For The Use of a Psychiatrist Only

NEXTRIL 50

(Tofisopam Tablets 50mg)

COMPOSITION

Each uncoated tablet contains:
Tofisopam JP…….50mg
Excipients …….. q.s.

DOSAGE FORM

Uncoated tablet

INDICATION

For the treatment of anxiety and depression.

DOSE AND METHOD OF ADMINISTRATION

Dose

Adults

It is essential to determine the dosage individually and it depends on the patient, the severity of the disease, and the tolerance of the drug.

A typical dosage for adults is: 1 to 2 tablets 1 to 3 times per day (a total of from 50 to 300 mg per day).

Paediatric population

Has not been established safety and efficacy of tofisopam in children and adolescents under 18 years of age.

Method of administration

Oral administration

USE IN SPECIAL POPULATIONS

Pregnancy

Tofisopam can cross the placenta. Animal studies do not indicate direct effects with respect to reproductive toxicity.

As a precaution, it is advisable to avoid the use of tofisopam during the first trimester pregnancy. In the later period of pregnancy should be tofisopam is administered based on careful assessment of the health risks and benefits of treatment.

Breast-feeding

Tofisopam is excreted into breast milk.

Tofisopam should not be used during breastfeeding.

CONTRAINDICATIONS

- Hypersensitivity to benzodiazepines or other or any of the other substances of tablet.
- Decompensated respiratory insufficiency.
- Sleep apnea history. Coma history.
- Concomitant administration tofisopam with tacrolimus, sirolimus and cyclosporine is contraindicated.

WARNINGS AND PRECAUTIONS

It is not recommended during the first trimester of pregnancy and during lactation.

Administration of particular caution is required in case of non-decompensated chronic respiratory insufficiency or in patients with a history of acute respiratory insufficiency.

Treatment of elderly and mentally ill patients or patients with kidney or liver disease also requires caution because unwanted effects in such cases more frequent.

When administered together with substances central nervous system depressants (alcohol, antidepressants, antihistamines, sedative hypnotics, neuroleptics, opioid analgesics, general anesthetics), Tofisopam may potentiate the effects of other medicinal products.

Tofisopam is not recommended for chronic psychosis, and obsessive compulsive phobic disorders. Treatment with tofisopam lowers inhibitions, therefore, may increase the risk of suicide or aggressive behavior. Therefore tofisopam monotherapy is not recommended for the treatment of depression and depression associated with anxiety. Treatment of patients with personality disorders also requires special care.

Particular caution is advised when administering tofisopam in patients with organic disorders of brain (e.g. atherosclerosis).

In epileptic patients, the preparation can cause seizures.

Tofisopam is not recommended for narrow-angle glaucoma.

Effects on ability to drive and use machines

Tofisopam does not cause drowsiness or depression, nor does it affect attention and concentration ability. Nevertheless, it should be taken into consideration that high doses can cause hyperactivity and aggressiveness, therefore limitations depend on individual patient response.

DRUG INTERACTIONS

In the case of co-administration with tofisopam may increase plasma concentrations products metabolized by CYP3A4. Therefore, co-administration of tacrolimus, tofisopam, sirolimus and cyclosporine is contraindicated.

When co-administered with drugs central nervous system depressants (analgesics, total anesthetics, antidepressants, H_1-antihistaminics, sedative hypnotics, neuroleptics), these preparations mutually enhance their effects (sedation, respiratory depression).

Inducer (alcohol, nicotine, barbiturates, antiepileptics, etc.) may increase tofisopam metabolism, which may decrease the plasma concentrations and therapeutic efficacy.

Certain antifungals (ketoconazole, itraconazole) may increase the plasma concentration of tofisopam by inhibition of its metabolism in the liver.

Some antihypertensives (clonidine, calcium channel blockers) may intensify the effects of tofisopam. Beta-receptors could inhibit the metabolism of tofisopam, but this interaction is not significant.

Tofisopam may increase plasma concentrations of digoxin.

Benzodiazepine compounds can alter the anticoagulant activity of warfarin.

Chronic administration of disulfiram can inhibit the metabolism tofisopam.

Antacids can have different effects on the absorption tofisopam. Cimetidine and omeprazole inhibited tofisopam metabolism.

Oral contraceptives may inhibit the metabolism of tofisopam.

Tofisopam reduces the depressant effects of alcohol on the CNS.

UNDESIRABLE EFFECTS

Classification of undesirable effects is based on the following convention: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (from the available data do not specify).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. There are no adequate data on cancer incidence.

Metabolism and nutrition disorders: loss of appetite.

Psychiatric disorders: very rarely confusion, restlessness, irritability, tension.

Nervous system disorders: very rarely tofisopam can cause seizures in epileptic patients. Headache, insomnia

Respiratory, thoracic and mediastinal disorders: respiratory depression.

Gastrointestinal: vomiting, nausea, constipation, flatulence, dry mouth.

Hepatobiliary disorders: very rarely cholestatic jaundice.

Skin and subcutaneous tissue disorders: rash, scarlatiniform rash, itching.
Disorders of the musculoskeletal system and connective tissue disorders: muscle tension, muscle aches.

OVERDOSE
Symptoms
The CNS depression only occurs if swallowed extreme doses (50-120 mg / kg body weight). Such doses can cause vomiting, confusion, coma, respiratory depression and seizures.

Treatment of overdose
Gastric lavage may be beneficial, but is not appropriate to induce vomiting due to CNS depression.

To inhibit or reduce the absorption of tofisopam, activated charcoal and laxatives may be used.

It is recommended to monitor vital functions and symptomatic treatment is consistent with the results monitoring. Severe respiratory depression can be applied to support respiration. Application of stimulants of the central nervous system is not recommended. Hypotension can be treated with intravenous supplementation fluids having the patient in trendelenburg position, or if these methods are ineffective administration of dopamine or norepinephrine.

Tofisopam is not dialyzable, forced diuresis is of no benefit.

Flumazenil is a specific, benzodiazepine antagonist, but there is regarding the use of tofisopam. Use of this product is rather reserved for emergent cases.

PHARMACODYNAMIC AND PHARMACOKINETIC PROPERTIES
Pharmacodynamic properties
Pharmacotherapeutic group: Anxiolytics, benzodiazepine derivatives.
ATC code: N05BA23

Mechanism of action
Tofisopam is short-acting, weak anxiolytic with a wide therapeutic index.
The mechanism of action is not precisely known. Tofisopam differs from classical 1,4-benzodiazepines, namely not only the chemical structure, but also goes on its pharmacological properties.

Pharmacodynamic effects
Tofisopam can effectively treat vegetative symptoms, fatigue and apathy associated with anxiety. Unlike other benzodiazepines,tofisopam has no hypnotic sedative, muscle relaxant and anticonvulsant effects and does not impair psychomotor, cognitive and memory function, also has mildly stimulating effect. It does not have muscle relaxant activity, and it is useful in the treatment of patients with neuromuscular diseases in which the administration of classical benzodiazepines contraindicated.

When using tofisopam, even after prolonged use, it develops somatic or psychological dependence.

Pharmacokinetic properties

Absorption

Tofisopam is rapidly absorbed from the gastro intestinal tract, the maximum plasma concentration reached within about 1-1.5 hours.

Distribution in the body

About 50% of circulating tofisopam is bound to plasma proteins.

Biotransformation

After absorption tofisopam is subject to intense first-pass metabolism in the liver. The primary metabolic path is demethylation.

Elimination

About 60% of the dose is excreted as metabolites in urine and 40% in feces. The half life is 6-8 hours.

Preclinical safety

Preclinical data based on conventional studies of safety pharmacology, toxicity repeated administration, genotoxicity, carcinogenicity, and reproductive and developmental toxicity reveal no special hazard for humans.

EXPIRY DATE

Do not use later than the date of expiry.

PACKAGING INFORMATION

Nextril 50 is available as blister strips of 10 Tablets.

STORAGE AND HANDLING INSTRUCTIONS

STORE IN A COOL, DRY PLACE. Keep all medicines out of reach of children.

MARKETED BY

torrent PHARMA

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