Extended-release tablets: 600 mg. (3)

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THE USE OF ZILEUTON EXTENDED-RELEASE TABLETS ARE CONTRAINDICATED IN PATIENTS WITH:

- 4 CONTRAINDICATIONS

Zileuton extended-release tablets are not indicated for use in the reversal of bronchospasm in acute asthma in adults and children 12 years of age and older.

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Zileuton extended-release tablets may be used in patients with active liver disease or repeated blood tests showing elevated liver function enzymes ≥3 times the upper limit of normal. (4, 5, 8.7)

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- 5.1 Hepatotoxicity

Most common adverse reactions (≥5%) included: sinusitis, nausea, and abdominal pain. In pediatric patients aged 6 to 17 years with active asthma, abdominal pain, nausea, and vomiting occurred in 51% of patients who received zileuton extended-release tablets compared to 0.7% in patients treated with placebo. The majority of elevations (82%) were transaminase elevations and occurred within the first 6 months of treatment.

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- 6.3 Adverse Reactions

In a clinical trial of 16 healthy male subjects who received zileuton immediate-release tablets 600 mg every 6 hours for 6 days, the motility of sperm cells and the percentage of normal sperm cells (i.e., those with normal morphology) decreased in a dose-related manner. There was an increase in the percentage of sperm cells with hypotonic morphology, which is an indicator of apoptosis. These effects were reversible with time. In a 12-week, placebo-controlled trial in patients with acute asthma, patients who received zileuton extended-release tablets for 12 weeks showed a decrease in the percentage of normal sperm cells compared to placebo, although the clinical significance of this finding is unknown.

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- 8.1 Pregnancy

Zileuton has the molecular formula C36H45ClN5O4. It is a white or almost white, crystalline powder, which is practically insoluble in water and soluble in ethanol. Zileuton is an inhibitor of the enzymes that catalyze the synthesis of leukotriene A4, the precursor of leukotrienes, which are mediators of inflammation and bronchoconstriction.

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- 12.3 Pharmacokinetics

Adverse reactions that may occur during administration of zileuton extended-release tablets in clinical trials included:

- 16 healthy male subjects who received zileuton immediate-release tablets 600 mg every 6 hours for 6 days, the motility of sperm cells and the percentage of normal sperm cells (i.e., those with normal morphology) decreased in a dose-related manner. There was an increase in the percentage of sperm cells with hypotonic morphology, which is an indicator of apoptosis. These effects were reversible with time. In a 12-week, placebo-controlled trial in patients with acute asthma, patients who received zileuton extended-release tablets for 12 weeks showed a decrease in the percentage of normal sperm cells compared to placebo, although the clinical significance of this finding is unknown.
What are the possible side effects of zileuton extended-release tablets?

Zileuton extended-release tablets can cause serious side effects.

**Liver problems.** Liver function enzymes and bilirubin can increase while taking zileuton extended-release tablets, and severe liver injury can occur. Sleep disorders and changes in your behavior can happen while you take zileuton extended-release tablets. Tell your healthcare provider if you have any sleep problems or changes in behavior.

• Keep all of your health care provider’s appointments and be sure to follow all of your health care provider’s instructions. Have your blood tests done as ordered to check your liver enzymes.

• Take your health care provider right away if you get any of the following signs or symptoms: pain on the right side of your abdomen (stomach area), nausea, tiredness, lack of energy, itching, yellow skin or yellow color in the whites of your eyes, dark urine, or “flu-like” symptoms.

Some of the most common side effects are:

- nose and throat irritation
- sneezing
- upper respiratory infection
- painful stomach
- headache
- diarrhea
- nausea
- dizziness

Allergic reactions can happen while taking zileuton extended-release tablets. Tell your health care provider right away if you get any of the following signs or symptoms:

• rash or hives
• muscle aches
• throat pain
• sleep problems, including headache, restlessness, or irritability
• joint pain
• chest pain

Tell your health care provider if you have any new or unusual symptoms that bother you or do not go away while taking zileuton extended-release tablets.

These are not all of the possible side effects of zileuton extended-release tablets. For more information, ask your health care provider or pharmacist.

How should I store zileuton extended-release tablets?

Store zileuton extended-release tablets between 68°F to 77°F (20° to 25°C).

Protect zileuton extended-release tablets from light and replace the cap each time after use.

Keep zileuton extended-release tablets and all medicines out of the reach of children.

General information about zileuton extended-release tablets. What are the ingredients in zileuton extended-release tablets?

Active ingredient: zileuton

Inactive ingredients: colloidal silicon dioxide, dicalcium phosphate, hydroxypropyl cellulose, hypromellose, iron oxide red, magnesium stearate, mannitol, microcrystalline cellulose, polyethylene glycol, pregelatinized starch and sodium starch glycolate.

Manufactured by:

Par Pharmaceutical

750 Chestnut Ridge Road

Chestnut Ridge, NY 10977

For more information go to www.parpharm.com or call 1-800-828-9393.

For more information about zileuton extended-release tablets, talk with your health care provider or pharmacist for information about zileuton extended-release tablets that is written for health professionals.

For more information go to www.parpharm.com or call 1-800-828-9393.

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