NEUXAM
(ALPRAZOLAM) USP

TABLETS

1- COMPOSITION

- **NEUXAM TABLETS 0.25 mg**

Each tablet contains Alprazolam (USP).....0.25 mg

- **NEUXAM TABLETS 0.5 mg**

Each tablet contains Alprazolam (USP).....0.5 mg

- **NEUXAM TABLETS 1 mg**

Each tablet contains Alprazolam (USP).....1 mg

2- PROPERTIES

Alprazolam is chemically 8-ChIoro-1-methyl-6-phenyl-4H-s-triazolo [4,3-α] [1,4] benzodiazepine

3- PHARMACODYNAMICS

NEUXAM Tablets contain a triazolobenzodiazepam. The benzodiazepines have qualitatively similar properties: anxiolysis, hypnosedation, myorelaxation, anticonvulsion. There are, however, quantitative differences in their pharmacodynamic properties that have led to varying patterns of therapeutic application. Currently, there is a general agreement that the action of benzodiazepines is a result of the potentiation of the neural inhibition that is mediated by gamma-aminobutyric acid (GABA).

4- PHARMACOKINETICS

Following oral administration, peak concentrations in the plasma occur in 1 to 2 hours following administration. The mean half-life of Alprazolam is 12-15 hours. Alprazolam is mainly oxidized. The predominant metabolites are alpha-hydroxy-Aiprazolam and a benzophenone derived from Alprazolam. Plasma levels of these metabolites are extremely low. The biological activity of alpha-hydroxy-Alprazolam is approximately one-half that of Alprazolam. Their half-lives appear to be of the same order of magnitude as that of Alprazolam. The benzophenone metabolite is essentially inactive.

Alprazolam and its metabolites are excreted primarily in the urine. In vitro, Alprazolam is bound (80%) to human serum protein.

5- INDICATIONS

NEUXAM (alprazolam) tablets are indicated for the treatment of:

- ANXIETY STATES (ANXIETY NEUROSES)

Symptoms which occur in such patients include anxiety, tension, agitation, insomnia, apprehension, irritability and/or autonomic hyperactivity resulting in a variety of somatic complaints.

- MIXED ANXIETY-DEPRESSION

Symptoms of both anxiety and depression occur simultaneously in such patients.

- NEUROTIC OR REACTIVE DEPRESSION

Such patients primarily exhibit a depressed mood or a pervasive loss of interest or pleasure. Symptoms of anxiety, psychomotor agitation and insomnia are usually present. Other characteristics include appetite disturbances, changes in weight, somatic complaints, cognitive disturbances, decreased energy, feeling of worthlessness or guilt or thoughts of death or suicide.

- ANXIETY STATES, MIXED ANXIETY-DEPRESSION OR NEUROTIC DEPRESSION

Associated with other diseases such as the chronic phase of alcohol withdrawal and functional or organ disease particularly certain gastrointestinal, cardiovascular or dermatological disorders.

- PANIC RELATED DISORDERS

NEUXAM is indicated in the treatment of panic disorder with or without some phobic avoidance. NEUXAM is also indicated for the blocking or attenuation of panic attacks and phobias in patients who have agoraphobia with panic attacks.

The effectiveness of NEUXAM in the treatment of anxiety, anxiety associated with depression and neurotic (reactive) depression for long term use exceeding six months has not been established by systematic clinical trials; however, patients with panic-related disorders have been effectively treated for up to eight months. The physician should periodically reassess the usefulness of the drug for the individual patient.

6- DOSAGE AND ADMINISTRATION

The optimum dosage of NEUXAM (Alprazolam) should be individualized based upon the severity of the symptoms and individual patient response. The daily dosage (see TABLE) will meet the needs of most patients. In the few patients who require higher doses, dosage should be increased cautiously to avoid adverse effects. When higher dosage is required, the evening dose should be increased before the day time doses. In general, patients who have not previously treated with minor tranquilizers, antidepressants, or hypnotics or those with a history of chronic alcoholism. It is recommended that the general principle of using the lowest effective dosage be followed in elderly or debilitated patients to preclude the development of over sedation or ataxia. Patients should be periodically re-assessed and dosage adjustments made, as appropriate.

	Usual Starting Dosage	Usual Starting Range
Anxiety	0.25 to 0.5 mg given three times daily	0.5 to 4 mg in dividend doses.
Depression	0.5 mg given three times daily	1.5 to 4.5 mg given in dividend doses.
Geriatric patients or in the presence of debilitating disease	0.25 given two to three times daily	0.5 to 0.75 mg given in dividend dose; to be gradually increased if needed and tolerated.
Panic-related disorders	0.5 mg to 1.0 mg given at bed time	The dose should be adjusted to patient response. Dosage adjustments should be increments no greater than 1mg every 3-4 days. Additional doses can be added until a TID or QID schedule is achieved. The mean dose in a large multi clinic study was 5.7+2.3mg/day with rare patients requiring a maximum of 10mg daily.

If side effects occur, the dose should be lowered.

7- DISCONTINUATION THERAPY

The dosage should be reduced slowly in keeping with good medical practice. It is suggested that the daily dosage of NEUXAM be decreased by no more than 0.5 mg every three days. Some patients may require an even slower dosage reduction.

8- CONTRAINDICATIONS

NEUXAM is contraindicated in patients with known sensitivity to the benzodiazepines.

9- ADVERSE REACTIONS

Side effects, if they occur, are generally observed at the beginning of therapy and usually disappear upon continued medication or decreased dosage. In patients treated for anxiety, anxiety associated with depression and neurotic (reactive) depression, the most common adverse reactions to NEUXAM were drowsiness and light-headedness/ dizziness.

Less common adverse reactions were blurred vision, headache, depression, insomnia, nervousness/anxiety, tremor, change in weight, memory impairment/ amnesia, co-ordination disorders, various

gastrointestinal symptoms and autonomic manifestations.
In addition, the following adverse events have been reported in association with the use of anxiolytic benzodiazepines including Alprazolam: dystonia, irritability, anorexia, fatigue, slurred speech, jaundice, musculoskeletal weakness, changes in libido, menstrual irregularities, incontinence, urinary retention and abnormal liver function. Increased intraocular pressure has been rarely reported.
The most common adverse reactions in patients with panic-related disorders were sedation/ drowsiness, fatigue, ataxia/ impaired coordination and slurred speech. Less common adverse reactions were altered mood, gastrointestinal symptoms, dermatitis, memory problems, sexual dysfunction, intellectual impairment and confusion. As with other benzodiazepines, reaction such as concentration difficulties, confusion, hallucination, stimulation and adverse behavioural effects such as irritability, agitation, rage and aggressive or hostile behaviour have been reported rarely. In many of the spontaneous case reports of adverse behavioural effects, patients were receiving other CNS drugs concomitantly and/or were described as having underlying psychiatric conditions.
Isolated published reports involving small numbers of patients have suggested that patients who have borderline personality disorder, a prior history of violent or aggressive behaviour or alcohol or substance abuse may be at risk for such events. Instances of irritability, hostility and intrusive thoughts have been reported during discontinuance of Alprazolam in patients with post-traumatic stress disorder.

10- SPECIAL PRECAUTIONS
Usage has not been established in depression with psychiatric features in bipolar disorders or in "endogenous" depression (i.e. severely depressed). Habituation and emotional/physical dependence may occur with benzodiazepines, including Alprazolam. Caution should be particularly used when prescribing benzodiazepines, to patients who are prone to abuse drugs (e.g., alcoholics and drug addicts) because of their predisposition to habituation and dependence. Withdrawal symptoms have occurred following rapid decrease or abrupt discontinuance of benzodiazepines including Alprazolam. These can range from mild dysphoria and insomnia to a major syndrome which may include abdominal and muscle cramps, vomiting, sweating, tremor and convulsions. The signs and symptoms, especially the more serious ones, are generally more common in those patients who have received excessive doses over an extended period of time. However, withdrawal symptoms have also been reported following abrupt discontinuance of benzodiazepines taken at therapeutic levels.
Consequently, abrupt discontinuations should be avoided and a gradual tapering in dosage followed (see DOSAGE AND ADMINISTRATION - Discontinuation therapy). When therapy is discontinued in patients with panicrelated disorders, the symptoms associated with recurrence of panic attacks often mimic those of withdrawal.
Administration to severely depressed or suicidal patients should be done with appropriate precaution and appropriate size of prescription. Panic-related disorders have been associated with primary and secondary major depressive disorders and increased reports of suicide among untreated patients.
Therefore, the same precaution must be exercised when using the higher doses of NEUXAM in treating patients with panic-related disorders as is exercised with the use of any psychotropic drug in treating depressed patients or those-in whom there is reason to expect concealed suicidal ideation or plans. The usual precaution for treating patients with impaired renal or hepatic function should be observed.
The safety and efficacy of NEUXAM in children less than 18 years of age has not been established.

11- PREGNANCY AND LACTATION
Because of experience with other members of the benzodiazepine class, NEUXAM is assumed to be capable of causing an increased risk of congenital abnormalities when administered to a pregnant woman during the first trimester. If NEUXAM is used during pregnancy; or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus. Benzodiazepines are known to be excreted in human milk. As a general rule, nursing should not be undertaken by mothers who must use NEUXAM.

12- INTERACTIONS
Benzodiazepines, including alprazolam, produce additive central nervous system (CNS) depressant effects when co-administered with other psychotropic medications, anticonvulsants, antihistamines, alcohol and other drugs which themselves produce CNS depression.
The steady state plasma concentrations of imipramine and desipramine have been reported to be increased an average of 31% and 20% respectively, by the concomitant administration of NEUXAM tablets in doses up to 4 mg/day. The clinical significance of these changes is unknown
Pharmacokinetic interactions of benzodiazepines with other drugs have been reported. For example, the clearance of alprazolam and certain other benzodiazepines can be delayed by the co-administration of cimetidine or macrolide antibiotics. The clinical significance of this is unclear.

13- ABILITY TO DRIVE AND TO OPERATE MACHINERY
As with other CNS active drugs, patients receiving NEUXAM should be advised not to operate motor vehicles or dangerous machinery until it is established that they do not become drowsy or dizzy while receiving NEUXAM.

14- OVERDOSAGE
Manifestations of alprazolam overdosage include somnolence, confusion, impaired coordination, diminished reflexes and coma. Overdosage reports with NEUXAM tablets are limited. As in all cases of drug overdosage, respiration, pulse rate and blood pressure should be monitored. General supportive measures should be employed, along with immediate gastric lavage.
Intravenous fluids should be administered and an adequate airway maintained. If hypotension occurs, it may be combated by the use of vasopressors. Dialysis is of limited value. As with the management of intentional overdosing with any drug, it should be borne in mind that multiple agents may have been ingested.
WARNING: Do not exceed the stated dose.

15- DOSAGE
Use as directed by the physician.

16- INSTRUCTIONS
Store at 25°C. Protect from heat, light & moisture. Keep all medicines out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

17- PRESENTATION
NEUXAM 0.25mg tablets: Available in blister pack of 3x10's.
NEUXAM 0.5mg tablets: Available in blister pack of 3x10's.
NEUXAM 1mg tablets: Available in blister pack of 3x10's.

نیوزیم ٹیبلیٹس
(ایلپریزولیم) یو ایس پی

ہدایات: دوا کو **25°** سینٹی گریڈ پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔
تمام دوائیں بچوں کی پہنچ سے دُور رکھیں۔ صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

STANDPHARM
Manufactured by:
STANDPHARM PAKISTAN (PVT) LTD
20 km Ferozepur Road Lahore, Pakistan.