evaluated in human studies.

Dependence:

Topiramate has not been systemically studied in animals or humans for its potential for tolerance or physical dependence.

PEDIATRIC USE:

Safety and efficacy in the pediatric population has not been established.

DOSAGE AND ADMINISTRATION:

	Initial Dose	Titration	Recommended Dose
Epilepsy monotherapy: children 2 to <10 years	25 mg/day administered nightly for the first week	The dosage should be titrated over 5-7 weeks	Daily doses in two divided doses based on weight
Epilepsy monotherapy: adults and pediatric patients >10 years	50 mg/day in two divided doses	The dosage should be increased weekly by increments of 50 mg for the first 4 weeks then 100 mg for weeks 5 to 6.	400 mg/day in two divided doses
Epilepsy adjunctive therapy: adults with partial onset seizures or LGS	25 to 50 mg/day	The dosage should be increased weekly to an effective dose by increments of 25 to 50 mg.	200-400 mg/day in two divided doses
Epilepsy adjunctive therapy: adults with primary generalized tonic- clonic seizures	25 to 50 mg/day	The dosage should be increased weekly to an effective dose by increments of 25 to 50 mg.	400 mg/day in two divided doses
Epilepsy adjunctive therapy: Pediatric patients with partial onset seizures, primary generalized tonic-clonic seizures or LGS.	25 mg/day (or less, based on a range of 1 to 3 mg/kg/day) nightly for the first week	The dosage should be increased at 1- or 2-week intervals by increments of 1 to 3 mg/kg/day (administered in two divided doses). Dose titration should be guided by clinical outcome.	5 to 9 mg/kg/day in two divided doses
Migraine	25 mg/day administered nightly for the first week	The dosage should be increased weekly by increments of 25 mg. Dose and titration should be guided by clinical outcome.	100 mg/day administered in two divided doses

Adjunctive Therapy Use:

As adjunctive therapy, the recommended daily dose of Topiramate in adults with partial onset serious is 200 to 400mg/day in two devided doses and in adults with primary generalized tonic clonic seizures is 400mg/day in two divided doses.

Usual Pediatric Dose for Seizure Prophylaxis:

1 to 3 mg/kg/day given nightly.

Renal Dose Adjustments:

In renally impaired subjects, one half of the usual adult dose is recommended.

HOW SUPPLIED:

Eminant 25mg Tablets:

Available in pack size of 60's.

Eminant 50mg Tablets:

Available in pack size of 60's.

Eminant 100mg Tablets:

Available in pack size of 30's.

INSTRUCTION:

Store at 15-30°C. Protect from heat, light and moisture.

Keep out of the reach of children. To be sold on the prescription of a registered medical practitioner only.

ایمی نینٹ

〈ٹوپیرامیٹ〉

گولیاں

خوراک: دواڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات: دوا کو 15-30° سینٹی گریڈ پر رکھیں۔

گرمی، روشنی اور نمی سے محفوظ رکھیں۔ 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.
0638-00

Eminant

(Topiramate) **Tablets**

COMPOSITION:

Eminant 25mg:

Each film coated tablet contains:

Topiramate (USP)..... 25mg

Eminant 50mg:

Each film coaled tablet contains:

Topiramate (USP).....50mg

Eminant 100mg:

Each film coated tablet contains:

Topiramate (USP).....100mg

DESCRIPTION

Eminant (Topiramate) is an anticonvulsant or anti epileptic drug.

CLINICAL PHARMACOLOGY

Mechanism of Action:

The precise mechanisms by which Topiramate exerts its anticonvulsant and migraine prophylaxis effects are unknown; however, preclinical studies have revealed four properties that may contribute to Topiramate's efficacy for epilepsy and migraine prophylaxis. Electrophysiological and biochemical evidence suggests that Topiramate, at pharmacologically relevant concentrations, blocks voltage-dependant sodium channels, augments the activity of the neurotransmitter gamma-aminobutycic acid at some subtypes of the GABA-A receptor, antagonizes the AMPA/kainate subtype of the glutamate receptor and inhibits the carbonic anhydrase enzyme, particularly isozymes II and IV.

Pharmacokinetics:

Absorption and distribution:

Absorption of Topiramate is rapid, with peak plasma concentrations occurring at approximately 2 hours following a 400mg oral dose. The relative bioavailability of Topiramate from the tablet formulation is about 80% compared to a solution. The bioavailability of Topiramate is not affected by food. Topiramate is 15% to 41% bound to human plasma proteins over the blood concentration range 0.5 to 250ug/mL. The fraction of bound topiramate is decreased as blood concentration is increased.

Metabolism and Excretion:

Topiramate is not extensively metabolized and is primarily eliminated unchanged in urine (approximately 70% of an administered dose). Oral plasma clearance is approximately 20 to 30mL/min in humans following oral administration.

Special Populations:

Renal Impairment:

The clearance of Topiramate may reduce by 42% in moderately renally impaired and by 54% in severely renally impaired subjects compared to normal renal function subjects.

Hepatic Impairment:

In hepatically impaired subjects, the clearance of Topiramate may decrease; however its underlying mechanism is not well understood.

Hemodialysis:

Topiramate is cleared by hemodialysis, using a high efficiency, counterflow, single pass-dialysate hemodialysis procedure. Topiramate clearance by dialysis is 120mL/min with blood flow through the dialyzer at 400mL/min. This high clearance

will remove a clinically significant amount of Topiramate from the patient over the hemodialysis treatment period. Therefore, a supplemental dose may be required.

Indications:
For epilepsy:
As monotherapy:
Topiramate is indicated as initial monotherapy in patients 10 years of age and older with partial onset or primary generalized tonic-clonic seizure.
As Adjunctive Therapy:
Topiramate is indicated as adjunctive therapy for adults and pediatric patients ages 2 to 16 years with partial onset seizures or primary generalized tonic-clonic seizures.
In prophylaxis of migraine:
Topiramate is indicated for adults for the prophylaxis of migraine headache.

WARNINGS:
Acute Myopia and Secondary Angle Closure Glaucoma:
A syndrome consisting of acute myopia associated with secondary angle closure glaucoma has been reported in patients receiving Topiramate. Symptoms include acute onset of decreased visual acuity and/or ocular pain Ophthalmologic findings can include myopia, ocular hyperemia (redness) and increased intraocular pressure. Primary treatment to reverse symptoms is discontinuation of Topiramate as rapidly as possible.
Suicidal Behavior and Ideation:
Antiepileptic drugs (AEDs), including Topiramate, increase the risk of suicidal thoughts/behavior in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior and/or any unusual changes in mood or behavior.
Withdrawal of Antiepileptic Drugs (AEDs):
In patients with or without a history of seizures or epilepsy, antiepileptic drugs including Topiramate should be gradually withdrawn to minimize the potential for seizures or increased seizure frequency.
Fetal Toxicity:
Topiramate can cause fetal harm when administered to a pregnant woman. Data from pregnancy registries indicate that infants exposed to Topiramate in utero have an increased risk for cleft lip and/or cleft palate (oral clefts). When multiple species of pregnant animals received Topiramate at clinically relevant doses, structural malformations including craniofacial defects, and reduced fetal weights occurred in offspring.

ADJUSTMENT OF DOSE:
In Renal Failure:
The major route of elimination of unchanged Topiramate and its metabolites is via the kidney. Dosage adjustment may be required in patients with reduced renal function.
Decreased Hepatic Function:
In hepatically impaired patients, Topiramate should be administered with caution as the clearance of Topiramate may be decreased.
Labor and Delivery:
Although the effect of Topiramate on labor and delivery in humans has not been established. The development of Topiramate-induced metabolic acidosis in mother and/or in fetus might affect the fetus' ability to tolerate labor.

Nursing Mothers:
Caution should be exercised when administered to a nursing woman. Topiramate may excrete in milk.

DRUG INTERACTIONS:
Anti-epileptic Drugs:
Concomitant administration of phenytoin or carbamazepine with Topiramate, decrease plasma concentrations of Topiramate by 48% and 40% respectively when compared to Topiramate given alone.
CNS Depressants:
Concomitant administration of Topiramate and alcohol or other CNS depressant drugs has not been evaluated in clinical studies. Because of the potential of Topiramate to cause CNS depression as well as other cognitive and/or neuropsychiatric adverse events, Topiramate should be used with extreme caution if used in combination with alcohol and other CNS depressants.
Oral Contraceptives:
The possibility of decreased contraceptive efficacy and increased breakthrough bleeding should be considered in patients taking oral contraceptive products in combination with Topiramate.
Metformin:
Topiramate treatment can frequently cause metabolic acidosis, a condition for which the use of metformin is contraindicated.
Other Carbonic Anhydrase Inhibitors:
Concomitant use of Topiramate with any other carbonic anhydrase inhibitor (e.g., zonisamide, acetazolamide or dichlorphenamide) may increase the severity of metabolic acidosis and may also increase the risk of kidney stone formation.

ADVERSE REACTIONS
Body as a whole:
Frequent: syncope.
Infrequent: abdomen enlargement.
Rare: alcohol intolerance.
Cardiovascular Disorders:
Infrequent: hypotension, postural hypotension, angina pectoris.
Gastrointestinal System Disorders:
Infrequent: Stomatitis, melena, gastritis, esophagitis.
Rare: tongue edema.
Urinary System Disorders:
Infrequent: urinary retention, face edema, renal pain, albuminuria, polyuria, oliguria.

OVERDOSE:
Overdose with Topiramate has occurred predominantly in combination with alcohol and/or other drugs. The most commonly reported events in overdosage include tachycardia, vomiting and seizures.
Management of Overdose:
In Acute Topiramate overdose, if the ingestion is recent, the stomach should be emptied immediately by lavage or by induction of emesis. Activated charcoal has been shown to adsorb Topiramate in vitro. Treatment should be appropriately supportive. Hemodialysis is an effective mean of removing Topiramate from the body.
DRUG ABUSE AND DEPENDENCE:
Controlled Substance:
Topiramate is not a controlled substance.
Abuse:
The abuse potential of Topiramate has not been