Brolite
(Bromazepam)

TABLETS

COMPOSITION
Each tablet contains: Bromazepam (J.P).....3mg

PROPERTIES AND EFFECTS
Brolite is a psychotropic agent. In low dosage, it selectively reduces tension and anxiety.
In high dosage, sedative and muscle-relaxing properties appear.

PHARMACOKINETICS
ABSORPTION: Peak plasma concentration is reached within 2 hours of oral administration of bromazepam. The absolute (versus i.v. solution) and relative (versus oral solution) bio-availability of the tablet is 60 % and 100% respectively.

DISTRIBUTION: On average, 70% of bromazepam is bound to plasma proteins. The volume of distribution is 50 liters.

METABOLISM AND ELIMINATION: Bromazepam is metabolized in the liver. Quantitatively, two metabolites predominate: 3-hydroxy-bromazepam and 2-(2-amino-5-bromo-3-hydroxybenzoyl) pyridine.
The urinary recovery of intact bromazepam and the glucuronide conjugates of 3-hydroxy-bromazepam and 2-(2-amino-5-bromo-3-hydroxybenzoyl) pyridine is 2%, 27% and 40% of the administered dose.
Bromazepam has an elimination half-life of about 20 hours. The clearance is 40 ml/min.

PHARMACOKINETICS IN SPECIAL POPULATIONS
ELDERLY: The elimination half-life may be prolonged in elderly patients (see Special dosage instructions).

INDICATIONS
EMOTIONAL DISTURBANCES: Acute tension and anxiety states. Difficulties in interpersonal contact. Agitation, insomnia, anxious and agitated depressive reactions.
Functional disturbances in the cardiovascular and respiratory systems (pseudoangina pectoris, precordial anxiety, tachycardia, emotiogenic hypertension, dyspnea, hyperventilation); in the gastrointestinal system (irritable bowel syndrome, epigastric pain, spasm, bloating diarrhea, etc.); in the genitourinary system (frequency, irritable bladder, dysmenorrhea).

PSYCHOSOMATIC DISORDERS: Psychogenic headache, Psychogenic dermatosis, Asthma, Gastric and duodenal ulcer and ulcerative colitis. Emotional reactions to chronic organic disease. Adjuvant to psychotherapy in psychoneurosis.

DOSAGE AND ADMINISTRATION
STANDARD DOSAGE: Average dosage for outpatient therapy 1.5-3 mg up to three times daily. Severe cases, especially in hospital: 6-12 mg two or three times daily.
These amounts are general recommendations, and dosage should be individually determined. Treatment of outpatients should begin with low doses, gradually increasing to the optimum level. The duration of treatment should be as short as possible. The patient should be reassessed regularly and the need for continued treatment should be evaluated, especially in case the patient is symptom free. The overall treatment generally should not be more than 8-12 weeks, including a tapering-off process. In certain cases extension beyond the maximum treatment period may be necessary, if so, it should not take place without re-evaluation of the patient's status with special expertise.

SPECIAL DOSAGE INSTRUCTIONS: Brolite is usually not indicated in children, but if the physician feel **Brolite** treatment is appropriate, then the dose should be adjusted to their low body weight (about 0.1-0.3 mg/kg body weight).
Elderly patients (see Pharmacokinetics in special populations) and those with impaired hepatic function require lower doses because of individual variations in sensitivity and pharmacokinetics.

CONTRAINDICATIONS
Brolite must not be administered to patients with known hypersensitivity to benzodiazepines, severe respiratory insufficiency, severe hepatic insufficiency (benzodiazepines are not indicated to treat patients with severe hepatic insufficiency as they may cause encephalopathy) or sleep apnea syndrome.

PRECAUTIONS
DEPENDENCE: The use of benzodiazepines and benzodiazepine-like agents may lead to the development of physical and psychological dependence upon these products (see Undesirable effects). The risk of dependence increases with dose and duration of treatment; it is also greater in predisposed patients with a history of alcohol or drug abuse.

WITHDRAWAL: Once physical dependence has developed, termination of treatment will be accompanied by withdrawal symptoms. These may consist of headaches, muscle pain, extreme anxiety, tension, restlessness, confusion and irritability.
In severe cases the following symptoms may occur: Derealization, depersonalization, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures (see Undesirable effects).
Rebound anxiety, a transient syndrome whereby the symptoms that lead to treatment with **Brolite** recur in an enhanced form, may occur on withdrawal of treatment. It may be accompanied by other reactions including mood changes, anxiety or sleep disturbances and restlessness.
Since the risk of withdrawal phenomena and rebound phenomena is greater after abrupt discontinuation of treatment, it is recommended that the dosage should be decreased gradually.

AMNESIA: Benzodiazepines may induce anterograde amnesia. Anterograde amnesia may occur using higher therapeutic dosages (documented at 6 mg).

DURATION OF TREATMENT
It may be useful to inform the patient when treatment is started, that it will be of limited duration and to explain precisely how the dosage will be progressively decreased. It is important that the patient should be aware of the possibility of rebound phenomena that occur while the drug is being discontinued.

GENERAL PRECAUTIONS
The patient should be checked regularly at the start of treatment in order to minimize the dosage and/or the frequency of administration and to prevent overdose due to accumulation.
When benzodiazepines are used, withdrawal symptoms may develop when changing to a benzodiazepine with a considerably shorter elimination half-life.
Benzodiazepines should not be used alone to treat depression or anxiety associated with depression (suicide may be precipitated in such patients). Benzodiazepines are not recommended for the primary treatment of psychotic illness.

Patients with known or presumed dependence on alcohol, medicines or drugs should not take Benzodiazepines, except in rare situations under medical supervision.

SPECIFIC PATIENT GROUPS
In patients with myasthenia gravis who are prescribed **Brolite,** care should be taken on account of pre-existing muscle weakness. Particular care is required in patients with chronic respiratory insufficiency due to the risk of respiratory depression.

EFFECTS ON ABILITY TO DRIVE OR TO USE MACHINES
Sedation, amnesia and impaired muscular function may adversely affect the ability to drive or to use machinery. This effect is increased if the patient has taken alcohol.

PREGNANCY & NURSING MOTHERS
The safety of bromazepam for use in human pregnancy has not been established. A review of spontaneously reported adverse drug events shows no greater incidence than would be anticipated from a similar untreated population. An increased risk of congenital malformations associated with the use of minor tranquillizers (diazepam, meprobamate and chlordiazepoxide) during the first trimester of pregnancy has been suggested in several studies. Bromazepam should be avoided during pregnancy unless there is no safer alternative.
If the product is prescribed to a woman of childbearing potential, she should be warned to contact her physician regarding discontinuance of the product if she intends to become or suspects that she is pregnant.
Administration of bromazepam during the last three months of pregnancy or during labor is allowed only in the event of a strict medical indication as, due to the pharmacological action of the product, effects on the neonate can be expected, such as hypothermia, hypotonia and moderate respiratory depression.
Moreover, infants born to mothers who took benzodiazepines chronically during the latter stages of pregnancy may have developed physical dependence and may be at some risk for developing withdrawal symptoms in the postnatal period.
As benzodiazepines pass into breast milk, nursing mothers should not take **Brolite**.

UNDESIRABLE EFFECTS
Brolite is well tolerated in therapeutic doses. The following undesirable effects may occur: fatigue, drowsiness, muscle weakness, numbed emotions, reduced alertness, confusion, headache, dizziness, ataxia or double vision. These phenomena occur predominantly at the start of therapy and usually disappear with prolonged administration. Gastrointestinal disturbances, changes in libido and skin reactions have been reported occasionally. Anterograde amnesia may occur using therapeutic dosages, the risk increasing at higher dosages. Amnesiac effects may be associated with inappropriate behaviour. Pre-existing depression may be unmasked during benzodiazepine use.
Paradoxical reactions like restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour and other adverse behavioural effects are known to occur when using benzodiazepines or benzodiazepine-like agents (see Precautions). If this occur, then the use of the drug should be discontinued. They are more likely to occur in children and elderly patients than in other patients.
Chronic use (even at therapeutic doses) may lead to the development of physical dependence: discontinuation of therapy may result in withdrawal or rebound phenomena (see Precautions). Psychological dependence may occur. Abuse of benzodiazepines has been reported.

INTERACTIONS
As with all psychoactive substances, the effect of **Brolite** may be intensified by alcohol. Concomitant intake of alcohol should be avoided.
If **Brolite** is combined with other centrally active drugs, its central-sedative effect may be enhanced. These drugs may include antidepressants, hypnotics, narcotic analgesics, anti-psychotics, anxiolytics/sedatives, anti-epileptic drugs, sedative antihistamines and anesthetics.
In the case of narcotic analgesics enhancement of euphoria may also occur, leading to an increase in psychological dependence.
There is a possibility that compounds which inhibit certain hepatic enzymes may influence the activity of those benzodiazepines that are metabolized by these enzymes.
Co-administration of cimetidine may prolong the elimination half-life of Bromazepam.

OVER-DOSAGE
As with other benzodiazepines, intentional or accidental over-dosage of **Brolite** alone is seldom life-threatening unless combined with other CNS depressants (including alcohol). Overdose of benzodiazepines is usually manifested by degrees of central nervous system depression ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, mental confusion and lethargy. In most cases it is sufficient to monitor the vital functions and await recovery. Higher overdoses, especially in combination with other centrally acting drugs, can result in ataxia, hypotonia, hypotension, respiratory depression, rarely coma and very rarely death.
In the management of overdose with any medicinal product, it should be borne in mind that multiple agents may have been taken.
Following overdose with oral benzodiazepines, vomiting should be induced (within one hour) if the patient is conscious or gastric lavage undertaken with the airway protected if the patient is unconscious. If there is no advantage in emptying the stomach activated charcoal should be given to reduce the absorption. Special attention should be paid to respiratory and cardiac function in intensive care. Flumazenil may be useful as an antagonist. Flumazenil is not recommended in patients with epilepsy who have been treated with benzodiazepines. Antagonism in such patients may produce seizures.

STABILITY
See expiry on the pack.

INSTRUCTIONS
Store below 30°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.

PRESENTATION
Brolite Tablets: Available in blister pack of 3x10s.

بروالائٹ ٹیبلیٹس
(برومیزی پام)

ہدایات: **30°** سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔
تمام دوائیں بچوں کی پہنچ سے دُور رکھیں۔ صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

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

0663-00