Drug Update

Vilazodone

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Composition: Vilazodone Hydrochloride

Strengths: 20 mg and 40 mg tablets.

Molecular Structure / Formula

Class

Chemically, Vilazodone is a 2-benzofurancarboxamide. Serotonin Partial Agonist and Reuptake Inhibitor (SPARI).

Pharmacodynamic properties

Vilazodone is both SSRI and a 5-HT1A partial agonist. As an SSRI, it blocks serotonin reuptake by serotonin transporter to increase serotonin accumulation in the synapse, indirectly leading to nonspecific 5-HT receptor activation. As a 5HT1A partial agonist, it directly activates 5HT1A autoreceptors as well as postsynaptic heteroreceptors and may also potentially hasten desensitization of 5HT1A autoreceptors. Faster receptor desensitization may lead to a more rapid onset of therapeutic efficacy, decrease side effects attributed to serotonin reuptake inhibition (e.g. sexual dysfunction), and provides enhanced benefits for symptoms of anxiety.

Pharmacokinetic properties

The pharmacokinetics of Vilazodone(5-80mg) are dose proportional. Accumulation of Vilazodone is predictable from single dose data, does not vary with dose, and steady-state is achieved in about 3 days. Vilazodone concentration peaks at a median of 4-5 hours (T_max) after administration. The absolute bioavailability of vilazodone is 72% with food. It is widely distributed and approximately 96-99% protein-bound. It is extensively metabolized through CYP and non-CYP pathways with 1% of dose in urine and 2% of dose in feces recovered in unchanged form.
Tolerability

As per trials conducted in initial phases, finding noted in some of studies shows that Vilazodone is safe and well tolerated with a very low rate of adverse events and discontinuation due to adverse events. No impairment of psychomotor functions or cognition. No effect on ECG, BP or laboratory parameters. The adverse effects commonly noted are nausea, diarrhoea and headache (> 10%), vomiting, dry mouth, dizziness, and insomnia (1-10%) while the uncommon side effects are somnolence, paraesthesia, tremors, abnormal dreams, decreased libido, restlessness and in rare cases serotonin syndrome with mania or hypomania.

Indications

Vilazodone is approved by FDA for treatment of Major Depressive Disorder in adults. The safety and efficacy of vilazodone have not been established in paediatric patients.

Contradictions

Vilazodone is contraindicated in patients currently taking MAOIs, or within 14 days of stopping monoamine oxidase inhibitors (MAOIs), linezolid or intravenous methylene blue, because of an increased risk of serotonin syndrome.

Pregnancy and lactation

Even though, in a case report, no hazardous effects were seen on the child, careful consideration should be made when determining if potential benefits outweigh risk of treatment in pregnant women. Vilazodone is excreted into milk of lactating rats. It is unknown as to whether it is excreted into human milk.

Drug Interactions

- As with all antidepressants concomitant use with MAOIs is to be avoided.
- Concurrent use with NSAIDS may increase the risk of gastrointestinal bleeding or bleeding in general.
- Prolonged bleeding times may occur with anticoagulants such as warfarin.
- Concomitant use with potent CYP3A4 inhibitors (e.g. ketoconazole) may increase vilazodone's plasma concentrations by approximately 50%.
- Drugs that induce CYP3A4 (e.g. carbamazepine) may reduce vilazodone systematic exposure by approximately 45%.
- Vilazodone is highly bound to protein plasma and may increase free concentration of other highly protein bound drugs.

Dosage and Administration

The recommended dose for vilazodone is 40mg once daily. When starting vilazodone, the drug must be titrated. Start at 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. The maximum daily dose is 40mg/day. No dose adjustment is recommended in mild, moderate, or severe renal impairment or hepatic impairment or on the basis of age. Vilazodone should be taken with food. Administration without food may decrease drug concentration by 50% and may diminish effectiveness. The dose of vilazodone should be reduced to 20 mg if co-administered with strong (e.g. ketoconazole) or moderate (e.g. erythromycin) inhibitor of CYP3A4. Gradual dose reduction is recommended to prevent withdrawal symptoms.
Suggested References and Further Reading

6. Citrome L. Vilazodone for major depressive disorder: a systematic review of the efficacy and safety profile for this newly approved antidepressant—what is the number needed to treat, number needed to harm and likelihood to be helped or harmed. Int J Clin Pract 2012;66(4):356-68.

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