Tics-G® (TOPIRAMATE) Tablets U.S.P.

25mg
50mg
100mg

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(ٹوپیرامیٹ)
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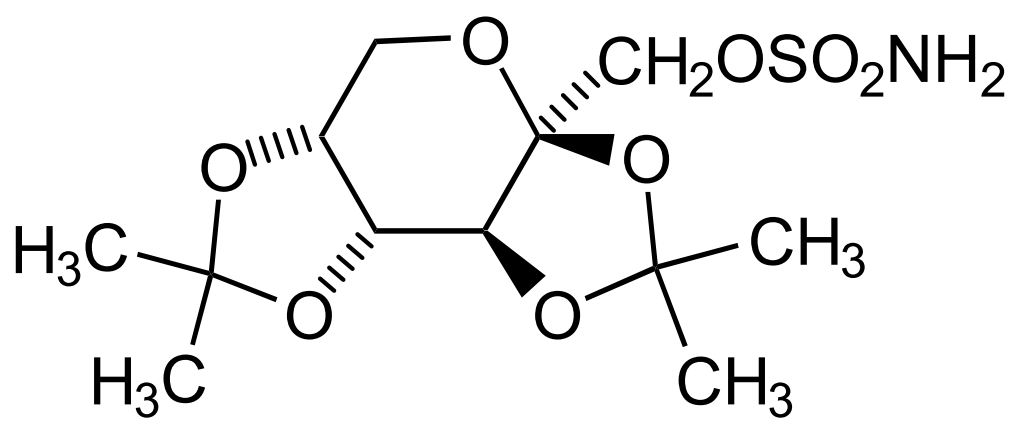
DESCRIPTION:
Topiramate is an oral drug that is used to prevent the seizures of epilepsy is used primarly among patient who are not controlled by other anti epileptic drugs.



COMPOSITION:
Tics-G 25mg Tablets U.S.P.
Each film-coated tablet contains:
Topiramate U.S.P. 25mg

Tics-G 50mg Tablets U.S.P.
Each film-coated tablet contains:
Topiramate U.S.P. 50mg

Tics-G 100mg Tablets U.S.P.
Each film-coated tablet contains:
Topiramate U.S.P. 100mg

CLINICAL PHARMACOLOGY
Mechanism of Action
The precise mechanisms by which topiramate exerts its anticonvulsant and migraine prophylaxis effects are unknown; Electrophysiological and biochemical evidence suggests that topiramate, at pharmacologically relevant concentrations, blocks voltage-dependent sodium channels, augments the activity of the neurotransmitter gamma-aminobutyrate 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.

Pharmacodynamics
Topiramate is only weakly effective in blocking clonic seizures induced by the GABAA receptor antagonist, pentylenetetrazole. Topiramate is effective in epilepsy which include tonic and absence-like seizures and tonic and clonic seizures. Changes (increases and decreases) from baseline in vital signs (systolic blood pressure-SBP, diastolic blood pressure-DBP, pulse) occurred more frequently in pediatric patients (6 to 17 years) treated with various daily doses of topiramate (50 mg, 100 mg, 200 mg, 2 to 3 mg/kg) than in patients treated with placebo in controlled trials for migraine prophylaxis.

Pharmacokinetics
The pharmacokinetics of topiramate are linear with dose proportional increases in plasma concentration over the dose range studied (200 to 800 mg/day). 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% to 41% bound to human plasma proteins over

the blood concentration range of 0.5 to 250μg/mL. The fraction bound decreased as blood concentration increased.
Carbamazepine and phenytoin do not alter the binding of topiramate. Sodium valproate, at 500 μg/mL (a concentration 5 to 10 times higher than considered therapeutic for valproate) decreased the protein binding of topiramate from 23% to 13%. Topiramate does not influence the binding of sodium valproate.

INDICATIONS AND USAGE

- Monotherapy Epilepsy
- Adjunctive Therapy Epilepsy
- Migraine

DOSAGE AND ADMINISTRATION

Epilepsy

Monotherapy Use

Adults and Pediatric Patients 10 Years and Older

The recommended dose for Topiramate monotherapy in adults and pediatric patients 10 years of age and older is 400 mg/day in two divided doses. Approximately 58% of patients randomized to 400 mg/day achieved this maximal dose in the monotherapy controlled trial the mean dose achieved in the trial was 275 mg/day

Children Ages 2 to <10 Years

Dosing in patients 2 to <10 years is based on weight. During the titration period, the initial dose of Topiramate should be 25 mg/day administered nightly for the first week. Based upon tolerability, the dosage can be increased to 50 mg/day (25 mg twice daily) in the second week. Dosage can be increased by 25-50 mg/day each subsequent week as tolerated. Titration to the minimum maintenance dose should be attempted over 5-7 weeks of the total titration period. Based upon tolerability and clinical response, additional titration to a higher dose (up to the maximum maintenance dose) can be attempted at 25-50 mg/day weekly increments. The total daily dose should not exceed the maximum maintenance dose for each range of body weight.

Adjunctive Therapy Use

Adults 17 Years of Age and Over - Partial Onset Seizures, Primary Generalized Tonic-Clonic Seizures, or Lennox-Gastaut Syndrome The recommended total daily dose of Topiramate as adjunctive therapy in adults with partial onset seizures is 200 to 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 to 50 mg/day followed by titration to an effective dose in increments of 25 to 50 mg/day every week. Titrating in increments of 25 mg/day every week may delay the time to reach an effective dose. Doses above 400 mg/day (600, 800 or 1,000 mg/day) have not been shown to improve responses in dose-response studies in adults with partial onset seizures. Daily doses above 1,600 mg have not been studied Pediatric Patients Ages 2 - 16 Years – Partial Onset Seizures, Primary Generalized Tonic-Clonic Seizures, or Lennox-Gastaut Syndrome The recommended total daily dose of Topiramate as adjunctive therapy for pediatric patients with partial onset 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/day (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 Topiramate as treatment for adults and adolescents 12 years of age and older 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:

Migraine Prophylaxis Titration Schedule for Adults and Adolescents Patients 12 Years and Older.

	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

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
- Acute Myopia and Secondary Angle Closure Glaucoma
- Visual Field Defects
- Oligohidrosis and Hyperthermia
- Metabolic Acidosis
- Suicidal Behavior and Ideation
- Cognitive/Neuropsychiatric Adverse Reactions
- Fetal Toxicity
- Withdrawal of Antiepileptic Drugs (AEDs)
- Sudden Unexplained Death in Epilepsy (SUDEP)
- Hyperammonemia and Encephalopathy
- Kidney Stones
- Hypothermia with Concomitant Valproic Acid (VPA)
- Paresthesia

DRUG INTERACTIONS
In vitro studies indicate that topiramate does not inhibit enzyme activity for CYP1A2, CYP2A6, CYP2B6, CYP2C9, CYP2D6, CYP2E1, and CYP3A4/5 isozymes. In vitro studies indicate that topiramate is a mild inhibitor of CYP2C19 and a mild inducer of CYP3A4.

ADVERSE REACTIONS:
The most common (≥10% more frequent than placebo or low-dose Topiramate in monotherapy) adverse reactions at recommended dosing in adult and pediatric controlled, epilepsy clinical trials were paresthesia, anorexia, weight decrease, speech disorder related speech problem, fatigue, dizziness, somnolence, nervousness, psychomotor slowing, abnormal vision, and fever. The most common (≥ 5% more frequent than placebo) adverse reactions at recommended dosing in adult and adolescent controlled, migraine clinical trials were paresthesia, anorexia,weight decrease, difficulty with memory, taste perversion, upper respiratory tract infection, abdominal pain, diarrhea, hypoesthesia, and nausea.

DOSAGE:
As directed by the physician.

INSTRUCTIONS:
Store below 30ºC. Protect from heat, light & moisture. Keep all medicines out of the reach of children.

PRESENTATION:
Tics-G 25mg Tablets U.S.P. are available in ALU/ALU Blister pack of 6x10's.
Tics-G 50mg Tablets U.S.P. are available in ALU/ALU Blister pack of 6x10's.
Tics-G 100mg Tablets U.S.P. are available in ALU/ALU Blister pack of 3x10's.

خوراک : معالج کی ہدایت کے مطابق استعمال کریں۔

ہدایات : ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

گرمی، روشنی اور نمی سے محفوظ رکھیں۔

تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

For detailed information:

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ISO 14001:2015 CERTIFIED TÜV AUSTRIA — **ISO 14001:2015**

ISO 45001:2018 CERTIFIED TÜV AUSTRIA — **ISO 45001:2018**

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