Since June 2018, the Access Pathways® Program for VIGADRONE® has helped physicians overcome the obstacles of prescribing vigabatrin. At no additional cost to patients, we provide a dedicated, experienced team that surrounds patients and caregivers with support, in an effort to shorten time to therapy.

300 PATIENTS SERVED—AND GROWING

Access Pathways® Program for VIGADRONE®

93% OF ELIGIBLE PATIENTS* receive starter treatment within 48 hours following referral.1

SUCCESS STORIES

Access Pathways® is fully committed to providing the support patients and caregivers need, regardless of when they need it.

**AFTER-HOURS CARE**

VIGADRONE® was personally delivered to the airport for overnight delivery the same day a patient received their diagnosis.

**WEEKEND SUPPORT**

A Saturday priority overnight delivery of VIGADRONE® to a patient caregiver was arranged.

* Does not include patients who at time of referral are missing REMS or Access Pathways® consent, need Rx clarification or opt to not start treatment.

Please see Important Safety Information, including Boxed Warning for Risk of Permanent Vision Loss, on page 3-4, and accompanying full Prescribing Information.
INDICATIONS

VIGADRONE® (vigabatrin) powder for Oral Solution is indicated for the treatment of:

- Infantile Spasms (IS) – monotherapy in infants 1 month to 2 years of age for whom the potential benefits outweigh the potential risk of vision loss.
- Refractory Complex Partial Seizures as adjunctive therapy in patients 2 years of age and older who have responded inadequately to several alternative treatments and for whom the potential benefits outweigh the potential risk of vision loss; VIGADRONE is not indicated as a first line agent.

IMPORTANT SAFETY INFORMATION

WARNING: PERMANENT VISION LOSS

See full Prescribing Information for complete Boxed Warning.

- VIGADRONE can cause permanent bilateral concentric visual field constriction, including tunnel vision that can result in disability. In some cases, VIGADRONE may also decrease visual acuity.
- Risk increases with increasing dose and cumulative exposure, but there is no dose or exposure to VIGADRONE known to be free of risk of vision loss.
- Risk of new and worsening vision loss continues as long as VIGADRONE is used, and possibly after discontinuing VIGADRONE.
- Baseline and periodic vision assessment is recommended for patients on VIGADRONE. However, this assessment cannot always prevent vision damage.
- The onset of vision loss from VIGADRONE is unpredictable, and can occur within weeks of starting treatment or sooner, or at any time after starting treatment, even after months or years.
- Because of the risk of permanent vision loss, VIGADRONE is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Vigabatrin REMS Program. Further information is available at www.vigabatrinREMS.com or call 1-866-244-8175.

WARNINGS & PRECAUTIONS

- Permanent Vision Loss. VIGADRONE can cause permanent vision loss. The risk of vision loss increases with increasing the dose and cumulative exposure, but there is no dose or exposure known to be free of risk of vision loss. Patient response should be periodically assessed. Patients can be affected with bilateral concentric visual field constriction ranging in severity from mild to severe. Severe cases may be characterized by tunnel vision, which can result in disability. In some cases, VIGADRONE can damage the central retina and may decrease visual acuity. Symptoms of vision loss from VIGADRONE are unlikely to be recognized by patients or caregivers before vision loss is severe. Vision loss of milder severity, while often unrecognized by the patient or caregiver, can still adversely affect function.
- Monitoring of Vision. Monitoring of vision by an ophthalmic professional with expertise in visual field interpretation and the ability to perform dilated indirect ophthalmoscopy of the retina is recommended. Because vision testing in infants is difficult, vision loss may not be detected until it is severe. For patients receiving VIGADRONE, vision assessment is recommended at baseline, at least every 3 months while on therapy, and about 3 to 6 months after the discontinuation of therapy. Once detected, vision loss due to VIGADRONE is not reversible. It is expected that even with frequent monitoring, some VIGADRONE patients will develop severe vision loss.
- Magnetic Resonance Imaging (MRI) Abnormalities in Infants. Abnormal MRI signal changes have been reported in some infants with Infantile Spasms receiving VIGADRONE. These changes generally resolved with discontinuation of treatment.

Continued on next page...
• **Suicidal Behavior and Ideation.** Antiepileptic drugs, including VIGADRONE, increase the risk of suicidal thoughts and behavior. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. 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 and report behaviors of concern immediately to healthcare providers.

• **Neurotoxicity.** Based on animal data, VIGADRONE may cause neurotoxicity. Intramyelinic edema (IME), was seen in animals at doses within the human therapeutic range.

• **Anemia.** VIGADRONE may cause anemia.

• **Somnolence and Fatigue.** VIGADRONE causes somnolence and fatigue. Advise patients not to drive or operate machinery until they have gained sufficient experience on VIGADRONE.

• **Peripheral Neuropathy.** VIGADRONE causes symptoms of peripheral neuropathy in adults.

• **Weight Gain.** VIGADRONE causes weight gain in adult and pediatric patients.

• **Edema.** VIGADRONE causes edema in adults.

• **Withdrawal of AEDs.** As with all AEDs, VIGADRONE should be withdrawn gradually.

**USE IN SPECIFIC POPULATIONS**

• **Pregnancy:** Based on animal data, VIGADRONE may cause fetal harm.

• **Nursing Mothers:** VIGADRONE is excreted in human milk.

**DRUG INTERACTIONS**

VIGADRONE may decrease phenytoin plasma levels: dosage adjustment may be needed.

**ADVERSE REACTIONS**

**Refractory Complex Partial Seizures**

Most common adverse reactions in controlled studies include (incidence ≥5% over placebo):

• Adults: blurred vision, somnolence, dizziness, abnormal coordination, tremor, and fatigue

• Pediatric patients (3 to 16 years of age): weight gain

**Infantile Spasms (incidence >5% and greater than on placebo)**

• Somnolence, bronchitis, ear infection, and acute otitis media

The most serious adverse reactions are listed above in the WARNINGS AND PRECAUTIONS section.

Refer to the DOSAGE AND ADMINISTRATION section of the full Prescribing Information for recommended dosing guidelines for VIGADRONE, including specific populations.

This safety information is not comprehensive. Please refer to the full Prescribing Information, including Boxed Warning for vision loss for VIGADRONE, WARNINGS AND PRECAUTIONS and Medication Guide. You can also visit www.vigadrone.com, www.upsher-smith.com or call 1-888-650-3789.

You are encouraged to report suspected adverse reactions to Upsher-Smith Laboratories, LLC at 1-855-899-9180 or to the FDA by visiting www.fda.gov/medwatch.

References

## INDICATIONS AND USAGE

Seizures (CPS) in adults and children 2 years of age and older, including patients who are refractory to other AEDs.

### CPS in Adults

- **Lowest Dosage:** Use the lowest dosage and shortest exposure to VIGADRONE consistent with clinical objectives.
- **Alternative Treatments:** Consider alternative treatments and for whom the potential benefits outweigh the risk of vision loss.
- **Caveats:**
  - Risk of new and worsening vision loss.
  - Decreased phenytoin plasma levels: dosage is increased if no clinical benefit is noted, as shown in adult clinical trials.
  - Pregnancy: Based on animal data, may impair fertility. Inform patients of potential risks prior to treatment.
  - Geriatric Use: Decreased in efficacy due to age-related changes in renal and hepatic function.
  - Pediatric Use: Not recommended for use in infants and children below 2 years of age.
  - Lactation: Excretion in breast milk. Assess the potential risk of exposure to the infant and benefits of nursing.

### CPS in Children

- **Multinational Study:**
  - **2,034 patients:** CPS in children aged 2 to 12 years with treatment duration of 12 weeks.
  - **Objectives:** To evaluate clinical benefit of vigabatrin compared to placebo.
  - **Results:**
    - **Clinical benefit:** Superiority of vigabatrin over placebo was seen in children aged 4 to 12 years.
    - **Common Adverse Reactions:** Decreased appetite, vomiting, and weight gain were most frequently reported in children treated with vigabatrin.

### Infantile Spasms

- **Low Dose:**
  - **Maintenance Dose:** Based on 3000 mg/day adult-equivalent dose.
  - **Children:** Administration of 300 mg/kg/day to 500 mg/kg/day.

### Predose Monitoring

- **Visual Assessment:**
  - **Baseline:** At least 4 weeks after starting drug treatment with AEDs.
  - **During Treatment:** Weekly monitoring for vision changes.

### Data Pooled from Randomized Controlled Trials

- **Pediatric Patients:**
  - **Comparison:** Vigabatrin vs. placebo.
  - **Outcome:**
    - **Suicide Risk:**
      - Four suicides in drug treated patients in the trials and none in placebo group.
    - **Weight Gain:**
      - Weight gain in 40% of patients treated with vigabatrin.
    - **Other Adverse Reactions:**
      - Somnolence, bronchitis, ear infection, and skin rash were the most commonly reported adverse reactions.

### Pharmacokinetic Parameters

- **Pharmacokinetic Parameters of Vigabatrin in Infants:**
  - **Half-Life:**Terminal half-life of vigabatrin is about 5.7 hours for infants (5 months to 2 years of age).

### Other AEDs

- **Phenobarbital:**
  - **Decreased Phenytoin Plasma Levels:** Dosage of phenytoin is increased if no clinical benefit is noted, as shown in adult clinical trials.

### Metabolism

- **Gastrointestinal System:** Decreased in efficacy due to age-related changes in renal and hepatic function.

### Magnetic Resonance Imaging (MRI)

- **Abnormalities in Infants:**
  - **Prevalence:** MRI signal changes were observed in the brain of young rats when administered by intraperitoneal injection on postnatal days 5 to 7.
  - **Implications:** Impaired neurobehavioral effects were also observed following vigabatrin treatment of young rats.
  - **Resolving:** MRI signal changes resolved despite continued use.

### Clinical Trials

- **Effectiveness:**
  - **Placebo Patients:**
    - **Response Rate:**
      - 51% of patients randomized to vigabatrin 3 g/day and 53% of patients randomized to placebo.
  - **Other AEDs:**
    - **Adverse Effects:**
      - Common (≥5%) adverse reactions associated with the use of vigabatrin in combination with other AEDs were headache, somnolence, fatigue, dizziness, convulsion, nasopharyngitis, weight gain, and urinary tract infection.
  - **Clinical Trials for Psychiatric or Other Conditions:**
    - **Absolute Risk Differences:** Similar for pediatric patients on vigabatrin and placebo.

### Preparation and Administration Instructions

- **Vigabatrin Powder for Oral Solution:**
  - **Stability:** Stable for at least 2 years when stored at room temperature (25°C).
  - **Dosage Form:** White to off-white powder for oral solution.
  - **Dosing:**
    - **Low Dose:**
      - **Maintenance Dose:** Based on 3000 mg/day adult-equivalent dose.
      - **Children:** Administration of 300 mg/kg/day to 500 mg/kg/day.
    - **High Dose:**
      - **Maintenance Dose:** Based on adult-equivalent dose for patients weighing >20 kg.
      - **Children:** Administration of 300 mg/kg/day to 500 mg/kg/day.
  - **Dosage Adjustments:**
    - **Weight Gain:** Decreasing the daily dose at a rate of 25 mg/kg to 50 mg/kg every 3 to 4 days.
    - **Patient Monitoring:** Regular monitoring of visual function is recommended.
  - **Compliance:**
    - **Recommended:** Assistance from caregivers in taking the medication.
    - **Clinical Trials:** Compliance with the recommended dosing was high in clinical trials.
  - **Discontinuation:** Treatment should be discontinued at that time.
**Permanent vision loss:**

Call your healthcare provider between visits as needed.

**Risk of suicidal thoughts or actions:**

In study of adults treated with AEDs, including VIGADRONE, there was an increased risk of suicidal thoughts or actions compared to placebo. The risk was different for each individual and is not predictable from the individual's characteristics or the characteristics of the condition you are treating. However, if you or your child is experiencing any of the following symptoms of suicidal thoughts or actions, stop using VIGADRONE and call your healthcare provider or the FDA MedWatch at 1-800-FDA-1088 immediately:

- thoughts about suicide or dying
- attempts to run away from home or school
- planning or thinking about self-harm
- talking with others about wanting to harm yourself or kill yourself
- acting on this need, such as looking for a weapon or毒药
- a plan for how you would kill yourself, such as writing instructions on how to do so
- actions to support suicide that are new or increased, such as giving away prized possessions or making arrangements for your death

**MRI Abnormalities in Infants:**

VIGADRONE is available only through a restricted program called the Vigabatrin REMS Program. Patients and caregivers should be informed that if changes in vision are suspected, they should contact their healthcare provider immediately. Monitoring of vision, including assessment of visual fields and visual acuity, is recommended at pre-defined and consistent time points during treatment.

**How Supplied:**

VIGADRONE comes in a packet containing a small spoon for measuring VIGADRONE powder and a ready-to-use oral syringe. Two oral syringes are supplied with each packet of VIGADRONE. Do not use a different oral syringe than the one supplied with your VIGADRONE packets. For Instructions for Use, please visit www.upsher-smith.com or call 1-888-650-3789.

**Limitations:**

- VIGADRONE is a registered trademark of Upsher-Smith Laboratories, LLC.
- IN0556AU
- Revisted 0220

**Monitoring of vision:**

Healthcare providers may not find vision loss in all patients. Patients and caregivers should be informed that if changes in vision are suspected, they should contact their healthcare provider immediately. Monitoring of vision, including assessment of visual fields and visual acuity, is recommended at pre-defined and consistent time points during treatment. The number of packets of VIGADRONE needed for each dose depends on the number of mLs of mixture your healthcare provider tells you to use. VIGADRONE comes in a packet containing a small spoon for measuring VIGADRONE powder and a ready-to-use oral syringe. Two oral syringes are supplied with each packet of VIGADRONE. For Instructions for Use, please visit www.upsher-smith.com or call 1-888-650-3789.

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