Vilazodone HCl (Viibryd) Tablets

**Manufacturer:** Trovis/Clinical Data/PGx Health, New Haven, Conn.

**Indication:** Vilazodone HCl is indicated for the treatment of major depressive disorder (MDD). MDD consists of one or more major depressive episodes, defined as a prominent and relatively persistent dysphoric mood that occurs nearly every day for at least two weeks and usually interferes with daily functioning. Vilazodone is not approved for pediatric patients.

**Drug Class:** The chemical formula is 2-benzofurancarboxamide, 5-4-[4-(5-cyano-1H-indol-3-yl)butyl]-1-piperazinyl]-HCl(1:1). The molecular weight is 477.99.

**Uniqueness of Drug:** Vilazodone is a selective serotonin reuptake inhibitor (SSRI) and a 5-hydroxytryptamine (5-HT1A) receptor partial agonist. The mechanism of the antidepressant effect is not fully understood, but it is thought to be related to the drug’s enhancement of serotonergic activity in the central nervous system through selective inhibition of serotonin reuptake. The net result of this action on serotonergic transmission and its role in vilazodone’s antidepressant effect are unknown.

**Boxed (Black-Box) Warning.** In short-term studies of MDD and other psychiatric disorders, antidepressants have been associated with an increased risk of suicidal thinking and behavior in children, adolescents, and young adults. Anyone considering the use of vilazodone or any other antidepressant in these patients must balance this risk with the clinical need. Short-term studies have not shown an increase in the risk of suicidality with antidepressants, compared with placebo, in adults older than age 24, and there was a reduction in risk with antidepressants, compared with placebo, in adults 65 years of age and older.

Depression and other psychiatric disorders are associated with an increased risk of suicidal thinking and behavior in children, adolescents, and young adults. Anyone considering the use of vilazodone or any other antidepressant in these patients must balance this risk with the clinical need. Short-term studies have not shown an increase in the risk of suicidality with antidepressants, compared with placebo, in adults older than age 24, and there was a reduction in risk with antidepressants, compared with placebo, in adults 65 years of age and older.

Depression and other psychiatric disorders are associated with an increased risk of suicide. Patients of all ages who begin antidepressant therapy should be monitored appropriately and observed closely for worsening of depression, suicidal thinking, or unusual changes in behavior.

Families and caregivers should be advised of the need for close observation and communication with the prescriber. Vilazodone is not approved for pediatric patients.

**Warnings and Precautions:**

**Worsening of depression and risk of suicide.** Patients with MDD, both adult and pediatric, may experience worsening of their depression, the emergence of suicidal ideation and behavior (suicidality), or unusual changes in behavior, whether or not they are taking antidepressant medications. This risk may persist until significant remission occurs. Anti-depressants may play a role in inducing worsening of depression and the emergence of suicidality in some patients during early phases of treatment. Antidepressants increase the risk of suicidal thinking and behavior in children, adolescents, and young adults (18 to 24 years of age) with MDD and other psychiatric disorders.

All patients receiving antidepressants should be monitored for clinical worsening of depression, suicidality, and atypical changes in behavior, especially during the first few months of drug therapy and when the dose is increased or decreased.

Although a causal link has not been established between the emergence of behavioral changes and either the worsening of depression or the emergence of suicidal impulses, these symptoms may represent precursors to emerging suicidality.

**Serotonin syndrome or neuroleptic malignant syndrome–like reactions.** Potentially life-threatening serotonin syndrome or neuroleptic malignant syndrome (NMS)–like reactions have been reported with antidepressants alone, and particularly when serotonergic drugs (including triptans) are given with drugs that impair serotonin metabolism. Examples include monoamine oxidase (MAO) inhibitors, antipsychotic agents, and other dopamine antagonists.

Symptoms of serotonin syndrome were noted in 0.1% of patients who received vilazodone. In its most severe form, the syndrome can resemble NMS, with manifestations of hyperthermia, muscle rigidity, autonomic instability with rapid fluctuation of vital signs, and changes in mental status. Patients should be monitored for the emergence of serotonin syndrome or NMS-like signs and symptoms.

The concomitant use of vilazodone is contraindicated with MAO inhibitors that are intended to treat depression. The concomitant use of vilazodone with serotonin precursors (such as tryptophan) is not recommended.

Treatment with vilazodone and any concomitant serotonergic agent, such as serotonin–norepinephrine reuptake inhibitors (SNRIs), triptans, buspirone (BuSpar, Bristol-Myers Squibb), tramadol (Ultram, PriCara/Johnson & Johnson), or antidepressive drugs, including antipsychotic agents, should be discontinued immediately if adverse symptoms occur. Supportive symptomatic treatment should be initiated.

**Seizures.** Because vilazodone has not been systematically evaluated in patients with a seizure disorder, like other antidepressants, it should be prescribed with caution in these patients.

**Abnormal bleeding.** The use of drugs that interfere with serotonin reuptake inhibition, including vilazodone, may increase the risk of bleeding. The concomitant use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), warfarin (Coumadin, Bristol-Myers Squibb), and other anticoagulants may add to this risk. Studies have demonstrated an association between the use of drugs that interfere with serotonin reuptake and the occurrence of gastrointestinal (GI) bleeding.
Patients should be cautioned about the risk of bleeding associated with the concomitant use of vilazodone and NSAIDs, aspirin, or other drugs that affect coagulation or bleeding.

**Activation of mania and hypomania.** In clinical studies, symptoms of mania and hypomania were reported in 0.1% of patients using vilazodone. Activation of mania and hypomania has also been reported in a small proportion of patients with major affective disorder who used other antidepressants. Vilazodone should be used cautiously in patients with a history or a family history of bipolar disorder, mania, or hypomania.

**Discontinuation of therapy.** Adverse events may occur upon cessation of serotonergic antidepressants, particularly when cessation is abrupt. Effects may include dysphoric mood, irritability, agitation, dizziness, sensory disturbances, paresthesia (e.g., electric shock–like sensations), anxiety, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. Although these events are generally self-limiting, patients should be monitored for these symptoms when they discontinue vilazodone.

When possible, the vilazodone dose should be tapered gradually when patients are discontinuing therapy. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, resuming the previously prescribed dose may be considered. Subsequently, the dose may be decreased but at a more gradual rate.

**Hyponatremia.** Although hyponatremia resulting from vilazodone treatment has not been reported in clinical studies, it has occurred after treatment with SSRIs and SNRIs. In many cases, hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Serum sodium levels lower than 110 mmol/L have been reported. Elderly patients taking SSRIs and patients taking diuretics or who are otherwise volume-depleted can be at risk. Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness, which can lead to falls. Signs and symptoms associated with more severe hyponatremia have included hallucinations, syncope, seizures, coma, respiratory arrest, and death.

**Contraindications:** The concomitant use of vilazodone is contraindicated with MAO inhibitors that are intended to treat depression.

**Drug Interactions:** The concomitant use of vilazodone with serotonin precursors (such as tryptophan) is not recommended. Treatment with vilazodone and any concomitant serotonergic agent, such as SNRIs, triptans, buspirone, tramadol, or antidopaminergic drugs, including antipsychotic agents, should be discontinued immediately if adverse symptoms occur.

**Dosage and Administration:** Vilazodone should be taken with food. The tablets contain the polymorphic form of vilazodone (vilazodone HCl, Form IV). The recommended dose is 40 mg once daily. The drug should be titrated, starting with an initial dose of 10 mg once daily for seven days, followed by 20 mg once daily for seven more days. The dose is then increased to 40 mg once daily.

Patients with acute episodes of MDD require sustained pharmacological therapy for several months or longer; however, the efficacy of vilazodone has not been systematically studied beyond eight weeks.

Symptoms have been reported with discontinuation of serotonergic drugs such as vilazodone; therefore, a gradual dose reduction is recommended when possible. Patients should be monitored for symptoms when they stop taking vilazodone. At least 14 days must elapse between the discontinuation of an MAO inhibitor and the initiation of vilazodone, and at least 14 days must be allowed after stopping vilazodone before starting an MAO inhibitor.

**Commentary:** MDD is the leading cause of disability in the U.S. in people 15 to 44 years of age. Symptoms can interfere with the patient’s ability to work, sleep, study, eat, and enjoy once-pleasurable activities. In a given year, MDD affects approximately 14.8 million American adults, or about 6.7% of the population 18 years of age and older. Although MDD can develop at any age, the median age at onset is 32 years. MDD is more prevalent in women than in men.

Because medications affect everyone differently, a variety of treatment options should be available to depressed patients. Vilazodone is the only antidepressant that works as an SSRI as well as a 5-HT1A receptor partial agonist, thereby affecting serotonin, a mood regulator, in two ways: by restoring a sense of well-being and by not interfering with sexual function.

Like other antidepressants, vilazodone contains a boxed warning and a patient medication guide describing an increased risk of suicidal thinking and behavior in children, adolescents, and young adults during initial treatment.

**Source:** www.vilibryd.com

**Spinosad (Natroba Topical Suspension 0.9%)**

**Manufacturer:** Perrinex Therapeutics, Magnolia, Tex./ParaPro LLC, Carmel, Ind.

**Indication:** Spinosad is indicated for the topical treatment of head lice infestation in patients four years of age and older. This agent is to be used on the scalp and scalp hair only; it is not intended for oral, ophthalmic, or intravaginal use. Spinosad should be used in the context of an overall lice-management program (see Commentary).

**Drug Class:** Spinosad, the active ingredient in the 0.9% viscous, slightly opaque, light-orange suspension, is derived from the fermentation of a soil actinomycete bacterium, Saccharopolyspora spinosa. The product is a mixture of spinosyn A and spinosyn D in a ratio of approximately 5 to 1.

**Uniqueness of Drug:** Spinosad causes neuronal excitation in insects. After periods of hyperexcitation, lice become paralyzed and die.

**Warnings and Precautions:** The topical suspension contains benzyl alcohol and is not recommended for use in neonates and infants younger than six months of age. Systemic exposure to benzyl alcohol has been associated with serious adverse reactions and death in neonates and low-birth-weight infants.

**Dosage and Administration:** The bottle should be shaken well. A sufficient amount of the suspension should be applied to cover the dry scalp, and the product is then applied to dry hair. Depending on the patient’s hair length, up to 120 mL (one bottle) should be applied. The suspension should be left on for 10 minutes and then thoroughly rinsed off with warm water. The hair can be washed with regular shampoo any time after
The chemical name of this cocaine analogue is 2-fluoropropyl-2β-carbomethoxy-3β-(4-iodophenyl) nor-tropane, or \(^{123}\)FP-CIT. Spinosad is synthesized from a basic starting material, stannum (tin)—Sn FP-CT—via oxidative iododestannylation with sodium \(^{123}\)I iodide (123I).

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Spinosad may have additional advantages, other than efficacy, over the current standard of care, permethrin (e.g., Nix). Lice have become resistant to permethrin, which can be dangerous in children if it is overused. Individuals often apply more permethrin than the recommended dose when treatment fails to fully eradicate permethrin-resistant lice. Pyrethrin (e.g., RID shampoo) is also susceptible to resistance.

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Proper and consistent use of spinosad will result in easier and less time-consuming application. Adult lice should be removed from the hair and scalp, and nits from the hair and scalp. However, combing is not required, resulting in easier and less time-consuming application.

Spinosad should be stored at room temperature out of the reach of children.

Commentary: A lice-management program includes washing (in hot water) or dry cleaning all recently worn clothing, hats, used linens, and towels. Combs, brushes, barrettes, and hair clips should also be washed in hot water.

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Sources: www.natroba.com; www.drugs.com

Ioflupane \(^{123}\)I Injection (DaTscan)

Manufacturer: GE Healthcare, Princeton, N.J.

Indication: DaTscan is a radiopharmaceutical agent used to detect the loss of dopaminergic neurons using single photon emission computed tomography (SPECT) brain imaging to assist in evaluating adults with suspected parkinsonian syndromes. Used as an adjunct to other diagnostic evaluations, DaTscan helps to differentiate essential tremor from tremor caused by these syndromes, which include idiopathic Parkinson’s disease (PD), multiple system atrophy, and progressive supranuclear palsy.

Drug Class: The chemical name of this cocaine analogue is \(N\)-\(\omega\)-fluoropropyl-2\(\beta\)-carbomethoxy-3\(\beta\)-(4-iodophenyl) nor-tropane, or \(^{123}\)FP-CIT. Spinosad is synthesized from a basic starting material, stannum (tin)—Sn FP-CT—via oxidative iododestannylation with sodium (I-123) iodide (\(^{123}\)I).

Uniqueness of Product: DaTscan works by binding to dopamine transporters (DaT) in the brain. A specific marker for DaT, the agent produces images that display the presence of dopamine transporters. DaTscan is classified as a Schedule II controlled substance, which has a high potential for abuse that may lead to severe psychological or physical dependence.

Warnings and Precautions:

Hypersensitivity reactions. Patients have experienced hypersensitivity reactions after receiving DaTscan, generally consisting of skin erythema and pruritus. These reactions have resolved either spontaneously or following the administration of corticosteroids and antihistamines. Before DaTscan is given, the patient should be asked about any previous reactions to this agent. If the patient has had or is thought to have had a hypersensitivity reaction to this product, the decision of whether to administer DaTscan should be based upon an assessment of the expected benefits and potential risks. Anaphylactic and hypersensitivity treatments should be available before administration. After the agent is administered, the patient should be observed for symptoms or signs of a hypersensitivity reaction.

Thyroid accumulation. The injection may contain up to 6% of free iodide (iodine 123, or \(^{123}\)I). To decrease thyroid accumulation of \(^{123}\)I, a thyroid-blocking agent should be given first. Potassium iodide oral solution and Lugol’s solution should be avoided in patients who are sensitive to these products. Failure to block thyroid uptake of \(^{123}\)I may result in an increased risk of thyroid neoplasia.

Dosage and Administration: DaTscan emits gamma radiation and must be handled with safety measures. The recommended dose is 111 to 185 MBq (3 to 5 mCi). The dose should be measured by an appropriate radioactivity calibration system immediately before administration. A thyroid-blocking agent must be given at least one hour before DaTscan is given. SPECT imaging should begin between three and six hours after the injection.

Commentary: DaTscan is the first FDA-approved imaging agent that can be used as an adjunct to other diagnostic evaluations to detect neurodegenerative movement disorders, such as idiopathic PD. DaTscan can distinguish essential tremor from tremor caused by parkinson syndromes, although it does not differentiate between various types of parkinson syndromes; therefore, a diagnostic diagnosis is essential for selecting the appropriate treatment for patients with movement disorders.

The FDA granted a priority review for DaTscan because of an unmet need for an imaging agent to assist physicians in managing patients according to their dopaminergic status. Parkinsonian syndromes comprise several neurodegenerative disorders, including multiple system atrophy, progressive supranuclear palsy, and idiopathic PD, which are characterized by rigidity, tremor, and an impaired ability to walk.

Clinical examinations, blood tests, and neuropsychological evaluations are currently used to diagnose movement disorders; however, these modalities are not definitive and may lead to misdiagnosis. As a new diagnostic adjunct to existing assessments, DaTscan represents a meaningful contribution to the field of movement disorders and should benefit patients.

Source: http://us.datscan.com