuton is either added or discontinued during warfarin therapy.

Coadministration of drugs that could result in QT prolongation should zileuton compete for the same metabolic pathway, like cisapride and pimozide should be avoided when possible.

Zileuton is likely to inhibit the metabolism of alosetron, resulting in increased alosetron plasma concentrations. Coadministration of alosetron with zileuton has not been studied. Appropriate clinical monitoring is recommended if these drugs must be used concomitantly.

Adverse reactions: Most adverse reactions attributed to zileuton administration have been mild and self-limited. A flu-like syndrome (e.g., chills, fever, fatigue, myalgia) has been reported in 3.9% of healthy volunteers treated with zileuton compared to 1.9% treated with placebo. Other adverse events reported for zileuton vs. placebo in Phase I and Phase II trials involving 754 patients include: headache (25.4% vs. 21.7%), asthenia (11.1% vs. 8.4%), dizziness (5.9% vs. 4.3%), dyspepsia (5.2% vs. 3.7%), drowsiness (4.5% vs. 3.4%), abdominal pain (4.1% vs. 1.9%), insomnia (2.3% vs. 0.9%), pain (2.0% vs. 0.6%), and back pain (2.0% vs. 0.9%).

REQUIREMENTS FOR APPROVAL:

Patients must have failed or be intolerant to Singulair.

LENGTH OF APPROVAL:

1 year.