

Vilazodone (Viibryd®)

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Learning Objectives

- * Describe vilazodone's mechanism of action and how it impacts its antidepressant effect
- * Provide dosing recommendations
- * List vilazodone's most common side effects
- * Describe vilazodone's place in therapy

Mechanism of Action

- * Inhibits reuptake of 5HT
- * Partial agonism at 5HT_{1A} receptors

Viibryd (vilazodone) package insert, Forest Laboratories, January 2011.

Pharmacokinetics

Parameter	Vilazodone
Metabolism	Hepatic via CYP3A4 (Primary), CYP2C19 and CYP2D6 (Minor); also possibly by carboxylesterase
Elimination	Urine (1%), feces (2%) unchanged
Half - Life	~ 25 hours
Protein Binding	96 - 99%
Bioavailability	72% with food

Viibryd (vilazodone) package insert, Forest Laboratories, January 2011.

Dosage

- * Recommended dose for MDD
 - * 40 mg once daily
- * Initiation of treatment
 - * Start at 10 mg once daily x 7 days, followed by 20 mg once daily x 7 days, and then increased to 40 mg once daily

MDD = Major Depressive Disorder

Viibryd (vilazodone) package insert, Forest Laboratories, January 2011.

Dose Adjustments

Specific Patient Factors	FDA Recommendation
Renal Impairment	None
Hepatic Impairment	Mild-to-Moderate: None Severe: Not studied
Geriatric	None
Strong Inhibitor of CYP3A4	Reduce dose to 20 mg daily
Mild Inhibitor of CYP3A4	None unless intolerable side effects then consider reducing dose to 20 mg daily

Viibryd (vilazodone) package insert, Forest Laboratories, January 2011.

Administration

- * Take with food
 - * Administration without food may decrease drug concentrations by approximately 50% and may diminish effectiveness
- * Discontinuation of treatment
 - * Taper to prevent withdrawal symptoms

Vilbryd (vilazodone) package insert, Forest Laboratories, January 2011.

Side Effects

Common	Serious
GI: • Diarrhea (28%) • Nausea (23%) • Vomiting (5%)	CV: • Palpitations (2%) • Ventricular premature beats (0.1% to 1%)
Neurologic: • Dizziness (9%) • Insomnia (6%)	Other: • Serotonin syndrome (0.1%)

Vilbryd (vilazodone) package insert, Forest Laboratories, January 2011.

Cost

Drug	Dose	Cost/Day/ Patient (\$)	Cost/Year/ Patient (\$)
Vilazodone	10 mg/d	4.74	1706.40
Vilazodone	20 mg/d	4.74	1706.40
Vilazodone	40 mg/d	4.74	1706.40

**AWP prices

McKesson Computerized Ordering System, Accessed 5/22/12

Efficacy Trials

Two Phase III Randomized Placebo-Controlled Trials

- * Duration: 8 weeks
- * Primary Efficacy Endpoint:
 - * Mean change from baseline to week 8 on Montgomery-Asberg Depression Rating Scale (MADRS) total score
 - * There was significant improvement in MADRS score for patients on vilazodone compared to placebo for both studies
 - * Only 1 study assessed remission: no difference from placebo

Ricketts K. J Clin Psychiatry. 2009;70(3):326-33.
Khan A. J Clin Psychiatry. 2011;72(4):441-7.
Robinson D. J Clin Psychopharmacol. 2011;31:643-6.

Claim To Fame

- * Faster onset compared to SSRIs
- * No sexual dysfunction

"The overall percentage of vilazodone-treated patients spontaneously reporting sexual dysfunction were quite low (5% or less), but such low rates are observed with all SSRIs and it is well recognized that reporting of sexual dysfunction is severely underreported in trials that do not devote particulate attention to eliciting such effects."

Laughren T. J Clin Psychiatry. 2011;72(9):1166-73.

Conclusion

ADVANTAGES

- * No proven advantages compared to other antidepressants

DISADVANTAGES

- * Expensive
- * Requires initial dose titration & tapering upon discontinuation to prevent withdrawal side effects
- * Must be taken with food
- * Has not been studied in randomized controlled studies beyond 8 weeks

Place in Therapy

- * Vilazodone may be used as a 1st line agent for Major Depressive Disorder given that no head-to-head trials comparing vilazodone to other antidepressants have been performed.
- * Vilazodone cannot be recommended for treatment resistant depression, as these patients were excluded from the phase III clinical trials.

References

- * Vibryd (vilazodone) package insert. Forest Laboratories. January 2011.
- * Khan A. Vilazodone, a novel dual-acting serotonergic antidepressant for managing major depression. *Expert Opin. Investig. Drugs* (2009)18(11):1753-64.
- * Dawson L and Watson J. Vilazodone: A 5HT_{1c} receptor agonist/serotonin transporter inhibitor for the treatment of affective disorders. *CNS Neuroscience & Therapeutics*. 15(2009)107-17.
- * Rickels K, Athanasiou M, Robinson D, et al. Evidence for efficacy and tolerability of vilazodone in the treatment of major depressive disorder: a randomized, double-blind, placebo-controlled trial. *J Clin Psychiatry* 2009;70(3):326-33.
- * Khan A, Cutler A, Kajdasz K, et al. A randomized, double-blind, placebo-controlled, 8-week study of vilazodone, a serotonergic agent for the treatment of major depressive disorder. *J Clin Psychiatry* 2011;72(4):441-7.
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- * Laughren T, Gobburu J, Temple R, et al. Vilazodone: Clinical Basis for the US Food and Drug Administration's Approval of a New Antidepressant. *J Clin Psychiatry*. 2011;72(9):1166-73.

Question 1

- * Which of the following choices best reflects the evidence based advantages of vilazodone compared to SSRIs?
 - A faster onset of action
 - Less gastrointestinal side effects
 - Less sexual dysfunction
 - There is no advantage
- * Answer: D

Question 2

- * Which of the following is the most frequent side effect of vilazodone?
 - Gastrointestinal upset
 - Serotonin syndrome
 - Blurred vision
 - Sexual dysfunction
- * Answer: A

Question 3

- * Vilazodone's place in therapy based on the published literature is?
 - A first line agent for Major Depression
 - Treatment Resistant Major Depression
 - Post-Traumatic Stress Disorder
 - Generalized Anxiety Disorder
- * Answer: A