Felbamate Tablets 400 mg and 600 mg
Oral Suspension 600 mg/5 mL

IN-0321-02
Rev. 9/11

Before Prescribing Felbamate, the physician should be thoroughly familiar with the details of this prescribing information.

FELBAMATE SHOULD NOT BE USED BY PATIENTS UNLESS THERE IS A COMPLETE DISCUSSION OF THE RISKS AND THE PATIENT, PARENT, OR GUARDIAN HAS BEEN PROVIDED THE FELBAMATE WRITTEN ACKNOWLEDGMENT (SEE PATIENT/PHYSICIAN ACKNOWLEDGMENT FORM).

1. APLASTIC ANEMIA

The use of felbamate is associated with a marked increase in the incidence of aplastic anemia in patients whose epilepsy is so severe that the risk of death from seizures would have outweighed the benefits conferred by its use (see INDICATIONS AND USAGE).

Felbamate should be discontinued if evidence of bone marrow depression occurs (see WARNINGS). The risk of death in patients with aplastic anemia generally varies as a function of its severity and etiology; current estimates of the overall case fatality rate are in the range of 20 to 90%.

Felbamate does not appear to affect the incidence of aplastic anemia. However, the risk of aplastic anemia may be increased in patients taking felbamate concomitantly with another antiepileptic drug or drugs which are associated with a risk of aplastic anemia.

It is not known whether or not the risk of developing felbamate-associated aplastic anemia changes with duration of felbamate therapy. It is not known whether or not the dosage of felbamate affects the incidence of aplastic anemia.

Description

Felbamate is an antiepileptic available as 400 mg and 600 mg tablets and as a 600 mg/mL suspension for oral administration.

Felbamate is a white or off-white crystalline powder with a characteristic odor. It is very slightly soluble in water, slightly soluble in methanol, sparingly soluble in dichloromethane, and soluble in dimethyl sulfoxide. The molecular weight is 238.24.

2. HEPATIC FAILURE

Evaluation of postmarketing experience suggests that acute liver failure is associated with the use of felbamate. It is possible that the reporting rate is 67% resulted in death or liver transplantation, usually within 5 weeks of the onset of signs and symptoms of liver failure. The earliest onset of severe hepatic dysfunction, followed subsequently by liver failure was 2 weeks after initiation of felbamate. Several reports described dark urine and biliopancreatic nodular, or pseudoneoplastic, symptoms. In addition, it was not clear if any other neurologic symptoms preceded the onset of jaundice.

It is not known whether or not the risk of developing hepatic failure changes with duration of exposure.

It is not known whether or not the dosage of felbamate affects the incidence of hepatic failure.

It is not known whether concomitant use of other antiepileptic drugs affects the incidence of hepatic failure.

Felbamate should not be prescribed for anyone with a history of hepatic dysfunction.

Treatment with felbamate should be initiated only in patients without active liver disease and with normal baseline serum transaminases.

It has not been proved that periodic serum transaminase determinations are helpful in identifying patients who are at risk for developing a clinical consequence.

It is not known whether or not the dose of felbamate affects the risk of hepatic failure.

Felbamate should be continued if it is not known whether or not concomitant use of antiepileptic drugs and/or other drugs affects the risk of hepatic failure.

Aplastic anemia typically develops without premonitory clinical or laboratory signs, the full clinical syndrome developing within weeks to months. Severe aplastic anemia is manifested by profound pancytopenia in the presence of a bone marrow biopsy showing depleted hematopoietic precursors. The anemia is a function of decreased red blood cell production and subsequent anemia. The white blood cell count and platelet count may be low as a result of a decrease in their production or an increase in bone marrow cell death. The degree of hematopoietic depression is variable, ranging from mild to severe, with bone marrow aspiration showing depletion of hematopoietic precursors. The bone marrow biopsy may show normal cellularity or bone marrow aplasia, with cellularity that is decreased to 5% or less of normal.

Felbamate should be discontinued if evidence of bone marrow depression occurs. The risk of death in patients with aplastic anemia generally varies as a function of its severity and etiology; current estimates of the overall case fatality rate are in the range of 20 to 90%.

Felbamate may increase seizure threshold, an effect considered to be predictive of potential efficacy in absence seizures.

The inactive ingredients for felbamate oral suspension are sodium, lactose, magnesium stearate, FD&C Yellow No. 6, D&C Yellow No. 10, and FD&C Red No. 40 (600 mg tablets only).

Felbamate is effective in mice and rats in the maximal electroshock test, the subcutaneous pentylenetetrazol seizure test, and the subacute pentylenetetrazol seizure test. Felbamate also exhibits anticonvulsant activity by intracerebroventricular administration of glutamate in rats and N-Methyl-D-aspartic acid in mice. Protection against maximal electroshock-induced seizures was noted at an oral dose of 50 mg/kg in the maximal electroshock-induced seizure test in mice. The monocarbamate and p-hydroxy metabolites had only weak (0.2 to 0.6) activity compared with felbamate in the subcutaneous pentylenetetrazol seizure test. These metabolites did not contribute significantly to the anticonvulsant action of felbamate.

The numbers in the pharmacokinetic section are mean ± standard deviation.

Felbamate is well absorbed following oral administration. Over 90% of the radioactivity after a dose of 1000 mg of felbamate was found in the urine within 10 days. The tablet and suspension were each shown to be bioequivalent to the capsules used in clinical trials, and pharmacokinetic parameters of the tablet and suspension were similar. There was no effect of food on absorption of the tablet, the effect of food on absorption of the suspension has not been evaluated.

Following oral administration, felbamate is the predominant plasma species (about 80% of plasma radioactivity). Almost 40-50% of the radioactivity is excreted in the urine within 24 hours in the form of a metabolite which is an ionophore complex. The other portion of the radioactivity is excreted as conjugates. About 15% is present as paraxylotetrahydroxy, 2-hydroxylamino, and felbamate mononitrate, none of which are active. The urinary radioactivity of the metabolite ionophore complex was approximately 10% of the administered dose.

Tolerance of felbamate plasma protein was independent of felbamate concentrations between 10 and 310 micrograms/mL. Binding ranged from 22% to 25%, mostly to albumin, and was dependent on the albumin concentration.

Felbamate was excreted as a terminal half-life of 20-23 hours, which is unaltered after multiple doses. Clearance of a single 1200 mg dose is 26±2 mL/min/1.73 m2 and for a single 3600 mg dose is 35±2 mL/min/1.73 m2. The volume of distribution was 75±2 mL/kg after a 1200 mg dose. Felbamate Cmax and AUC are proportionate to dose single and multiple doses over a range of 100-3600 mg single doses and 1050-3600 mg daily doses. Cmin (blood) was also dose proportional. Multiple daily doses of 1200, 2400, and 3600 mg gave Cmin values of 30x, 55x, and 88x, respectively. Linear and dose proportional pharmacokinetics were also observed at doses above 3620 micrograms/day up to the maximum dose studied of 6000 micrograms. Felbamate gave dose proportional steady-state peak plasma concentrations in children age 4-12 over a range of 15, 30, and 45 mg/kg/day with peak concentrations of 17, 32, and 49 micrograms/mL, respectively.

The effects of race and gender on felbamate pharmacokinetics have not been systematically evaluated, but plasma concentrations of felbamate were not significantly different between races or genders.

Felbamate pharmacokinetics in patients on felbamate were shown to be similar to those in patients not taking felbamate. The effects of felbamate pharmacokinetics on hepatic functional impairment have not been evaluated.

The risk of death in patients with blood pressure. Small but statistically significant mean increase in heart rate were seen during adjunctive therapy and monotherapy; however, these mean increases of up to 5 bpm were not clinically significant.

In children, no statistically relevant changes in blood pressure or heart rate were seen during adjunctive therapy or monotherapy with felbamate.

Other Physiologic Effects:

The incidence of muscle cramps was a mean decrease of approximately 18% in respiratory rate in patients taking felbamate. In adults, statistically significant mean reductions in body weight were observed during felbamate monotherapy and adjunctive therapy. In children, there were decreases in body weight during adjunctive therapy with felbamate which were statistically significant. These mean reductions in adults and children were approximately 5% of the mean weights at baseline.

Clinical Studies

The results of controlled clinical trials established the efficacy of felbamate as monotherapy and adjunctive therapy in adults with partial-onset seizures with or without secondary generalization and in partial and generalized seizures associated with Lennox-Gastaut syndrome in children.

Felbamate Monotherapy Trials in Adults

Felbamate (3600 mg/day given QID) and low-dose valproate (15 mg/kg/day) were compared as monotherapy during a 112-day period in the multicenter Felbhamate Adjunctive Therapy Trials in Adults.

In the multicenter trial, the percentage of patients who met escape criteria was 40% (8/15) in the Felbamate group and 23% (3/13) in the Valproate group. The mean reduction percentage of seizures was 40% (1/3) among patients with 10 or more seizures per month while receiving therapeutic dosages of one or two other antiepileptic drugs.

Felbamate Adjunctive Therapy Trials in Adults

A double-blind, placebo-controlled crossover trial consisted of two 1-week outpatient treatment periods. Patients with refractory partial-onset seizures who were receiving phenytoin and carbamazepine at therapeutic levels were administered felbamate or placebo in a 4-week period. Felbamate was increased to a maximum of 3600 mg/day in three divided doses. Among the 56 patients who completed the study, the baseline seizure frequency was 20 per month for patients treated with felbamate and 26 per month for patients treated with placebo. The mean percentage reduction in seizures was 40% for felbamate and 12% for placebo.

In the multicenter trial, the percentage of patients who met escape criteria was 40% (8/15) in the Felbamate group and 75% (9/12) in the low-dose valproate group. In both trials, the difference in the percentage of patients meeting escape criteria was statistically significant (P=0.001) in favor of Felbamate. These two studies by themselves could not be interpreted to demonstrate equivalent efficacy of the two drugs. For example, valproate was not used at the maximally effective dose in the Felbamate group and 90% (53/58) in the low-dose valproate group. In both trials, the difference in the percentage of patients meeting escape criteria was statistically significant (P=0.001) in favor of Felbamate. These two studies by themselves could not be interpreted to demonstrate equivalent efficacy of the two drugs. For example, valproate was not used at the maximally effective dose in the Felbamate group and 90% (53/58) in the low-dose valproate group.
Phenytoin: Felbamate causes an increase in steady-state phenytoin plasma concentrations. In 10 otherwise healthy subjects who received felbamate as a feed additive for 50 weeks at doses of 300 mg/kg/day and 1000 mg/kg/day of rats were also fed by administration, the steady-state trough (Cmin) phenytoin plasma concentration was 17±5 micrograms/mL, 2400 mg/day of felbamate was monitored. Patients randomized to one of the AEDs had approximately twice the risk (adjusted Relative Risk 1.8, 95% CI:1.2, 2.7) of increased risk of these interactions is summarized in Table 2:

**Specific Effects of Felbamate on Other Antiepileptic Drugs:**

**Phenytoin:** Felbamate causes an increase in steady-state phenytoin plasma concentrations. In 10 otherwise healthy subjects who received felbamate as a feed additive for 50 weeks at doses of 300 mg/kg/day and 1000 mg/kg/day of rats were also fed by administration, the steady-state trough (Cmin) phenytoin plasma concentration was 17±5 micrograms/mL, 2400 mg/day of felbamate was monitored. Patients randomized to one of the AEDs had approximately twice the risk (adjusted Relative Risk 1.8, 95% CI:1.2, 2.7) of

<table>
<thead>
<tr>
<th>Interaction</th>
<th>Placebo Patients with Events Per 1000 Patients</th>
<th>Drug Patients with Events Per 1000 Patients</th>
<th>Relative Risk: Placebo Patients with Events Per 1000 Patients/Drug Patients with Events Per 1000 Patients</th>
<th>Risk Difference: Additional Drug Patients with Events Per 1000 Patients</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>1.0</td>
<td>3.4</td>
<td>3.5</td>
<td>0.6±0.9</td>
<td>0.004</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>5.7</td>
<td>8.5</td>
<td>1.5</td>
<td>0.9±1.9</td>
<td>0.41</td>
</tr>
<tr>
<td>Other</td>
<td>1.0</td>
<td>1.8</td>
<td>1.9</td>
<td>0.3±1.3</td>
<td>0.99</td>
</tr>
<tr>
<td>Total</td>
<td>2.4</td>
<td>4.3</td>
<td>1.8</td>
<td>0.9±1.9</td>
<td>0.99</td>
</tr>
</tbody>
</table>

The relative risk for suicidal thoughts or behavior was higher in clinical trials for epilepsy than in clinical trials for psychiatric or other conditions, but the absolute risk differences were similar for the epilepsy and psychiatric indications. Anyone considering prescribing Felbamate or any other AED must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Should suicidal thoughts and behavior emerge during treatment, the prescriber needs to consider whether the emergence of these symptoms in any given patient is related to the initial illness, or is part of a differential diagnosis. Patients, their caregivers, and families should be informed that AEDs increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of the symptoms and to report such symptoms to their prescriber immediately. Behavior or thoughts about self-harm. Behaviors of concern should be reported immediately to healthcare providers.

PRECAUTIONS

Drug/Laboratory Test Interactions: There are no known interactions of Felbamate with commonly used laboratory tests.

Effects on Pregnancy and Reproductive Function: Fetal studies were conducted in mice and rats. Mice received felbamate as a feed additive for 50 weeks at doses of 300 mg/kg/day and 1000 mg/kg/day of rats were also fed by administration, the steady-state trough (Cmin) phenytoin plasma concentration was 17±5 micrograms/mL, 2400 mg/day of felbamate was monitored. Patients randomized to one of the AEDs had approximately twice the risk (adjusted Relative Risk 1.8, 95% CI:1.2, 2.7) of

Effects of Antacids on Felbamate: The rate and extent of absorption of a 2400 mg dose of felbamate as monotherapy given as tablets was not affected when coadministered with antacids.

Effects of Ethyromycin on Felbamate: The coadministration of ethyromycin (1000 mg/day) for 10 days did not alter the pharmacokinetic parameters of Oxicam, Cmx, AUC, Cl/A or Tmx or felbamate daily doses of 3000 or 3600 mg/day in 10 otherwise healthy subjects with epilepsy.

Other Antiepileptic Drugs: The net

Labor and Delivery: The effect of felbamate on labor and delivery in humans is unknown.

Nursing Mothers: Felbamate has been detected in human milk. The effect on nursing infants is unknown (see Pregnancy section).

Pediatric Use: The safety and effectiveness of Felbamate in children other than those with Lennox-Gastaut syndrome has not been established.

Geriatric Use: No systematic studies in geriatric patients have been conducted. Clinical studies of Felbamate did not include
ADVERSE REACTIONS

The most common adverse reactions seen in association with Felbamate in adults during monotherapy are anorexia, vomiting, insomnia, headache, and dizziness. The most common adverse reactions seen in association with Felbamate in children during adjunctive therapy are anorexia, vomiting, insomnia, nausea, dizziness, somnolence, and headache.

The dropout rate because of adverse experiences or intercurrent illnesses among adult felbamate patients was 12 percent (12/977). The dropout rate because of adverse experiences or intercurrent illnesses among pediatric felbamate patients was six percent (20/357). In adults, the body systems associated with causing these withdrawals in order of frequency were: digestive (34.3%), psychological (21.7%), and musculoskeletal (13.1%). In children, the body systems associated with causing these withdrawals in order of frequency were: digestive (17.5%), neurological (14.1%), dermatological (14.1%), psychological (12.1%), and whole body (10.0%). In adults, specific events with an incidence of 1% or greater associated with causing these withdrawals, in order of frequency was: anorexia (16.4%), nausea (14.4%), rash (12.1%), and weight decrease (11.0%). In children, specific events with an incidence of 1% or greater associated with causing these withdrawals, in order of frequency was rash (11.0%).

Incidence in Clinical Trials – Monotherapy Studies in Adults:
The table that follows enumerates adverse events that occurred at an incidence of 2% or more of 58 adult patients who received felbamate monotherapy at dosages of 3600 mg/day in double-blind controlled trials. Table 3 presents reported adverse events that were classified using standard WHO-based adverse event terminology.

Incidence in Controlled Add-on Clinical Studies in Adults:
Table 4 enumerates adverse events that occurred at an incidence of 2% or more among 114 adult patients who received Felbamate adjunctive therapy in add-on controlled trials at dosages up to 3600 mg/day. Reported adverse events were classified using standard WHO-based adverse event terminology. Many adverse experiences that occurred during adjunctive therapy may be a result of drug interactions. Adverse experiences during adjunctive therapy typically resolved with conversion to monotherapy, or with adjustment of the dosage of other antiepileptic drugs.

Children

In a Controlled Add-on Trial in Children with Lennox-Gastaut Syndrome:
Table 5 enumerates adverse events that occurred more than once among 31 pediatric patients who received felbamate up to 45 mg/kg/day at a maximum of 3600 mg/day. Reported adverse events were classified using standard WHO-based adverse event terminology.

Other Events Observed in Association with the Administration of Felbamate:
In the paragraphs that follow, the adverse clinical events, other than those in the preceding tables, that occurred in a total of 577 adult and 357 children exposed to felbamate and that are reasonably associated with its use are presented. They are listed in order of decreasing frequency. Because the reports cite events observed in open-label and uncontrolled studies, the role of felbamate in their causation cannot be reliably determined.

Table 3: Adults Treatment-Emergent Adverse Event Incidence in Controlled Monotherapy Trials

<table>
<thead>
<tr>
<th>Body System/Event</th>
<th>Felbamate * (N=58)</th>
<th>Valproate ** (N=50)</th>
<th>%</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body as a Whole</td>
<td>Fatigue</td>
<td>6.9</td>
<td>4.0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Weight Decrease</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Face Edema</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>Insomnia</td>
<td>8.6</td>
<td>4.0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>6.9</td>
<td>18.0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Anxiety</td>
<td>5.2</td>
<td>2.0</td>
<td>0</td>
</tr>
<tr>
<td>Dermatological</td>
<td>Acne</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Rash</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Digestive</td>
<td>Diarrhea</td>
<td>6.8</td>
<td>2.0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>5.1</td>
<td>2.0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td>2.7</td>
<td>2.0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Diarthrosis</td>
<td>4.2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>SGPT increased</td>
<td>5.2</td>
<td>2.0</td>
<td>0</td>
</tr>
<tr>
<td>Metabolic/Nutritional</td>
<td>Hypophosphatemia</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Respiratory</td>
<td>Upper Respiratory Tract Infection</td>
<td>8.6</td>
<td>4.0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Rhinitis</td>
<td>6.9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Special Senses</td>
<td>Diaphoresis</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Urticaria</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Urogenital</td>
<td>Infarcturen Blinding</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Urinary Infection</td>
<td>3.4</td>
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<tr>
<td>*3600 mg/day, **15 mg/kg/day</td>
<td>2.5</td>
<td>0</td>
<td>0</td>
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</table>

Table 4: Adults Treatment-Emergent Adverse Event Incidence in Controlled Add-on Trials

<table>
<thead>
<tr>
<th>Body System/Event</th>
<th>Felbamate (N=114)</th>
<th>Placebo (N=43)</th>
<th>%</th>
<th>%</th>
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<tbody>
<tr>
<td>Body as a Whole</td>
<td>Fatigue</td>
<td>16.8</td>
<td>7.0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Fever</td>
<td>2.6</td>
<td>4.7</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Chest Pain</td>
<td>2.6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>Insomnia</td>
<td>18.4</td>
<td>14.0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Somnolence</td>
<td>9.3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td>12.1</td>
<td>7.0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Insomnia</td>
<td>9.3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Sinusitis</td>
<td>2.3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Anorexia</td>
<td>2.3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Asthenia</td>
<td>2.6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Nervousness</td>
<td>2.6</td>
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<td>0</td>
</tr>
<tr>
<td></td>
<td>Gait Abnormal</td>
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<td>0</td>
</tr>
<tr>
<td></td>
<td>Abdominal Pain</td>
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<td>0</td>
</tr>
<tr>
<td></td>
<td>Pharyngitis</td>
<td>2.6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Myalgia</td>
<td>5.2</td>
<td>2.0</td>
<td>0</td>
</tr>
<tr>
<td>Metabolic/Nutritional</td>
<td>Pruritus</td>
<td>3.4</td>
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<td>0</td>
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<tr>
<td>Respiration</td>
<td>Rhinitis</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td>3.4</td>
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<tr>
<td></td>
<td>Diarrhea</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
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<tr>
<td></td>
<td>SGPT increased</td>
<td>3.4</td>
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<td>0</td>
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<tr>
<td>Drug Interactions</td>
<td>Myalgia</td>
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<td>Nausea</td>
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<td></td>
<td>Diarrhea</td>
<td>12.3</td>
<td>7.0</td>
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<tr>
<td></td>
<td>Constipation</td>
<td>11.4</td>
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<td></td>
<td>Urinary Pain</td>
<td>5.2</td>
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<td>Drug Interactions</td>
<td>Myalgia</td>
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<td>Metabolic/Nutritional</td>
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<td>Respiratory</td>
<td>Rhinitis</td>
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<tr>
<td></td>
<td>Vomiting</td>
<td>5.2</td>
<td>0</td>
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<tr>
<td></td>
<td>Diarrhea</td>
<td>3.4</td>
<td>0</td>
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<tr>
<td></td>
<td>SGPT increased</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Drug Interactions</td>
<td>Myalgia</td>
<td>2.6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Metabolic/Nutritional</td>
<td>Pruritus</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Rhinitis</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>5.2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Diarrhea</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>SGPT increased</td>
<td>3.4</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
| Other Events Observed in Association with the Administration of Felbamate:
In the paragraphs that follow, the adverse clinical events, other than those in the preceding tables, that occurred in a total of 357 children exposed to felbamate and that are reasonably associated with its use are presented. They are listed in order of decreasing frequency. Because the reports cite events observed in open-label and uncontrolled studies, the role of felbamate in their causation cannot be reliably determined.

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It is strongly recommended that you retain a copy of the Patient/Physician Acknowledgment Form with the patient’s medical records.

**SUPPLY OF PATIENT/PHYSICIAN ACKNOWLEDGMENT FORMS:**

A supply of “Patient/Physician Acknowledgment” Forms as printed above is available, free of charge, from your local Wallace Pharmaceuticals representative, or may be obtained by calling 1-800-352-4047. Permission to use the above Patient/Physician Acknowledgment Form by photocopy reproduction is also hereby granted by Wallace Pharmaceuticals Inc.
Read this Medication Guide before you start taking FELBAMATE and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment.

**What is the most important information I should know about FELBAMATE?**

Do not stop taking FELBAMATE without first talking to your healthcare provider. Stopping FELBAMATE suddenly can cause serious problems.

FELBAMATE can cause serious side effects, including:

1. **FELBAMATE may cause serious blood problems that may be life-threatening.**
   - Call your healthcare provider right away if you have any of the following symptoms:
     - Fever, sore throat or other infections that come and go or do not go away
     - Frequent infections or an infection that does not go away
     - Easy bruising
     - Bleeding gums or nose bleeds
     - Red or purple spots on your body
     - Severe fatigue or weakness

2. **Liver problems that may be life-threatening.**
   - Call your healthcare provider right away if you have any of these symptoms:
     - Yellowing of your skin or the whites of your eyes (jaundice)
     - Dark urine
     - Nausea or vomiting
     - Loss of appetite
     - Pain on the right side of your stomach (abdomen)

3. **Like other antiepileptic drugs, FELBAMATE may cause suicidal thoughts or actions in a very small number of people, about 1 in 500.**
   - Call your healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you:
     - Thoughts about suicide or dying
     - New or worse depression
     - Attempts to commit suicide
     - Feeling agitated or restless
     - New or worse anxiety
     - Trouble sleeping (insomnia)
     - Panic attacks
     - Acting aggressive, being angry, or violent
     - New or worse irritability
     - Acting on dangerous impulses
     - An extreme increase in activity and talking (mania)
     - Other unusual changes in behavior or mood

**How can I watch for early symptoms of suicidal thoughts and actions?**

- Pay attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings.
- Keep all follow-up visits with your healthcare provider as scheduled.

Call your healthcare provider between visits as needed, especially if you are worried about symptoms.

**Do not stop FELBAMATE without first talking to a healthcare provider.**

Stopping FELBAMATE suddenly can cause serious problems. You should talk to your healthcare provider before stopping. Stopping a seizure medicine suddenly in a patient who has epilepsy can cause seizures.

Suicidal thoughts or actions can be caused by things other than medicines. If you have suicidal thoughts or actions, your healthcare provider may check for other causes.

**What is FELBAMATE?**

FELBAMATE is a prescription medicine used when other treatments have failed in:

- Adults alone or with other medicines to treat:
  - Partial seizures with and without generalization
- Children with other medicines to treat:
  - Seizures associated with Lennox-Gastaut syndrome

**Who should not take FELBAMATE?**

Do not take FELBAMATE if you:

- Are allergic to felbamate, carbamates or any of the ingredients in FELBAMATE.
- Have kidney problems
- Have or have had blood problems
- Have or have had liver problems

**What should I tell my healthcare provider before taking FELBAMATE?**

Before you take FELBAMATE, tell your healthcare provider if you:

- Have kidney problems
- Have or have had depression, mood problems, or suicidal thoughts or behavior
- Have any other medical conditions
- Are pregnant or plan to become pregnant. It is not known if FELBAMATE can harm your unborn baby. Tell your healthcare provider right away if you become pregnant while taking FELBAMATE. You and your healthcare provider will decide if you should take FELBAMATE.
- If you become pregnant while taking FELBAMATE, talk to your healthcare provider about registering with the North American Antiepileptic Drug (NAAED) Pregnancy Registry. The purpose of this registry is to collect information about the safety of antiepileptic medicine during pregnancy. You can enroll in this registry by calling 1-888-233-2334.
- Are breastfeeding or plan to breastfeed. FELBAMATE may pass into your breast milk. You and your healthcare provider should decide if you should take FELBAMATE while you breastfeed.
Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Taking FELBAMATE with certain other medicines can cause side effects or affect how well they work. Do not start or stop other medicines without talking to your healthcare provider.

Know the medicines you take. Keep a list of them and show it to your healthcare provider and pharmacist when you get a new medicine.

How should I take FELBAMATE?
- Take FELBAMATE exactly as your healthcare provider tells you. Your healthcare provider will tell you how much FELBAMATE to take and when to take it.
- Your healthcare provider may change your dose of FELBAMATE. Do not change your dose of FELBAMATE without talking to your healthcare provider.
- Because of the risk of serious blood and liver problems, your healthcare provider may do blood tests before you start and while you take FELBAMATE.
- If you take too much FELBAMATE, call your healthcare provider or local Poison Control Center right away.
- Do not stop FELBAMATE without first talking to your healthcare provider.

What should I avoid while taking FELBAMATE?
- FELBAMATE can cause drowsiness and dizziness. Do not drink alcohol or take other medicines that make you sleepy or dizzy while taking FELBAMATE, until you talk with your doctor. Taking FELBAMATE with alcohol or drugs that cause sleepiness or dizziness may make your sleepiness or dizziness worse.

What are the possible side effects of FELBAMATE?
See “What is the most important information I should know about FELBAMATE?” FELBAMATE may cause serious side effects including:

The most common side effects of FELBAMATE include:
- weight loss
- trouble sleeping
- vomiting
- nausea
- headache
- changes in the way that food tastes
- dizziness
- double-vision

These are not all the possible side effects of FELBAMATE. For more information, ask your healthcare provider or pharmacist.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store FELBAMATE?
- Store FELBAMATE at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep FELBAMATE and all medicines out of the reach of children.

General information about FELBAMATE.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use FELBAMATE for a condition for which it was not prescribed. Do not give FELBAMATE to other people, even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about FELBAMATE. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about FELBAMATE that is written for health professionals.

What are the ingredients in FELBAMATE?
Active Ingredient: felbamate

Tablet Inactive Ingredients: starch, microcrystalline cellulose, croscarmellose sodium, lactose, magnesium stearate, FD&C Yellow No. 6, D&C Yellow No. 10, and FD&C Red No. 40 (600 mg tablets only).
Suspension Inactive Ingredients: sorbitol, glycerin, microcrystalline cellulose, carboxymethylcellulose sodium, simethicone, polysorbate 80, methylparaben, saccharin sodium, propylparaben, FD&C Yellow No. 6, FD&C Red No. 40, flavorings, and purified water.

For more information, go to www.wallacepharmaceuticals.com or call 1-800-352-4047. This Medication Guide has been approved by the U.S. Food and Drug Administration. 
Mfd. By: Meda Pharmaceuticals Inc. For: Wallace Pharmaceuticals Inc.
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