## Topiramate May Cut Basilar Migraine Frequency

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CHICAGO — Topiramate reduced the frequency of basilar migraine by up to 75% in almost 90% of children who took the drug for migraine prevention, Dr. Donald Lewis reported in a poster presentation at the annual meeting of the American Headache Society.

Migraine drugs are considered successful if they produce at least a 50% improvement in at least 50% of patients, said Dr. Lewis, a pediatric neurologist at Children's Hospital of the King's Daughters, Norfolk, Va.

Using this standard, 86% of the patients in Dr. Lewis' study responded to the medication.

Although the study was small—just 14 children—the robust results are a signifi-

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cant finding, he said in an interview.

"We had a much-better-than-usual clinical response for migraine preventatives. This study cries out to be replicated in a large multicenter trial," he said.

Topiramate (Topamax),

manufactured by Ortho-McNeil, previously has been approved as an adjunctive therapy for seizures. However, the drug is not approved for any headache indication in children, but is used off label, Dr. Lewis said.

The study randomized 14 children with basilar migraine to 25 mg or 100 mg/day of topiramate. Their mean age was 13 years; age of onset of basilar migraine ranged from age 2 to 13 years.

At baseline, they had from 4 to 12 migraine days per month, with most reporting severe or excruciating pain (only two reported moderate pain). The mean duration of migraine was 5 hours (range 1-10 hours).

After a 4-week washout period, the children took topiramate for 12 weeks. Both groups experienced a significant decrease in mean monthly migraine days: 3 days (64%) for the 25-mg group and 3.6 days (75%) for the 100-mg group.

Patients in the 25-mg group experienced a 75% reduction in the mean monthly rate of basilar type migraine, while those in the 100-mg group experienced an 82% reduction.

The overall reduction of basilar type migraine attacks per month was 79%.

There also was a median decrease in migraine duration (18 minutes for the 25-mg group and 89 minutes for the 100-mg group). There were no significant differences in migraine severity between the two groups.

Parents rated six of the seven children taking 25 mg/day as very much or much improved, Dr. Lewis reported. In the 100-mg group, parents rated three of the sev-

en children as very much or much improved.

Dr. Lewis used the PedMidas functionality scale to assess disability. The mean rating decreased from severe to moderate.

There were 35 adverse events noted among 10 children (five children in each group). Only 15 events were possibly or probably related to the study drug, and there were no significant differences in adverse events between the groups.

Adverse events included tingling in the face, intermittent numbness and tingling of the upper extremities, nausea, increased thirst, fatigue, and cognitive issues, including blocked thoughts, difficulty with word finding, and learning problems.

In light of the similar efficacy in both groups and slightly higher responder rate in the 25-mg group (100% vs. 71% in the 100-mg group), Dr. Lewis recommends the "start low, go slow" approach to topi-

ramate titration for basilar migraine in children.

"Sometimes in pediatrics, we have a mindset based on a dose per kilogram. In this situation, we should start with the lower dose, reassess how the patient is doing, then go up slowly. "A titration to 'effectiveness' rather than a targeted dose per weight is the way to go."

The study was investigator initiated, and Ortho-McNeil provided financial support.



GEODON is indicated for the treatment of acute manic or mixed episodes associated with bipolar disorder and for the treatment of schizophrenia.

Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. GEODON is not approved for the treatment of patients with dementia-related psychosis.

GEODON is contraindicated in patients with a known history of QT prolongation, recent acute myocardial infarction, or uncompensated heart failure, and should not be used with other QT-prolonging drugs. GEODON has a greater capacity to prolong the QT $_{\rm c}$  interval than several antipsychotics. In some drugs, QT prolongation has been associated with torsade de pointes, a potentially fatal arrhythmia. In many cases this would lead to the conclusion that other drugs should be tried first.

As with all antipsychotic medications, a rare and potentially fatal condition known as neuroleptic malignant syndrome (NMS) has been reported with GEODON. NMS can cause hyperpyrexia, muscle rigidity, diaphoresis, tachycardia, irregular pulse or blood pressure, cardiac dysrhythmia, and altered mental status. If signs and symptoms appear, immediate discontinuation, treatment, and monitoring are recommended.

Please see brief summary of prescribing information on adjacent page.

Prescribing should be consistent with the need to minimize tardive dyskinesia (TD), a potentially irreversible dose- and duration-dependent syndrome. If signs and symptoms appear, discontinuation should be considered since TD may remit partially or completely.

Hyperglycemia-related adverse events, sometimes serious, have been reported in patients treated with atypical antipsychotics. There have been few reports of hyperglycemia or diabetes in patients treated with GEODON, and it is not known if GEODON is associated with these events. Patients treated with an atypical antipsychotic should be monitored for symptoms of hyperglycemia.

Precautions include the risk of rash, orthostatic hypotension, and seizures

The most common adverse events associated with GEODON in bipolar mania were somnolence, extrapyramidal symptoms, dizziness, akathisia, and abnormal vision.

In short-term schizophrenia trials, the most commonly observed adverse events associated with GEODON at an incidence of  ${\ge}5\%$  and at least twice the rate of placebo were somnolence and respiratory tract infection.

In short-term schizophrenia clinical trials, 10% of GEODON-treated patients experienced a weight gain of ≥7% of body weight vs 4% for placebo.