HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VIIBRYD® safely and effectively. See full prescribing information for VIIBRYD.

VIIBRYD® (vilazodone HCl) Tablets for oral administration
Initial U.S. Approval: 2011

WARNING: SUICIDALITY AND ANTIDEPRESSANT DRUGS

See full prescribing information for complete boxed warning.
Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants for major depressive disorder (MDD) and other psychiatric disorders (5.1).
VIIBRYD is not approved for use in pediatric patients (8.4).

RECENT MAJOR CHANGES

Dosage and Administration (2.5, 2.6)	MM/YYYY
Contraindications (4.1)	MM/YYYY
Warnings and Precautions (5.2)	MM/YYYY

INDICATIONS AND USAGE

VIIBRYD is indicated for the treatment of major depressive disorder (MDD). The efficacy of VIIBRYD was established in two 8-week, placebo-controlled trials in adult patients with MDD (1, 14).

DOSAGE AND ADMINISTRATION

- The recommended dose for VIIBRYD is 40 mg once daily (2.1).
- VIIBRYD should be titrated to the 40 mg dose, starting with an initial dose of 10 mg once daily for 7 days, followed by 20 mg once daily for an additional 7 days, and then increased to 40 mg once daily (2.1).
- VIIBRYD should be taken with food. Administration without food can result in inadequate drug concentrations and may diminish effectiveness (2.1, 12.3).
- When discontinuing treatment, reduce the dose gradually (2.4).

DOSAGE FORMS AND STRENGTHS

VIIBRYD is available as 10 mg, 20 mg and 40 mg tablets (3).

CONTRAINDICATIONS

- **Serotonin Syndrome and MAOIs**: Do not use MAOIs intended to treat psychiatric disorders with VIIBRYD or within 14 days of stopping treatment with VIIBRYD. Do not use VIIBRYD within 14 days of stopping an MAOI intended to treat psychiatric disorders. In addition, do not start VIIBRYD in a patient who is being treated with linezolid or intravenous methylene blue (4.1).

WARNINGS AND PRECAUTIONS

Clinical Worsening/Suicide Risk: Monitor patients for clinical worsening and suicidal thinking or behavior (5.1).
Serotonin Syndrome: Serotonin syndrome has been reported with SSRIs and SNRIs, including VIIBRYD, both when taken alone, but especially when co-administered with other serotonergic agents (including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, trytophan, buspirone and St. John's Wort). If such symptoms occur, discontinue VIIBRYD and initiate supportive treatment. If concomitant use of VIIBRYD with other serotonergic drugs is clinically warranted, patients should be made aware of a potential increased risk for serotonin syndrome, particularly during treatment initiation and dose increases (5.2).
Seizures: Can occur with treatment. Use with caution in patients with a seizure disorder (5.3).
Abnormal Bleeding: Treatment can increase the risk of bleeding. Use with caution in association with nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, or other drugs that affect coagulation (5.4).
Activation of Mania/Hypomania: Can occur with treatment. Screen patients for bipolar disorder (5.5).
Discontinuation of Treatment with VIIBRYD: A gradual reduction in dose is recommended rather than an abrupt cessation (5.6).
Hyponatremia: Can occur in association with the syndrome of inappropriate antidiuretic hormone secretion (SIADH) (5.7).

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥ 5% and at least twice the rate of placebo) are: diarrhea, nausea, vomiting, and insomnia (6).

To report SUSPECTED ADVERSE REACTIONS, contact Forest Laboratories, Inc. at 1-800-678-1605 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

DRUG INTERACTIONS

MAOIs: Do not use VIIBRYD concomitantly with an MAOI or within 14 days of stopping or starting an MAOI (4.1, 7.2).
CYP3A4 inhibitors: The VIIBRYD dose should be reduced to 20 mg when co-administered with CYP3A4 strong inhibitors (7.5).
CYP3A4 inducers: Concomitant use of VIIBRYD with inducers of CYP3A4 can result in inadequate drug concentrations and may diminish effectiveness. The effect of CYP3A4 inducers on systemic exposure of vilazodone has not been evaluated (7.5).

USE IN SPECIFIC POPULATIONS

Pregnancy: There are no controlled human data regarding VIIBRYD use during pregnancy. Use only if the potential benefits outweigh the potential risks (2.3, 8.1).
Nursing Mothers: There are no human data regarding VIIBRYD concentrations in breast milk. Women should breast feed only if the potential benefits outweigh the potential risks (8.3, 2.3).
Pediatric Use: The safety and efficacy of VIIBRYD in pediatric patients have not been studied (2.3, 8.4).
Geriatric Use: No dose adjustment is recommended on the basis of age (8.5).
Hepatic Impairment: No dose adjustment is recommended in patients with mild or moderate hepatic impairment. VIIBRYD has not been studied in patients with severe hepatic impairment (2.3, 8.6).
Renal Impairment: No dose adjustment is recommended in patients with mild, moderate, or severe renal impairment (2.3, 8.7).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: Month Year

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FULL PRESCRIBING INFORMATION: CONTENTS*

***Sections or subsections omitted from the full prescribing information are not listed**

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FULL PRESCRIBING INFORMATION

WARNING: SUICIDALITY AND ANTIDEPRESSANT DRUGS

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of VIIBRYD or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. VIIBRYD is not approved for use in pediatric patients [*see Warnings and Precautions (5.1), Use in Specific Populations (8.4), and Patient Counseling Information (17.1)*]

1 INDICATIONS AND USAGE

VIIBRYD® is indicated for the treatment of major depressive disorder (MDD). The efficacy of VIIBRYD was established in two 8-week, randomized, double-blind, placebo-controlled trials in adult patients with a diagnosis of MDD *[see Clinical Studies (14)]*.

Major depressive disorder consists of one or more major depressive episodes. A major depressive episode (DSM-IV-TR) implies a prominent and relatively persistent (nearly every day for at least 2 weeks) depressed or dysphoric mood that usually interferes with daily functioning, and includes at least 5 of the following 9 symptoms: depressed mood, loss of interest in usual activities, significant change in weight and/or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, or a suicide attempt or suicidal ideation.

2 DOSAGE AND ADMINISTRATION

2.1 Initial Treatment of Major Depressive Disorder

The recommended dose for VIIBRYD is 40 mg once daily. VIIBRYD should be titrated, starting with an initial dose of 10 mg once daily for 7 days, followed by 20 mg once daily for an additional 7 days, and then an increase to 40 mg once daily. VIIBRYD should be taken with food. VIIBRYD blood concentrations (AUC) in the fasted state can be decreased by approximately 50% compared to the fed state, and may result in diminished effectiveness in some patients *[see Clinical Pharmacology (12.3)]*.

2.2 Maintenance/Continuation/Extended Treatment

The efficacy of VIIBRYD has not been systematically studied beyond 8 weeks. It is generally agreed that acute episodes of major depressive disorder require several months or longer of sustained pharmacologic therapy. Patients should be reassessed periodically to determine the need for maintenance treatment and the appropriate dose for treatment.

2.3 Dosing in Special Populations

Pregnant Women: Neonates exposed to serotonergic antidepressants late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. When treating pregnant women with VIIBRYD, consider whether the potential benefits outweigh the potential risks of treatment *[see Use in Specific Populations (8.1)]*.

Nursing Mothers: There are no clinical data regarding the effect of VIIBRYD on lactation and nursing *[see Use in Specific Populations (8.3)]*. Breastfeeding in women treated with VIIBRYD should be considered only if the potential benefit outweighs the potential risk.

Pediatric Patients: The safety and efficacy of VIIBRYD have not been studied in pediatric patients *[see Use in Specific Populations (8.4)]*.

Geriatric Patients: No dose adjustment is recommended on the basis of age *[see Use in Specific Populations (8.5)]*.

Hepatic Impairment: No dose adjustment is recommended in patients with mild or moderate hepatic impairment. VIIBRYD has not been studied in severe hepatic impairment *[see Use in Specific Populations (8.6)]*.

Renal Impairment: No dose adjustment is recommended in patients with mild, moderate, or severe renal impairment *[see Use in Specific Populations (8.7)]*.

Gender: No dose adjustment is recommended on the basis of gender *[see Use in Specific Populations (8.8)]*.

2.4 Discontinuing Treatment

Discontinuation symptoms have been reported with discontinuation of serotonergic drugs such as VIIBRYD. Gradual dose reduction is recommended, instead of abrupt discontinuation, whenever possible. Monitor patients for these symptoms when discontinuing VIIBRYD. If intolerable symptoms occur following a dose decrease or upon discontinuation of treatment, consider resuming the previously prescribed dose and decreasing the dose at a more gradual rate *[see Warnings and Precautions (5.6)]*.

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2.5 Switching a Patient To or From a **Monoamine Oxidase Inhibitor (MAOI)** Intended to Treat Psychiatric Disorders

At least 14 days should elapse between discontinuation of an MAOI intended to treat psychiatric disorders and initiation of therapy with VIIBRYD. Conversely, at least 14 days should be allowed after stopping VIIBRYD before starting an MAOI intended to treat psychiatric disorders *[see Contraindications (4.1)]*.

2.6 Use of VIIBRYD with Other MAOIs such as Linezolid or Methylene Blue

Do not start VIIBRYD in a patient who is being treated with linezolid or intravenous methylene blue because there is an increased risk of serotonin syndrome. In a patient who requires more urgent treatment of a psychiatric condition, other interventions, including hospitalization, should be considered *[see Contraindications (4.1)]*.

In some cases, a patient already receiving VIIBRYD therapy may require urgent treatment with linezolid or intravenous methylene blue. If acceptable alternatives to linezolid or intravenous methylene blue treatment are not available and the potential benefits of linezolid or intravenous methylene blue treatment are judged to outweigh the risks of serotonin syndrome in a particular patient, VIIBRYD should be stopped promptly, and linezolid or intravenous methylene blue can be administered. The patient should be monitored for symptoms of serotonin syndrome for 2 weeks or until 24 hours after the last dose of linezolid or intravenous methylene blue, whichever comes first. Therapy with VIIBRYD may be resumed 24 hours after the last dose of linezolid or intravenous methylene blue *[see Warnings and Precautions (5.2)]*.

The risk of administering methylene blue by non-intravenous routes (such as oral tablets or by local injection) or in intravenous doses much lower than 1 mg/kg with VIIBRYD is unclear. The clinician should, nevertheless, be aware of the possibility of emergent symptoms of serotonin syndrome with such use *[see Warnings and Precautions (5.2)]*.

3 DOSAGE FORMS AND STRENGTHS

VIIBRYD Tablets are available as 10 mg, 20 mg and 40 mg immediate-release, film-coated tablets.

10 mg pink, oval tablet, debossed with 10 on one side
20 mg orange, oval tablet, debossed with 20 on one side
40 mg blue, oval tablet, debossed with 40 on one side

4 CONTRAINDICATIONS

4.1 Monoamine Oxidase Inhibitors (MAOIs)

The use of MAOIs intended to treat psychiatric disorders with VIIBRYD or within 14 days of stopping treatment with VIIBRYD is contraindicated because of an increased risk of serotonin syndrome. The use of VIIBRYD within 14 days of stopping an MAOI intended to treat psychiatric disorders is also contraindicated *[see Dosage and Administration (2.5), and Warnings and Precautions (5.2)]*.

Starting VIIBRYD in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue is also contraindicated because of an increased risk of serotonin syndrome *[see Dosage and Administration (2.6), and Warnings and Precautions (5.2)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Clinical Worsening and Suicide Risk

Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled studies of antidepressant drugs (selective serotonin reuptake inhibitors [SSRIs] and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with MDD and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older.

The pooled analyses of placebo-controlled studies in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term studies of 9 antidepressant drugs in over 4,400 patients. The pooled analyses of placebo-controlled studies in adults with MDD or other psychiatric disorders included a total of 295 short-term studies (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug vs. placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1000 patients treated) are provided in Table 1.

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Table 1

Age Range	Drug-Placebo Difference in Number of Cases of Suicidality per 1000 Patients Treated
	Increases Compared to Placebo
<18	14 additional cases
18-24	5 additional cases
	Decreases Compared to Placebo
25-64	1 fewer case
≥65	6 fewer cases

No suicides occurred in any of the pediatric studies. There were suicides in the adult studies, but the number was not sufficient to reach any conclusion about drug effect on suicide.

It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial evidence from placebo-controlled maintenance studies in adults with depression that the use of antidepressants can delay the recurrence of depression.

All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.

The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality.

Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms [*see Warnings and Precautions (5.6) and Dosage and Administration (2.4)*].

Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to healthcare providers. Such monitoring should include daily observation by families and caregivers. Prescriptions for VIIBRYD should be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose *[see also Patient Counseling Information (17.1)]*.

Screening patients for bipolar disorder

A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled studies) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that VIIBRYD is not approved for use in treating bipolar depression.

5.2 Serotonin Syndrome

The development of a potentially life-threatening serotonin syndrome has been reported with SNRIs and SSRIs, including VIIBRYD, alone but particularly with concomitant use of other serotonergic drugs (including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John's Wort) and with drugs that impair metabolism of serotonin (in particular, MAOIs, both those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue).

Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea). Patients should be monitored for the emergence of serotonin syndrome.

The concomitant use of VIIBRYD with MAOIs intended to treat psychiatric disorders is contraindicated. VIIBRYD should also not be started in a patient who is being treated with MAOIs such as linezolid or intravenous methylene blue. All reports with methylene blue that provided information on the route of administration involved intravenous administration in the dose range of 1 mg/kg to 8 mg/kg. No reports involved the administration of methylene blue by other routes (such as oral tablets or local tissue injection) or at lower doses. There may be circumstances when it is necessary to initiate treatment with an MAOI such as linezolid or intravenous methylene blue in a patient taking VIIBRYD. VIIBRYD should be discontinued before initiating treatment with the MAOI *[see Contraindications (4.1) and Dosage and Administration (2.5 and 2.6)]*.

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