TOPAMAX® tablets sprinkle capsules (topiramate/topiramate capsules)

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News Center

September 4, 2001
New Treatment Option Approved for Lennox-Gastaut Syndrome, One of Most Debilitating Forms of Epilepsy

May 15, 2000
FDA Approves Slower Dose And Titration Schedule For TOPAMAX® (topiramate)

October 5, 1999
FDA Approves TOPAMAX® (topiramate) To Treat Common Seizure Type In Adults And Pediatric Patients

July 26, 1999
FDA Approves TOPAMAX® For Pediatric Patients (Ages 2-16) With Epilepsy

November 4, 1998
New Sprinkle Capsule Formulation Available for Antiepileptic Drug TOPAMAX® (topiramate) tablets

TOPAMAX® (topiramate) Tablets &
TOPAMAX® (topiramate capsules) Sprinkle Capsules

Uncontrolled Epilepsy Takes Toll on Children in U.S., Report Finds

Full U.S. Prescribing Information

Please see the full U.S. prescribing information for:

TOPAMAX® (topiramate) Tablets and
TOPAMAX® (topiramate capsules) Sprinkle Capsules

*note: these documents will open in a new browser window.

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Frequently Asked Questions about...

TOPAMAX® (topiramate) Tablets &
TOPAMAX® (topiramate capsules) Sprinkle Capsules

Frequently asked questions

Common Seizure Types

Side Effects of Antiseizure Medicines

First aid for Seizures

When To Call an Ambulance

General Questions

What is TOPAMAX?
TOPAMAX is an antiseizure medication that can improve the control of several types of seizures when patients are still having seizures with other treatments. TOPAMAX is indicated as adjunctive therapy for adults and pediatric patients ages 2-16 years with partial onset seizures or primary generalized tonic-clonic seizures and in patients 2 years of age and older with seizures associated with LGS.

What formulations of TOPAMAX are available?
TOPAMAX is available as a tablet in strengths of 25 mg, 100 mg, and 200 mg. TOPAMAX is also available as a sprinkle capsule in strengths of 15 mg and 25 mg.

Do TOPAMAX tablets or sprinkle capsules contain the following:

Gluten? TOPAMAX tablets and sprinkle capsules do not contain gluten.
Wheat? TOPAMAX tablets and sprinkle capsules do not contain wheat.
Lactose? TOPAMAX tablets do contain lactose but the sprinkle capsule does not contain lactose.

What is a TOPAMAX Sprinkle Capsule?
TOPAMAX Sprinkle Capsules contain topiramate-coated beads in a hard gelatin capsule. The capsule may be swallowed as a whole capsule or may be opened and sprinkled onto soft food such as applesauce, custard, ice cream, oatmeal, pudding, or yogurt.

How should TOPAMAX be stored?
TOPAMAX tablets should be stored at a room temperature (59-86ºF) in a tightly-closed container, such as the prescription bottle your drugstore uses. TOPAMAX sprinkle capsules are best stored at or below 77ºF in a tightly-closed container. Your antiseizure medicines should be protected from moisture.

TOP

Taking TOPAMAX

How should I take TOPAMAX Sprinkle Capsules?
TOPAMAX Sprinkle Capsules may be swallowed as whole capsules or may be opened and poured over food in the following way:

- You may sprinkle the contents of TOPAMAX Sprinkle Capsules on a small amount (teaspoon) of soft food, such as applsauce, custard, ice cream, oatmeal, pudding, or yogurt.
- Hold the capsule upright so that you can read the word "TOP"
- Carefully twist off the clear portion of the capsule. You may find it best to do this over a small portion of the food onto which you will be pouring the sprinkles.
- Sprinkle all of the capsule's contents onto a spoonful of soft food, taking care to see that the entire prescribed dosage is sprinkled onto the food.
- Be sure to swallow the entire spoonful of the sprinkle/food mixture immediately. Chewing should be avoided. It may be helpful to drink fluids immediately in order to make sure all of the mixture is swallowed.
- **IMPORTANT:** Never store any sprinkle/food mixture for use at a later time.

Can TOPAMAX sprinkles be chewed?
Chewing TOPAMAX sprinkles should be avoided because of the bitter taste.

Can I take TOPAMAX with food?
Yes, TOPAMAX can be taken with food. Many people take their medicine at breakfast and dinner.

For those people who have difficulty swallowing pills or in whom doctors want to use smaller doses, TOPAMAX is available as a sprinkle capsule that can be opened and sprinkled onto food or swallowed whole. If your doctor has prescribed TOPAMAX Sprinkle Capsules, your pharmacist will provide an instruction sheet with pictures that illustrate how to use the sprinkle capsules.

How often should I take TOPAMAX?
TOPAMAX is typically taken twice a day, usually in the morning and the evening. Choose two times in the day that are convenient for you so you will remember to take your medication.

Carefully follow your doctor's instructions about starting TOPAMAX and about continuing your other medicine. Even when you are not having seizures, you should continue to take your medication every day to prevent seizures from occurring.

Are there any foods, drinks, or activities I need to avoid when taking TOPAMAX?
There are no specific foods you need to avoid while taking TOPAMAX. Be

sure to drink plenty of water to reduce the risk of kidney stones. In general, people with seizures should avoid alcohol because it can trigger seizures or make seizures more severe.

People with seizures can lead physically active lives. Just as people without seizures should exercise regularly, so should you, particularly if your antiseizure medicine may cause weight gain.

Talk with your doctor before you participate in higher risk activities such as biking, skiing, skateboarding, scuba diving or sky diving. Even if you do not have seizures, you should take appropriate safety precautions in terms of supervision and safety equipment such a helmet.

What is the recommended total daily dose of TOPAMAX?

Adults:	The recommended total daily dose of TOPAMAX as adjunctive therapy in partial onset seizures, primary generalized tonic-clonic seizures or seizures associated with LGS, is 400 mg/day in two divided doses.
Pediatric Patients Ages 2-16:	The recommended total daily dose of TOPAMAX as adjunctive therapy in partial onset seizures or primary generalized tonic-clonic seizures is approximately 5 to 9mg/kg/day in two divided doses.

What is the recommended starting dose of TOPAMAX and how should the dose be increased?

Adults:	For adjunctive therapy in partial onset seizures, primary generalized tonic-clonic seizures, or seizures associated with LGS, it is recommended that TOPAMAX 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:	For adjunctive therapy in partial onset seizures or primary generalized tonic-clonic seizures or seizures associated with LGS, titration of TOPAMAX 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). Dose titration should be guided by clinical outcome.

What if I forget to take my medicine? Can I skip the missed dose?
Successful control of seizures is often determined by whether people take their medicine as the doctor prescribed. By taking your medications at the same time every day, you replace the amount your body has used since the last dose, keeping a steady level of medicine in your blood. Missing a dose

can cause the blood levels to drop too low and allow seizures to break through.

Ask your doctor about what to do if you forget a dose. Do not try to "catch up" by taking twice your normal dose since this may release too much drug into the blood and cause side effects.

Why is my doctor adding or changing to TOPAMAX?
Your doctor is hoping that TOPAMAX is the best medicine for you to reach the goal that both of you are working towards - freedom from seizures with the least amount of side effects.

As you have most likely learned from being treated with other antiseizure medicines, finding the best medicine is sometimes a matter of trial and error. Every antiseizure medicine is different. Plus, different patients do not respond in exactly the same way even if they are taking the same medicine.

Your doctor has probably chosen TOPAMAX because it is effective against partial-onset seizures and primary generalized tonic-clonic seizures when added to other antiseizure medicines. Your doctor may also have chosen TOPAMAX because of its safety record or because you have another medical condition that makes TOPAMAX a good choice at this time. Your doctor may have selected TOPAMAX based on discussions with you about possible side effects of different antiseizure medicines, choosing TOPAMAX based on your input. Doctors also select TOPAMAX because it can be combined with other medicines without causing big changes in their blood levels. TOPAMAX may also have been chosen because it can be taken twice a day, which tends to be more convenient than frequent dosing.

Will TOPAMAX affect my other medicines?
Blood levels of other antiseizure medicines change very little, if at all, when TOPAMAX is added. However, the doctor may reduce the dose of other antiseizure medicine when adding TOPAMAX. When people take more than one medicine, they are more likely to have side effects such as dizziness, fatigue, sleepiness and mental slowing.

If you are a woman who also takes birth control pills, be sure to tell the doctor who prescribed the birth control pills that you are taking TOPAMAX and other antiseizure medicines. The effectiveness of birth control pills can be reduced by antiseizure medicines such as TOPAMAX.

Before starting any new medicine, tell your doctor about all the medicines you take, including non-prescription products, food supplements, vitamins or herbals. Just because a medicine is not prescribed by a doctor does not mean that is free of side effects, and that it will not negatively affect other medicines that the doctor prescribes. In fact, some herbals can make seizures worse.

Are there any medicines I should avoid while taking TOPAMAX?
Probably the most important medicines to avoid are drugs what can cause kidney stones such as Zonegranâ (zonisamide) and Diamoxâ (acetazolamide). Kidney stones have occurred in people taking TOPAMAX, and the risk could increase when combined with other drugs that can cause

kidney stones.

Also, some children may be on a ketogenic diet - a special high-fat, low-carbohydrate diet to help control seizures. The ketogenic diet can also cause kidney stones. Combined use of TOPAMAX and the ketogenic diet should be avoided.

TOP

Side Effects

What are the most common side effects associated with TOPAMAX?

Adults:	The most commonly reported side effects during clinical trials in adult patients receiving 200 - 400 mg/day of topiramate (TOPAMAX) were somnolence, dizziness, coordination proplems, speech disorders, psychomotor slowing, abnormal vision, difficulty with memory, sensory distortion and double vision. Because of these side effects, patients are advised not to drive or operate machinery until they have gained sufficient experience on TOPAMAX to determine whether it adversely affects their mental and/or motor performance.
Pediatric Patients Ages 2-16:	The most commonly reported side effects in pediatric patients receiving 5 to 9 mg/kg/day of topiramate (TOPAMAX) were fatigue, sleepiness, loss of appetite, nervousness, difficulty with concentration/attention, difficulty with memory, aggressive reaction, and weight decrease. Additional food intake may be considered if the patient is losing weight while on TOPAMAX.

Should I expect the same side effects with TOPAMAX that I have had with other antiseizure medicines?
Doctors cannot predict how a person will respond to an antiseizure medicine in terms of side effects. People can respond very differently to the same drug.

TOPAMAX and other antiseizure medicines can all cause "brain side effects" such as dizziness, slowness, fatigue, and sleepiness. However, just because a person had intolerable dizziness, for example, on one antiseizure medicine does not mean that dizziness will be a side effect of a different medicine. Even though antiseizure medicines can have similar "brain side effects", antiseizure medicines can still have distinctly different side effects. For example, some medicines are more like to cause tremor, hair loss, weight gain, or skin rash than others; some medicines are more likely to cause weight loss than weight gain.

Side effects that seem to be "different" or at least more notable with

TOPAMAX are myopia and secondary angular closure glaucoma, kidney stones, tingling in the fingers and toes (known as "paresthesia"), loss of appetite and weight loss. When TOPAMAX is first added to other antiseizure medicines, some people taking TOPAMAX or their family members may notice "word-finding difficulty" - not being able to come up with a particular word when talking. This effect and many of the other side effects that can occur during treatment with TOPAMAX tend to disappear with time or when doses of TOPAMAX (or even the other antiseizure medicine) are reduced. If a side effect is truly intolerable and does not respond to dose reductions, TOPAMAX can be discontinued with the expectation that the side effect will disappear.

What are the symptoms of myopia and secondary angle-closure glaucoma associated wtih TOPAMAX?
The primary symptoms of this syndrome are blurred vision and eye pain. Patients should seek immediate medical attention if they experience these symptoms.

How early or late in therapy can this syndrome develop?
Symptoms have typically occurred within the first month of therapy.

Are there any risk factors or predisposing conditions for developing this syndrome?
No risk factors have been identified.

What is the risk of developing kidney stones with the use of TOPAMAX?
A total of 32/2,086 (1.5%) of adults exposed to topiramate (TOPAMAX) during its development reported the occurrence of kidney stones, an incidence about 2-4 times that expected in a similar, untreated population. As in the general population, the incidence of stone formation among topiramate (TOPAMAX) treated patients was higher in men. Kidney stones have also been reported in pediatric patients. To reduce the risk of developing kidney stones it is recommended to increase fluid intake. Increased fluid intake increases urinary output, lowering the concentration of substances involved in stone formation.

Are there steps that I can take to avoid side effects such as kidney stones?
You can reduce your risk of kidney stones by drinking plenty of water, especially if you spend a lot of time outdoors in warm weather. In the absence of TOPAMAX, men are more prone than women to developing kidney stones, as are people who have had kidney stones in the past or have blood relatives who have had kidney stones. If you fit any of these categories, you may be at higher risk of developing a kidney stone when taking TOPAMAX and way want to be especially careful in drinking plenty of fluids.

Can TOPAMAX decrease the effectiveness of oral contraceptives?
The efficacy of oral contraceptives may be compromised by topiramate (TOPAMAX). Patients taking oral contraceptives while on TOPAMAX should report any change in their bleeding patterns to their health care provider.

Should patients on TOPAMAX drive automobiles?

In clinical trials with TOPAMAX, some common side effects reported in adult patients included sleepiness, dizziness, confusion, abnormal vision, and difficulty with concentration and memory. Because of these side effects, patients are advised not to drive or operate machinery until they have gained sufficient experience on TOPAMAX to determine whether it adversely affects their mental and/or motor performance.

What should I do if I get what I think are side effects from TOPAMAX?
Talk with your doctor before making any changes in your antiseizure medicine, whether it is TOPAMAX or one of the other agents. Your doctor has probably talked with you about side effects that might occur and perhaps given you instructions on when to call the office, particularly since a number of the side effects that might occur when starting TOPAMAX may disappear on their own. However, if you have any questions or concerns about your medicine or if you develop anything different than what your doctor described, call your doctor's office.

Side effects that emerge when starting TOPAMAX may or may not be due to TOPAMAX. In other words, a side effect may be due to the combination of medicines rather than TOPAMAX itself.

Your doctor has a number of options to help you overcome side effects. Sometimes it is simply a matter of waiting and the side effect will resolve. Or, delaying a dose increase until the side effect disappears. Or, the doctor may decide to reduce the dose of your other antiseizure medicine since the drug combination may be the cause. Temporarily reducing the TOPAMAX dose may be necessary. However, if none of these tactics seem to help, your doctor may decide to discontinue TOPAMAX.

It is very important to remember that you should not stop taking TOPAMAX or any of your antiseizure medicines without first talking with your doctor. A sudden drop in blood levels of antiseizure medicine can trigger severe seizures in some people.

TOP

Other Information

If my seizures stop, how long will I have to keep taking TOPAMAX?
Your doctor is the best judge of how long treatment with TOPAMAX and other antiseizure medicines should continue. Antiseizure medicines suppress seizures - take the medicines away and the seizures may recur. Your doctor will consider such factors as how long you have been seizure-free and the type of epilepsy that you have. You and your doctor will only want to stop treatment when the risk that seizures will recur is acceptably low.

If you go 6 months or 12 months without a seizure and get a driver's license, it does not mean that your epilepsy is cured and that you can stop your medicines. Your doctor may want you to go several years without a single seizure before gradually reducing doses of your antiseizure medicines and

stopping treatment. Some people may need to take antiseizure medicines for very long periods. Remember, never stop taking your medicine without talking to your doctor first. Abruptly stopping antiseizure medicine can trigger severe seizures in some patients.

Do I need to have blood tests while taking TOPAMAX?
Blood tests may still be needed due to other antiseizure medicine that you may be taking. It is important to understand why blood tests are done during treatment with antiseizure medicines.

Some antiseizure medicines can, in some people, injure organs such as the liver or blood-forming cells. In people who need these medicines, doctors are encouraged to monitor patient health and safety with periodic blood tests. Based on its safety record, such guidelines have not been established for people taking TOPAMAX. For the medicines you have been taking, your doctor may also have been measuring the amount of medicine in your blood in order to modify the dose and keep the blood level within a particular range. Such tests can be helpful if seizures are not controlled despite what seems to be an adequate dose, if seizures break through or worsen, or if you have side effects that are not explained by increases in dose, for example.

Your doctor may decide to measure the amount of TOPAMAX in your blood, particularly when you get to a stable dose that gives you the best effect. Beyond that, however, the doctor may only check the blood level of TOPAMAX if there is evidence that you are not getting the right amount of medicine.

Where can I get more information on epilepsy and its treatment?
Your local chapter of the Epilepsy Foundation of America (EFA) can provide information on education, counseling, job placement, social support, and other resources. To find your nearest local chapter, contact the EFA at:
Epilepsy Foundation of America
4351 Garden City Drive
Landover, MD 20785
(301) 459-3700
1-800-EFA-1000
www.efa.org

Other Internet resources:
www.epilepsy.com
www.seizures.net
www.familydoctor.org
www.drkoop.com
www.healthwatch.com

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Resources:

Organizations and Links

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American Association of Neuroscience Nurses
The American Association of Neuroscience Nurses is a national organization of 3,400 registered nurses and other healthcare professionals dedicated to improving the care of the neuroscience patient and to furthering the interests of health professionals in the neurosciences.
www.aann.org

American Epilepsy Society
The American Epilepsy Society promotes research and education for professionals dedicated to the prevention, treatment and cure of epilepsy.
www.aesnet.org

American Medical Association
AMA's work includes the development and promotion of standards in medical practice, research, and education; strong advocacy agenda on behalf of patients and physicians; and the commitment to providing timely information on matters important to the health of America.
www.ama-assn.org

American Neurological Association
The American Neurological Association is a professional society of academic neurologists and neuroscientists devoted to advancing the goals of academic neurology; to training and educating neurologists and other physicians in the neurologic sciences; and to expanding both our understanding of diseases of the nervous system and our ability to treat them.
www.aneuroa.org

American Psychiatric Association
The American Psychiatric Association is a medical specialty society recognized worldwide which specializes in the diagnosis and treatment of mental and emotional illnesses and substance use disorders.
www.psych.org

BrainTalk
Online patient support groups for neurology.
www.braintalk.org

Epilepsy Foundation
The Epilepsy Foundation is a national, charitable organization wholly dedicated to the welfare of people with epilepsy.
www.efa.org

Medscape
Medscape.com offers health professionals the Web's most robust medical health information and education site.
www.medscape.com

National Medical Association
The National Medical Association is a national professional and scientific organization committed to preventing the diseases, disabilities and adverse health conditions that disproportionately or differentially impact African American and underserved populations.
www.nmanet.org

Neurology Channel
The Internet's most comprehensive resource for neurology-related consumer health care. The Neurology Channel community is monitored and developed by leading neurologists.
www.neurologychannel.com—Home Page
www.neurologychannel.com/seizures—Epilepsy and Seizures section

Prescription for Safety
The Ortho-McNeil guide to the safe use of prescription medicines.
www.orthomcneil.com/about/rxforsafety/

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All required fields are marked with an asterisk(*)

Salutation*

Name*

Address1*

Address2

City*

State* **Zip***

Phone

Fax

E-mail*

What is your preferred method of response?*

○ Email ○ Phone ○ US Mail ○ Fax

Are you a:*

○ Consumer ○ Healthcare Professional

If Healthcare Professional, which of the following best describes your job functions?

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1000 Route 202 South
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- Full U.S. Prescribing Information

Frequently Asked Questions

Patient Information

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- About Epilepsy and Epileptic Seizures
- Facts About Epilepsy

Physician Information

- The Fastest Growing AED
- TURN TO TOPAMAX For Broad-Spectrum Coverage
- TURN TO TOPAMAX For Proven Efficacy
- 25 mg Titration Improves Tolerability

TOPAMAX News

- May 15, 2000—FDA Approves Slower Dose And Titration Schedule For TOPAMAX® (topiramate)
- October 5, 1999—FDA Approves TOPAMAX® (topiramate) To Treat Common Seizure Type In Adults And Pediatric Patients
- July 26, 1999—FDA Approves TOPAMAX® For Pediatric Patients (Ages 2-16) With Epilepsy
- November 4, 1998—New Sprinkle Capsule Formulation Available for Antiepileptic Drug TOPAMAX® (topiramate) tablets
- TOPAMAX® (topiramate) Tablets & TOPAMAX® (topiramate capsules) Sprinkle Capsules
- Uncontrolled Epilepsy Takes Toll on Children in U.S., Report Finds

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Lennox-Gastaut Syndrome

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TOPAMAX® (topiramate) Tablets & TOPAMAX® (topiramate capsules) Sprinkle Capsules

TOPAMAX® (topiramate) Tablets and TOPAMAX® (topiramate capsules) Sprinkle Capsules is an antiepileptic drug proven to reduce the frequency of seizures, particularly among patients who are not controlled by other antiepileptic drugs (AEDs). TOPAMAX is indicated as adjunctive therapy for adults and pediatric patients ages 2-16 years with partial onset seizures or primary generalized tonic-clonic seizures and in patients 2 years of age and older with seizures associated with Lennox-Gastaut Syndrome.

In October of 1998, the U.S. Food and Drug Administration approved a new sprinkle formulation of TOPAMAX. The sprinkle formulation offers more convenience and ease to patients taking the drug. With this formulation, the TOPAMAX capsule can be opened and its contents can be sprinkled onto soft food for easier swallowing, or the capsule can be swallowed whole, offering patients greater flexibility.

TOPAMAX has been studied in more than one million epilepsy patients worldwide.

Although the exact mechanism of action is unknown, TOPAMAX appears to work in three ways to help balance electrical activity in the brain to reduce the frequency of seizures. Specifically, TOPAMAX enhances a chemical substance that inhibits electrical activity in the brain, while blocking other substances that increase activity.

Epilepsy is a chronic condition characterized by recurrent, unprovoked seizures, or electrical disturbances in the brain that can alter a patient's consciousness, movement or behaviors. Seizures are characterized as either partial or generalized, depending on where they originate in the brain.

TOPAMAX was discovered and developed by the R.W. Johnson Pharmaceutical Research Institute and is marketed in the United States by Ortho-McNeil Pharmaceutical. Both companies are located in Raritan, NJ.

In the pediatric trial, the most common side effects associated with TOPAMAX as add-on therapy included excessive drowsiness, loss of appetite, fatigue, nervousness, difficulty with concentration/attention, weight decrease, aggressive reaction and difficulty with memory. The safety and effectiveness in patients younger than two have not been established.

In adults, the most common side effects were somnolence, dizziness, coordination problems, speech disorders, psychomotor slowing, abnormal vision, difficulty with memory, sensory distortion and double vision.

Please see full U.S. Prescribing Information for TOPAMAX® (topiramate) Tablets and TOPAMAX® (topiramate capsules) Sprinkle Capsules.

All full U.S. Prescribing Information on this web site is in Adobe Acrobat form. If you need information about any Ortho-McNeil Pharmaceutical product, please contact your doctor, pharmacist or other health care professional. You can also call Ortho-McNeil Medical Information, 1-800-682-6532, 8:30am - 4:30pm(EST).

This information is intended for use by our customers, patients and healthcare professionals in the United States only. Ortho-McNeil Pharmaceutical recognizes that the Internet is a global communications medium; however, laws, regulatory requirements and medical practices for pharmaceutical products vary from country to country. The prescribing information included here may not be appropriate for use outside the United States.

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Facts About Epilepsy and Epileptic Seizures

- Epilepsy is a disorder characterized by recurrent and unprovoked seizures and temporary impairment of brain function. There currently is no known cure.
- More than 2 million people, or one percent of the population, in the United States have epilepsy.

- It is estimated that approximately 70,000-129,000 new cases of epilepsy occur each year in the United States, which corresponds to approximately 30 to 53 cases per 100,000 people. About one-third of these new cases begin in childhood. Incidence is also high in the elderly.
- Epilepsy tends to affect slightly more men than women, but it can strike anyone, at any age.
- In most cases, epilepsy is not genetic. However, hereditary factors can play a role—almost 9 percent of children whose mothers have epilepsy and 2.4 percent whose fathers have epilepsy will develop the condition.
- Head injuries, strokes, brain tumors, infections and genetic conditions are potential causes of approximately 35 percent of all cases of epilepsy. In the remaining 65 percent, no cause can be found.
- Epileptic seizures can be broadly categorized into two groups: 1) generalized seizures that begin on both sides of the brain simultaneously and 2) partial seizures that begin in only one area of the brain. Partial seizures can evolve into generalized seizures.
- Antiepileptic drugs (AEDs) are the principal therapy for epilepsy. Currently available medications do not control seizures adequately in 30 percent of patients. Many patients whose seizures are under control with current AEDs still suffer from the side effects of the medication.
- Non-compliance with AED therapy is the most common cause of breakthrough seizures in people with epilepsy. Sleep deprivation, alcohol withdrawal, and stress can also increase the risk of having epileptic seizures.
- People with forms of epilepsy that have no known cause and onset in early to middle childhood (except neonatal seizures) sometimes respond better to medication. People who may not respond well to AEDs include those whose symptoms started as neonatal seizures and those who have epilepsy associated with cerebral palsy, mental retardation or brain damage.

Information for People Taking TOPAMAX® (topiramate) Tablets and TOPAMAX (topiramate capsules) Sprinkle Capsules

Introduction

The following information for patients taking TOPAMAX® (topiramate) Tablets and TOPAMAX® (topiramate capsules) Sprinkle Capsules does not take the place of a discussion with your doctor, pharmacist, or other healthcare professional about the risks and benefits associated with this prescription product. It is important to speak with one of these healthcare professionals about any prescribed medication. **Click here for PRxESCRIPTION FOR SAFETY: The Ortho-McNeil Guide to Safe Use of Prescription Medicines.**

If you would like immediate information about TOPAMAX, please contact your doctor, pharmacist, or other healthcare professional. Click here to access the Full full U.S. Prescribing Information for TOPAMAX Tablets or TOPAMAX Sprinkle capsules.

Information For Patients Taking TOPAMAX
(see **PRECAUTIONS** section of Full U.S. Prescribing Information)

- Patients, particularly those with predisposing factors, should maintain an adequate fluid intake in order to minimize the risk of renal stone formation. (See PRECAUTIONS: General Section of Full U.S. prescribing information on this web site, for support regarding hydration as a preventative measure);
- Patients should be aware of the potential for somnolence (sleepiness), dizziness, confusion, and difficulty concentrating and are advised not to drive or operate machinery until they have gained sufficient experience on TOPAMAX to gage whether it adversely affects their mental and/or motor performance.

Click here for information on how to read a prescription drug package insert.

Please see package insert for full U.S. Prescribing Information for TOPAMAX® (topiramate) Tablets and TOPAMAX® (topiramate capsules) Sprinkle Capsules.

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About Epilepsy and Epileptic Seizures

Q. What is epilepsy?
Epilepsy is a neurological disorder that causes recurrent seizures—abnormal electrical discharges in the brain that temporarily disrupt normal brain function.

Q. How common is epilepsy?
Epilepsy is one of the most common neurological disorders. An estimated 2.3 million Americans, at least 750,000 of them age 18 or younger, have epilepsy.

Q. What causes epilepsy?
Roughly 30 percent of epilepsy cases are attributed to severe head injury, brain tumor, poisoning, infection affecting the brain, or stroke. Some forms of epilepsy appear to have a genetic basis. But in most cases, the cause of the disorder is unknown.

Q. Can people with epilepsy live normal lives?
People who are able to bring their seizures under control with anti-seizure medications are able to live personally and professionally fulfilling lives. But those whose seizures resist treatment face many obstacles. Uncontrolled seizures can disrupt careers and personal lives. In children, uncontrolled seizures can interfere with learning, and, in extreme cases in which seizures are frequent and uncontrolled, lead to brain damage.

Q. What are seizures?
Seizures are abnormal electrical discharges in the brain that temporarily disrupt normal brain function. During seizures, brain cells, or neurons, discharge, or "fire,"erratically.

Epileptic seizures are usually categorized as "generalized," affecting both sides of the brain simultaneously, or "partial," affecting just one part of the brain initially. There are a number of different types of seizures, and adults and children with epilepsy may experience more than one kind.

Q. What are partial onset seizures?
A partial onset seizure can cause sensory distortion, uncontrolled movements, and in some cases, an altered state of consciousness in which the patient appears to be in a trance. A patient in the midst of a partial seizure may make random movements, walk about, run, mumble, or scream. These seizures last only a minute or two. Afterward, the patient usually has no memory of the seizure.

Q. What are primary generalized tonic-clonic seizures?
Often referred to as "grand mal seizures," primary generalized tonic-clonic seizures are the most common form of generalized seizure. These seizures cause a temporary loss of consciousness and muscle control. An adult or child suffering a primary generalized tonic-clonic seizure will lapse into unconsciousness, fall, stiffen, and experience forceful muscle jerking before slowly regaining consciousness.


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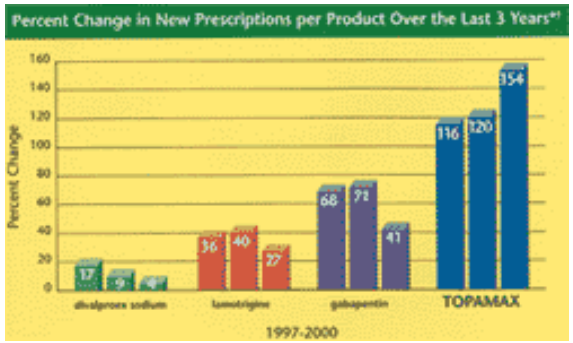
Physician Information

Topiramate has been available in the US only since 1997 and in parts of Europe since 1995. The drug is approved for monotherapy in Europe, but to date, only as adjunctive therapy in the US. Topiramate's efficacy as adjunctive therapy for uncontrolled partial onset seizures was established in both adults and children in double-blind, placebo-controlled trials. [1-6] Many patients with therapy-resistant partial onset seizures achieved ≥ 50% seizure reductions (in 44% of adults and 39% of children in double blind trials with target doses of 400 mg/day). [4,6]

Studies show that use of topiramate is of significant add-on benefit in patients with PGTC seizures previously resistant to AED therapy. Double blind treatment with topiramate for 20 weeks resulted in 56% of patients achieving a 50% or greater reduction on monthly PGTC seizures.[7]

See the TOPAMAX

- Anti-Epileptic Drug Chart
- Established Safety Record
- Broad Spectrum Coverage
- Proven Efficacy
- Tolerability
- Full US Prescribing Information



References

1. Sharief M, Viteri C, Ben-Menachem E, et al. Double-blind, placebo-controlled study of topiramate in patients with refractory epilepsy. *Epilepsy Res* 1996;25:217-24.
2. Tassinari CA, Michelucci R, Chauvel P, et al. Double-blind, placebo- controlled trial of topiramate (600 mg daily) for the treatment of refractory partial epilepsy. *Epilepsia* 1996;37:763-8.
3. Ben-Menachem E, Henriksen O, Dam M, et al. Double-blind, placebo-controlled trial of topiramate as add-on therapy in patients with refractory partial seizures. *Epilepsia* 1996;37:539-43.
4. Faught E, Wilder BJ, Ramsay RE, et al. Topiramate placebo-controlled dose-ranging trial in refractory partial epilepsy using 200-, 400-, and 600-mg daily dosages. *Neurology* 1996;46:1684-90.
5. Priviters M, Fincham R, Penry J, et al. Topiramate placebo-controlled dose-ranging trial in refractory partial epilepsy using 600-, 800-, and 1,000-mg daily dosages. *Neurology* 1996;46:1678-83.
6. Elterman R, Glauser TA, Wyllie E, et al. A double-blind, randomized trial of topiramate as adjunctive therapy for partial-onset seizures in children. *Neurology* 1999;52:1338-44.

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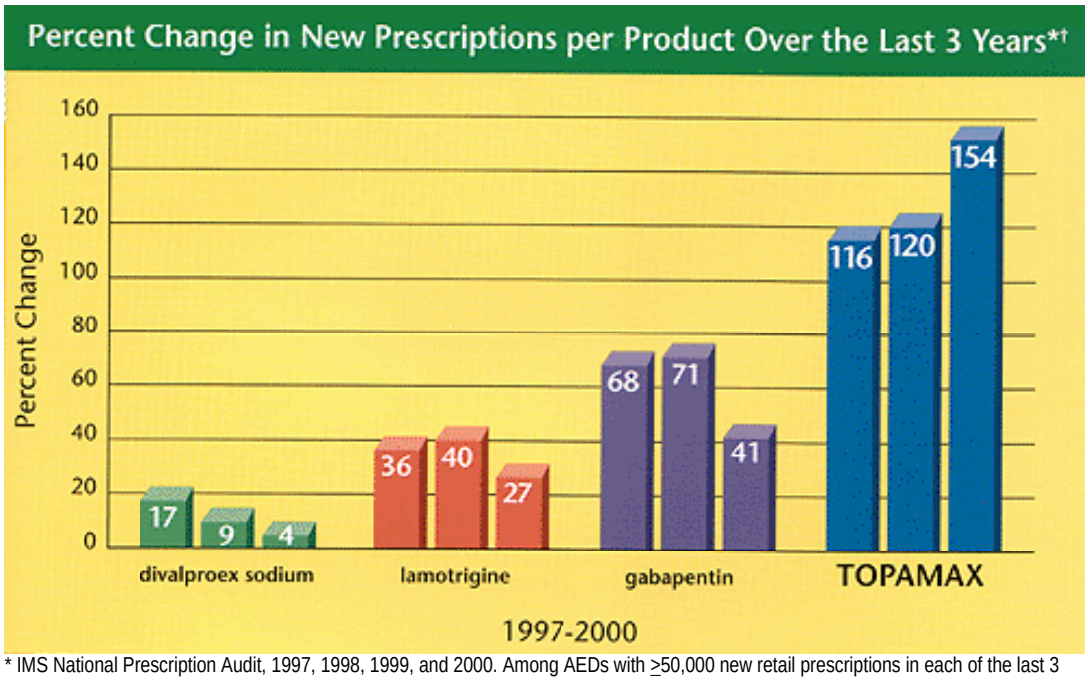
The Fastest Growing AED



* IMS National Prescription Audit, 1997, 1998, 1999, and 2000. Among AEDs with ≥50,000 new retail prescriptions in each of the last 3 years. Specific indications and dosage vary by product.
†Bar graph and statement represent the following time frames: 1997-1998, 1998-1999, 1999-2000. Data represent new prescription present growth per product.

The Established Worldwide Safety Record of Topiramate

- **1,000,000 patients treated**
- **8 years of clinical experience**
- **Available in over 80 countries worldwide**

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TURN TO TOPAMAX For Even Broader-Spectrum Coverage

	FDA-Approved Indication — Adjunctive Therapy				
	Partial-Onset Seizures in Adults	Partial-Onset Seizures in Pediatric Patients ≥2 Years of Age	Primary Generalized Tonic-Clonic Seizures in Adults	Primary Generalized Tonic-Clonic Seizures in Pediatric Patients ≥2 years of Age	Seizures of Lennox-Gastaut Syndrome in Pediatric Patients and in Adults
TOPAMAX	X	X	X	X	X
divalproex sodium*	X	X†			
lamotrigine±	X				X§
gabapentin	X	X"			
levetiracetam	X				
zonisamide	X				

*Indicated as monotherapy in partial-onset seizures that occur in isolation or with other types of seizures.
†Patients ≥10 years of age.
±Indicated for conversion to monotherapy in adults with partial-onset seizures who are receiving treatment with a single enzyme-inducing antiepileptic drug.
§Indicated for generalized seizures of Lennox-Gastuat syndrome
"Patients ≥3 years of age.

Effective Seizure Control May Be Attributable to Multiple Mechanisms of Action

- Electrophysiological and biochemical studies of the effects of topiramate on cultured neurons suggest that TOPAMAX affects excitatory and inhibitory neurotransmission

  Blocks sodium channels

  Blocks non-NMDA subtype of the glutamate receptor

  Enhances the effect of GABA


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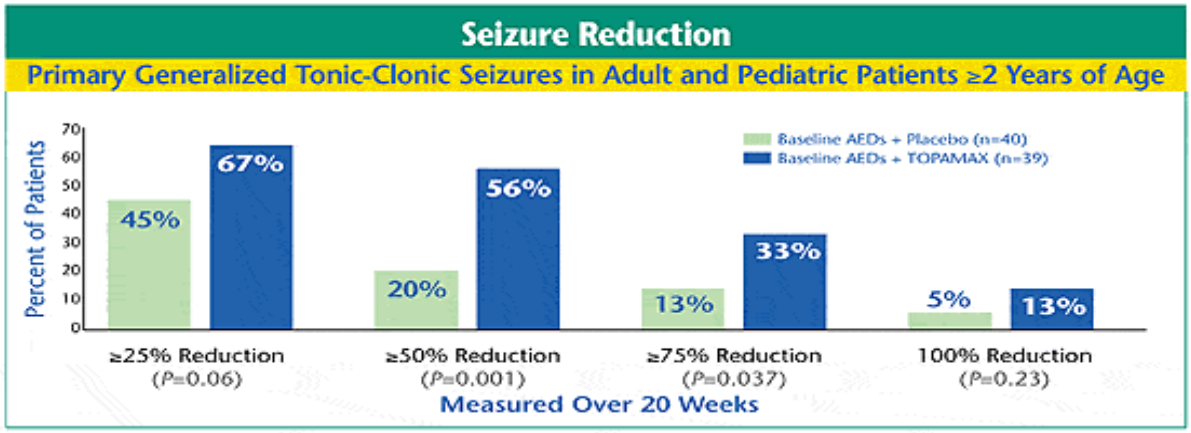
TURN TO TOPAMAX For Proven Efficacy

In Primary Generalized Tonic-Clonic Seizures in Adult and Pediatric Patients ≥2 years of Age



In Partial-Onset Seizures

In double-blind, placebo-controlled, add-on trials:

- **Among adults** (n=90), TOPAMAX plus baseline AEDs resulted in ≥**50% seizure reduction for 44% of patients** (vs 18% for placebo plus baseline AEDs)
- **Among patients 2 to 16 years of age** (n=86), TOPAMAX plus baseline AEDs resulted in ≥**50% seizure reduction for 39% of patients** (vs 20% for placebo plus baseline AEDs)

No Demonstrated Evidence of Tolerance

In combination with other traditional antiepileptic drugs (AEDs), the most common side effects of TOPAMAX in pediatric patients (5 to 9 mg/kg/day) were somnolence (26% vs 16%, TOPAMAX + baseline AEDs vs placebo + baseline AEDs), anorexia (24% vs 15%), fatigue (16% vs 5%), nervousness (14% vs 7%), difficulty with concentration/attention (10% vs 2%), weight decrease (9% vs 1%), aggressive reaction (9% vs 4%), and memory difficulty (5% vs 0%); and in adults (200 to 400 mg/day), somnolence (29% vs 12%), dizziness (25% vs 15%), ataxia (16% vs 7%), speech disorders and related problems (13% vs 2%), psychomotor slowing (13% vs 2%), abnormal vision (13% vs 2%), difficulty with memory (12% vs 3%), paresthesia (11% vs 4%), and diplopia (10% vs 5%).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Well Tolerated

- In controlled clinical trials:
  - Among pediatric patients receiving TOPAMAX adjunctive therapy at 5 to 9 mg/kg/day, there was no discontinuation due to adverse events
  - Among adults patients receiving TOPAMAX adjunctive therapy at 200 to 400 mg/day, 11% discontinued due to adverse events vs 6% for baseline AEDs + placebo
- Minimal interactions with baseline AEDs
- The incidence of kidney stones was 0.6% in pediatric patients and 1.5% in adults

In combination with other traditional antiepileptic drugs (AEDs), the most common side effects of TOPAMAX in pediatric patients (5 to 9 mg/kg/day) were somnolence (26% vs 16%, TOPAMAX + baseline AEDs vs placebo + baseline AEDs), anorexia (24% vs 15%), fatigue (16% vs 5%), nervousness (14% vs 7%), difficulty with concentration/attention (10% vs 2%), weight decrease (9% vs 1%), aggressive reaction (9% vs 4%), and memory difficulty (5% vs 0%); and in adults (200 to 400 mg/day), somnolence (29% vs 12%), dizziness (25% vs 15%), ataxia (16% vs 7%), speech disorders and related problems (13% vs 2%), psychomotor slowing (13% vs 2%), abnormal vision (13% vs 2%), difficulty with memory (12% vs 3%), paresthesia (11% vs 4%), and diplopia (10% vs 5%).

25 mg Titration Improves Tolerability

Commonly Used BID Titration Schedule for Adults

	Week 1	Week 2	Week 3	Week 4	After Week 4
AM Dose		25 mg	25 mg	50 mg	Increase in weekly increments of 25-50 mg/day to effect
PM Dose	25 mg	25 mg	50 mg	50 mg	

- Recommended target dose is 400 mg/day in two divided doses
- Some patients may begin to see a clinical response at TOPAMAX 200 mg/day
- Titrating in increments of 25 mg/week may delay the time to reach an effective dose

Recommended Dosing for Pediatric Patients

	AM DOSE	PM DOSE
Week 1	None	25 mg or less*
At 1 to 2 week intervals	Titrate by increments of 1 to 3 mg/kg/day (in two divided doses) to achieve optimal clinical response	

*Based on a range of 1 to 3 mg/kg/day

- In pediatric patients (ages 2 to 16 years), the recommended daily dose is approximately 5 to 9 mg/kg/day in two divided doses

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FDA APPROVES SLOWER DOSE AND TITRATION SCHEDULE FOR TOPAMAX® (topiramate)

Could Improve Tolerability For Epilepsy Patients Experiencing Majority Of Seizure Types

RARITAN, N.J., May 15, 2000—A slower initial titration schedule for the anti-epileptic medication TOPAMAX® (topiramate) Tablets and TOPAMAX® (topiramate capsules) Sprinkle Capsules has been approved by the U.S. Food and Drug Administration (FDA). TOPAMAX is indicated as add-on treatment for the majority of seizures affecting the 2.3 million Americans diagnosed with epilepsy.

Post-marketing data from physicians with clinical experience with TOPAMAX have shown that slower titration improves tolerability and may reduce the rate of discontinuation due to a lessening of side effects. The new dosing schedule recommends that TOPAMAX be administered initially at 25-50 mg per day, and titrated in increments of 25-50 mg per week until an effective daily dose is reached.

A commonly used titration schedule is to initiate TOPAMAX at 25 mg/day, with weekly increases of 25 mg for the first four weeks. Thereafter, the daily dose may be increased by 25-50 mg weekly to an effective daily dose. Although time to reach an efficacious dose may be delayed relative to the faster rate in the original label, some adult patients may begin to see a clinical response at 200 mg per day of TOPAMAX.

"My own clinical experience and that of my peers, published in the medical literature, shows that TOPAMAX is better tolerated when initiated at a low dose and increased slowly. This new dosing schedule may allow more adults and children with seizures that have not been controlled with other medications to obtain better control with TOPAMAX," said B. J. Wilder, M.D., Professor Emeritus of Neurology and Neuroscience at the College of Medicine at the University of Florida in Gainesville. "It also provides greater flexibility to prescribing physicians in their treatment of patients," he added.

TOPAMAX was first approved by the FDA in 1996 as add-on treatment for adults with partial onset seizures. In July 1999, TOPAMAX was approved as the first "newer generation" anti-epileptic drug to treat partial onset seizures as add-on therapy in pediatric patients as young as two, and in October 1999 was approved as add-on treatment for primary generalized tonic-clonic seizures in adults and pediatric patients ages 2-16.

Seizures, the hallmark of epilepsy, are abnormal electrical discharges in the brain that temporarily disrupt normal brain function. Seizures are classified as either "generalized," when the abnormal discharge affects both sides of the brain simultaneously, or "partial," when the discharge affects one part of the brain initially.

Approximately 25 percent of Americans diagnosed with epilepsy have seizures that resist treatment with traditional anti-epileptic drugs, according to a recent report by the Epilepsy Foundation, a national organization serving people with epilepsy. Physicians may prescribe an add-on medication, such as TOPAMAX, when their patients fail to respond to a single anti-epileptic drug. The newer generation anti-epileptic drugs, developed since 1993, generally are associated with fewer side effects than earlier medications.

TOPAMAX is approved for marketing in more than 65 countries and to date, has been used to treat more than 500,000 patients worldwide.

In clinical trials, in combination with traditional AEDs, the most common side effects associated with

TOPAMAX in pediatric patients included excessive drowsiness, loss of appetite, fatigue, nervousness, difficulty with concentration/attention, weight decrease, aggressive reaction and difficulty with memory. The safety and effectiveness in patients younger than two have not been established. In adults, the most common types of side effects were somnolence, dizziness, coordination problems, speech disorders, psychomotor slowing, abnormal vision, difficulty with memory, sensory distortion and double vision.

TOPAMAX is available as a tablet and in a capsule formulation that can be opened and sprinkled onto food for easy swallowing. The capsule also can be swallowed whole, offering patients greater flexibility.

TOPAMAX was discovered and developed by the R.W. Johnson Pharmaceutical Research Institute, and is marketed in the United States by Ortho-McNeil Pharmaceutical, both Johnson & Johnson companies. Ortho-McNeil markets TOPAMAX and other pharmaceutical products in several therapeutic categories including infectious diseases, central nervous system, wound healing and women's health.

Additional information about TOPAMAX is available by calling 1-800-682-6532

Please see Full U.S. Prescribing Information.

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FDA APPROVES TOPAMAX® (topiramate) TO TREAT COMMON SEIZURE TYPE IN ADULTS AND PEDIATRIC PATIENTS

TOPAMAX Now Indicated as Add-On Treatment for Majority of Seizure Types; Could Benefit Thousands with Uncontrolled Seizures

RARITAN, N.J., October 5, 1999—The U.S. Food and Drug Administration (FDA) approved a new use for the anti-epileptic drug TOPAMAX (topiramate) Tablets and TOPAMAX (topiramate capsules) Sprinkle Capsules as add-on treatment for primary generalized tonic-clonic seizures in adults and pediatric patients ages 2-16. With its previous indication as add-on treatment of partial onset seizures in adults and pediatric patients (ages 2-16), TOPAMAX can now be used to treat the majority of seizures affecting the 2.3 million Americans diagnosed with epilepsy.

Seizures, the hallmark of epilepsy, are abnormal electrical discharges in the brain that temporarily disrupt normal brain function. Seizures are classified as either "generalized," when the abnormal discharge affects both sides of the brain simultaneously, or "partial," when the discharge affects one part of the brain initially.

About 40 percent of people with epilepsy have generalized seizures, and more than half of them experience primary generalized tonic-clonic seizures, sometimes referred to as "grand mal seizures." An individual suffering a primary generalized tonic-clonic seizure will lose consciousness, fall, stiffen, and experience forceful muscle jerking before slowly regaining consciousness.

Roughly 57 percent of people with epilepsy experience partial onset seizures, including about half of the 750,000 children in the U.S. with epilepsy. Partial onset seizures can cause sensory distortion, uncontrolled movements and, in some cases, an altered, trance-like consciousness.

"Topiramate now offers hope to many patients diagnosed with either type of seizure that has not been controlled with other medications," said Victor Biton, M.D., director of the Arkansas Epilepsy Program and lead investigator in the TOPAMAX clinical trials. "With this new indication, topiramate is an effective medication to treat most seizures, in patients ranging from young children to adults."

TOPAMAX was first approved by the FDA in 1996 as add-on treatment for adults with partial onset seizures. In July 1999, TOPAMAX was approved as the first "newer generation" anti-epileptic drug to treat partial onset seizures as add-on therapy in pediatric patients as young as two. Topiramate is approved for marketing in more than 60 countries and to date, has been used to treat seizures in more than 300,000 patients worldwide.

Approximately 25 percent of Americans diagnosed with epilepsy have seizures that resist treatment with traditional anti-epileptic drugs, according to a recent report by the Epilepsy Foundation, a national organization serving people with epilepsy. Physicians may prescribe an add-on medication, such as TOPAMAX, when their patients fail to respond to a single anti-epileptic drug. The newer generation anti-epileptic drugs, developed since 1993, generally are associated with fewer side effects than earlier medications.

TOPAMAX was tested in patients with primary generalized tonic-clonic seizures in a double-blind, randomized, placebo-controlled study at 20 sites with a total of 80 patients. In that trial, 56 percent of patients receiving TOPAMAX as add-on therapy with baseline AEDs experienced at least a 50 percent reduction in primary generalized tonic-clonic seizures vs. 20 percent of patients given placebo. A reduction in seizure frequency of at least 75 percent was experienced by 33 percent of TOPAMAX-treated patients

vs. 13 percent of patients given placebo.

In clinical trials, in combination with traditional AEDs, the most common side effects associated with TOPAMAX in pediatric patients included excessive drowsiness, loss of appetite, fatigue, nervousness, difficulty with concentration/attention, weight decrease, aggressive reaction and difficulty with memory. The safety and effectiveness in patients younger than two have not been established. In adults, the most common types of side effects were somnolence, dizziness, coordination problems, speech disorders, psychomotor slowing, abnormal vision, difficulty with memory, sensory distortion and double vision.

TOPAMAX is available as a tablet and in a capsule formulation that can be opened and sprinkled onto food for easy swallowing. The capsule also can be swallowed whole, offering patients greater flexibility.

TOPAMAX was discovered and developed by the R.W. Johnson Pharmaceutical Research Institute, and is marketed in the United States by Ortho-McNeil Pharmaceutical, both Johnson & Johnson companies. Additional information about TOPAMAX is available by calling 1-800-682-6532

Please see Full U.S. Prescribing Information.

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FDA APPROVES TOPAMAX® FOR PEDIATRIC PATIENTS (AGES 2-16) WITH EPILEPSY

Medication could help thousands of children who experience partial onset seizures

RARITAN, N.J., July 26, 1999—The U.S. Food and Drug Administration (FDA) has approved a new use of the anti-epileptic drug TOPAMAX® (topiramate) Tablets as add-on treatment for pediatric patients (ages 2-16) who experience partial onset seizures. TOPAMAX is the first "new-generation" anti-epileptic drug to be approved for the treatment of partial onset seizures in patients as young as two.

Partial onset seizures affect nearly half of the 750,000 patients seizures under the age of 18 who have epilepsy, according to the Epilepsy Foundation, a national organization serving people with epilepsy.

TOPAMAX was first approved by the FDA in 1996 as add-on treatment for adults with partial onset seizures. It is marketed in more than 45 countries and to date, has been used to treat seizures in more than 270,000 patients worldwide. The newer anti-epileptic drugs, developed since 1993, generally are associated with fewer side effects than earlier mediacations.

"Topiramate is a very important treatment, particularly for the many thousands of pediatric patients in the U.S. who have not been able to achieve freedom from seizures with other anti-epileptic drugs," said W. Edwin Dodson, M.D., professor of pediatrics and neurology at Washington University School of Medicine, and an investigator in the TOPAMAX clinical trials. "Uncontrolled partial onset seizures can severely undermine quality of life."

Partial onset seizures can cause sensory distortion, uncontrolled movements and, in some cases, an altered, trance-like consciousness.

Approximately 25 percent of the 2.3 million people in the U.S. diagnosed with epilepsy have seizures that resist treatment with traditional anti-epileptic drugs, according to a recent report by the Epilepsy Foundation. Physicians may prescribe an add-on medication, such as TOPAMAX, when their patients fail to respond to a single anti-epileptic drug.

Roughly 30 percent of epilepsy cases are attributed to severe head injury, brain tumor, infection affecting the brain, or stroke. But in most cases, the cause is unknown. Although the onset of epilepsy can occur at any age, 20 percent of cases develop before age five.

Seizures, the hallmark of epilepsy, are abnormal electrical discharges in the brain that temporarily disrupt normal brain function. They are categorized as either "generalized," affecting both sides of the brain simultaneously, or "partial," affecting just one part of the brain.

In a double-blinded, randomized, placebo-controlled trial of 86 patients between the ages of two and 16 at 17 clinical sites, TOPAMAX effectively reduced the frequency of partial onset seizures in children. Pediatric patients who received TOPAMAX as add-on therapy with baseline anti-epileptic drugs (AEDs) over the course of the 16-week trial experienced a 33 percent reduction in seizures, compared to 11 percent for placebo and baseline AEDs.

In the pediatric trial, the most common side effects associated with TOPAMAX as add-on therapy included excessive drowsiness, loss of appetite, fatigue, nervousness, difficulty with concentration/attention, weight decrease, aggressive reaction and difficulty with memory. The safety and effectiveness in patients younger than two have not been established.

TOPAMAX is available as a tablet and in a capsule formulation that can be opened and sprinkled onto food

for easy swallowing. The capsule also can be swallowed whole, offering patients greater flexibility.

TOPAMAX was discovered and developed by the R.W. Johnson Pharmaceutical Research Institute, and is marketed in the United States by Ortho-McNeil Pharmaceutical, both Johnson & Johnson companies. Additional information about TOPAMAX is available by calling 1-800-682-6532

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NEW SPRINKLE CAPSULE FORMULATION AVAILABLE FOR ANTIEPILEPTIC DRUG TOPAMAX®; (topiramate) TABLETS

RARITAN, N.J., November 4, 1998 The U.S. Food and Drug Administration has approved a new sprinkle formulation of TOPAMAX® (topiramate) tablets, an antiepileptic drug (AED). The new formulation offers more convenience and ease to patients taking the drug.

With this new formulation, the TOPAMAX Sprinkle Capsule can be opened and its contents sprinkled onto soft food for easier swallowing, or the capsule can be swallowed whole, offering patients greater flexibility.

The new formulation is available in 15 mg and 25 mg capsules. TOPAMAX also is available as 25 mg, 100 mg and 200 mg round tablets for oral use. The new sprinkle capsule formulation is bioequivalent to TOPAMAX tablets and therefore needs no conversion.

TOPAMAX is indicated as adjunctive therapy for adults with partial onset seizures, the most common seizure type. It has been prescribed to more than 180,000 patients worldwide.

In a clinical trial of TOPAMAX tablets, the median average monthly seizure frequency in patients was 11.25 before the addition of TOPAMAX. When TOPAMAX was added to the regimen, 22 percent of patients achieved a 75 percent or greater reduction in seizures (compared to seven percent for baseline AEDs plus placebo). Forty-four percent of patients achieved a 50 percent or greater reduction in seizures (compared to 18 percent for baseline AEDs plus placebo).

The effective seizure control offered by TOPAMAX may be attributable to its multiple mechanisms of action. Electrophysiological and biochemical studies of the effects of topiramate on cultured neurons suggest that TOPAMAX affects excitatory and inhibitory neurotransmission. Specifically, TOPAMAX blocks non-NMDA subtype of the glutamate receptor, enhances the effect of GABA, and blocks sodium channels.

TOPAMAX generally is well-tolerated by patients and has minimal drug interactions with traditional AEDs. In combination with traditional AEDs, the most common side effects of TOPAMAX (200 to 400 mg/day) were somnolence (drowsiness), dizziness, ataxia (coordination problems), psychomotor slowing, speech disorders, nervousness, nystagmus (involuntary eye movement) and paresthesia (numbness or tingling in the skin). Most side effects were mild to moderate in severity.

TOPAMAX Tablets initially was approved by the FDA in December 1996. Discovered and developed by The R.W. Johnson Pharmaceutical Research Institute, TOPAMAX is marketed in the United States by Ortho-McNeil Pharmaceutical. Both are Johnson & Johnson companies headquartered in Raritan, N.J. Topiramate is marketed in more than 25 countries including the United Kingdom, France, Sweden, Australia, Hong Kong and Canada.

Ortho-McNeil manufactures and markets pharmaceutical products in several therapeutic categories, including central nervous system, infectious diseases, women's health and wound healing.

Additional information about TOPAMAX is available by calling 1-800-682-6532

Please see Full U.S. Prescribing Information.

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TOPAMAX®(topiramate) TABLETS & TOPAMAX (topiramate capsules) SPRINKLE CAPSULES

Indications

- TOPAMAX (topiramate) Tablets and TOPAMAX (topiramate capsules) Sprinkle Capsules are indicated as adjunctive therapy for adults and pediatric patients ages 2-16 with partial onset seizures, or primary generalized tonic-clonic seizures.
- TOPAMAX can now be used to treat a majority of seizure types in people with epilepsy.
  Note: Seizures are classified as either "generalized,"affecting both sides of the brain simultaneously, or "partial", affecting one part of the brain initially. About 40 percent of people with epilepsy experience generalized seizures; about 57 percent experience partial seizures.
- TOPAMAX is the first "new generation" anti-epileptic drug (AED) approved for the treatment of partial onset seizures in patients as young as two.
  Note:" New generation" AEDs are those that have been approved by the FDA since 1993.

Mechanism of Action—Although the exact mechanism of action is unknown, studies on cultured neurons suggest that TOPAMAX works in three ways to reduce seizure frequency:

- It blocks non-NMDA subtype of the glutamate receptor, a neurotransmitter that increases nerve cell excitation in the brain.
- It enhances the activity of gamma-aminobutyric acid (GABA), a neurotransmitter that inhibits nerve-cell excitation in the brain.
- It blocks sodium channels.

Efficacy—Clinical trials show that:

- **Primary Generalized Tonic-Clonic Seizures**
  TOPAMAX was tested in a double-blind, randomized, placebo-controlled study at 20 sites with a total of 80 patients. In that trial, 56 percent of patients receiving TOPAMAX as add-on therapy with baseline AEDs experienced at least a 50 percent reduction in primary generalized tonic-clonic seizures vs. 20 percent of patients given placebo. A reduction in seizure frequency of at least 75 percent was experienced by 33 percent of TOPAMAX-treated patients vs. 13 percent of patients given placebo.

- **Partial Onset Seizures**
  - **Pediatric**—Pediatric patients who received TOPAMAX and baseline AEDs experienced a median reduction in seizure frequency of 33 percent, vs. 11 percent for placebo and baseline AEDs. A reduction in seizure frequency of 75 percent or greater was experienced by 17 percent of patients in the TOPAMAX group, compared with two percent of those in the placebo group.

  - **Adult**—Before the addition of TOPAMAX and baseline AEDs, the median average monthly seizure frequency in patients was 11.25. Twenty-two percent of patients achieved a 75 percent or greater reduction in seizures (compared to seven percent for baseline AEDs plus

placebo). Forty-four percent of patients achieved a 50 percent or greater reduction in seizures (compared to 18 percent for baseline AEDs plus placebo).

Safety—More than 500,000 people worldwide have used topiramate. TOPAMAX generally is well tolerated by patients and has minimal drug interactions with traditional AEDs.

- **Pediatric**—In clinical trials, in combination with traditional anti-epileptic drugs, the most common side effects associated with TOPAMAX in pediatric patients included excessive drowsiness, loss of appetite, fatigue, nervousness, difficulty with concentration/attention, weight decrease, aggressive reaction and difficulty with memory. The safety and effectiveness in patients younger than two have not been established.

- **Adult**—In adults, the most common side effects were somnolence, dizziness, coordination problems, speech disorders, psychomotor slowing, abnormal vision, difficulty with memory, sensory distortion and double vision.

Dosage—

- **Pediatric**— According to product labeling, therapy for patients ages 2 to 16 with partial onset seizures should be initiated at 25mg or less, nightly for the first week, based on the range of 1 to 3 mg/kg/day. The dose should be increased at one to two week intervals by increments of 1 to 3 mg/kg/day in two divided doses. The recommended daily dose is approximately 5 to 9 mg/kg/day in two divided doses

  In the study of primary generalized tonic-clonic seizures the initial titration rate was slower then in previous studies; the assigned dose of 6mg/kg/day was reached at the end of 8 weeks.

- **Adult**—According to product labeling, it is recommended that therapy for adults age 17 and older with partial onset seizures 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.

  A commonly used titration schedule is to initiate TOPAMAX at 25 mg/day, with weekly increases of 25 mg for the first four weeks. Thereafter, the daily dose may be increased by 25-50 mg weekly to an effective daily dose.

  In the study of primary generalized tonic-clonic seizures the initial titration rate was slower than in previous studies; the assigned dose was reached at the end of 8 weeks.

Dosage Forms—25, 100 and 200 mg tablets in bottles of 60; 15 and 25 mg sprinkle capsules in bottles of 60

Developed by—The R. W. Johnson Pharmaceutical Research Institute

U.S. marketer/manufacturer—Ortho-McNeil Pharmaceutical, Inc.

International Availability—Topiramate is approved for marketing for a variety of indications in epilepsy in more than 65 countries including the United Kingdom, France, Sweden, Australia, Hong Kong, China, Germany and Canada.

Additional information about TOPAMAX is available by calling 1-800-682-6532

Please see Full U.S. Prescribing Information.

UNCONTROLLED EPILEPSY TAKES TOLL ON CHILDREN IN U.S., REPORT FINDS

Epilepsy, a neurological disorder that causes recurrent seizures, affects hundreds of thousands of pediatric patients in the United States, and can take a devastating toll on young lives, according to "Epilepsy: A Report to the Nation," a recently released Epilepsy Foundation-sponsored report.

Approximately 2.3 million Americans—at least 750,000 of them age 18 or younger—have epilepsy, according to the Epilepsy Foundation. The Foundation reports that 20 percent of those with epilepsy develop the condition before age five. Approximately 30 percent of epilepsy cases are attributed to severe head injury, brain tumor, infection affecting the brain, or stroke. But in most cases, the cause of the disorder is unknown.

Seizures and their treatment
Seizures are the hallmark of epilepsy. Defined as abnormal electrical discharges in the brain that temporarily disrupt normal brain function, epileptic seizures are categorized as either "generalized," affecting both sides of the brain simultaneously, or "partial," affecting just one part of the brain. There are a number of different types of seizures; adults and pediatric patients with the disorder may experience more than one kind. [See information below.]

Treatment with anti-epileptic drugs is standard therapy for people with epilepsy and can often control, and in some cases, eliminate seizures. But roughly 25 percent of those with the disorder—many of them under age 18 -- have uncontrolled seizures that resist treatment, according to "Epilepsy: A Report to the Nation."

Uncontrolled seizures and the need for new therapies
Uncontrolled, recurring seizures can have a particularly devastating effect on pediatric patients. They can lead to repeated seizure-related injuries, learning difficulties and social problems—limiting educational opportunity and undermining quality of life. Such "intractable seizures" may permanently damage developing brains, the authors of the report write.

"Although intractable seizures cut across all demographic lines, the medical literature and new findings by leading experts clearly demonstrate one cruel fact: the young bear an inordinate burden," the authors conclude. "Perhaps the most persuasive evidence in favor of aggressive, focused research into new epilepsy treatments comes from consideration of how epilepsy impacts the social and intellectual development of children."

Fortunately, a promising treatment for pediatric patients with epilepsy is now available. TOPAMAX® (topiramate) Tablets is an anti-epileptic drug that has just been approved by the U.S. Food and Drug Administration as add-on therapy for pediatric patients (ages 2-16) with partial onset seizures. Up to half of the 750,000 patients under age 18 in the United States with epilepsy experience partial onset seizures. TOPAMAX has been shown to significantly reduce seizure frequency in pediatric patients with partial onset seizures. It was first approved in 1996 as add-on therapy for the treatment of adult partial onset seizures.

Clinical trials indicate that TOPAMAX is generally well tolerated and is associated with few clinically significant drug interactions with traditional anti-epileptic drugs (AEDs). In combination with traditional AEDs, the most common side effects associated with TOPAMAX as add-on therapy (5 to 9 mg/kg/day) in pediatric patients (ages 2-16) and under included excessive drowsiness, loss of appetite, fatigue, nervousness, difficulty with concentration/attention, weight decrease, aggressive reaction and difficulty with memory. The safety and effectiveness in patients below age two have not been established.

Note: Patients who have any doubts or questions about their medical treatment should discuss this with their physicians.

Epilepsy in Children: Recognizing and Handling Seizures

Patients with epilepsy may experience a variety of different types of seizures. The information below, based on information from the Epilepsy Foundation, identifies the most common types, and explains what you should do if you see a child having a seizure.

Generalized tonic-clonic

Characteristics: Loss of consciousness and convulsive movements. Child may lose bladder and bowel control. Breathing may stop briefly, then resume. Seizure usually lasts a minute or two.
What to do: Ease the child gently to the floor and clear the area of anything that might hurt him. Put something flat and soft under the child's head so it will not strike the floor during convulsions. Turn the child gently onto his side, to keep his airway clear and allow fluid in his mouth to drain. If breathing halts and does not resume promptly, check the child's airway for obstructions. When the seizure ends, let the child rest until he regains full consciousness.
What not to do: Do not hold the child's tongue. Contrary to popular belief, people with epilepsy do not swallow their tongues during seizures. Do not put anything in the child's mouth or restrain his movements.
When to seek emergency medical help: Most generalized tonic-clonic seizures are not medical emergencies and do not require immediate medical attention. However, if the child exhibits any of the following symptoms, medical attention is warranted:

- A second seizure begins shortly after the first—before the child regains consciousness.
- The seizure shows no sign of ending after five minutes.
- The child hits his head forcefully and does not regain consciousness after a minute or two, is vomiting, is having difficulty regaining full alertness after 20 minutes, complains of vision problems, has a persistent headache, or has dilated pupils or pupils unequal in size.
- The child has a seizure while swimming and there is any possibility that he has swallowed large amounts of water.
- The child has no known history of epilepsy (In this case, some other medical problem may be causing the seizure.)

Other generalized seizures

Characteristics: Sudden changes in muscle tone that may cause the child to fall, or move in an uncoordinated, jerky manner.
What to do: Help the child up if he falls, check for injuries due to the fall, reassure the child, and encourage him to sit quietly until fully recovered.

Absence seizures

Characteristics: Momentary loss of awareness, sometimes accompanied by blinking or other facial or arm movements.
What to do: No first aid or intervention is necessary. However, if the child has no prior history of seizures, medical evaluation is warranted.

Simple partial seizure

Characteristics: The child does not lose consciousness, but may not be able to control his movements. He may hear, smell or experience strange sensations.
What to do: Comfort and reassure the child if he seems confused or frightened.

Complex partial seizure

Characteristics: Automatic behaviors - repeated tapping, muttering, or pacing - and either loss of or clouded consciousness. The child may appear to be sleepwalking or drugged.
What to do: Speak calmly to the child, and gently guide him to a safe place to sit. (If the child resists, simply ensure that he is not in any jeopardy). Help re-orient the child after he regains consciousness.

Additional information about TOPAMAX is available by calling 1-800-682-6532

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TOPAMAX® Approved for Seizures Associated with Lennox-Gastaut Syndrome

Adults and children 2 years of age or older who suffer from seizures associated with Lennox-Gastaut Syndrome - a severe, debilitating form of epilepsy - now have a much-needed new treatment option with the announcement today that the U.S. Food and Drug Administration has approved TOPAMAX® (topiramate) tablets and sprinkle capsules as an adjunctive (add-on) treatment for this condition.

- PRESS RELEASE: New Treatment Option Approved for LENNOX-GASTAUT SYNDROME, one of most debilitating forms of EPILEPSY
- FACT SHEET: TOPAMAX® (topiramate) Tablets & TOPAMAX® (topiramate capsules) Sprinkle Capsules
- FACT SHEET: Lennox-Gastaut Syndrome
- BACKGROUNDER ON: Epilepsy
- JACKIE DISANTE, commenting on: WHEN YOUR CHILD HAS LENNOX-GASTAUT SYNDROME

New Treatment Option Approved for Lennox-Gastaut Syndrome, One of Most Debilitating Forms of Epilepsy

Ortho-McNeil Pharmaceutical Receives New Indication for Topamax® (topiramate)

RARITAN, N.J., Sept. 4 /PRNewswire/ — Adults and children (age 2-16) who suffer from seizures associated with Lennox-Gastaut Syndrome -- a severe, debilitating form of epilepsy -- now have a much-needed new treatment option with the announcement today that the U.S. Food and Drug Administration has approved Topamax(R) (topiramate) tablets and sprinkle capsules as an adjunctive (add-on) treatment for this condition. Lennox-Gastaut Syndrome (LGS) is one of the most severe forms of epilepsy. Individuals who suffer from this illness experience dozens of seizures a day, many of which are resistant to most anti-epileptic drugs. In some cases, LGS seizures are fatal. The condition typically first occurs in early childhood and accounts for up to 10 percent of all cases of pediatric epilepsy. "Lennox-Gastaut is a devastating form of epilepsy, particularly for children. Patients are often developmentally delayed and suffer seizures that are severe, very tough to control and may even lead to injuries," says Tracy Glauser, MD, director of the Children's Comprehensive Epilepsy Program at Cincinnati Hospital Medical Center and a member of the professional advisory board of the Epilepsy Foundation of America. "Until now, anti-epileptic drugs have either not been effective for Lennox-Gastaut, or have had significant side effects, so topiramate offers hope for children and adults with this disease."

Mysterious Condition; Serious Impact
Epileptic seizures are abnormal electrical discharges in the brain that temporarily disrupt normal brain function. Seizures are either classified as "generalized," when the abnormal discharge affects both sides of the brain simultaneously, or "partial," when the discharge affects just one side of the brain. Patients with Lennox-Gastaut Syndrome may experience both generalized and partial seizures. A significant number of patients with Lennox-Gastaut Syndrome are mentally retarded, and/or suffer from developmental delays and behavioral disturbances. The cause of LGS is unknown, although some cases are believed to result from brain injury, malformation or infection. Some evidence suggests that hereditary factors also may play a role in the syndrome's development. There is currently no cure.

Clinical Data and Experience
A study of Topamax was conducted at 12 sites, involving 98 patients who had a history of symptoms associated with Lennox-Gastaut Syndrome and had experienced a minimum of 60 seizures during the month before the study started. Patients continued to receive any previously-prescribed anti- epileptic drugs and were randomized to receive either Topamax or placebo as adjunctive medication. "The results of the study of topiramate in Lennox-Gastaut Syndrome are impressive, given how difficult this condition can be to treat -- particularly in young children," says John Pellock, MD, chairman of child neurology at the Medical College of Virginia and one of the investigators in the study. "The evidence suggests that topiramate will be a valuable addition to our arsenal against this serious condition." The 11-week, double-blinded portion of the study showed that Topamax -- when used in combination with one or two other anti-epileptic drugs -- can significantly reduce both the severity of seizures and the number of "drop attacks" (serious seizures characterized by complete loss of muscle tone and sudden falls). During the study, 52 percent of family members caring for individuals who received Topamax reported that seizures had improved overall, compared to 28 percent of caregivers of patients receiving placebo. Overall, in clinical trials in which Topamax was combined with traditional anti-epileptic drugs, the most common side effects observed in children included excessive drowsiness, loss of appetite, fatigue, nervousness, difficulty with concentration/attention, weight loss, aggressive reaction and memory difficulties. Safety and effectiveness in patients younger than two have not been established. In adults, the most common types of side effects

were sleepiness, dizziness, poor coordination, speech difficulties, slowed thinking (psychomotor slowing), blurred or double vision, memory difficulties and changes in sensation. However, these effects were generally temporary.Topamax is available in tablets and in capsules that can be opened and sprinkled onto food for easy swallowing. The capsules also can be swallowed whole, offering patients greater flexibility.

Product Background
Topamax is marketed under various brand names in more than 75 countries and to date, has been used to treat seizures in approximately 825,000 patients worldwide. The FDA first approved Topamax in 1996 as add-on treatment for adults with partial-onset seizures. In July 1999, the drug was the first "new-generation" anti-epileptic drug to be approved to treat partial-onset seizures as adjunctive therapy in children as young as two years old. In October of 1999, Topamax also was approved as add-on treatment for primary, generalized "tonic-clonic" seizures (in which a temporary loss of consciousness and muscle control occurs) in adults and children aged 2-16. Topamax was discovered and developed by the R.W. Johnson Pharmaceutical Research Institute, and is marketed in the United States by Ortho-McNeil Pharmaceutical, a Johnson & Johnson company. Based in Raritan, NJ, Ortho- McNeil markets pharmaceutical products in several therapeutic categories, including central nervous system disorders, infectious diseases, wound healing and women's health. For more information, please read the full U.S. prescribing information, available upon request by calling 1-800-682-6532 or by visiting http://www.topamax.com or http://www.ortho-mcneil.com.

A Video News Release is available via On The Scene Productions. Feed information:
Tuesday, September 4, 2001
10:00 am - 10:30 am et & 3:00 pm - 3:30 pm et
Telstar 4 , transponder 10 c-band
Audio subcarriers: 6.2/6.8

For more information or to request a hard copy, Please contact On The Scene Productions at 323-930-1030

Fact Sheet:
TOPAMAX®(topiramate) Tablets &
TOPAMAX® (topiramate capsules) Sprinkle Capsules

INDICATIONS

TOPAMAX® (topiramate) tablets and sprinkle capsules are indicated as adjunctive therapy for adults and children aged 2-16 who experience partial-onset seizures; primary, generalized tonic-clonic seizures; and seizures associated with Lennox-Gastaut Syndrome. TOPAMAX was the first "new-generation" anti-epileptic drug (AED) approved for the treatment of partial-onset seizures in children as young as 2 years old.

> Note: Seizures are classified as either "generalized," affecting both sides of the brain simultaneously, or "partial," initially affecting just one part of the brain. About 40 percent of individuals with epilepsy experience generalized seizures; about 57 percent suffer from partial seizures. "New-generation" AEDs are those that have been approved by the FDA since 1993.

MECHANISM OF ACTION

Although the exact mechanism of action is unknown, laboratory studies suggest that TOPAMAX works in three ways to calm the activity of nerve cells and reduce seizure frequency. It:

- Decreases nerve-cell excitation by blocking certain neurotransmitters from binding to glutamate receptors in the brain.
- Enhances the activity of GABA (gamma-aminobutyric acid), a neurotransmitter that inhibits nerve-cell excitation in the brain.
- Blocks sodium channels, thus decreasing excessive nerve-cell firing.

EFFICACY

Lennox-Gastaut Syndrome

A double-blind, placebo-controlled study was conducted of 98 individuals who had a history of Lennox-Gastaut Syndrome and who had experienced a minimum of 60 seizures during the month before entering the trial. These patients, drawn from 12 different study sites, were followed for 11 weeks. The findings demonstrated that when added to traditional anti-epileptic drugs, TOPAMAX was effective in significantly reducing both the severity of seizures and the number of drop attacks (a severe seizure type associated with the disorder that is characterized by a complete loss of muscle control and sudden collapse). In addition, 52 percent of caregivers of patients who received TOPAMAX reported that seizures had improved overall, compared to 28 percent of individuals caring for patients receiving placebo.

Primary, Generalized Tonic-Clonic Seizures

TOPAMAX was tested in a double-blind, randomized, placebo-controlled study at 20 sites involving 80 patients. In that trial, 56 percent of individuals receiving TOPAMAX along with traditional AEDs experienced at least a 50 percent reduction in primary, generalized tonic-clonic (or "grand mal") seizures - compared to 20 percent of patients who took supplemental placebo instead. A reduction in seizure frequency of at least 75 percent was experienced by 33 percent of TOPAMAX-treated patients, vs. 13 percent of patients given placebo instead.

Partial-Onset Seizures

Children (ages 2-16)

- In clinical research, children who received TOPAMAX in addition to a first-line anti-epileptic drug experienced a median reduction in seizure frequency of 33 percent, vs. 11 percent for children who took placebo instead. A reduction in seizure frequency of 75 percent or greater was experienced by 17 percent of patients in the TOPAMAX group, compared with two percent of those in the placebo group.

Adults

- In research involving adults, the median number of seizures experienced by patients was 11.25 per month before TOPAMAX was added to a first-line AED. Twenty-two percent of patients who received adjunctive TOPAMAX achieved a 75 percent or greater reduction in seizures, compared to just 7 percent of individuals who took a first-line AED plus placebo. Forty-four percent of the TOPAMAX group achieved a 50 percent or greater reduction in seizures, compared to 18 percent who received placebo instead.

SAFETY

More than one million people worldwide have taken topiramate. TOPAMAX generally is well tolerated and has minimal drug interactions with traditional AEDs.

Children (ages 2-16)

- When TOPAMAX (5 to 9 mg/kg/day) was taken in clinical trials in combination with traditional AEDs, the most common side effects in children were excessive drowsiness, loss of appetite, fatigue, nervousness, difficulty with concentration/attention, weight loss, aggressive reaction to stimuli and memory difficulties. However, when they occurred, these effects were typically transient.

Adults

- When TOPAMAX (200 to 400 mg/day) was taken in clinical trials in combination with traditional AEDs, the most common side effects were sleepiness, dizziness, poor coordination, speech difficulties, slowed thinking (psychomotor slowing), blurred or double vision, memory difficulties and changes in sensation. However, when they occurred, these effects were generally temporary.

DOSAGE

Children (ages 2-16)

- The recommended daily dose of TOPAMAX as adjunctive treatment for partial-onset seizures; primary, generalized, tonic-clonic seizures; or seizures associated with Lennox-Gastaut Syndrome is approximately 5 to 9 mg/kg/day taken in two divided doses (twice daily).
- It is recommended that the initial dose of TOPAMAX be no more than 25 mg (based on a range of 1 to 3 mg/kg/day), taken nightly for the first week. The dose 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 response. Dose increases should be determined by the prescribing physician based on outcomes in each individual.

Adults

- The recommended daily dose of TOPAMAX as adjunctive therapy is 400 mg per day in two divided doses. It is further recommended that treatment be started at 25-50 mg per day, with the dose increased in increments of 25-50 mg per week until a maximally effective dose is reached for the individual. Daily doses above 1,600 mg have not been studied.

AVAILABLE DOSAGE FORMS

- 25, 50, 100 and 200 mg tablets in bottles of 60
- 15 and 25 mg sprinkle capsules in bottles of 60

DEVELOPER

- The R.W. Johnson Pharmaceutical Research Institute

U.S. MARKETER/ MANUFACTURER

- Ortho-McNeil Pharmaceutical, Inc.

INTERNATIONAL AVAILABILITY

- Topiramate is approved for the treatment of various types of epilepsy in more than 80 countries, including the United Kingdom, France, Sweden, Australia, Hong Kong, China, Germany and Canada.

Fact Sheet:
Lennox-Gastaut Syndrome

- Lennox-Gastaut Syndrome is one of the most severe forms of epilepsy. It accounts for up to 10 percent of all cases of childhood epilepsy, with slightly more males than females affected. It usually develops in children between one and eight years of age, with three the average age of onset.
- Children with Lennox-Gastaut Syndrome experience delays in their development and as many as dozens of different, mixed types of seizures a day. The most common seizure types associated with Lennox-Gastaut Syndrome are tonic, atonic ("drop attacks"), myoclonic and atypical absence seizures.
    - **Tonic**: stiffening of the body, with the eyes rolling upwards, dilation of the pupils and shallow, irregular breathing.
    - **Atonic or "drop attacks"**: brief loss of muscle tone and consciousness, causing abrupt falls.
    - **Myoclonic**: sudden muscle jerks.
    - **Atypical absence**: staring spells.
- Approximately 50 percent of patients with Lennox-Gastaut Syndrome experience status epilepticus, a potentially life-threatening condition that is characterized by either a prolonged seizure lasting 30 minutes or more or the occurrence of repeated seizures without return of consciousness between attacks. Status epilepticus can last for hours, days or even months, and the physical affects include stupor, dementia, greatly impaired balance and, in some cases, death.
- There is no known cause for Lennox-Gastaut Syndrome, although some cases are thought to be the result of the following:
    - Brain injury due to problems associated with pregnancy and birth, including prematurity, asphyxia (lack of oxygen) and/or low birth weight.
    - Severe brain infections, including encephalitis, meningitis, toxoplasmosis and rubella.
    - Genetic brain disease, such as tuberous sclerosis and inherited metabolic brain diseases.
    - Malformations of the brain that occur during development.
- Lennox-Gastaut Syndrome seizures are resistant to most anti-epileptic drugs and thus are difficult to control. There is no cure for the disorder, and complete recovery (absence of any seizure activity and normal development) is unusual.


ORTHO-McNEIL

JACKIE DISANTE, commenting on:
WHEN YOUR CHILD HAS LENNOX-GASTAUT SYNDROME

"She's a little miracle to us every day." That's how Jackie DiSante describes her daughter, Alyssa, an 11-year-old with Lennox-Gastaut Syndrome (LGS). A severe form of epilepsy that accounts for up to 10 percent of all childhood cases, LGS can, in some cases, be fatal.


Alyssa Disante and her mother, Jackie

Alyssa experienced her first seizure a day before her second birthday. "I was called at work and told that there was an emergency and that I needed to go home," Jackie remembers. "That drive home was the worst half-hour of my life."

Alyssa was taken to a hospital emergency room, where she was diagnosed as having a seizure disorder. Within a few weeks, she was experiencing about 80 to 100 seizures a day. "She either seized or she slept. We held her 24 hours a day."

Alyssa suffered from drop seizures - severe seizures characterized by a brief loss of muscle tone and unconsciousness that causes the affected person to fall. "The drop seizures were the worst part; they were violent and came on without any warning," says Jackie. Like many children with Lennox-Gastaut, Alyssa was required to wear a helmet, along with elbow and knee pads, to protect herself from serious injury.

Because Alyssa needed full-time care, Jackie was forced to quit her job to be with her child around the clock. While at home, her free time was spent researching her daughter's condition.

"At the time, I didn't realize that 'seizure disorder' meant 'epilepsy,'" Jackie recalls. And Alyssa's doctors still hadn't confirmed her diagnosis. Frustrated, but driven, Jackie

searched for whatever information she could find and sought a second opinion. "My first question to the neurologist in the initial meeting was, 'Do you think Alyssa has Lennox-Gastaut?' to which he immediately responded, 'yes, absolutely.'"

At this point, Alyssa was taking five anti-epileptic drugs (AEDs) a day, but those medications couldn't control her seizures. The physician gradually weaned Alyssa off these medications, and tried a combination of two new ones instead. "With the new medications, her seizures lessened, but they still weren't controlled," Jackie says.

When Alyssa was six, her physician enrolled her in a research study investigating the use of TOPAMAX® (topiramate) tablets - a new-generation AED - to treat Lennox-Gastaut Syndrome in children. "When Alyssa began taking TOPAMAX, we saw immediate improvement," Jackie remembers. "Her seizures lessened, and now they usually only occur when she's sick, or sometimes when she's sleeping."

Four years later, Alyssa's seizures are still under control with a combination of TOPAMAX and a traditional AED, and life has taken on new meaning. "For so long, we never saw our daughter smile, and it's hard to explain how much that hurt," Jackie says. "Now, she amazing - so full of personality and able to enjoy her life. She is truly a little miracle."

Note to editors: TOPAMAX is approved as add-on therapy for adults and children ages 2-16 with seizures associated with Lennox-Gastaut Syndrome, partial-onset seizures or primary, generalized tonic-clonic seizures.

When used in combination with traditional anti-epileptic drugs in clinical trials, some side effects occurred, but were generally temporary. The most common side effects associated with TOPAMAX in children included excessive drowsiness, loss of appetite, fatigue, nervousness, poor concentration, weight loss, aggressive reaction and memory difficulty. Safety and

effectiveness in children younger than two have not been established. In adults, the most common types of side effects were sleepiness, dizziness, poor coordination, speech difficulty, slowed thinking, blurred or double vision, memory difficulties and changes in sensation.

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Common Seizure Types

There are two basic types of seizures. Generalized seizures start at the same time in both sides of the brain. Partial-onset seizures start in one site of the brain; these seizures may spread to involve more of the brain. Partial-onset seizures that spread very rapidly may actually be mistaken for generalized seizures. About 80% of people with epilepsy have partial-onset seizures or a kind of generalized seizure called primary generalized tonic-clonic seizures (once known as "grand mal").

Primary generalized tonic-clonic seizures are the convulsions that come to mind when the term "seizure" is used. The person may suddenly cry out and fall down with muscle jerks. The person looses consciousness, breathing becomes shallow, and the skin may take on a bluish appearance. Bladder control may also be lost. Usually after no more than 1 or 2 minutes, normal breathing returns and the person regains consciousness, although he/she may feel confused and tired.

Partial-onset seizures can be divided into those in which the person maintains consciousness (simple partial seizures) and those in which consciousness may be clouded or lost (complex partial seizures and secondarily generalized tonic-clonic seizures). Simple partial seizures may start with facial tics or the jerking of an arm or leg. Or, the person may sense a sudden unusual smell or have an abrupt change in mood (especially sudden fear or anxiety). These pre-seizure events are all clues to the area of the brain affected by the seizure. Complex partial seizures often start with a blank stare, followed by involuntary motions like chewing or rubbing the hands. The person appears dazed and unaware of the surroundings, may pick at clothing or pick up objects, and may try to run away or struggle against restraint. The seizure lasts only a few minutes, but the person has no memory of what happened. Seizures can also worsen. Simple partial seizures may spread and become complex partial seizures; complex partial seizures may spread and become convulsions that look exactly like primary generalized tonic-clonic seizures.

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Side Effects of Antiseizure Medicines

All medicines - those that are prescribed by doctors and those that are available at pharmacies without a doctor's prescription - can cause side effects. When used inappropriately, they can even be dangerous. When medicines are combined, the likelihood of side effects increases.

The combination of two or more antiseizure medicines can greatly increase side effects where medicines work - the brain. In general, all antiseizure medicines have side effects that affect the brain, such as sleepiness, dizziness, clumsiness, slow thinking, nervousness and blurred vision.

These side effects usually occur when you are starting a new medicine. However, they will often disappear as your brain adjusts. They reappear as the dose is increased, then disappear again. Your doctor may actually use these side effects as a means of finding the maximum dose you can tolerate or how fast the dose can be increased. If these kinds of side effects do not disappear within a few days or weeks, the doctor may reduce the dose of one of the medicines.

More serious but rare side effects, such as skin rash, liver problems, or blood-related problems, have been reported with various antiseizure medications. While your doctor may have prescribed a medicine that may be less likely to cause such injury, notify your doctor of any unusual or suspicious findings such as rash, unprovoked bruising, bleeding or pain, or unexplained illness.

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First Aid for Seizures

Many people do not know how to properly help someone who is having a seizure. People even have absolutely wrong and potentially dangerous information (dangerous for the person having the seizure).

For example, have you ever heard of putting something such as a stick between the teeth of a person who is having seizure? This can actually cause great harm. Therefore, family and friends need to know what and what not to do when someone is having a seizure.

The two goals of seizure first aid are 1) making the person safe and comfortable during the seizure, and 2) give assistance as the person recovers. Important points for potential caregivers:

- There is nothing to be afraid of - epilepsy is not contagious
- Cushion the person's head to protect against injury
- Loosen neckties and shirt collars
- Turn the person on his or her side to keep the airway clear
- Make sure there is nothing in the mouth (never put something in the mouth to prevent "choking on the tongue"; the tongue cannot be swallowed!)
- Guide the person away from nearby hazards if necessary (do not try to restrain or hold someone down during a seizure; they may resist and inadvertently hurt themselves or you)
- Look for medical ID
- Offer help as the seizure ends

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When To Call an Ambulance

In a person who is known to have epilepsy, an uncomplicated seizure is generally not a medical emergency if the seizure stops after a few minutes. After the seizure and a rest period, most people should be able to continue what they were doing with little or no assistance.

Situations when it would be important to call an ambulance and get a person who has had a seizure to an emergency department for evaluation include when:

- An injury occurs during the seizure
- The seizure occurs in water
- The person is pregnant
- You cannot find an epilepsy medical ID bracelet or card
- The person is diabetic
- The seizure does not stop after 5 minutes
- A second seizure follows the first
- Consciousness does not return after the seizure

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