xxxxxxxx-5343

TOPIRAMATE

EPIMATE-50

50 mg Film-Coated Tablet
ANTICONVULSANT

FORMULATION:
Each film-coated tablet contains:
Topiramate ..... 50 mg
PRODUCT DESCRIPTION:
Topiramate (Epimate-50) 50 mg Tablet is a yellow colored, round, biconvex, film coated tablet debossed with breakline on both sides, separating '10' and '32' on one side and '50' 'on other side
CLINICAL PHARMACOLOGY
MECHANISM OF ACTION:
The precise mechanism by which topiramate exerts its antiseizure effect is unknown; however, electrophysiological and biochemical studies of the effects of topiramate on cultured neurons have revealed three properties that may contribute to topiramate's antiepileptic efficacy. First, action potentials elicited repetitively by a sustained depolarization of the neurons are blocked by topiramate in a time-dependent manner, suggestive of a state-dependent sodium channel blocking action. Second, topiramate increases the frequency at which γ-aminobutyrate (GABA) activates GABAA receptors, and enhances the ability of GABA to induce a flux of chloride ions into neurons, suggesting that topiramate potentiates the activity of this inhibitory neurotransmitter. This effect was not blocked by flumazenil, a benzodiazepine antagonist, nor did topiramate increase the duration of the channel open time, differentiating topiramate from barbiturates that modulate GABAA receptors. Third, topiramate antagonizes the ability of kainate to activate the kainate/AMPA (α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid; non-NMDA) subtype of excitatory amino acid (glutamate) receptor, but has no apparent effect on the activity of N-methyl-D-aspartate (NMDA) at the NMDA receptor subtype. These effects of topiramate are concentration-dependent within the range of 1 μM to 200 μM.
Topiramate also inhibits some isoenzymes of carbonic anhydrase (CA-II and CA-IV). This pharmacologic effect is generally weaker than that of acetazolamide, a known carbonic anhydrase inhibitor, and is not thought to be a major contributing factor to topiramate's antiepileptic activity.
Pharmacodynamics
Topiramate has anticonvulsant activity in rat and mouse maximal electroshock seizure (MES) tests. Topiramate is only weakly effective in blocking clonic seizures induced by the GABAA receptor antagonist, pentylenetetrazole. Topiramate is also effective in rodent models of epilepsy, which include tonic and absence-like seizures in the spontaneous epileptic rat (SER) and tonic and clonic seizures induced in rats by kindling of the amygdala or by global ischemia.
PHARMACOKINETICS:
Topiramate is readily absorbed after oral doses, with peak plasma concentrations achieved after 2 hours. Bioavailability is not affected by the presence of food. Protein binding is about 9 to 17%. The volume of distribution in women is approximately half that in men. Topiramate crosses placental barrier and is distributed in breast milk.
In healthy subjects topiramate is not extensively metabolized; however, up to 50% of a dose may undergo metabolism in the liver in patients receiving enzyme-inducing drug concomitantly. It is eliminated chiefly in urine; as unchanged drug and metabolites; mean plasma elimination half-life is about 21 hours. Steady-state concentrations are achieved after 4 to 8 days in patients with normal renal function. Clearance is decreased in patients with impaired renal or hepatic function, and steady- state plasma concentrations may not be achieved for 10 to 15 days in the former. Children exhibit a higher clearance and shorter elimination half-life than adults.
The pharmacokinetics of topiramate may be affected by concurrent administration of other antiepileptics.
INDICATIONS:
Monotherapy in adults and children with newly diagnosed epilepsy. Adjunctive therapy in adults and children under 2 years for refractory partial seizures with or without secondary generalization, seizures associated with Lennox-Gestaut Syndrome and primary generalized tonic-clonic seizures.
Also used for the treatment and prophylaxis of migraine headache in adults.
DOSAGE AND ADMINISTRATION:
EPILEPSY: Adult - 25 mg once daily by mouth for one week increased thereafter by increments of 25 to 50 mg at intervals of one to two weeks. Daily dose of more than 25 mg should be taken in 2 divided doses. **Adjunctive Therapy** - The usual dose for adjunctive therapy is 200 to 400 mg, although some patients may require up to 800 mg daily. **Monotherapy** - Usual ranges range from 100 mg to a maximum of 400 mg daily.
Children - Adjunctive Therapy - Children aged 2 to 16 years is 25 mg nightly for the first week, increased at intervals of one to two weeks by increments of 1 to 3 mg/kg/day. The recommended dose thereafter is about 5 to 9 mg/kg/day given in 2 divided doses, though up to 30 mg/kg/day may be given. **Monotherapy** - Children aged 6 years and over may be started on 0.5 to 1 mg /kg at night for the first week, increased at intervals of one to two weeks by increments of 0.5 to 1 mg/kg/day. The usual dose is 3 to 6 mg/kg/day in 2 divided doses, although higher doses have been tolerated.
MIGRAINE: Adult - 25 mg per day administered nightly for the first week and increased thereafter by increments of 25 mg. Dosage of more than 25 mg should be taken in 2 divided doses. Usual dose is 100 mg. Dose and titration should be guided by clinical outcome.
Administration in Patients with Renal Impairment: In renally impaired patients (creatinine clearance less than 70 mL/min/1.73 m2), one half of the adult dose is recommended.
Patients Undergoing Hemodialysis: Topiramate is cleared by hemodialysis, a prolonged period of dialysis may cause topiramate concentration to fall below that required to maintain an anti-seizure effect. Thus, in patients undergoing hemodialysis a supplemental dose equal to about one-half of the daily dose should be given in divided doses (at the start and finish of the procedure).
Topiramate tablets may be taken with or without food. Swallow whole, do not chew or crush.
CONTRAINDICATIONS:
Topiramate is contraindicated in patients with a history of hypersensitivity to any component of this product.
WARNINGS:
There have been rare reports of acute myopia with secondary angle-closure glaucoma in adults and children receiving topiramate. Symptoms include decreased visual acuity and ocular pain which generally appear within one month of starting treatment; hyperaemia and raised intra-ocular pressure may be present with or without mydriasis. Choroidal effusions resulting in anterior displacement of lens and iris have been reported. Appropriate measures to reduce intra-ocular pressure should be taken, and discontinuation of topiramate as rapidly as possible to reverse the symptoms. Elevated intra-ocular pressure of any etiology, if left untreated, can lead to serious sequelae including permanent vision loss.
Decreased sweating and hyperthermia have been reported in patients given topiramate. Children appeared to be at an increased risk in developing these adverse reactions and should be monitored closely for such effects especially during warm or hot weather. Caution was also advised when topiramate was given with other drugs known to cause similar effects (eg. Carbonic anhydrase inhibitors ans antimuscarinics).
Metabolic acidosis has been associated with topiramate treatment. Generally, the decreases in serum bicarbonate are mild to moderate and occur as soon after starting topiramate. Clinical signs such as hyperventilation may develop. Baseline and periodic serum bicarbonate levels should be monitored during topiramate treatment. If metabolic acidosis develops or persists, it may be necessary to reduce the dose or discontinue topiramate although, in some cases, correcting the acidosis with alkali therapy may be appropriate.
Topiramate may cause serious adverse fetal effects. Topiramate should be used during pregnancy only if the potential benefit outweighs the potential risk of the fetus.
As with other antiepileptics, withdrawal of topiramate therapy or transition to or from another type of antiepileptic therapy should be made gradually to avoid precipitating an increase in the frequency of seizures.
PRECAUTIONS:
Topiramate should be used with caution in patients with renal or hepatic impairment. Adequate hydration is recommended to reduce the risk of developing renal calculi, especially in predisposed patients.
There is an increased risk for the development of cleft lip and / or cleft palate (oral clefts) in infants born to women treated with topiramate during pregnancy.
PREGNANCY AND LACTATION:
Pregnancy: Category C
Topiramate should be used during pregnancy only if the potential benefit outweighs the potential risk to the fetus.
Lactation
Topiramate should not be used during breast feeding.
DRUG INTERACTIONS:
Phenytoin and Carbamazepine - both decreased the plasma concentration to topiramate.
CNS Depressants - Because of potential to 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 - Topiramate increased plasma clearance of the estrogenic component significantly.
Others - Concomitant use of topiramate, a weak carbonic anhydrase inhibitor, with other carbonic anhydrase inhibitors, e.g. Acetazolamide or dichlorophenamide, may create a physiological environment that increases the risk of renal stone formation, and should therefore be avoided.
ADVERSE EFFECTS:
Adverse effects associated with topiramate therapy include ataxia, impaired concentrations, confusion, dizziness, fatigue, paraesthesia, drowsiness, and difficulties with memory or cognition. Agitation, anxiety, nervousness, emotional lability (with mood disorders), and depression may also occur. Other reported adverse effects include abdominal pain, anorexia, asthenia, diplopia, leucopenia, nausea, nystagmus, insomnia, psychomotor retardation, impaired speech, altered taste, visual disturbances, and weight loss. The risk of developing renal calculi is increased, especially in predisposed patients. Reduced sweating with hyperthermia has occurred particularly in children. Rare cases of myopia with secondary angle-closure glaucoma have been reported.
"For suspected adverse drug reaction, report to FDA: www.fda.gov.ph or to TORRENT: www.torrentpharma.com".
Patient to seek medical attention immediately at the first sign of any adverse drug reaction shall appear
OVERDOSAGE AND TREATMENT:
Overdoses of topiramate have been reported. Signs and symptoms included convulsions, drowsiness, speech disturbance, blurred vision, diplopia, mentation impaired, lethargy, metabolic acidosis, abnormal coordination, stupor, hypotension, abdominal pain, agitation, dizziness and depression. The clinical consequences were not severe in most cases, but deaths have been reported after poly-drug overdoses involving topiramate.
A patient who ingested a dose between 96 and 110 g topiramate was admitted to hospital with coma lasting 20-24 hours followed by full recovery after 3 to 4 days.
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 means of removing topiramate from the body.
CAUTION:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.
Caution for Children: Keep out of children reach.
STORAGE:
Store at temperatures not exceeding 25^{o}C.
AVAILABILITY:
Topiramate (Epimate-50) 50 mg Film-Coated Tablet - Alu-Alu Blister Pack of 10's (Box of 100's) - DRP-2763
DATE OF FIRST AUTHORIZATION
July 8, 2009
DATE OF REVISION
August 2016

torrent PHARMA

Manufactured by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA.

Imported and Distributed by :
TORRENT PHARMA PHILIPPINES INC.
Units 3 & 4, 34th Floor, Zuellig Building
Makati Avenue Corner Paseo de Roxas
Makati City, PHILIPPINES

PRODUCT NAME	: EPIMATE	**COUNTRY :** Philippines	**LOCATION :** Chhatral	**Supersedes A/W No.:**				
ITEM / PACK	: Insert	**NO. OF COLORS: 1**	**REMARK : Folded Size 30 mm**					
DESIGN STYLE	: Front-Back	**PANTONE SHADE NOS.:**	**SUBSTRATE :**					
CODE	: xxxxxxxxxx-5343	■ Black	**Activities**	**Department**	**Name**	**Signature**	**Date**	
DIMENSIONS (MM)	: 150 x 210		Prepared By	**Pkg.Dev**				
ART WORK SIZE	: S/S		Reviewed By	**Pkg.Dev**				
DATE	: 01-04-2017		Approved By	**Quality**				

This colour proof is not colour binding. Follow Pantone shade reference for actual colour matching.