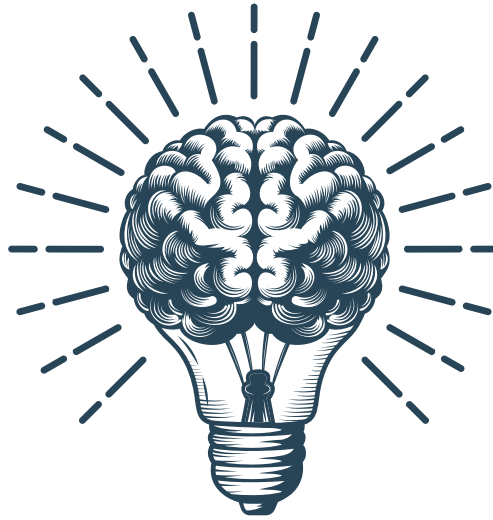


— Focus —

# CYP450 Enzymes





**Shine brightly.**

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## CYP450 Focused Mental Health Medications for Inducers and Inhibitors

(Various other classes are reviewed in the comprehensive flashcard deck)

Chart listing some of the strongest CYP450 inhibitors, organized by enzyme:

| CYP450 Enzyme | Strong Inhibitors                                     | Medications/Classes Inhibited                                              |
|---------------|-------------------------------------------------------|----------------------------------------------------------------------------|
| CYP1A2        | Fluvoxamine, Ciprofloxacin                            | Antidepressants (e.g., clomipramine, imipramine), antipsychotics, caffeine |
| CYP2C9        | Fluconazole, Amiodarone                               | Antiepileptics (e.g., phenytoin), anticoagulants (e.g., warfarin)          |
| CYP2C19       | Omeprazole, Fluconazole, Ticlopidine                  | Antidepressants (e.g., citalopram, clomipramine), proton pump inhibitors   |
| CYP2D6        | Paroxetine, Fluoxetine, Quinidine                     | Antidepressants (e.g., TCAs, SSRIs), antipsychotics, beta-blockers         |
| CYP3A4        | Ketoconazole, Itraconazole, Ritonavir, Clarithromycin | Benzodiazepines, statins, calcium channel blockers, some antipsychotics    |
| CYP2B6        | Orphenadrine, Clopidogrel                             | Antidepressants (e.g., bupropion), antiretrovirals                         |

### Key Points:

- **CYP1A2:** Fluvoxamine is particularly potent and can significantly raise levels of drugs metabolized by CYP1A2.
- **CYP2C9:** Fluconazole and Amiodarone are strong inhibitors and can increase the risk of bleeding with warfarin or toxicity with phenytoin.
- **CYP2C19:** Omeprazole and Fluconazole can inhibit the metabolism of drugs like citalopram, leading to increased concentrations.
- **CYP2D6:** Paroxetine and Fluoxetine are among the strongest inhibitors, affecting drugs like beta-blockers and certain antidepressants.
- **CYP3A4:** Ketoconazole, Itraconazole, and Ritonavir are some of the most potent inhibitors, affecting many medications.
- **CYP2B6:** Inhibition by Orphenadrine can significantly affect drugs like bupropion.

Chart listing some of the strongest CYP450 inducers, organized by enzyme:

| CYP450 Enzyme | Strong Inducers                            | Medications/Classes Affected                                            |
|---------------|--------------------------------------------|-------------------------------------------------------------------------|
| CYP1A2        | Tobacco (smoking), Rifampin, Carbamazepine | Antipsychotics (e.g., clozapine, olanzapine), caffeine, theophylline    |
| CYP2C9        | Rifampin, Carbamazepine, Phenobarbital     | Anticoagulants (e.g., warfarin), NSAIDs, antidiabetic drugs             |
| CYP2C19       | Rifampin, Carbamazepine, Phenytoin         | Proton pump inhibitors (e.g., omeprazole), clopidogrel, antidepressants |

|               |                                                     |                                                                         |
|---------------|-----------------------------------------------------|-------------------------------------------------------------------------|
| <b>CYP2D6</b> | There are no strong inducers of CYP2D6              | (N/A)                                                                   |
| <b>CYP3A4</b> | Rifampin, Carbamazepine, Phenytoin, St. John's Wort | Benzodiazepines, statins, calcium channel blockers, oral contraceptives |
| <b>CYP2B6</b> | Rifampin, Efavirenz                                 | Antidepressants (e.g., bupropion), antiretrovirals                      |

### Key Points:

- **CYP1A2:** Tobacco smoking is a strong inducer, which can lower levels of drugs like clozapine and theophylline. Rifampin and Carbamazepine also induce CYP1A2, affecting similar drugs.
- **CYP2C9:** Rifampin, Carbamazepine, and Phenobarbital are strong inducers, reducing the effectiveness of warfarin and certain NSAIDs.
- **CYP2C19:** Induced by Rifampin, Carbamazepine, and Phenytoin, leading to decreased efficacy of drugs like omeprazole and certain antidepressants.
- **CYP3A4:** One of the most widely affected enzymes, with Rifampin, Carbamazepine, Phenytoin, and St. John's Wort significantly reducing the efficacy of many medications.
- **CYP2B6:** Rifampin and Efavirenz are strong inducers, particularly affecting the metabolism of bupropion and antiretrovirals.

When inhibitors and inducers of the same CYP450 enzyme are taken together, the overall effect will depend on several factors, including the potency of the inhibitor and inducer, their concentrations, and the specific drugs involved. Generally:

1. **Inhibitors typically have a more immediate and stronger effect** than inducers because they can quickly reduce the enzyme's activity, leading to an increase in the levels of drugs metabolized by that enzyme. Depending on the drug and the strength of the inhibitor, this increase can happen within hours to days.
2. **Inducers tend to take longer to exert their effects** because they work by increasing the production of the enzyme, which can take days to weeks. The induced enzyme levels will increase the metabolism of drugs, leading to a decrease in their levels.

### Strongest Effect:

- **Inhibitors usually have the strongest immediate effect** when taken with drugs metabolized by the same enzyme. They can rapidly increase drug concentrations, potentially leading to toxicity.
- **Inducers, over time, can significantly lower drug levels**, but their effect is typically slower to develop.

### Example Scenario:

- **If a strong inhibitor and a strong inducer are taken together:** The inhibitor is likely to dominate in the short term, leading to higher drug levels initially. However, over time, if

the inducer remains in the system, it could eventually counteract the inhibitor by increasing the enzyme levels, potentially reducing the drug levels.

**Clinical Implication:**

- In practice, the presence of a strong inhibitor is often more concerning due to the risk of acute toxicity. Clinicians might monitor the patient closely for signs of drug accumulation.
- The long-term impact of an inducer may require dosage adjustments of the affected drug to maintain therapeutic levels.

In summary, while both inhibitors and inducers can significantly affect drug metabolism, **inhibitors generally have a stronger and more immediate impact when taken together with drugs metabolized by the same enzyme.**

Specific categories of mental health medications or supplements:

1. Herbal Supplements and Natural Products
2. Benzodiazepines, Hypnotics, and Anxiolytics
3. Beta Blockers, Alpha Agonists, and Miscellaneous Anxiolytics
4. Antipsychotics
5. Stimulants
6. Mood Stabilizers
7. Antidepressants

**1. Herbal Supplements and Natural Products**

| Substance               | CYP450 Enzyme             | Known Inhibitors                              | Known Inducers                             |
|-------------------------|---------------------------|-----------------------------------------------|--------------------------------------------|
| <b>St. John’s Wort</b>  | CYP3A4, 2C9, 2E1          | CYP3A4: Ketoconazole, Itraconazole, Ritonavir | CYP3A4: Rifampin, Carbamazepine, Phenytoin |
| <b>SAM-e</b>            | No significant CYP impact | Not applicable                                | Not applicable                             |
| <b>Omega-3</b>          | No significant CYP impact | Not applicable                                | Not applicable                             |
| <b>Folic Acid</b>       | No significant CYP impact | Not applicable                                | Not applicable                             |
| <b>N-acetylcysteine</b> | No significant CYP impact | Not applicable                                | Not applicable                             |
| <b>Chamomile</b>        | CYP1A2, CYP3A4            | CYP3A4: Ketoconazole, Itraconazole, Ritonavir | Not significant                            |
| <b>5-HTP</b>            | No significant CYP impact | Not applicable                                | Not applicable                             |
| <b>Kava kava</b>        | CYP3A4                    | CYP3A4: Ketoconazole, Itraconazole, Ritonavir | Not significant, potential mild induction  |

|                              |                           |                                                                      |                             |
|------------------------------|---------------------------|----------------------------------------------------------------------|-----------------------------|
| <b>L-methylfolate</b>        | No significant CYP impact | Not applicable                                                       | Not applicable              |
| <b>Melatonin</b>             | CYP1A2, CYP2C19           | CYP1A2: Fluvoxamine, Ciprofloxacin; CYP2C19: Omeprazole, Fluconazole | CYP1A2: Tobacco, Omeprazole |
| <b>Magnesium L-Threonate</b> | No significant CYP impact | Not applicable                                                       | Not applicable              |

## 2. Benzodiazepines, Hypnotics, and Anxiolytics

| <b>Medication</b>       | <b>Brand Name</b> | <b>CYP450 Enzyme</b>      | <b>Known Inhibitors</b>                                                     | <b>Known Inducers</b>                                                   |
|-------------------------|-------------------|---------------------------|-----------------------------------------------------------------------------|-------------------------------------------------------------------------|
| <b>Temazepam</b>        | Restoril          | No significant CYP impact | Not applicable                                                              | Not applicable                                                          |
| <b>Suvorexant</b>       | Belsomra          | CYP3A4                    | Ketoconazole, Itraconazole, Ritonavir                                       | Rifampin, Carbamazepine, Phenytoin                                      |
| <b>Zolpidem</b>         | Ambien            | CYP3A4                    | Ketoconazole, Itraconazole, Ritonavir, Clarithromycin, Erythromycin         | Rifampin, Carbamazepine, Phenytoin                                      |
| <b>Zaleplon</b>         | Sonata            | Aldehyde oxidase, CYP3A4  | CYP3A4: Ketoconazole, Itraconazole, Ritonavir                               | CYP3A4: Rifampin, Carbamazepine, Phenytoin                              |
| <b>Diphenhydramine</b>  | Benadryl          | CYP2D6                    | Paroxetine, Fluoxetine, Quinidine                                           | Not significant                                                         |
| <b>Ramelteon</b>        | Rozerem           | CYP1A2 (major), CYP3A4    | CYP1A2: Ciprofloxacin, Fluvoxamine; CYP3A4: Ketoconazole, Itraconazole      | CYP1A2: Tobacco, Omeprazole; CYP3A4: Rifampin, Carbamazepine, Phenytoin |
| <b>Doxepin</b>          | Sinequan, Silenor | CYP2D6                    | Paroxetine, Fluoxetine, Quinidine                                           | Not significant                                                         |
| <b>Eszopiclone</b>      | Lunesta           | CYP3A4                    | Ketoconazole, Itraconazole, Ritonavir, Clarithromycin, Erythromycin         | Rifampin, Carbamazepine, Phenytoin                                      |
| <b>Daridorexant</b>     | Quviviq           | CYP3A4                    | Ketoconazole, Itraconazole, Ritonavir                                       | Rifampin, Carbamazepine, Phenytoin                                      |
| <b>Diazepam</b>         | Valium            | CYP2C19, CYP3A4           | CYP3A4: Ketoconazole, Itraconazole, Ritonavir, Clarithromycin, Erythromycin | CYP3A4: Rifampin, Carbamazepine, Phenytoin                              |
| <b>Chlordiazepoxide</b> | Librium           | CYP3A4                    | CYP3A4: Ketoconazole, Itraconazole, Ritonavir                               | CYP3A4: Rifampin, Carbamazepine, Phenytoin                              |
| <b>Clorazepate</b>      | Tranxene          | CYP3A4                    | CYP3A4: Ketoconazole, Itraconazole, Ritonavir                               | CYP3A4: Rifampin, Carbamazepine, Phenytoin                              |
| <b>Clonazepam</b>       | Klonopin          | CYP3A4                    | CYP3A4: Ketoconazole, Itraconazole, Ritonavir                               | CYP3A4: Rifampin, Carbamazepine, Phenytoin                              |

|                    |                  |                         |                                                                               |                                            |
|--------------------|------------------|-------------------------|-------------------------------------------------------------------------------|--------------------------------------------|
| <b>Lorazepam</b>   | Ativan           | Glucuronidation         | Not applicable                                                                | Not applicable                             |
| <b>Alprazolam</b>  | Xanax            | CYP3A4                  | CYP3A4: Ketoconazole, Itraconazole, Ritonavir, Clarithromycin, Erythromycin   | CYP3A4: Rifampin, Carbamazepine, Phenytoin |
| <b>Buspirone</b>   | Buspar           | CYP3A4                  | CYP3A4: Ketoconazole, Itraconazole, Ritonavir                                 | CYP3A4: Rifampin, Carbamazepine, Phenytoin |
| <b>Gabapentin</b>  | Neurontin        | Not metabolized by CYPs | Not applicable                                                                | Not applicable                             |
| <b>Hydroxyzine</b> | Vistaril, Atarax | CYP3A4, CYP2D6          | CYP3A4: Ketoconazole, Itraconazole, Ritonavir; CYP2D6: Paroxetine, Fluoxetine | CYP3A4: Rifampin, Carbamazepine, Phenytoin |

### 3. Beta Blockers, Alpha Agonists, and Miscellaneous Anxiolytics

| Medication         | Brand Name     | CYP450 Enzyme             | Known Inhibitors                      | Known Inducers                     |
|--------------------|----------------|---------------------------|---------------------------------------|------------------------------------|
| <b>Propranolol</b> | Inderal        | CYP2D6                    | Paroxetine, Fluoxetine, Quinidine     | Not significant                    |
| <b>Atenolol</b>    | Tenormin       | Not metabolized by CYPs   | Not applicable                        | Not applicable                     |
| <b>Guanfacine</b>  | Intuniv, Tenex | CYP3A4                    | Ketoconazole, Itraconazole, Ritonavir | Rifampin, Carbamazepine, Phenytoin |
| <b>Clonidine</b>   | Catapres       | Not metabolized by CYPs   | Not applicable                        | Not applicable                     |
| <b>Prazosin</b>    | Minipress      | No significant CYP impact | Not applicable                        | Not applicable                     |
| <b>Pregabalin</b>  | Lyrica         | Not metabolized by CYPs   | Not applicable                        | Not applicable                     |

### 4. Antipsychotics

| Medication            | Brand Name | CYP450 Enzyme  | Known Inhibitors                                                              | Known Inducers                                                          |
|-----------------------|------------|----------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| <b>Chlorpromazine</b> | Thorazine  | CYP2D6, CYP1A2 | CYP2D6: Paroxetine, Fluoxetine, Quinidine; CYP1A2: Ciprofloxacin, Fluvoxamine | CYP1A2: Tobacco, Omeprazole; CYP2D6: Rifampin, Carbamazepine, Phenytoin |
| <b>Brexipiprazole</b> | Rexulti    | CYP3A4, CYP2D6 | CYP3A4: Ketoconazole, Itraconazole, Ritonavir; CYP2D6: Paroxetine, Fluoxetine | CYP3A4: Rifampin, Carbamazepine, Phenytoin                              |

|                                    |           |                                           |                                                                                                        |                                                                         |
|------------------------------------|-----------|-------------------------------------------|--------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| <b>Clozapine</b>                   | Clozaril  | CYP1A2, CYP3A4, CYP2D6                    | CYP1A2: Ciprofloxacin, Fluvoxamine; CYP3A4: Ketoconazole, Itraconazole; CYP2D6: Paroxetine, Fluoxetine | CYP1A2: Tobacco, Omeprazole; CYP3A4: Rifampin, Carbamazepine, Phenytoin |
| <b>Quetiapine</b>                  | Seroquel  | CYP3A4                                    | Ketoconazole, Itraconazole, Ritonavir                                                                  | Rifampin, Carbamazepine, Phenytoin                                      |
| <b>Perphenazine</b>                | Trilafon  | CYP2D6                                    | Paroxetine, Fluoxetine, Quinidine                                                                      | Rifampin, Carbamazepine, Phenytoin                                      |
| <b>Cariprazine</b>                 | Vraylar   | CYP3A4                                    | Ketoconazole, Itraconazole, Ritonavir                                                                  | Rifampin, Carbamazepine, Phenytoin                                      |
| <b>Olanzapine/<br/>Samidorphan</b> | Lybalvi   | CYP1A2 (Olanzapine), CYP3A4 (Samidorphan) | CYP1A2: Ciprofloxacin, Fluvoxamine; CYP3A4: Ketoconazole, Itraconazole                                 | CYP1A2: Tobacco, Omeprazole; CYP3A4: Rifampin, Carbamazepine, Phenytoin |
| <b>Fluphenazine</b>                | Prolixin  | CYP2D6                                    | Paroxetine, Fluoxetine, Quinidine                                                                      | Rifampin, Carbamazepine, Phenytoin                                      |
| <b>Lumateperone</b>                | Caplyta   | CYP3A4                                    | Ketoconazole, Itraconazole, Ritonavir                                                                  | Rifampin, Carbamazepine, Phenytoin                                      |
| <b>Haloperidol</b>                 | Haldol    | CYP2D6, CYP3A4                            | CYP2D6: Paroxetine, Fluoxetine, Quinidine; CYP3A4: Ketoconazole, Itraconazole                          | CYP3A4: Rifampin, Carbamazepine, Phenytoin                              |
| <b>Pimozide</b>                    | Orap      | CYP3A4                                    | Ketoconazole, Itraconazole, Ritonavir                                                                  | Rifampin, Carbamazepine, Phenytoin                                      |
| <b>Risperidone</b>                 | Risperdal | CYP2D6                                    | Paroxetine, Fluoxetine, Quinidine                                                                      | Rifampin, Carbamazepine, Phenytoin                                      |
| <b>Paliperidone</b>                | Invega    | Not metabolized by CYPs                   | Not applicable                                                                                         | Not applicable                                                          |
| <b>Olanzapine</b>                  | Zyprexa   | CYP1A2, CYP2D6                            | CYP1A2: Ciprofloxacin, Fluvoxamine; CYP2D6: Paroxetine, Fluoxetine                                     | CYP1A2: Tobacco, Omeprazole; CYP2D6: Rifampin, Carbamazepine, Phenytoin |
| <b>Ziprasidone</b>                 | Geodon    | CYP3A4, CYP1A2                            | CYP3A4: Ketoconazole, Itraconazole; CYP1A2: Ciprofloxacin, Fluvoxamine                                 | CYP3A4: Rifampin, Carbamazepine, Phenytoin; CYP1A2: Tobacco, Omeprazole |

|                     |         |                |                                                                    |                                            |
|---------------------|---------|----------------|--------------------------------------------------------------------|--------------------------------------------|
| <b>Iloperidone</b>  | Fanapt  | CYP2D6, CYP3A4 | CYP2D6: Paroxetine, Fluoxetine; CYP3A4: Ketoconazole, Itraconazole | CYP3A4: Rifampin, Carbamazepine, Phenytoin |
| <b>Asenapine</b>    | Saphris | CYP1A2         | Ciprofloxacin, Fluvoxamine                                         | Tobacco, Omeprazole                        |
| <b>Lurasidone</b>   | Latuda  | CYP3A4         | Ketoconazole, Itraconazole, Ritonavir                              | Rifampin, Carbamazepine, Phenytoin         |
| <b>Aripiprazole</b> | Abilify | CYP2D6, CYP3A4 | CYP2D6: Paroxetine, Fluoxetine; CYP3A4: Ketoconazole, Itraconazole | CYP3A4: Rifampin, Carbamazepine, Phenytoin |

## 5. Stimulants

| Medication                  | Brand Name        | CYP450 Enzyme               | Known Inhibitors                                                                | Known Inducers                             |
|-----------------------------|-------------------|-----------------------------|---------------------------------------------------------------------------------|--------------------------------------------|
| <b>Methylphenidate</b>      | Ritalin, Concerta | CES1A1 (Carboxylesterase 1) | Not applicable                                                                  | Not applicable                             |
| <b>Dexmethylphenidate</b>   | Focalin           | CES1A1                      | Not applicable                                                                  | Not applicable                             |
| <b>Dextroamphetamine</b>    | Dexedrine         | CYP2D6                      | Paroxetine, Fluoxetine, Quinidine                                               | Not significant                            |
| <b>Lisdexamfetamine</b>     | Vyvanse           | Not metabolized by CYPs     | Not applicable                                                                  | Not applicable                             |
| <b>D- and L-Amphetamine</b> | Adderall          | CYP2D6                      | Paroxetine, Fluoxetine, Quinidine                                               | Not significant                            |
| <b>Modafinil</b>            | Provigil          | CYP3A4, CYP2C19             | CYP3A4: Ketoconazole, Itraconazole, Ritonavir; CYP2C19: Omeprazole, Fluconazole | CYP3A4: Rifampin, Carbamazepine, Phenytoin |
| <b>Armodafinil</b>          | Nuvigil           | CYP3A4, CYP2C19             | CYP3A4: Ketoconazole, Itraconazole, Ritonavir; CYP2C19: Omeprazole, Fluconazole | CYP3A4: Rifampin, Carbamazepine, Phenytoin |

## 6. Mood Stabilizers

| Medication                   | Brand Name         | CYP450 Enzyme           | Known Inhibitors                    | Known Inducers                                 |
|------------------------------|--------------------|-------------------------|-------------------------------------|------------------------------------------------|
| <b>Lithium</b>               | Lithobid, Eskalith | Not metabolized by CYPs | Not applicable                      | Not applicable                                 |
| <b>Olanzapine/Fluoxetine</b> | Symbyax            | CYP1A2, CYP2D6          | CYP1A2: Ciprofloxacin, Fluvoxamine; | CYP1A2: Tobacco, Omeprazole; CYP2D6: Rifampin, |

|                      |           |                          |                                                                                   |                                            |
|----------------------|-----------|--------------------------|-----------------------------------------------------------------------------------|--------------------------------------------|
|                      |           |                          | CYP2D6: Paroxetine, Quinidine, Fluoxetine                                         | Carbamazepine, Phenytoin                   |
| <b>Carbamazepine</b> | Tegretol  | CYP3A4, CYP1A2           | CYP3A4: Ketoconazole, Itraconazole, Ritonavir; CYP1A2: Ciprofloxacin, Fluvoxamine | CYP3A4: Rifampin, Carbamazepine, Phenytoin |
| <b>Divalproex</b>    | Depakote  | CYP2C9, CYP2C19          | CYP2C9: Fluconazole, Amiodarone; CYP2C19: Omeprazole, Fluconazole                 | CYP2C9: Rifampin; CYP2C19: Rifampin        |
| <b>Lamotrigine</b>   | Lamictal  | UGT1A4 (Glucuronidation) | Valproic acid (UGT inhibitor)                                                     | Carbamazepine, Phenytoin (UGT inducers)    |
| <b>Oxcarbazepine</b> | Trileptal | CYP3A4, CYP2C19          | CYP3A4: Ketoconazole, Itraconazole, Ritonavir; CYP2C19: Omeprazole, Fluconazole   | Not applicable                             |

## 7. Antidepressants

| Medication           | Brand Name | CYP450 Enzyme   | Known Inhibitors                                                              | Known Inducers                                                          |
|----------------------|------------|-----------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| <b>Imipramine</b>    | Tofranil   | CYP2D6          | Paroxetine, Fluoxetine, Quinidine                                             | Not significant                                                         |
| <b>Desipramine</b>   | Norpramin  | CYP2D6          | Paroxetine, Fluoxetine, Quinidine                                             | Not significant                                                         |
| <b>Amitriptyline</b> | Elavil     | CYP2D6          | Paroxetine, Fluoxetine, Quinidine                                             | Not significant                                                         |
| <b>Nortriptyline</b> | Pamelor    | CYP2D6          | Paroxetine, Fluoxetine, Quinidine                                             | Not significant                                                         |
| <b>Clomipramine</b>  | Anafranil  | CYP2D6, CYP1A2  | CYP2D6: Paroxetine, Fluoxetine, Quinidine; CYP1A2: Ciprofloxacin, Fluvoxamine | CYP1A2: Tobacco, Omeprazole; CYP2D6: Rifampin, Carbamazepine, Phenytoin |
| <b>Trazodone</b>     | Desyrel    | CYP3A4          | Ketoconazole, Itraconazole, Ritonavir                                         | Rifampin, Carbamazepine, Phenytoin                                      |
| <b>Nefazodone</b>    | Serzone    | CYP3A4          | Ketoconazole, Itraconazole, Ritonavir                                         | Rifampin, Carbamazepine, Phenytoin                                      |
| <b>Fluoxetine</b>    | Prozac     | CYP2D6, CYP2C19 | CYP2D6: Paroxetine, Quinidine; CYP2C19:                                       | Not significant                                                         |

|                       |            |                            |                                                                                                                          |                                                                                     |
|-----------------------|------------|----------------------------|--------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
|                       |            |                            | Omeprazole,<br>Fluconazole                                                                                               |                                                                                     |
| <b>Bupropion</b>      | Wellbutrin | CYP2B6                     | Orphenadrine,<br>Ticlopidine                                                                                             | Not significant                                                                     |
| <b>Sertraline</b>     | Zoloft     | CYP2D6                     | Paroxetine,<br>Fluoxetine, Quinidine                                                                                     | Not significant                                                                     |
| <b>Paroxetine</b>     | Paxil      | CYP2D6                     | Paroxetine itself is a<br>strong CYP2D6<br>inhibitor                                                                     | Not significant                                                                     |
| <b>Venlafaxine</b>    | Effexor    | CYP2D6, CYP3A4<br>(minor)  | CYP2D6: Paroxetine,<br>Fluoxetine,<br>Quinidine; CYP3A4:<br>Ketoconazole,<br>Itraconazole                                | Rifampin,<br>Carbamazepine,<br>Phenytoin                                            |
| <b>Desvenlafaxine</b> | Pristiq    | CYP3A4 (minor)             | Ketoconazole,<br>Itraconazole,<br>Ritonavir                                                                              | Rifampin,<br>Carbamazepine,<br>Phenytoin                                            |
| <b>Fluvoxamine</b>    | Luvox      | CYP1A2, CYP2C19            | CYP1A2:<br>Ciprofloxacin,<br>Fluvoxamine;<br>CYP2C19:<br>Omeprazole,<br>Fluconazole                                      | CYP1A2: Tobacco,<br>Omeprazole                                                      |
| <b>Mirtazapine</b>    | Remeron    | CYP1A2, CYP2D6,<br>CYP3A4  | CYP1A2:<br>Ciprofloxacin,<br>Fluvoxamine;<br>CYP2D6: Paroxetine,<br>Fluoxetine; CYP3A4:<br>Ketoconazole,<br>Itraconazole | CYP1A2: Tobacco,<br>Omeprazole;<br>CYP3A4: Rifampin,<br>Carbamazepine,<br>Phenytoin |
| <b>Citalopram</b>     | Celexa     | CYP2C19, CYP3A4<br>(minor) | CYP2C19:<br>Omeprazole,<br>Fluconazole;<br>CYP3A4:<br>Ketoconazole,<br>Itraconazole                                      | Rifampin,<br>Carbamazepine,<br>Phenytoin                                            |
| <b>Escitalopram</b>   | Lexapro    | CYP2C19, CYP3A4<br>(minor) | CYP2C19:<br>Omeprazole,<br>Fluconazole;<br>CYP3A4:<br>Ketoconazole,<br>Itraconazole                                      | Rifampin,<br>Carbamazepine,<br>Phenytoin                                            |
| <b>Duloxetine</b>     | Cymbalta   | CYP2D6, CYP1A2             | CYP2D6: Paroxetine,<br>Fluoxetine,<br>Quinidine; CYP1A2:<br>Ciprofloxacin,<br>Fluvoxamine                                | CYP1A2: Tobacco,<br>Omeprazole;<br>CYP2D6: Rifampin,<br>Carbamazepine,<br>Phenytoin |
| <b>Vilazodone</b>     | Viibryd    | CYP3A4                     | Ketoconazole,<br>Itraconazole,<br>Ritonavir                                                                              | Rifampin,<br>Carbamazepine,<br>Phenytoin                                            |

|                                        |                        |                                                     |                                                                                      |                                                                                     |
|----------------------------------------|------------------------|-----------------------------------------------------|--------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| <b>Atomoxetine</b>                     | Strattera              | CYP2D6                                              | Paroxetine,<br>Fluoxetine, Quinidine                                                 | Not significant                                                                     |
| <b>Vortioxetine</b>                    | Trintellix             | CYP2D6                                              | Paroxetine,<br>Fluoxetine, Quinidine                                                 | Not significant                                                                     |
| <b>Levomilnacipran</b>                 | Fetzima                | CYP3A4                                              | Ketoconazole,<br>Itraconazole,<br>Ritonavir                                          | Rifampin,<br>Carbamazepine,<br>Phenytoin                                            |
| <b>Phenelzine</b>                      | Nardil                 | Not metabolized by<br>CYPs                          | Not applicable                                                                       | Not applicable                                                                      |
| <b>Tranlycypromine</b>                 | Parnate                | Not metabolized by<br>CYPs                          | Not applicable                                                                       | Not applicable                                                                      |
| <b>Selegiline</b>                      | Emsam<br>(transdermal) | CYP2B6, CYP3A4                                      | CYP3A4:<br>Ketoconazole,<br>Itraconazole,<br>Ritonavir                               | CYP3A4: Rifampin,<br>Carbamazepine,<br>Phenytoin                                    |
| <b>Viloxazine</b>                      | Qelbree                | CYP1A2, CYP2D6                                      | CYP1A2:<br>Ciprofloxacin,<br>Fluvoxamine;<br>CYP2D6: Paroxetine,<br>Fluoxetine       | CYP1A2: Tobacco,<br>Omeprazole;<br>CYP2D6: Rifampin,<br>Carbamazepine,<br>Phenytoin |
| <b>Brexanolone</b>                     | Zulresso               | CYP3A4                                              | Ketoconazole,<br>Itraconazole,<br>Ritonavir                                          | Rifampin,<br>Carbamazepine,<br>Phenytoin                                            |
| <b>Esketamine</b>                      | Spravato               | CYP2B6, CYP3A4                                      | CYP2B6:<br>Orphenadrine,<br>Clopidogrel;<br>CYP3A4:<br>Ketoconazole,<br>Itraconazole | CYP2B6: Rifampin,<br>Efavirenz; CYP3A4:<br>Rifampin,<br>Carbamazepine,<br>Phenytoin |
| <b>Dextromethorphan/<br/>Bupropion</b> | Auvelity               | CYP2D6<br>(Dextromethorphan),<br>CYP2B6 (Bupropion) | CYP2D6: Paroxetine,<br>Fluoxetine; CYP2B6:<br>Orphenadrine,<br>Clopidogrel           | CYP2B6: Rifampin,<br>Efavirenz; Not<br>significant for<br>CYP2D6                    |