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 hydrochloride) tablets, for oral use
Initial U.S. Approval: 2011

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS
See full prescribing information for complete boxed warning.

- **Antidepressants increase the risk of suicidal thoughts and behaviors in pediatric and young adult patients (5.1).**
- **Closely monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors (5.1).**
- **Viibryd is not approved for use in pediatric patients (8.4).**

RECENT MAJOR CHANGES

Warnings and Precautions (5.9) 7/2021

INDICATIONS AND USAGE

VIIBRYD is indicated for the treatment of major depressive disorder (MDD) in adults (1).

DOSAGE AND ADMINISTRATION

- Recommended target dosage: 20 mg to 40 mg once daily with food (2.1, 12.3).
- To titrate: start with initial dosage of 10 mg once daily for 7 days, followed by 20 mg once daily. The dose may be increased up to 40 mg once daily after a minimum of 7 days between dosage increases (2.1).
- Prior to initiating VIIBRYD, screen for bipolar disorder (2.2, 5.4).
- When discontinuing VIIBRYD, reduce dosage gradually (2.4, 5.5).

DOSAGE FORMS AND STRENGTHS

Tablets: 10 mg, 20 mg, and 40 mg (3)

CONTRAINDICATIONS

- Concomitant use of monoamine oxidase inhibitors (MAOIs), or use within 14 days of stopping MAOIs (4).

WARNINGS AND PRECAUTIONS

- Serotonin Syndrome: Increased risk when co-administered with other serotonergic agents (e.g., SSRI, SNRI, triptans, amphetamines), but also when taken alone. If it occurs, discontinue VIIBRYD and initiate supportive treatment (5.2).
- Increased Risk of Bleeding: Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), other antiplatelet drugs, warfarin, and other anticoagulants may increase this risk (5.3).
- Activation of Mania/Hypomania: Screen patients for bipolar disorder (5.4).
- Seizures: Can occur with treatment. Use with caution in patients with a seizure disorder (5.6).
- Angle Closure Glaucoma: Avoid use of antidepressants, including VIIBRYD, in patients with untreated anatomically narrow angles (5.7).
- Sexual Dysfunction: VIIBRYD may cause symptoms of sexual dysfunction (5.9).

ADVERSE REACTIONS

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

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

DRUG INTERACTIONS

- CYP3A4 Inhibitors: The VIIBRYD dose should not exceed 20 mg once daily when co-administered with strong CYP3A4 inhibitors (2.4, 7).
- CYP3A4 Inducers: Consider increasing VIIBRYD dosage by 2-fold, up to 80 mg once-daily over 1 to 2 weeks when used concomitantly with strong CYP3A4 inducers for greater than 14 days (2.4, 7).

USE IN SPECIFIC POPULATIONS

- Pregnancy: Third trimester use may increase risk for persistent pulmonary hypertension and withdrawal in the newborn (8.1).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 7/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adult patients in short-term studies. Closely monitor all antidepressant-treated patients for clinical worsening and for emergence of suicidal thoughts and behaviors *[see Warnings and Precautions (5.1)]* . Viibryd is not approved for use in pediatric patients *[see Use in Specific Populations (8.4)]*.

1 INDICATIONS AND USAGE

VIIBRYD® is indicated for the treatment of major depressive disorder (MDD) in adults *[see Clinical Studies (14)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage for Treatment of Major Depressive Disorder

The recommended target dosage for VIIBRYD is 20 mg to 40 mg orally once daily with food *[see Clinical Pharmacology (12.3), Clinical Studies (14)]*. To achieve the target dosage, titrate VIIBRYD as follows:

- Start with an initial dosage of 10 mg once daily with food for 7 days,
- Then increase to 20 mg once daily with food.
- The dose may be increased up to 40 mg once daily with food after a minimum of 7 days between dosage increases.

If a dose is missed, it should be taken as soon as the patient remembers. If it is almost time for the next dose, the patient should skip the missed dose and take the next dose at the regular time. Two doses should not be taken at the same time.

2.2 Screen for Bipolar Disorder Prior to Starting VIIBRYD

Prior to initiating treatment with VIIBRYD or another antidepressant, screen patients for a personal or family history of bipolar disorder, mania, or hypomania *[see Warnings and Precautions (5.4)]*.

2.3 Switching to or from a Monoamine Oxidase Inhibitor Antidepressant

At least 14 days must elapse between discontinuation of a monoamine oxidase inhibitor (MAOI) antidepressant and initiation of VIIBRYD. In addition, at least 14 days must elapse after stopping VIIBRYD before starting an MAOI antidepressant *[see Contraindications (4), Warnings and Precautions (5.2)]*.

2.4 Dosage Adjustments with CYP3A4 Inhibitors or Inducers

Patients receiving concomitant CYP3A4 inhibitors:
During concomitant use of a strong CYP3A4 inhibitor (e.g., itraconazole, clarithromycin, voriconazole), the VIIBRYD dose should not exceed 20 mg once daily. The original VIIBRYD dose level, can be resumed when the CYP3A4 inhibitor is discontinued *[see Drug Interactions (7)]*.

Patients receiving concomitant CYP3A4 inducers:
Based on clinical response, consider increasing the dosage of VIIBRYD by 2-fold, up to a maximum 80 mg once daily, over 1 to 2 weeks in patients taking strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifampin) for greater than 14 days. If CYP3A4 inducers are discontinued, gradually reduce the VIIBRYD dosage to its original level over 1 to 2 weeks *[see Drug Interactions (7)]*.

2.5 Discontinuing Treatment with VIIBRYD

Adverse reactions may occur upon discontinuation of VIIBRYD *[see Warnings and Precautions (5.5)]*. A gradual reduction in dosage rather than abrupt cessation is recommended whenever possible. VIIBRYD should be down tapered from the 40 mg once daily dose to 20 mg once daily for 4 days, followed by 10 mg once daily for 3 days. Patients taking VIIBRYD 20 mg once daily should be tapered to 10 mg once daily for 7 days.

3 DOSAGE FORMS AND STRENGTHS

VIIBRYD Tablets are available as 10 mg, 20 mg and 40 mg 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

VIIBRYD is contraindicated in:

- Patients taking, or within 14 days of stopping, monoamine oxidase inhibitors (MAOIs), including MAOIs such as linezolid or intravenous methylene blue, because of an increased risk of serotonin syndrome *[see Warnings and Precautions (5.2), Drug Interactions (7)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Suicidal Thoughts and Behavior in Adolescents and Young Adults

In pooled analyses of placebo-controlled trials of antidepressant drugs (SSRIs and other antidepressant classes) that included approximately 77,000 adult patients, and over 4,500 pediatric patients, the incidence of suicidal thoughts and behaviors in antidepressant-treated patients age 24 years and younger was greater in antidepressant-treated patients than in placebo-treated patients. There was considerable variation in risk of suicidal thoughts and behaviors among drugs, but there was an increased risk identified in young patients for most drugs studied. There were differences in absolute risk of suicidal thoughts and behaviors across the different indications, with the highest incidence in patients with MDD. The drug-placebo differences in the number of cases of suicidal thoughts and behaviors per 1000 patients treated are provided in Table 1.

Table 1: Risk Differences of the Number of Patients with Suicidal Thoughts or Behaviors in the Pooled Placebo-Controlled Trials of Antidepressants in Pediatric and Adult Patients

Age Range (years)	Drug-Placebo Difference in Number of Patients with Suicidal Thoughts or Behaviors per 1000 Patients Treated
	Increases Compared to Placebo
<18	14 additional patients
18-24	5 additional patients
	Decreases Compared to Placebo
25-64	1 fewer patient
≥65	6 fewer patients

It is unknown whether the risk of suicidal thoughts and behaviors in children, adolescents, and young adults extends to longer-term use, i.e., beyond four months. However, there is substantial evidence from placebo-controlled maintenance studies in adults with MDD that antidepressants delay the recurrence of depression and that depression itself is a risk factor for suicidal thoughts and behaviors.

Monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy and at times of dosage changes. Counsel family members or caregivers of patients to monitor for changes in behavior and to alert the healthcare provider. Consider changing the therapeutic regimen, including possibly discontinuing VIIBRYD, in patients whose depression is persistently worse, or who are experiencing emergent suicidal thoughts or behaviors.

5.2 Serotonin Syndrome

Serotonin and norepinephrine reuptake inhibitors (SNRIs) and selective serotonin reuptake inhibitor (SSRIs), including VIIBRYD, can precipitate serotonin syndrome, a potentially life-threatening condition. The risk is increased with concomitant use of other serotonergic drugs (including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, amphetamines, and St. John's Wort) and with drugs that impair metabolism of serotonin, i.e., MAOIs [see Contraindications (4) and Drug Interactions (7)]. Serotonin syndrome can also occur when these drugs are used alone. Symptoms of serotonin syndrome were noted in 0.1% of MDD patients treated with VIIBRYD in premarketing clinical trials.

Serotonin syndrome signs and 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 gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea).

The concomitant use of VIIBRYD with MAOIs is contraindicated. In addition, do not initiate VIIBRYD in a patient being treated with MAOIs such as linezolid or intravenous methylene blue. No reports involved the administration of methylene blue by other routes (such as oral tablets or local tissue injection). If it is necessary to initiate treatment with an MAOI such as linezolid or intravenous methylene blue in a patient taking VIIBRYD, discontinue VIIBRYD before initiating treatment with the MAOI *[see*

Monitor all patients taking VIIBRYD for the emergence of serotonin syndrome. Discontinue treatment with VIIBRYD and any concomitant serotonergic agents immediately if the above symptoms occur, and initiate supportive symptomatic treatment. If concomitant use of VIIBRYD with other serotonergic drugs is clinically warranted, inform patients of the increased risk for serotonin syndrome and monitor for symptoms.

5.3 Increased Risk of Bleeding

Drugs that interfere with serotonin reuptake inhibition, including VIIBRYD, increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDS), other antiplatelet drugs, warfarin, and other anticoagulants may add to this risk. Case reports and epidemiological studies (case-control and cohort design) have demonstrated an association between use of drugs that interfere with serotonin reuptake and the occurrence of gastrointestinal bleeding. Bleeding events related to drugs that interfere with serotonin reuptake have ranged from ecchymosis, hematoma, epistaxis, and petechiae to life-threatening hemorrhages.

Inform patients about the risk of bleeding associated with the concomitant use of VIIBRYD and antiplatelet agents or anticoagulants. For patients taking warfarin, carefully monitor coagulation indices when initiating, titrating, or discontinuing VIIBRYD.

5.4 Activation of Mania or Hypomania

In patients with bipolar disorder, treating a depressive episode with VIIBRYD or another antidepressant may precipitate a mixed/manic episode. In controlled clinical trials, patients with bipolar disorder were excluded; however, symptoms of mania or hypomania were reported in 0.1% of undiagnosed patients treated with VIIBRYD. Prior to initiating treatment with VIIBRYD, screen patients for any personal or family history of bipolar disorder, mania, or hypomania *[see Dosage and Administration (2.2)]*.

5.5 Discontinuation Syndrome

Adverse reactions after discontinuation of serotonergic antidepressants, particularly after abrupt discontinuation, include: nausea, sweating, dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesia, such as electric shock sensations), tremor, anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. A gradual reduction in dosage rather than abrupt cessation is recommended whenever possible *[see Dosage and Administration (2.5)]*.

5.6 Seizures

VIIBRYD has not been systematically evaluated in patients with a seizure disorder. Patients with a history of seizures were excluded from clinical studies. VIIBRYD should be prescribed with caution in patients with a seizure disorder.

5.7 Angle-Closure Glaucoma

The pupillary dilation that occurs following use of many antidepressant drugs including VIIBRYD may trigger an angle closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy. Avoid use of antidepressants, including VIIBRYD, in patients with untreated anatomically narrow angles.

5.8 Hyponatremia

Hyponatremia may occur as a result of treatment with SNRIs and SSRIs, including VIIBRYD. Cases of serum sodium lower than 110 mmol/L have been reported. Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness, which may lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest, and death. In many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH).

In patients with symptomatic hyponatremia, discontinue VIIBRYD and institute appropriate medical intervention. Elderly patients, patients taking diuretics, and those who are volume-depleted may be at greater risk of developing hyponatremia with SSRIs and SNRIs *[see Use in Specific Populations (8.5)]*.

5.9 Sexual Dysfunction

Use of SSRIs, including VIIBRYD, may cause symptoms of sexual dysfunction [*see Adverse Reactions (6.1)]*. In male patients, SSRI use may result in ejaculatory delay or failure, decreased libido, and erectile dysfunction. In female patients, SSRI use may result in decreased libido and delayed or absent orgasm.

It is important for prescribers to inquire about sexual function prior to initiation of VIIBRYD and to inquire specifically about changes in sexual function during treatment, because sexual function may not be spontaneously reported. When evaluating changes in sexual function, obtaining a detailed history (including timing of symptom onset) is important because sexual symptoms may have other causes, including the underlying psychiatric disorder. Discuss potential management strategies to support patients in making informed decisions about treatment.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling:

- Suicidal Thoughts and Behaviors in Adolescents and Young Adults *[see Warnings and Precautions (5.1)]*.
- Serotonin Syndrome *[see Warnings and Precautions (5.2)]*.
- Increased Risk of Bleeding *[see Warnings and Precautions (5.3)]*.
- Activation of Mania or Hypomania *[see Warnings and Precautions (5.4)]*.
- Discontinuation Syndrome *[see Warnings and Precautions (5.5)]*.
- Seizures *[see Warnings and Precautions (5.6)]*
- Angle-Closure Glaucoma *[see Warnings and Precautions (5.7)]*.
- Hyponatremia *[see Warnings and Precautions (5.8)]*.
- Sexual Dysfunction *[see Warnings and Precautions (5.9)]*.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions and varying lengths of time, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect rates observed in practice.

The most commonly observed adverse reactions in VIIBRYD-treated patients with major depressive disorder (MDD) in placebo-controlled studies (incidence ≥ 5% and at least twice the rate of placebo) were diarrhea, nausea, vomiting, and insomnia.

Patient Exposure

The safety of VIIBRYD was evaluated in 3,007 patients (18-70 years of age) diagnosed with MDD who participated in clinical studies, representing 676 patient-years of exposure. In an open-label 52 week study at 40 mg daily, 599 patients were exposed to VIIBRYD for a total of 348 patient-years.

The adverse reaction information presented below was derived from studies of VIIBRYD 20 mg and 40 mg daily in patients with MDD including:

- Four placebo-controlled 8 to 10-week studies in 2,233 patients, including 1,266 VIIBRYD-treated patients; and
- An open-label 52-week study of 599 VIIBRYD-treated patients.

These studies included a titration period of 10 mg daily for 7 days, followed by 20 mg daily for 7 days or to 40 mg daily over 2 weeks. In these clinical trials, VIIBRYD was administered with food.

Adverse reactions reported as reasons for discontinuation of treatment

In these studies, 7.3% of the VIIBRYD-treated patients discontinued treatment due to an adverse reaction, compared with 3.5% of placebo-treated patients. The most common adverse reaction leading to discontinuation in at least 1% of the VIIBRYD-treated patients in the placebo-controlled studies was nausea (1.4%).

Common adverse reactions in placebo-controlled MDD studies

Table 2 shows the incidence of common adverse reactions occurring in ≥ 2% of VIIBRYD-treated patients and greater than the rate of placebo-treated patients in MDD Studies. There were no dose-related adverse reactions between 20 mg and 40 mg reported.

Table 2: Common Adverse Reactions Occurring in ≥ 2% of VIIBRYD-treated Patients and Greater than the Rate of Placebo-Treated Patients

System Organ Class Preferred Term	Placebo N=967	VIIBRYD 20 mg/day N=288	VIIBRYD 40 mg/day N=978
Gastrointestinal disorders			
Diarrhea	10%	26%	29%
Nausea	7%	22%	24%
Dry mouth	5%	8%	7%
Vomiting	2%	4%	5%
Abdominal pain[1]	3%	7%	4%
Dyspepsia	2%	2%	3%
Flatulence	1%	3%	3%
Gastroenteritis	1%	1%	2%

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