

Stresam®

International Non-Proprietary Name (INN): Etifoxine

Dosage Form: capsules (50 mg)

Structure: 1 capsule contains:

Active ingredient: Etifoxine hydrochloride 50 mg.

Excipients: Lactose monohydrate, talc, microcrystalline cellulose, anhydrous colloidal silicon dioxide, magnesium stearate.

Capsule shell composition: titanium dioxide, gelatin, indigo carmine.

Description:

Smooth, shiny gelatin capsules with a white body and a blue cap. The content is powder of white or white with a slight yellowish tint color.

Pharmacological classification: anxiolytic (tranquilizer)

ATC code: N05BX03

Pharmacological action: anxiolytic.

Pharmacodynamics:

Etifoxine hydrochloride is a benzoxazin derivative. As an anxiolytic, etifoxine has an autonomous controlling effect. In vitro and in vivo studies of rats and mice have shown that anxiolytic activity of etifoxine is driven by the dual mechanism of its action (direct and indirect) on GABA-A receptors, which improves GABAergic impulse transmission. When there is a direct effect on GABA-A receptor by allosteric modulation, etifoxine binds predominantly with $\beta 2$ or $\beta 3$ receptor subunits; studies have shown that etifoxine binds with GABA-A receptor at a binding site other than benzodiazepines. Indirect effect is provided by increasing the synthesis of neurosteroids (by

activation of mitochondrial translocator protein), such as allopregnanolone, which is also a positive allosteric modulator of the GABA-A receptor.

Pharmacokinetics:

Absorption: Stresam is quickly absorbed from the gastrointestinal tract. Maximum concentration in blood is reached within 2-3 hours.

Distribution: Stresam penetrates through the placental barrier.

Metabolism: Stresam metabolizes quickly in the liver until it forms several metabolites. One of the metabolites – diethyl-etifoxine – is active.

Excretion: Etifoxine's half-life is around 6 hours; the active metabolite's half-life is 20 hours. It is mainly excreted in urine in the form of metabolites and in small amounts in the unchanged form. It is also excreted in bile.

Intended uses:

Stresam is used for treatment of psychosomatic signs of anxiety, fear, inner tension, increased irritability and decreased mood (including associated with somatic diseases and especially diseases of cardiovascular nature).

Contraindications:

Hypersensitivity to the active ingredient or other components of the drug, shock state, myasthenia and severe disorders of liver and/or kidney function. Due to the presence of lactose in the drug, it should not be used if the patient suffers from galactosemia, glucose-galactose malabsorption syndrome, and lactase deficiency.

It is not recommended to use the drug at the age below 18 years old as well as during pregnancy or lactation.

Dosage and administration:

Ingest orally with a small amount of water. The dosage of the drug is determined by the doctor individually, depending on the

patient's condition. The usual dosage is 1 capsule three times a day, or 2 capsules twice a day (150-200 mg/day). The length of the treatment varies from several days to 4-6 weeks, depending on the patient's condition.

Side effects (rare):

Definition of the frequency of adverse events: rarely ($\geq 1 / 10,000$ and $< 1/1000$), very rarely ($< 1/10,000$) in decreasing order of frequency.

Central nervous system disorders: (rare) insignificant drowsiness during the first days of taking the drug. It usually disappears on its own in the process of treatment.

Skin and subcutaneous tissue disorders: (rare) maculopapular rash, erythema multiform, itching, facial edema; (very rare) urticaria, Quincke's edema; (frequency unidentified) anaphylactic shock, drug-induced hypersensitivity syndrome with eosinophilia, Stevens-Johnson syndrome, leukocytoclastic vasculitis.

Hepatobiliary disorders: (frequency unidentified) hepatitis, cytolytic hepatitis.

Reproductive system and breast disorders: (frequency unidentified) metrorrhagia among women who take oral contraceptive.

Gastrointestinal tract disorders: (frequency unidentified) lymphocytic colitis.

Overdose:

Symptoms: torpidity, excessive drowsiness. Treatment: if necessary, symptomatic treatment is provided. There is no specific antidote.

Interaction with other drugs:

Potentiates effects of drugs that inhibit the central nervous system such as opioid analgesics, barbiturates, opiates, antihistamines, neuroleptics, etc.

Also potentiates the effects of alcohol.

Pregnancy and lactation:

It is not recommended to take Stresam during pregnancy. If pregnancy is detected during the treatment, you should consult your doctor about the continuation of the treatment. It is not recommended to take Stresam during lactation.

Influence on the ability to drive vehicles and operate mechanisms:

Due to the risk of drowsiness, during the treatment you should avoid driving vehicles or engaging into activity, which requires increased attention such as operating various mechanisms.

Special precaution:

In case of skin or allergic reactions or liver complications administration of Stresam should be discontinued.

If you missed taking the drug, do not double the dose at the next intake.

IT IS NOT RECOMMENDED TO TAKE THE DRUG ALONG WITH ALCOHOL.

DO NOT EXCEED THE DOSE PRESCRIBED BY YOUR DOCTOR.

Terms of release from pharmacy: on prescription

Storage conditions: store at temperatures of 15-25°C. Keep out of reach of children.

Shelf life: 3 years. Do not use beyond the expiration date.

Country of manufacture: France