MaxLax®
(TIZANIDINE)
Tablets USP

میکس لیکس
(ٹیزانیڈین)
ٹیبلٹس
۲ ملی گرام
۴ ملی گرام

QUALITATIVE AND QUANTITATIVE DESCRIPTION

Maxlax 2mg Tablet
Each tablet contains:
Tizanidine (as HCl).....2mg
USP Specification

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

DESCRIPTION

Tizanidine belongs to a group of medicines called skeletal muscle relaxants. This medicine is used to relieve the stiffness and restriction of muscles resulting from multiple sclerosis, injury or diseases of the spinal cord.

INDICATIONS

Spasms of the skeletal muscles

- Associated with static and functional disorders of the spine (cervical and lumbar syndromes)
- After surgical interventions on the musculoskeletal system, e.g. herniated disc or joint disorders of the hip.

Spasticity due to neurological disorders

- Multiple sclerosis, chronic myelopathy, degenerative spinal cord disease, cerebrovascular accidents and cerebral palsy.

DOSAGE AND ADMINISTRATION

Spasms of the skeletal muscles
The recommended dose is 2-4 mg three times daily.
In severe cases, an extra dose of 2-4 mg may be given, preferably late in the evening to reduce the sedative effect.

Spasticity due to neurological disorders
The initial daily dose should not exceed 6 mg in three divided doses. This dose may be increased in steps by 2-4 mg at intervals of half or full week.
The total daily dose should not exceed 36 mg.

USE IN SPECIFIC POPULATIONS

Paediatric population
The safety and efficacy of tizanidine in children and adolescents under 18 years have not been established. Limited data are available. Tizanidine cannot be recommended for the use in children and adolescents

Elderly
Experience with tizanidine in the elderly is limited.
In this patient group the starting dose should be as low as possible and it should be increased in small increments, according to tolerability and efficacy.

Renal impairment
In patients with renal impairment (CRCL < 25 mL/min) treatment should be started with 2 mg once daily with slow titration to achieve the effective dose. Dosage increases should be in increments of no more than 2 mg according to tolerability and effectiveness. If efficacy has to be improved, it is advisable to slowly increase the once-daily dose before increasing the frequency of administration. Renal function should be monitored as appropriate in these patients

Hepatic impairment
Tizanidine is contraindicated in patients with severe hepatic impairment
Tizanidine should be used with caution in patients with mild and moderate he-

patic impairment. The starting dose should be as low as possible and it should be increased in small increments, according to tolerability and efficacy.

Pregnancy
The safety of tizanidine in pregnancy has not been established. Therefore, tizanidine should not be used in pregnant women unless the benefit clearly outweighs the risk.

Breast-feeding
The safety of tizanidine in breast-fed infants of mothers receiving tizanidine is not known. Therefore, tizanidine should not be used in nursing mothers unless the benefit clearly outweighs the risk.

CLINICAL PHARMACOLOGY

Pharmacodynamics
The exact mechanism of action of tizanidine has not been fully clarified. It is believed that the pharmacodynamic effects of tizanidine are primarily linked to its α2- adrenergic agonist properties, although its imidazoline receptor binding may play a role. The predominant effect of tizanidine appears to occur presynaptically in the spinal cord by reducing release of the excitatory amino acids glutamate and aspartate from the presynaptic terminal of spinal interneurons. There is some evidence of postsynaptic action on excitatory amino acid receptors.
In humans, tizanidine reduces pathologically increased muscle tone, including resistance to passive movements and alleviates painful spasms and clonus.

Pharmacokinetics
Absorption Tizanidine is rapidly and almost completely absorbed. The maximum plasma concentration is reached approximately 1 hour after administration. The mean absolute bioavailability is approximately 34% because of the strong first-pass metabolism. The average maximum plasma concentration (Cmax) of tizanidine is 12.3 ng/mL after a single administration and 15.6 ng/mL after repeated administration of 4 mg tizanidine. Concomitant use of food has no relevant influence on the pharmacokinetic profile of tizanidine. Food increases Cmax by about one third, but has no effect on the extent of absorption (AUC). The increase in Cmax is not considered clinically relevant.
Distribution Mean steady-state volume of distribution (VSS) following i.v. administration is 2.6 L/kg. Tizanidine is 30% bound to plasma proteins. Tizanidine has linear pharmacokinetics in the dose range of 1-20 mg.
Biotransformation Tizanidine undergoes rapid and extensive metabolism in the liver (about 95%). Tizanidine is mainly metabolised in vitro by CYP1A2. The metabolites appear to be inactive. Elimination The elimination half-life of tizanidine from plasma is 2 to 4 hours. The metabolites are primarily excreted via the renal route (approx. 70% of the dose). Only a small part of the active substance is excreted unchanged via the urine (approx. 4.5%).

CONTRAINDICATIONS

- Hypersensitivity to the active substance or to any of the excipients
- Severe hepatic impairment
- Concomitant use of tizanidine with potent CYP1A2 inhibitors such as fluvoxamine or ciprofloxacin

WARNINGS AND PRECAUTIONS

Hypotension
Tizanidine is an α2-adrenergic agonist that can produce hypotension. The chance of significant hypotension may possibly be minimised by titration of the dose and by focusing attention on signs and symptoms of hypotension prior to dose advancement.

Withdrawal syndrome
Withdrawal adverse reactions include rebound hypertension, tachycardia, and

hypertonia. To minimise the risk of these reactions, particularly in patients who have been receiving high doses (20 to 28 mg daily) for long periods (9 weeks or more) or who may be on concomitant treatment with narcotics, the dose should be decreased slowly (2 to 4 mg per day).

Hepatic impairment
Since hepatic dysfunction has been reported in association with tizanidine, but rarely at daily doses up to 12 mg, it is recommended that liver function tests should be monitored monthly for the first four months in patients receiving doses of 12 mg and higher and in patients who develop clinical symptoms suggestive of hepatic dysfunction, such as unexplained nausea, anorexia or tiredness. Treatment with tizanidine should be discontinued if serum levels of SGPT (serum glutamic-pyruvic transaminase) and/or SGOT (serum glutamic-oxaloacetic transaminase) are persistently above three times the upper limit of the normal range. Tizanidine should be discontinued in patients with symptoms compatible with hepatitis or where jaundice occurs.

Cardiovascular, hepatic or renal disorders
Caution is required in patients with cardiovascular disorders, coronary artery disease, or renal or hepatic disorders. Regular clinical laboratory and ECG monitoring is recommended during treatment with tizanidine.

Renal impairment
Tizanidine should be used with caution in patients with renal insufficiency (creatinine clearance < 25 mL/min), as clearance is reduced by more than 50%. In these patients, during titration, the individual doses should be reduced. If higher doses are required, individual doses rather than dosing frequency should be increased. These patients should be monitored closely for the onset or increase in severity of the common adverse events (dry mouth, somnolence, asthenia, and dizziness) as indicators of potential overdose.
Sedation
Tizanidine can cause sedation, which may interfere with everyday activity. In multiple dose studies, the prevalence of patients with sedation peaked following the first week of titration and then remained stable for the duration of the maintenance phase of the study.

Hallucinosis/Psychotic-like symptoms
Tizanidine use has been associated with hallucinations. Discontinuing should be considered in patients who develop hallucinations.
Hypersensitivity reactions
Tizanidine can cause anaphylaxis. Signs and symptoms including respiratory compromise, urticaria, and angioedema of the throat and tongue have been reported. Patients should be informed of the signs and symptoms of severe allergic reactions and instructed to discontinue tizanidine and seek immediate medical care if they occur.

Tizanidine contains lactose
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

ADVERSE REACTIONS
Many adverse effects have been found to be dose related and slow titration of doses appears to reduce the frequency of occurrence.
With low doses, such as those recommended for the relief of painful muscle spasms, somnolence, fatigue, dizziness, dry mouth, decreased blood pressure, nausea, gastrointestinal disturbances, and increased hepatic enzymes 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.

PRESENTATION

Maxlax (Tizanidine) 2mg tablets are available in ALU-ALU blister of ten tablets (10's) in a carton.
Maxlax (Tizanidine) 4mg tablets are available in ALU-ALU blister of ten tablets (10's) in a carton.

INSTRUCTIONS

Store below 30°C. Protect from heat, light and moisture. Keep all medicines out of the reach of children.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

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