Zukast®

Tablet

Description

Zukast contains Zafirlukast which is a synthetic, selective peptide leukotriene receptor antagonist (LTRA) that acts as a prophylactic agent against inflammation in asthma.

Cysteinyl leukotriene production and receptor occupation have been correlated with the pathophysiology of asthma, including airway oedema, smooth muscle constriction, and altered cellular activity associated with the inflammatory process, which contribute to the signs and symptoms of asthma.

Indications

Zukast is indicated for the treatment of asthma.

Dosage and Administration

Zukast should be taken continuously. *Children under 7 years of age* : There is no clinical experience of the use of Zukast in children under 7 years of age until safety information is available. *Children over 7 years through 11 years of age*: The recommended dose of Zukast in this age group is 10 mg twice daily. *Adult and children aged 12 years and over* : The dosage is one 20 mg tablet twice daily. This dosage should not be exceeded. Higher doses may be associated with elevations of one or more liver enzymes consistent with hepatotoxicity. As food may reduce the bioavailability of Zafirlukast, Zukast should not be taken with meals. *Elderly* : The clearance of Zafirlukast is significantly reduced in elderly patients (over 65 years old), and C_{max} and AUC are approximately double than those of younger adults. However, accumulation of Zafirlukast is not greater than that seen in multiple dose trials conducted in adult subjects with asthma and the consequences of the altered kinetic in the elderly are unknown. Clinical experience with Zukast in the elderly (over 65 years) is limited and caution is recommended until further information is available.

No dosage adjustment is necessary in patients with mild renal impairment.

Contraindications

Zukast should not be given to patients who have previously experienced hypersensitivity to the product or any of its ingredients. Zukast is contraindicated in patients with a history of moderate or severe renal impairment. Zukast is contraindicated in patients with hepatic impairment or cirrhosis; it has not been studied in patients with hepatitis or in long term studies of patients with cirrhosis. Zukast is contraindicated in children under 7 years of age until safety information is available.

Precautions

Zukast should be taken regularly to achieve benefit, even during symptom free periods. Zukast therapy should normally be continued during acute exacerbations of asthma. Zukast does not allow a reduction in existing steroid treatment. As with inhaled steroids and hormones (disodium cromoglycate, nedocromil sodium), Zukast is not indicated for use in the reversal of bronchospasm in acute asthma attacks. Zukast has not been evaluated in the treatment of labile (brittle) or unstable asthma.

Cases of Churg Strauss syndrome have been reported in association with Zukast usage. A causal relationship has neither been confirmed nor refuted. If a patient develops a Churg Strauss syndrome type illness, Zukast should be stopped, a re-challenge test should not be performed and treatment should not be restarted.

Elevations in serum transaminases can occur during treatment with Zukast. These are usually asymptomatic and transient but could represent early evidence of hepatotoxicity.

If clinical symptoms or signs suggestive of liver dysfunction occur (e.g., nausea, vomiting, right upper quadrant pain, fatigue, lethargy, flu-like symptoms, enlarged liver, pruritus and jaundice), the serum transaminases, in particular serum ALT, should be measured and the patient managed accordingly. A decision to discontinue Zukast should be individualized to the patient's condition, weighing the risk of hepatic dysfunction against the clinical benefit of Zukast to the patient.

Drug Interactions

Zukast may be administered with other therapies routinely used in the management of asthma and allergy. Inhaled steroids, inhaled and oral bronchodilator therapy, antibiotics and antihistamines are examples of agents which have been co-administered with Zukast without adverse interaction.

Zukast may be administered with oral contraceptives without adverse interaction. Co-administration with Warfarin results in an increase in maximum prothrombin time by approximately 35%. It is therefore recommended that if Zukast is co-administered with Warfarin, prothrombin time should be closely monitored. The interaction is probably due to an inhibition by Zafirlukast of the cytochrome P450 2C9 enzyme system. In clinical trials co-administration with Theophylline resulted in decreased plasma levels of Zafirlukast, by approximately 30%, but with no effect on plasma Theophylline levels. However, during post-marketing surveillance, there have been rare cases of patients experiencing increased Theophylline levels when co-administered with Zafirlukast.

Co-administration with Terfenadine resulted in a 54% decrease in AUC for Zafirlukast, but with no effect on plasma Terfenadine levels. Co-administration with Acetylsalicylic acid (650 mg four times a day) may result in increased plasma levels of Zafirlukast, by approximately 45%.

Co-administration with Erythromycin will result in decreased plasma levels of Zafirlukast, by approximately 40%. The clearance of Zafirlukast in smokers may be increased by approximately 20%.

Side Effects

Effect on ability to drive or operate machinery : There is no evidence that Zukast affects the ability to drive and use machinery. Administration of Zukast in clinical trials against placebo has been associated with headache (9.9% vs. 9.0%) or gastrointestinal disturbance (nausea 2.6% vs. 2.2%, vomiting 1.2% vs. 1.0%, diarrhoea 2.3% vs. 1.8%, abdominal pain 1.6% vs. 1.2%). These symptoms are usually mild and do not necessitate withdrawal from therapy. During post-marketing experience, bruising, bleeding disorders, including menorrhagia (rare), thrombocytopaenia and agranulocytosis (very rare) have also been reported.

Hypersensitivity reactions, including urticaria and angio-oedema have been reported. Rashes, including blistering, have also been reported. The above events have usually resolved during continued treatment or following cessation of therapy.

Infrequently, elevated serum transaminase levels have been observed in clinical trials against placebo with Zafirlukast (increased AST 1.0% vs. 0.9%, increased AST 0.6% vs. 0.6%); at recommended doses the incidence was equivalent to placebo. Rarely the transaminase profile has been consistent with drug-induced hepatitis, which resolved following cessation of Zukast therapy. During post-marketing experience there have been rare reports of hepatitis, with or without elevated bilirubin levels. These cases were usually reversible.

In placebo controlled clinical trials, an increased incidence of infection has been observed in elderly patients given Zafirlukast (7.8% vs. 1.4%). Infections were usually mild, predominantly affecting the respiratory tract.

Use in Special Populations

Pregnancy and lactation : The safety of Zukast in human pregnancy has not been established. In animal studies, Zafirlukast did not have any apparent effect on fertility and did not appear to have any teratogenic or selective toxic effect on the foetus. The potential risks should be weighed against the benefits of continuing therapy during pregnancy and Zukast should be used during pregnancy only if clearly needed.

Lactation : Zafirlukast is excreted in human breast milk. Zukast should not be administered to nursing mothers.

Commercial Pack

Zukast® Tablet : Box containing 10 tablets in 1 x 10's Alu-Alu form pack, each tablet contains Zafirlukast INN 20 mg.