Viibryd (Vilazodone): Viable option or for the byrds?

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ABSTRACT

Vilazodone was approved by the Food and Drug Administration (FDA) in January of 2011. This article reviews clinically significant aspects of this new drug including: the FDA-approved indications, mechanism of action, administration, drug interactions, adverse effects, clinical trial evidence, innovative properties and place in therapy.

KEYWORDS

Vilazodone, Viibryd, major depressive disorder

SB is a 25 year-old patient with General Anxiety Disorder and Major Depressive Disorder who arrives to your medication management clinic. She has a previous history of fluoxetine and duloxetine use, which she did not tolerate well. She is currently taking sertraline 150 mg daily and says the effect is wearing-off and that she would like to try something different. Her psychiatrist is considering augmentation, but is concerned about pill-burden. Are there any newer antidepressant treatment options for SB that may help provide better symptom control?

WHAT IS THE FDA-APPROVED INDICATION FOR VILAZODONE?

Viibryd™ (vilazodone) was FDA approved on January 21, 2011 for the treatment of major depressive disorder in adults.[1, 2]

WHAT IS THE RECEPTOR BINDING PROFILE AND MECHANISM OF ACTION FOR VILAZODONE?

Vilazodone is a combined serotonin reuptake inhibitor and 5HT-$_{1A}$ partial agonist.[3] Forest Pharmaceuticals is marketing Viibryd,™ highlighting its novel mechanism of action. The mechanism of action is based on the thought that the 5HT-$_{1A}$ receptor mediates negative-feedback circuitry of endogenous serotonin and limits serotonin concentration at the synapse.[3] Vilazodone, as a combined serotonin reuptake inhibitor and 5HT-$_{1A}$ partial agonist, may enhance neuroplastic adaptation, thus decreasing time to effect and may stimulate postsynaptic 5HT-$_{1A}$ heteroreceptors, thereby increasing therapeutic efficacy compared to current SSRIs.[3]

HOW IS VILAZODONE DOSED AND HOW SHOULD IT BE ADMINISTERED?

Vilazodone is available in 10, 20, and 40 mg immediate release tablets.[1] Vilazodone should be initiated at 10 mg once daily for one week, increased to 20 mg once daily for one week, then increased to the recommended maintenance dose of 40 mg once daily.[1] Vilazodone should be taken with food or a small meal. Food increases the peak plasma concentration and the AUC of vilazodone about two-fold.[1] Conversely, taking vilazodone on an empty stomach will result in a 50% decrease in peak plasma concentration and AUC. No dosage adjustment is recommended based on age, mild to moderate hepatic impairment, or mild to severe renal impairment.[1]

ARE THERE ANY CLINICALLY SIGNIFICANT DRUG INTERACTIONS WITH VILAZODONE?

Vilazodone is extensively metabolized primarily via hepatic enzyme CYP 3A4, while CYP 2C19 and 2D6 have a minor role in metabolism.[2] Vilazodone has no active metabolites.[2] Concomitant therapy with strong CYP 3A4 inhibitors may increase vilazodone's plasma concentrations approximately 50%.[2] The vilazodone dose should be reduced to 20 mg if given with a strong 3A4 inhibitor[1]. Combination with 3A4 inducers has yet to be evaluated, but would likely result in significant decreases in serum concentrations and may decrease effectiveness. Vilazodone has not been shown to inhibit or induce CYP hepatic enzymes.[1] Vilazodone is 96-99% protein-bound[1].

WHAT ADVERSE EFFECTS SHOULD I DISCUSS WITH MY PATIENT?

The most common side effects reported in clinical trials include diarrhea (28%), nausea (23%), insomnia (6%), and vomiting (5%).[1, 2] Adverse effects seen in clinical trials at a rate of at least 2% and twice the placebo rate include gastroenteritis, parasthesias, tremor, abnormal dreams, restlessness, decreased libido, abnormal orgasm, delayed ejaculation, erectile dysfunction, feeling jittery, palpitations, and increased appetite.[2] These findings differ from some claims of vilazodone having no sexual side effects and no weight gain.[4] Many of the noted adverse effects are dose-related with poor tolerability at doses greater than 40 mg per day.[2] Like other antidepressants, vilazodone carries a boxed warning for increased risk of suicidal thinking and behavior in children, adolescents, and young adults, ages 18-24, during treatment initiation.[1, 5] Patients aged 65 and older who take antidepressants have a decreased risk of suicidal thinking and behavior.[5] Serious treatment-emergent adverse effects are expected to be similar to SSRIs and include risk of serotonin syndrome, contraindication with MAOIs, activation of hypomania/mania, and increased risk of bleed[1]. Vilazodone is Pregnancy Category C due to inadequate data in pregnant women.[1]

HOW DID VILAZODONE PERFORM IN CLINICAL TRIALS?

Vilazodone has been studied in two randomized, placebo-controlled, multicenter 8-week clinical trials in adults, aged 18-70 years, experiencing a first episode or recurrence of major depressive disorder.[1, 2] The average change from baseline MADRS at week eight was -13.3 (baseline MADRS 32) and -12.9 (baseline MADRS 31) in trials one and two, respectively.[6] This corresponds to a MADRS response rate of 40% for vilazodone and 28% for placebo.[2] The number needed to treat (NNT) for achieving a response is noted to be eight[2]. Vilazodone statistically separated from placebo beginning at week one; however specific symptoms that responded to vilazodone were not described.[2] Thus, it is difficult to conclude that individuals treated with vilazodone will respond more rapidly than individuals treated with traditional SSRIs. There are currently no published active-comparator trials. Phase 4 studies in progress include: maintenance efficacy studies, use in pediatric populations 7-17 years, a CYP 3A4-inducer study, pharmacokinetics in severe hepatic impairment, and a p-glycoprotein in vitro study.[2]

WHAT IS INNOVATIVE ABOUT THIS NEW ANTIDEPRESSANT?

Similar to SSRIs, vilazodone blocks reuptake of serotonin and the adverse effects are similar to those of SSRIs. The clinical impact of 5HT-$_{1A}$ receptor partial agonism with respect to efficacy onset and side effects has yet to be fully elucidated. However, buspirone also has high affinity for the 5HT-$_{1A}$ receptor and has been studied for augmentation in treatment resistant depression and for anxiety disorders[4]. Chronic exposure to SSRIs is thought to desensitize the 5HT-$_{1A\ receptors'}$ negative feedback mechanism, a theory behind the delayed onset of efficacy.[3]

WHAT PLACE DOES VILAZODONE HAVE IN THE TREATMENT OF DEPRESSION?

Because of vilazodone's 5HT-$_{1A}$ receptor partial agonism, individuals who fail initial SSRI therapy and, in theory, those with co-morbid anxiety may benefit from vilazodone. Active comparator and maintenance therapy studies are needed to evaluate how vilazodone compares to SSRIs with respect to onset of efficacy, weight changes, and sexual side effects.

REFERENCES

1. Viibryd (vilazodone HCl) Prescribing Information. Available at: http://www.frx.com/pi/Viibryd_pi.pdf. Accessed November, 2011.
2. Laughren TP, Gobburu J, Temple RJ, Unger EF, Bhattaram A, Dinh PV, 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. DOI: 10.4088/JCP.11r06984. PubMed PMID: 21951984.
3. Dawson LA, Watson JM. Vilazodone: a 5-HT1A receptor agonist/serotonin transporter inhibitor for the treatment of affective disorders. CNS Neurosci Ther. 2009;15(2):107-17. PubMed PMID: 19499624.
4. Vilazodone (Viibryd)--a new antidepressant. Med Lett Drugs Ther. 2011;53(1368):53-4. PubMed PMID: 21738107.
5. FDA approves Viibryd to treat major depressive disorder. FDA News Release. 2011. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm240642.htm. Accessed November, 2011.
6. Lindsey WT. Vilazodone for the treatment of depression. Ann Pharmacother. 2011;45(7-8):946-53. DOI: 10.1345/aph.1P772. PubMed PMID: 21672888.

How to cite this editor-reviewed article
Gonzalez ML. Viibryd (Vilazodone): Viable option or for the byrds?. Ment Health Clin [Internet]. 2011;1(6):140-1. Available from: http://dx.doi.org/10.9740/mhc.n89810