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 5HT1a receptors

Pharmacokinetics

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

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

Dose Adjustments

<table>
<thead>
<tr>
<th>Specific Patient Factors</th>
<th>FDA Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Impairment</td>
<td>None</td>
</tr>
<tr>
<td>Hepatic Impairment</td>
<td>Mild-to-Moderate: None Severe: Not studied</td>
</tr>
<tr>
<td>Geriatric</td>
<td>None</td>
</tr>
<tr>
<td>Strong Inhibitor of CYP3A4</td>
<td>Reduce dose to 20 mg daily</td>
</tr>
<tr>
<td>Mild Inhibitor of CYP3A4</td>
<td>None unless intolerable side effects then consider reducing dose to 20 mg daily</td>
</tr>
</tbody>
</table>
**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

**Side Effects**

<table>
<thead>
<tr>
<th>Common</th>
<th>Serious</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GI:</strong></td>
<td></td>
</tr>
<tr>
<td>Diarrhea (28%)</td>
<td></td>
</tr>
<tr>
<td>Nausea (23%)</td>
<td></td>
</tr>
<tr>
<td>Vomiting (5%)</td>
<td></td>
</tr>
<tr>
<td><strong>Neurologic:</strong></td>
<td></td>
</tr>
<tr>
<td>Dizziness (9%)</td>
<td></td>
</tr>
<tr>
<td>Insomnia (6%)</td>
<td></td>
</tr>
<tr>
<td><strong>CV:</strong></td>
<td></td>
</tr>
<tr>
<td>Palpitations (2%)</td>
<td>Ventricular premature beats (0.1% to 1%)</td>
</tr>
<tr>
<td><strong>Other:</strong></td>
<td></td>
</tr>
<tr>
<td>Serotonin syndrome (0.1%)</td>
<td></td>
</tr>
</tbody>
</table>

**Cost**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Cost/Day/ Patient ($)</th>
<th>Cost/Year/ Patient ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vilazodone</td>
<td>10 mg/d</td>
<td>4.74</td>
<td>1706.40</td>
</tr>
<tr>
<td>Vilazodone</td>
<td>20 mg/d</td>
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**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

**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."

**Notes**

- **AWP prices**
- **Sources:**
**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**

**Question 1**
- Which of the following choices best reflects the evidence based advantages of vilazodone compared to SSRIs?
  - A. A faster onset of action
  - B. Less gastrointestinal side effects
  - C. Less sexual dysfunction
  - D. There is no advantage
  
  Answer: D

**Question 2**
- Which of the following is the most frequent side effect of vilazodone?
  - A. Gastrointestinal upset
  - B. Serotonin syndrome
  - C. Blurred vision
  - D. Sexual dysfunction
  
  Answer: A

**Question 3**
- Vilazodone’s place in therapy based on the published literature is?
  - A. A first line agent for Major Depression
  - B. Treatment Resistant Major Depression
  - C. Post-Traumatic Stress Disorder
  - D. Generalized Anxiety Disorder
  
  Answer: A