



PIC QUESTION OF THE WEEK: 10/20/06

Q: What are the most common drug interactions reported with linezolid?

A: Linezolid (Zyvox®) is a synthetic antibacterial agent and member of the class of compounds known as oxazolidinones. It is indicated for infections due to multi-resistant gram positive cocci including vancomycin-resistant *Enterococci*, multi-drug resistant *Streptococcus pneumoniae*, and methicillin-resistant *Staphylococcus aureus* or *epidermidis*. Linezolid is a weak, reversible, non-selective inhibitor of monoamine oxidase (MAO) and possesses the potential for interaction with adrenergic and serotonergic agents as well as tyramine containing foods such as certain cheeses, chocolate, wine, etc. Although, there are rare reports of possible interaction with drugs such as rifampin and diphenhydramine (unrelated to MAO), the most commonly cited interactions with linezolid are associated with serotonergic agents including selective serotonin reuptake inhibitors (SSRIs) and serotonin/norepinephrine reuptake inhibitors (SNRIs). Both classes of drugs inhibit reuptake of serotonin at the CNS neuronal membrane. This effect combined with linezolid's ability to decrease serotonin metabolism produces a relative excess of serotonin and possible development of *serotonin syndrome*. Serotonin syndrome is a progressive condition that typically manifests as a clinical triad of mental status changes, autonomic hyperactivity, and neuromuscular abnormalities. Findings include, but are not limited to, fever, mydriasis, akathisia, tachycardia, myoclonus, hyperreflexia, and diaphoresis. Life-threatening complications include rhabdomyolysis and shock. The onset of symptoms is generally one hour to several days after exposure to the causative agent or drug combination. In mild cases, symptoms usually resolve within 24 hours after discontinuation of the triggering drug. If the associated drug or active metabolite has an extended half-life, improvement may be significantly delayed. For most SSRIs, manufacturers recommend a wash-out period of two weeks prior to administration of MAO inhibitors (MAOIs). Because of its long half-life and that of its metabolites, fluoxetine should be discontinued five weeks before introduction of an MAOI. Additionally, MAOIs should be discontinued at least two weeks prior to administration of SSRIs to allow for resynthesis of monoamine oxidase. A recent retrospective review evaluated the frequency of serotonin syndrome in 72 patients receiving linezolid plus an SSRI or SNRI. The combinations had been used simultaneously or within 14 days of each other. There were only two suspected cases of serotonin syndrome and symptoms subsided quickly after stopping the serotonergic agent. The authors concluded that, if necessary, linezolid could be combined with an SSRI or SNRI; however, the patient must be carefully monitored for signs of serotonin syndrome. Although there are a number of serotonergic compounds available, thus far, the most commonly reported interactions of linezolid are those associated with SSRIs.

References:

- Taylor J, Wilson J, Estes L. Linezolid and serotonergic drug interactions: a retrospective survey. Clin Infect Dis 2006; 43:180-7.
- Boyer EW, Shannon M. The serotonin syndrome. N Engl J Med 2005; 352:1112-20.

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