Maxlax® 2mg 4mg
(Tizanidine) Tablets USP

میکس لیکس

Description
Maxlax (Tizanidine) is a central alpha2-adrenergic agonist with chemical name 5-chloro-4-(2- imidazolin-2-ylamino)-2,1, 3-benzothiadiazole monohydrochloride and molecular formula $C_9H_8ClN_5S$-HCl.

Composition
Maxlax 2mg Tablets
Each tablet contains:
Tizanidine (as HCl) USP.....2mg

Maxlax 4mg Tablets
Each tablet contains:
Tizanidine (as HCl) USP.....4mg

Pharmaceutical form: Tablets for oral administration
Clinical particulars
Therapeutic indications Tablets
Painful muscle spasms: Associated with static and functional disorders of the spine (cervical and lumber syndromes).
Following surgery, e.g. for herniated intervertebral disc or osteoarthritis of the hip.
Spasticity due to neurological disorders: Eg. multiple sclerosis, chronic myelopathy, degenerative spinal cord diseases, cerebrovascular accidents, and cerebral palsy.
Posology and method of administration
Relief of painful muscle spasms: 2 to 4 mg three times daily in tablet form. In severe cases an extra dose of 2 or 4 mg may be taken at night.
Spasticity due to neurological disorders: The dosage should be adjusted to the needs of the individual patient. The initial daily dose should not exceed 6 mg given in 3 divided doses. It may be increased stepwise at half weekly or weekly intervals by 2-4mg. The optimum therapeutic response is generally achieved with at daily dose of between 12 & 24mg, administrated in 3 or 4 equally spaced doses the daily doses of 36mg should not be exceeded.
Use in Children: Experience in children is limited and the use of Maxlax in this patient population is not recommended.
Use in Elderly: Experience with the use of Maxlax in the elderly is limited pharmacokinetic data suggest that renal clearance in the elderly may in some cases be significantly decreased. Caution is therefore indicated when using Maxlax in elderly patients.
Contraindications: Known hypersensitivity to tizanidine or any component of the formulation. Significantly impaired hepatic function. Concomitant use of tizanidine with fluvoxamine or ciprofloxacin is contraindicated.
Special warning & precautions for use: Concomitant use of tizanidine with CYP1A2 inhibitors is not recommended since hepatic dysfunction has been reported in association with tizanidine but rarely at daily dose upto 12gm, it is recommended that liver function test should be monitored monthly for the 1st 4-months in patients receiving dose of 12mg and higher and in patients to develop clinical symptoms suggestive of hepatic dysfunction such as unexplained nausea, anorexia or tiredness. Treatment with Maxlax should not be discontinued if serum levels of SGPT of SGOT are persistently above 3-times the upper limit of the normal range.
Special precaution for use: In patients with renal insufficiency (creatinine clearance <25ml /min), it is recommended to start treatment at 2mg once daily. Dosage increases should be done in small steps according to tolerability and efficacy. if efficacy has to be improved, it is advisable to increase first the once-daily dose before increasing the frequency of administration.
For Maxlax tablets: Maxlax tablets contain lactose. The medicine is not recommended in patients with rare hereditary problem of galactose intolerance, of severe lactase deficiency or of glucose galactose malabsorption.
Interaction with other medicinal products and other forms of interaction: Concomitant use of tizanidine with fluvoxamine or ciprofloxacin, both CYP4501A2 inhibitors in man, is contraindicated. Concomitant use of tizanidine with fluvoxamine or ciprofloxacin resulted in a 33-fold and 10-fold increase in tizanidine AUC, respectively. Clinically significant & prolong hypotension may result along with somnolence, dizziness and decrease psychomotor performance. Co-administration of tizanidine with other inhibitors of CYP1A2 such as some antiarrhythmics (amiodarone, mexiletine, propafenone) cimetidine, some fluoroquinolones (enoxacin, pefloxacin, norfloxacin) rofecoxaib, oral contraceptives and ticlopidine is not recommended.
Concomitant use of Maxlax with antihypertensives, including diuretics may occasionally cause hypotension and bradycardia. Alcohol and sedatives may enhance the sedative action of **Maxlax**
Pregnancy and lactation
Pregnancy: Tizanidine has no teratogenic effects in rats and rabbits. As there have been no controlled studies in pregnant women, how ever it should not be used during pregnancy unless the benefit clearly outweigh the risks.
Lactation: Although only small amount of tizanidine are excreted in animal milk, tizanidine should not be taken by women who are breast feeding.
Effect on ability to drive and use machines: Patients experiencing somnolence or dizziness should refrain from activity requiring a high degree of alertness. e.g: driving a vehicle or operating machine.
Undesirable effects: Adverse reaction are ranked under heading of frequency, the most frequent 1st, using the following convention very common (>_ 1/10) common (>_ 1/100),, < 1/10); uncommon (>_ 1/1,000, < 1/100); rare (>_ 1/10,000, < 1/1,000) very rare (< 1/10,000), including isolated reports. Within each frequency grouping, adverse reactions are ranked in order of decreasing seriousness.
Psychiatric disorders: Rare: Hallucination, insomnia, sleep disorder
Nervous system disorders: Common: Bradycardia
Vascular disorders
Common: Hypotension

Gastrointestinal disorders
Common: Dry mouth
Rare: Nausea, gastrointestinal disorder
Hepatobiliary disorders: Very rare: Hepatitis
Musculoskeletal and connective tissue disorders
Rare: Muscular weakness
General disorders and administration site conditions
Common: Fatigue
Investigations: Common: Blood pressure decrease
Rare: Transaminase increase With low doses, such as those recommended for the relief of painful muscle spasm, somnolence, fatigue, dizziness, dry mouth, blood pressure decrease, nausea, gastrointestinal disorder and Transaminase increase have been reported, usually as mild and transient adverse reactions. With the higher doses recommended for the treatment of Spasticity, the adverse reactions reported with low doses are more frequent and more pronounced, but seldom severe enough to require discontinuation of treatment.

Overdose: In the few reports of tizanidine covered received, recovery was uneventful, including by a patient who ingested 400mg tizanidine.
Symptoms: Nausea, vomiting, hypotension, dizziness, somnolence, miosis, restlessness, respiratory distress, coma.
Treatment: It is recommended to eliminate the ingested drug by repeated administration of high doses of activated charcoal. Forced diuresis is expected to accelerate the elimination of Tizanidine. Further treatment should be symptomatic.
Pharmacological properties
Pharmacodynamic properties: Pharmacotherapeutic group: Muscle relaxants, other centrally acting agents; ATC code: M03B X02. Tizanidine is a centrally acting skeletal muscle relaxant. Its principal site of action is the spinal cord, where the evidence suggests that, by stimulating presynaptic alpha2-receptors, it inhibits the release of excitatory aminoacids that simulate N-methyl-D-aspartate (NMDA) receptors. Polysynaptic signal transmission at spinal interneuron level, which is responsible for excessive muscle tone, is thus inhibited and muscle tone reduced. In addition to its muscle-relaxant properties, tizanidine also exerts a moderate central analgesic effect. Maxlax is effective in both acute painful muscle spasms and chronic Spasticity of spinal and cerebral origin. It reduces resistance to passive movements;alleviates spasms and clonus, and may improve voluntary strength.
Pharmacokinetic properties
Absorption and bioavailability: Tizanidine is rapidly and almost completely absorbed, reaching peak plasma concentration approximately-1 hour after dosing Mean absolute bioavailability is about 34% due to extensive first-pass metabolism.
Distribution: Mean steady-state volume of distribution (Vss) following i.v. administration is 2.6 L/kg. Plasma protein binding is 30%. Tizanidine has linear pharmacokinetic parameters (Cmax and AUC) which enables reliable prediction of plasma levels following oral administration. The pharmacokinetic parameters of tizanidine are not affected by gender.
Biotransformation: The drug has been shown to be rapidly and extensively metabolized by the liver. Tizanidine is mainly metabolized by cytochrome P450 1A2 in vitro. The metabolites appear to be inactive.
Elimination: Tizanidine is eliminated from the systemic circulation with a mean terminal half-life of 2 to 4 hours. Excretion is primarily via the kidneys (approximately 70% of dose) in the form of metabolites with unchanged drug accounting for only about 2.7% of urinary recovery.
Characteristics in special patient populations: In patients with renal insufficiency (creatinine clearance<25 mL/min), maximal mean plasma levels were found to be twice as high as in normal volunteers, and the terminal half-life was prolonged to approximately 14 hours, resulting in much higher (approximately 6-fold on average) AUC values.
Effect of food: Concomitant food intake has no relevant influence on the pharmacokinetic profile of tizanidine. Although Cmax is about one-third higher, this is not thought to be of any clinical relevance, and absorption (AUC) is not significantly affected.
Preclinical safety data: Acute toxicity: The acute toxicity of tizanidine is of a low order. After single doses>40mg/kg in animals, signs of overdosage were seen related to the drug's pharmacological action.
Chronic and subchronic toxicity: In a 13-week oral toxicity study in rats given average daily doses of 1.7, 8 and 40 mg/kg, the major findings were related to CNS stimulation (e.g. motor excitation, aggressiveness, tremor, and convulsions), and occurred mainly at the highest dose level. ECG changes and CNS effects were observed at daily doses of 1 mg/kg and higher in dogs in a 13-week study with 0.15, 0.45 and 1.5 mg/kg/day. These represent exaggerated pharmacological effects. Transient increases in SGPT seen at daily doses of 1 mg/kg and above were not related to histopathological findings but indicate that the liver is a potential target organ.
Mutagenicity: No evidence of mutagenic potential was found in in vitro, in vivo, or cytogenetic assays,
Carcinogenicity: No indication of carcinogenic potential was seen in rats or mice given doses of up to 9mg/kg/days and 16mg/kg/day, respectively, in the feed.
Reproductive toxicity: No embryotoxic or teratogenic effects were observed in pregnant rats and rabbits at dose levels up to 100mg/kg/day. Increased prenatal mortality due to prolongation of gestation and dystocia occurred at dose levels of 10 and 30 mg/kg/day in female rats doses at 3, 10 and 30 mg/kg/day from before mating through to lactation or from late pregnancy until weaning of the young.
Instructions: Store below 30°C. Protect from heat, light & moisture. Keep all medicine out of reach of children.
Presentation: Maxlax (Tizanidine) 2mg & 4mg tablets are available in Alu-Alu Blister Pack of 1x10's tablets.

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