Front

Torate®
(Topiramate)
Tablet

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COMPOSITION:
Torate Tablet 25 mg:
Each film coated tablet contains:
Topiramate USP ..... 25 mg.

Product Specs.: USP

Torate Tablet 50 mg:
Each film coated tablet contains:
Topiramate USP ..... 50 mg.

Product Specs.: USP

DESCRIPTION:
Torate is an anticonvulsant that is chemically unrelated to any other anticonvulsant or mood regulating medication for oral administration.

CLINICAL PHARMACOLOGY:
Mechanism of action: The precise mechanism by which Topiramate exert its antiseizure effect is unknown; however, four properties may contribute Topiramte's antiepileptic efficacy. Electrophysiological and biochemical evidence suggests that Topiramate, at pharmacologically relevant concentrations, blocks voltage dependent sodium channels, augments the activity of neurotransmitter gamma-aminobutyrate at some subtypes of the GABA-A receptor, antagonizes the kainate subtype of the glutamate receptor, and inhibits the carbonic anhydrase enzyme, particularly isoenzymes II and IV. It works by decreasing abnormal excitement in the brain.
Pharmacokinetics: The bioavailability of Topiramate is not affected by food.The pharmacokinetics of Topiramate are linear with dose proportional increases in plasma concentration. The mean plasma elimination half-life is 21 hours after single or multiple doses. Steady state is thus reached in about 4 days in patients with normal renal function. Topiramate is 15 - 41% bound to human plasma proteins over the blood concentration range of 0.5 - 250 mcg/mL. The fraction bound decreased as blood concentration increased.
Metabolism and excretion: Topiramate is not extensively metabolized and is primarily eliminated unchanged in the urine (approximately 70% of an administered dose). Six metabolites have been identified in humans, none of which constitutes more than 5% of an administered dose. The metabolites are formed via hydroxylation, hydrolysis, and glucuronidation. Overall, oral plasma clearance (CL/F) is approximately 20 to 30 mL/min in humans following oral administration.

INDICATIONS:
The drug is indicated for following conditions:
Monotherapy epilepsy: **Torate** is used to treat the seizure disorders (epilepsy).
Adjunctive therapy epilepsy: **Torate** may be used with other seizure medications to treat certain types of seizures in patients with epilepsy or Lennox-Gastaut syndrome (a disorder that causes seizures and developmental delays).
Migraine: **Torate** is also used to prevent migraine headaches.
Other uses: **Torate** has recently been shown to improve the drinking outcomes of alcohol-dependent individuals.

CONTRA-INDICATIONS: Hypersensitivity to any component of this product.

DOSAGE AND ADMINISTRATION:
Monotherapy use: The recommended dose for **Torate** monotherapy in adults and children 10 years of age and older is 400 mg/day in two divided doses.
The dose should be achieved by titrating according to the following schedule:

	Morning Dose	Evening Dose
Week 1	25 mg	25 mg
Week 2	50 mg	50 mg
Week 3	75 mg	75 mg
Week 4	100 mg	100 mg
Week 5	150 mg	150 mg
Week 6	200 mg	200 mg

Adjunctive therapy use: Adults (17 Years of Age and Over) - Partial Seizures, Primary Generalized Tonic-Clonic Seizures, or Lennox-Gastaut Syndrome. The recommended total daily dose of **Torate** as adjunctive therapy in adults with partial seizures is 200-400 mg/day in two divided doses, and 400 mg/day in two divided doses as adjunctive treatment in adults with primary generalized tonic-clonic seizures. It is recommended that therapy be initiated at 25-50 mg/day followed by titration to an effective dose in increments of 25-50 mg/week. Titrating in increments of 25 mg/week may delay the time to reach an effective dose. Pediatric Patients (Ages 2 - 16 Years) - Partial Seizures, Primary Generalized Tonic-Clonic Seizures, or Lennox-Gastaut Syndrome. The recommended total daily dose of **Torate** as adjunctive therapy for patients with partial seizures, primary generalized tonic-clonic seizures, or seizures associated with Lennox-Gastaut Syndrome is approximately 5 to 9 mg/kg/day in two divided doses. Titration should begin at 25 mg (or less, based on a range of 1 to 3 mg/kg/day) nightly for the first week. The dosage should then be increased at 1- or 2-week intervals by increments of 1 to 3 mg/kg/day (administered in two divided doses), to achieve optimal clinical response. Dose titration should be guided by clinical outcome.
Migraine: The recommended total daily dose of **Torate** for prophylaxis of migraine headache is 100 mg/day administered in two divided doses.
The recommended titration rate for Topiramate for migraine prophylaxis to 100 mg/day is:

	Morning Dose	Evening Dose
Week 1	None	25 mg
Week 2	25 mg	25 mg
Week 3	25 mg	50 mg
Week 4	50 mg	50 mg

Dose and titration rate should be guided by clinical outcome. If required, longer intervals between dose adjustments can be used. **Torate** can be taken with or without regards to food.
Patients with renal impairment: In renally impaired subjects (creatinine clearance less than 70 mL/min/1.73 m^2), one half of the usual adult dose is recommended. Such patients will require a longer time to reach steady-state at each dose.
Patients with hepatic disease: In hepatically impaired patients Topiramate plasma concentrations may be increased. So dose adjustment should be made accordingly.
Geriatric patients (Ages 65 Years and Over): Dosage adjustment may be indicated in the elderly patient when impaired renal function (creatinine clearance rate <70 mL/min/1.73 m^2) is evident.

ADVERSE EFFECTS:
More common side effects may include: Abdominal pain, abnormal co-ordination, abnormal vision, agitation, anxiety, appetite loss, back pain, breast pain, chest pain, confusion, constipation, depression, difficulty with concentration, difficulty with memory, dizziness, double vision, drowsiness, fatigue, flu-like symptoms, indigestion, involuntary eye movement, language problems, leg pain, loss of co-ordination, menstrual problems, mood problems, nausea, nervousness, rash, sinusitis, slowing of movements, sore throat, speech problems, tingling or burning sensations, tremors, upper respiratory infection, weakness, weight loss. Less common side effects may include: Abnormal gait, abnormal menstrual bleeding, acne, aggressiveness, apathy, bladder infection, changes in taste, bloody urine, body odor, bronchitis, cough, decreased awareness, decreased mobility, decreased sensitivity, diarrhea, digestive inflammation, dry mouth, exaggerated sense of well being, eye pain, feelings of illness, feelings of unreality, fever, fluid retention, frequent urination, gas, gum inflammation, hair loss, hallucinations, headache, hearing difficulties, heart palpitations, hot flushes, hyperactivity, impotence, increased sweating, irritable bladder, joint pain, kidney stones, loss of balance, loss of consciousness, low sex drive, mood swings, muscleache, muscle tension, muscle weakness, nosebleeds, painful or difficult urination, personality problems, pinkeye, ringing in the ears, sensitivity to touch, severe itching, shivers, shortness of breath, sleeplessness, suicidal tendencies, swelling, vaginal infection, vomiting, weight gain.

PRECAUTIONS:
Torate should be withdrawn gradually to minimize the potential of increased seizure frequency. Renal elimination is dependent on renal function and is independent of age. Patients with moderate or severe renal impairment may take 10 to 15 days to reach steady-state plasma concentrations as compared to 4 to 8 days in patients with normal renal function. Some patients, especially those with a predisposition to nephrolithiasis, may be at increased risk for renal stone formation. Adequate hydration is recommended to reduce this risk. Risk factors for nephrolithiasis include stone formation, a family history of nephrolithiasis and hypercalciuria. None of these risk factors can reliably predict stone formation during Topiramate treatment. In addition, patients taking other medication associated with nephrolithiasis may be at increased risk. In hepatically impaired patients, Topiramate should be administered with caution as the clearance of Topiramate may be decreased.
Pregnancy: Topiramate crosses the placental barrier. There is no data available for Topiramate in pregnant women. However, Topiramate therapy should be used during pregnancy only if the potential benefit outweighs the potential risk to the fetus.
Lactation: It is not known if Topiramate is excreted in human milk. Since many drugs are excreted in human milk, and because the potential for serious adverse reactions in nursing infants to Topiramate exists, the prescriber should decide whether to discontinue nursing or discontinue the drug, taking into account the risk/benefit ratio of the importance of the drug to the mother and the risks to the infant. The effect of Topiramate on labor and delivery in humans is unknown.
Children: Safety and effectiveness in children under 2 years of age have not been established.
Geriatrics: The possibility of age-associated renal function abnormalities should be considered when using Topiramate.

DRUG INTERACTIONS:
Antiepileptic drugs: Potential interactions between Topiramate and standard antiepileptic drugs (AEDs) occur in patients with epilepsy. The addition of Topiramate to other antiepileptic drugs (phenytoin, carbamazepine, valproic acid, phenobarbital, primidone) has no effect on their steady-state plasma concentrations, except in the occasional patient, where the addition of Topiramate to phenytoin may result in an increase of plasma concentrations of phenytoin. Phenytoin and carbamazepine decrease the plasma concentration of Topiramate. The addition or withdrawal of phenytoin and/or carbamazepine during adjunctive therapy with Topiramate may require adjustment of the dose of Topiramate. This should be done by titrating to clinical effect. The addition or withdrawal of valproic acid does not produce clinically significant changes in plasma concentrations of Topiramate, and therefore does not warrant dosage adjustment of Topiramate.
Digoxin: Concomitant administration of Topiramte and digoxin may decrease serum digoxin AUC to about 12%. When Topiramate is added or withdrawn in patients on digoxin therapy, careful attention should be given to the routine monitoring of serum digoxin.
CNS depressants: Concomitant administration of Topiramate and alcohol or other CNS depressant drugs has not been evaluated in clinical studies. It is recommended that Topiramate should not be used concomitantly with alcohol or other CNS depressant drugs.
Oral contraceptives: Efficacy of low-dose oral contraceptives may be reduced in combination with Topiramate. Patients taking oral contraceptives should be asked to report any change in their bleeding patterns.
Others: Concomitant use of Topiramate, a weak carbonic anhydrase inhibitor, with other carbonic anhydrase inhibitors, e.g., acetazolamide, may create a physiological environment that increases the risk of renal stone formation, and should therefore be avoided if possible.

OVERDOSE DOSAGE AND ITS MANAGEMENT:
The signs and symptoms of overdosage may include convulsions, drowsiness, speech disturbances, blurred vision, diplopia, mentation impaired, lethargy, abnormal co-ordination, stupor, hypotension, abdominal pain, agitation, dizziness, depression, and severe metabolic acidosis. If the ingestion is recent, the stomach should be emptied immediately by lavage or by the induction of emesis. Hemodialysis is effective for removing Topiramte from the body.

INSTRUCTIONS:
- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:
Torate Tablet 25 mg : Pack of 3 x 10 tablets.
Torate Tablet 50 mg : Pack of 3 x 10 tablets.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATION PLEASE CONTACT:

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