Vigabatrin for oral solution is indicated as monotherapy for pediatric patients with infantile spasms 1 month to 2 years of age who have not responded to treatment with conventional AEDs. Vigabatrin for oral solution should be withdrawn if a substantial clinical benefit is not observed within 3 months of initiating treatment. If, in the clinical judgment of the prescriber, the clinical benefit is not observed within 3 months of initiating treatment, the treatment should be discontinued. The decision to continue Vigabatrin for oral solution treatment must be periodically reassessed.

Dosage and Administration

1. Refractory Complex Partial Seizures

Vigabatrin for oral solution is indicated as monotherapy for pediatric patients with infantile spasms 1 month to 2 years of age who have not responded to treatment with conventional AEDs. Vigabatrin for oral solution should be withdrawn if a substantial clinical benefit is not observed within 3 months of initiating treatment. If, in the clinical judgment of the prescriber, the clinical benefit is not observed within 3 months of initiating treatment, the treatment should be discontinued. The decision to continue Vigabatrin for oral solution treatment must be periodically reassessed.

2. Preparation and Administration Instructions

Vigabatrin for oral solution should be mixed with water prior to administration. Vigabatrin tablets and powder for oral solution are bioequivalent. Either tablet or powder can be used for CPS. Vigabatrin for oral solution is indicated as monotherapy for pediatric patients with infantile spasms 1 month to 2 years of age who have not responded to treatment with conventional AEDs. Vigabatrin for oral solution should be withdrawn if a substantial clinical benefit is not observed within 3 months of initiating treatment. If, in the clinical judgment of the prescriber, the clinical benefit is not observed within 3 months of initiating treatment, the treatment should be discontinued. The decision to continue Vigabatrin for oral solution treatment must be periodically reassessed.

Contraindications

Vigabatrin can cause permanent bilateral concentric visual field constriction, ranging in severity from mild to severe. Severe cases may be characterized by tunnel vision to within 10 degrees of the center of the visual field. Visual field constriction may worsen with continued vigabatrin treatment. In patients with infantile spasms, vigabatrin should be withdrawn if a substantial clinical benefit is not observed within 3 months of initiating treatment. If, in the clinical judgment of the prescriber, the clinical benefit is not observed within 3 months of initiating treatment, the treatment should be discontinued. The decision to continue Vigabatrin for oral solution treatment must be periodically reassessed.

Vigabatrin is contraindicated in patients who have demonstrated a history of or are at risk for visual field constriction. Vigabatrin is contraindicated in patients who have demonstrated a history of or are at risk for visual field constriction. Vigabatrin is contraindicated in patients who have demonstrated a history of or are at risk for visual field constriction. Vigabatrin is contraindicated in patients who have demonstrated a history of or are at risk for visual field constriction.
5.6 Withdrawal of Antiepileptic Drugs (AEDs)

In adult patients, vigabatrin should be withdrawn gradually. However, it should be noted because of a sawtooth effect, rapid discontinuation can be harmful. Patients and caregivers should be told to slowly taper down vigabatrin therapy.

In clinical controlled studies in adults with partial seizures, vigabatrin was tapered by decreasing the daily dose about 10% every week over several weeks. In a clinical controlled study in patients with partial complex seizures, vigabatrin was tapered by decreasing the daily dose about 10% every week over several weeks.

In a controlled clinical study in patients with simple partial seizures, vigabatrin was tapered by decreasing the daily dose about 10% every week over several weeks.

5.7 Adverse Reactions

Nervous System Disorders

Gait disturbance

Somnolence

Fatigue

Sleep disorders

Nervous system disorders were common adverse reactions identified in clinical trials. Vigabatrin was associated with a higher risk of gait disturbance, somnolence, fatigue, and sleep disorders compared to placebo. In clinical studies, the incidence of these reactions was higher in the vigabatrin treatment group compared to the placebo group.

Metabolism & Nutrition Disorders

Weight gain

Decreased appetite

Increased appetite

Weight loss

These adverse reactions were more common in the vigabatrin treatment group compared to the placebo group.

Gastrointestinal Disorders

Diarrhea

Constipation

Nausea

Vomiting

These adverse reactions were more common in the vigabatrin treatment group compared to the placebo group.

Genitourinary Disorders

Urine frequency

Frequency

These adverse reactions were more common in the vigabatrin treatment group compared to the placebo group.

Table 5. Adverse Reactions in Pooled, Add-On Trials in Adults with Refractory Complex Partial Seizures

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Vigabatrin (n=108)</th>
<th>Placebo (n=99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gait disturbance</td>
<td>12%</td>
<td>4%</td>
</tr>
<tr>
<td>Somnolence</td>
<td>20%</td>
<td>8%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>17%</td>
<td>7%</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>19%</td>
<td>9%</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>35%</td>
<td>18%</td>
</tr>
<tr>
<td>Headache</td>
<td>13%</td>
<td>6%</td>
</tr>
<tr>
<td>Erythema multiforme</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Metabolism &amp; Nutrition Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight gain</td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td>Weight loss</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Increased appetite</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10%</td>
<td>6%</td>
</tr>
<tr>
<td>Constipation</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Nausea</td>
<td>8%</td>
<td>4%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5%</td>
<td>3%</td>
</tr>
<tr>
<td>Genitourinary Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine frequency</td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>Frequency</td>
<td>4%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Table 6 lists adverse reactions from controlled clinical studies of pediatric patients receiving vigabatrin or placebo as add-on or monotherapy efficacy trials. Vigabatrin and placebo patients had equal frequencies of adverse reactions. Vigabatrin patients had slightly higher frequencies of adverse reactions compared to placebo patients.

Table 6. Adverse Reactions in Pooled, Add-On Trials in Pediatric Patients 1 to 18 Years of Age with Refractory Complex Partial Seizures

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Vigabatrin (n=254)</th>
<th>Placebo (n=203)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gait disturbance</td>
<td>14%</td>
<td>5%</td>
</tr>
<tr>
<td>Somnolence</td>
<td>21%</td>
<td>10%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>14%</td>
<td>7%</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>12%</td>
<td>6%</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>38%</td>
<td>27%</td>
</tr>
<tr>
<td>Headache</td>
<td>11%</td>
<td>6%</td>
</tr>
<tr>
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<td>0%</td>
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<td></td>
</tr>
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<td>5%</td>
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<td>2%</td>
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<td>2%</td>
<td>1%</td>
</tr>
</tbody>
</table>

4.7 Discontinuation

Discontinuation in ≥1% of patients were infections, status epilepticus, developmental coordination disorder, dystonia, somnolence, fatigue, and eye problems. Discontinuation rates were similar between vigabatrin and placebo patients.

5.2 Pregnancy

Vigabatrin is contraindicated in women of childbearing potential due to the potential for teratogenicity. Vigabatrin is not a drug of choice for the treatment of epilepsy in women of childbearing potential or in women who may become pregnant.

5.9 Use in Special Populations

Pediatric Patients

In clinical trials of pediatric patients aged 2 to 16 years receiving vigabatrin (mean 3.6 years) for a mean of 35 weeks, the most common adverse reactions were gait disturbance (15%), somnolence (11%), and fatigue (8%). Vigabatrin patients had slightly higher frequencies of adverse reactions compared to placebo patients.

6.10 Indications

Epilepsy

Vigabatrin is indicated for the treatment of refractory complex partial seizures in adults 18 years of age and older.

6.11 Contraindications

Vigabatrin is contraindicated in patients with congenital or acquired defects of pyridoxine hydroxylation.

6.4 Pregnancy

Vigabatrin is not a drug of choice for the treatment of epilepsy in women of childbearing potential or in women who may become pregnant.

6.5 Nursing Mothers

Vigabatrin is not a drug of choice for the treatment of epilepsy in women of childbearing potential or in women who may become pregnant.

6.6 Other Drugs

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6.7 Drug Interactions

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11. DESCRIPTION

Vigabatrin is an oral agent. In oral solution form, vigabatrin is available under the trade name of Vigabatrin P.E. (USP 300 mg/5 mL) contains 60 mg/mL of vigabatrin as the hydrochloride salt (pH 7.0 to 7.2). Vigabatrin is supplied as an oral solution for use in the treatment of patients with intractable partial seizures, including those with secondarily generalized seizures, who have not responded to previously used anticonvulsants.

Vigabatrin is a white or almost white powder which is freely soluble in water, lightly soluble in alcohol, very slightly soluble in ether, insoluble in acetone, in ethyl acetate, in benzene, and in chloroform.

7.7 Pharmacokinetics

Vigabatrin was well absorbed in a double-blind, placebo-controlled, crossover study in 103 healthy volunteers. Peak plasma levels were reached at about 4 hours after a single dose of 250 mg and 8 hours after a single dose of 500 mg. Vigabatrin is extensively metabolized in vivo. Eight metabolites were identified in the plasma and urine of volunteers after a single oral dose of 1000 mg of vigabatrin. The major metabolites, each accounting for 10% or more of the dose, were the hydroxylated and glucuronidated forms of vigabatrin. The elimination of vigabatrin, its metabolites, and the parent drug is by urine, with less than 1% excreted in feces. The mean terminal half-life of vigabatrin was 10.5 hours for adults. Following administration of a single oral dose of 3 g, the mean terminal half-life was 10.7 hours. The mean AUC increased by 4.5-fold and the terminal half-life increased by 3.5-fold in adult patients with severe renal impairment as compared to healthy adult volunteers. Vigabatrin is not renally eliminated. Mean serum clearance was 2.4 L/hr for infants (5 months–2 years), 5.8 L/hr for children (10 years–16 years), and 8.5 L/hr for adults.

12. CLINICAL PHARMACOLOGY

12.1 Mechanisms of Action

Vigabatrin is a competitive and selective GABA transaminase inhibitor. It inhibits the metabolism of GABA, increasing its concentration at the synapse and altering central nervous system function. The precise mechanism of vigabatrin's anti-seizure effect is unknown, but it is believed to be the result of its action as a GABA agonist at the GABA-A receptor. Vigabatrin is not an agonist of the GABA-B receptor. Vigabatrin is believed to increase synaptic GABA availability at the synapse by inhibiting the metabolism of GABA.

12.2 Pharmacodynamics

12.2.1 GABA Levels

No significant changes in GABA levels have been observed in brain homogenates (2-5% increase) or in cerebrospinal fluid (20-30% decrease) compared to placebo, following the administration of vigabatrin.

12.2.2 Clinical Trials

The clinical trials assessing vigabatrin for adults are reviewed in the following paragraphs. The use of vigabatrin in pediatric patients is reviewed in sections 12.7 and 13.1.

14.2 Infantile Spasms

The term "infantile spasms" refers to a spectrum of disorders, including West syndrome, Lennox-Gastaut syndrome, hypsarrhythmia and other related disorders. Vigabatrin is indicated for the treatment of infantile spasms associated with West syndrome or Lennox-Gastaut syndrome in patients 1 to 16 years of age.
The CPS does not respond well enough to several other treatments, and

• Vigabatrin for oral solution causes sleepiness and tiredness. Adults taking vigabatrin for oral

• Solutions, medicines, and other medicines may affect each other, causing side effects.

How should I take vigabatrin for oral solution?

• Stopping vigabatrin for oral solution suddenly can cause serious problems. Stopping a seizure

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

• Like other antiepileptic drugs, vigabatrin for oral solution may cause suicidal thoughts or

• If you or your child has CPS, before taking vigabatrin for oral solution tell your

• How should I store vigabatrin for oral solution?

• If you become pregnant while taking vigabatrin for oral solution, talk to your healthcare provider

• If you are a parent or caregiver whose baby has IS, before giving vigabatrin for oral

• If you are using 2 packets of vigabatrin for oral solution, you will need to use 20 mL of water

• The water may be cold

• The most common side effects of vigabatrin for oral solution in

• The CPS does not respond well enough to several other treatments, and

• How often should I take vigabatrin for oral solution?

• Vigabatrin for oral solution causes sleepiness and tiredness. Adults taking vigabatrin for oral

• The number of packets of vigabatrin for oral solution needed for each dose

• The most common side effects of vigabatrin for oral solution in adults include

• You should tell your baby’s healthcare provider right away if your baby’s seizures do not get better.

• You see babies or air the oral syrup after drawing up the syrup, turn the oral syrup bottle upside down, then

• The baby can be tested. Your healthcare provider will determine if your

• You should follow your healthcare provider’s instructions for how to mix the medicine.

• Each dosage is complete when the bottom of the white plunger

• The number of packets of vigabatrin for oral solution needed for each dose

• Anyone who handles the oral solution must wash their hands before and after handling the oral solution.

• You can find this information by filling the packet of vigabatrin for oral solution and

• Your baby’s healthcare provider will talk to you about the

• You should follow your healthcare provider’s instructions for how to mix the medicine.

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