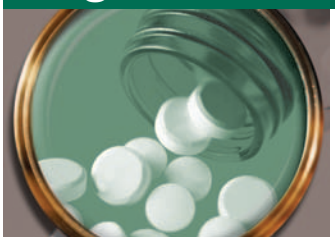

# Do All SSRIs Interact the Same Way?

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Selective serotonin reuptake inhibitors (SSRIs) are among the most widely used medications in the United States. Pharmacodynamic interactions of the SSRIs tend to be similar for all members of the group—when they are given with other serotonergic drugs, for example. Their pharmacokinetic drug interactions, however, can differ substantially because of differences in their pharmacokinetic properties (Table).

## Do Any Stand Out as Having More Pharmacokinetic Drug Interactions?

Fluvoxamine is the only SSRI that clearly stands out from the rest. It is a moderate-to-potent inhibitor of almost every important cytochrome P-450 isozyme, and it interacts with many other medications. The ability of fluvoxamine to moderately inhibit CYP3A4 substantially increases its interactive potential, because CYP3A4 metabolizes more drugs than any other cytochrome P-450 isozyme. Moreover, fluvoxamine is a remarkably potent inhibitor of CYP1A2, and it can produce dramatic (manyfold) increases in serum concentrations of such drugs as clozapine, theophylline, and tizanidine.[1]

## Do Any Stand Out as Having Fewer Pharmacokinetic Drug Interactions?

Theoretically, drugs that are not moderate or potent inhibitors of cytochrome P-450 isozymes—such as citalopram, escitalopram, sertraline, and venlafaxine—would be expected to have fewer drug interactions. Whether this expectation means a general increase in drug safety for these drugs over other SSRIs has not been established. For certain patients, it may be prudent to choose one of the SSRIs that is less likely to inhibit a certain enzyme.

## Does the CYP450 Profile Dictate Which SSRI Should Be Selected?

In most patients, the SSRI can be selected based on considerations other than the cytochrome P-450 system, because these patients are not receiving other medications, or the medications they are receiving do not interact significantly with SSRIs.

Nonetheless, particular attention must be paid to other psychotherapeutic drugs the patient may be taking. For example, many tricyclic antidepressants are metabolized by CYP2D6, and the addition of a potent CYP2D6 inhibitor such as fluoxetine or paroxetine can dramatically increase their levels. The combinations usually do not have to be avoided, but rather they may require dosage adjustment.

Also, one must be very cautious about giving CYP2D6 inhibitors to patients receiving CYP2D6 substrates that can prolong the QT interval, such as thioridazine or propafenone. Thioridazine can produce life-threatening ventricular arrhythmias when given with potent CYP2D6 inhibitors.

## Drugs *Activated* by CYP2D6

CYP2D6 acts upon a few prodrugs to form active metabolites, and in such cases one would expect CYP2D6 inhibitors, such as fluoxetine and paroxetine, to reduce the efficacy of these drugs. Indeed, clinical evidence suggests that prodrugs such as codeine and tramadol are less effective in patients who are genetically deficient in CYP2D6 or in patients receiving potent CYP2D6 inhibitors.[2] PT

*For a list of references, send a stamped, self-addressed envelope to: References Department, Attn. A. Stahl, Pharmacy Times, 241 Forsgate Drive, Jamesburg, NJ 08831; or send an e-mail request to: astahl@ascendmedia.com.*

**Table**

**Pharmacokinetic Properties of Selective Serotonin Reuptake Inhibitors**

| Antidepressant | CYP1A2 | CYP2C9 | CYP2C19 | CYP2D6 | CYP3A4 |
|---|---|---|---|---|---|
| Citalopram | | | • | ✧ | • |
| Duloxetin | • | | | • ❑ | |
| Escitalopram | | | • | ✧ | • |
| Fluoxetine | | ✧ | • ❑ | • ❑ | ✧ |
| Fluvoxamine | • ❑ | ✧ | ❑ | • ❑ | ❑ |
| Paroxetine | | | | • ❑ | |
| Sertraline | | | • | • ✧ | • ✧ |
| Venlafaxine | | | | • | • |

• = substrate for isozyme.
❑ = inhibits isozyme (moderate to strong).
✧ = inhibits isozyme (weak).