

**PSYCHIATRIC MEDICATIONS AND
HIV ANTIRETROVIRALS
ADULT MANAGEMENT
2010**

A DRUG INTERACTION GUIDE FOR CLINICIANS

Psychiatric Medications and HIV Antiretrovirals: A Drug Interaction Guide for Clinicians ADULT MANAGEMENT 2010

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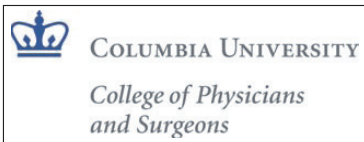
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This clinical support tool is sponsored by the New York/New Jersey AIDS Education and Training Center (NY/NJ AETC). The NY/NJ AETC is funded by the Health Resources and Services Administration (HRSA) and is part of the National AIDS Education and Training Center Program, a network of federally funded regional and national centers that conduct targeted multidisciplinary HIV/AIDS education and training programs for health care providers.

Disclaimer:

The data in this guide are intended for use by clinicians and other health care providers as guidance to minimize drug interactions and toxicities among adults being treated with psychiatric medications in conjunction with antiretrovirals. The information is intended for use in adult patients only. Additional/other references should be used when evaluating information for the treatment of adolescent and pediatric patients. These guidelines are for informational purposes only and cannot identify medical risks specific to an individual patient or recommend patient treatment. The absence of typographical errors is not guaranteed. These guidelines are not necessarily all-inclusive. Use of these guidelines indicates acknowledgement that neither NY/NJ AETC, nor the authors will be responsible for any loss or injury, sustained in connection with, or as a result of, the use of these guidelines. Users of this guide should consult other sources before prescribing medications or treatment. Data compiled through June 2010.



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Psychiatric Medications and HIV Antiretrovirals: A Drug Interaction Guide for Clinicians

NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS		
Generic Name	Brand Name	Route of Elimination/Metabolism
Delavirdine, DLV	Rescriptor®	CYP 3A4 inhibitor
Efavirenz, EFV	Sustiva®	CYP 3A4 inducer and inhibitor
Nevirapine, NVP	Viramune®	CYP 3A4 inducer
Etravirine, ETV	Intencele TM	CYP 3A4 inducer, inhibitor of 2C9, 2C19

NUCLEOSIDE/NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS		
Generic Name	Brand Name	Route of Elimination/Metabolism
Abacavir, ABC	Ziagen®	Metabolized by alcohol dehydrogenase and glucuronyl transferase
Didanosine, ddl	Videx EC®	Renal excretion 50%
Emtricitabine, FTC	Emtriva®	Renal
Lamivudine, 3TC	Epivir®	Renal
Stavudine, d4T	Zerit®	Renal excretion 50%
Tenofovir, TDF	Viread®	Renal
Zidovudine, AZT	Retrovir®	Metabolized to AZT glucuronide, renal excretion

COMBINATION REVERSE TRANSCRIPTASE INHIBITORS		
Generic Name	Brand Name	Route of Elimination/Metabolism
Abacavir and lamivudine	Epzicom®	See individual medications
Abacavir, zidovudine, and lamivudine	Trizivir®	See individual medications
Efavirenz, tenofovir, emtricitabine	Atripla®	See individual medications
Tenofovir and emtricitabine	Truvada®	See individual medications
Zidovudine and lamivudine	Combivir®	See individual medications

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PROTEASE INHIBITORS		
Generic Name	Brand Name	Route of Elimination/Metabolism
Atazanavir, ATV	Reyataz®	CYP 3A4 inhibitor and substrate
Darunavir, DRV	Prezista®	CYP 3A4 inhibitor and substrate
Fosamprenavir, FPV	Lexiva®	CYP 3A4 inhibitor, inducer and substrate
Indinavir, IDV	Crixivan®	CYP 3A4 inhibitor
Lopinavir/ritonavir, LPV/r	Kaletra®	CYP 3A4 inhibitor and substrate
Nelfinavir, NFV	Viracept®	CYP 3A4 inhibitor and substrate
Ritonavir, RTV	Norvir®	CYP 3A4 and 2D6 inhibitor
Saquinavir, SQV	Invirase®	CYP 3A4 inhibitor and substrate
Tipranavir, TPV	Aptivus®	CYP 3A4 and 2D6 inhibitor

FUSION INHIBITOR		
Generic Name	Brand Name	Route of Elimination/Metabolism
Enfuvirtide, ENF	Fuzeon®	Catabolism to amino acids

CCR5 INHIBITOR		
Generic Name	Brand Name	Route of Elimination/Metabolism
Maraviroc, MRV	Selzentry®	CYP 3A4 substrate

INTEGRASE INHIBITOR		
Generic Name	Brand Name	Route of Elimination/Metabolism
Raltegravir RAL	Isentress®	Metabolized by glucuronidation, not CYP 450

Abbreviations: **PK** - pharmacokinetics **NNRTI** - non-nucleoside reverse transcriptase inhibitor **NRTI** - nucleoside/tide reverse transcriptase inhibitor

Abbreviations: **PI** - protease inhibitor **CCR5I** - CCR5 inhibitor **I** - integrase inhibitor

Black Box Warnings for psychiatric medications are listed in bold in the Caution section.

CLASS

Antidepressants

INDICATIONS

Many antidepressants can be used to treat both depressive and anxiety disorders. Antianxiety drugs, such as benzodiazepines, however, are not a treatment for depression.



CATEGORY	Selective serotonin reuptake inhibitors (SSRIs) fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Pexeva, Paxil), citalopram (Celexa), escitalopram (Lexapro), fluvoxamine (Luvox)**	Tricyclics (TCAs) nortriptyline (Pamelor), desipramine (Norpramin), amitriptyline (Elavil), imipramine (Tofranil), doxepin (Sinequan), clomipramine (Anafranil)**, protriptyline (Vivactil)
BLACK BOX WARNINGS/ CAUTIONS	Increased suicide risk in <24 years old. * Monitor for serotonin syndrome (diaphoresis, hyperthermia, hypertension, tachycardia, pupillary dilatation, nausea, diarrhea, shivering, hyperreflexia, myoclonus, restlessness, tremor, incoordination, rigidity, clonus, trismus, seizure, confusion, agitation, anxiety, insomnia, hallucinations, headache). Fluoxetine is also formulated as a combination with olanzapine (Symbyax); refer to olanzapine (atypical antipsychotics) for further information.	Increased suicide risk in <24 years old. * TCAs are associated with dry mouth, constipation, urinary retention, and blurred vision; toxic levels of TCAs may prolong the PR interval on EKG, and lead to atrioventricular (AV) block and cardiac arrhythmia; patients with an existing AV conduction disturbance are at increased risk. Note: CNS side effects are more prominent in patients with advanced AIDS. It is best to start with low doses and titrate slowly.
PK	Fluoxetine: Inhibitor of CYP 2D6, 3A4, 2C19. Fluvoxamine: Inhibitor of CYP 3A4, 1A2, 2C19, 2C9. Citalopram, escitalopram, sertraline, and paroxetine: Inhibitors of CYP 2D6.	Metabolized by CYP 2D6
NNRTIs	Fluoxetine increased trough levels of delavirdine ~ 50%	No published data about drug interactions specific to this combination.
NRTIs	No published data about drug interactions specific to this combination.	No published data about drug interactions specific to this combination.

***Patients with major depressive disorder (MDD) may experience worsening of depression and/or emergence of suicidal ideation/behavior and/or unusual changes in behavior.**

****fluvoxamine(Luvox) and clomipramine (Anafranil) are generally used for obsessive compulsive disorder.**

CLASS

Antidepressants

INDICATIONS

Many antidepressants can be used to treat both depressive and anxiety disorders. Antianxiety drugs, such as benzodiazepines, however, are not a treatment for depression.



CATEGORY <i>(Continued)</i>	Selective serotonin reuptake inhibitors (SSRIs) fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Pexeva, Paxil), citalopram (Celexa), escitalopram (Lexapro), fluvoxamine (Luvox)**	Tricyclics (TCAs) nortriptyline (Pamelor), desipramine (Norpramin), amitriptyline (Elavil), imipramine (Tofranil), doxepin (Sinequan), clomipramine (Anafranil)**, protriptyline (Vivactil)
PIs	Ritonavir may increase levels of SSRIs and can lead to serotonin syndrome. Fluvoxamine increases levels of all PIs. Darunavir/ritonavir decreases sertraline levels by ~50% and decreases paroxetine levels by ~40%; monitor closely for antidepressant effect and increase dose as tolerated. Fosamprenavir/ritonavir decreases paroxetine levels 55%; monitor closely for antidepressant effect and increase dose as tolerated.	Ritonavir is a CYP 2D6 inhibitor, and decreases desipramine clearance by 59% causing higher blood levels of desipramine; Ritonavir may also increase levels of all TCAs. When used in combination with ritonavir or ritonavir - boosted protease inhibitors, caution is required. Reduced dosages may be required; monitor EKG and serum TCA levels.
CCR5I	No published data about drug interactions specific to this combination	No published data about drug interactions specific to this combination
II	No published data about drug interactions specific to this combination	No published data about drug interactions specific to this combination

**fluvoxamine(Luvox) and clomipramine (Anafranil) are generally used for obsessive compulsive disorder.

CLASS

Antidepressants

INDICATIONS

Many antidepressants can be used to treat both depressive and anxiety disorders. Antianxiety drugs, such as benzodiazepines, however, are not a treatment for depression.



CATEGORY	Other bupropion (Wellbutrin, Wellbutrin SR/XL, Zyban, Aplenzin)	Other nefazodone
BLACK BOX WARNINGS/ CAUTIONS	<p>Increased suicide risk in <24 years old. * Increased levels may induce seizures. Caution should be observed when bupropion is administered concomitantly with drugs that may inhibit its metabolism (e.g., cimetidine, PIs), increasing bupropion levels and increasing the risk of drug-induced seizures.</p>	<p>Increased suicide risk in <24 years old. * Cases of life-threatening hepatic failure have been reported with nefazodone; caution is indicated in patients with liver disease, such as hepatitis, or in combination with other potential hepatotoxins. This drug is usually avoided. Associated with somnolence and dizziness, especially at higher doses.</p>
PK	Metabolized by CYP 2D6, 3A4, 2B6.	Metabolized by and potent inhibitor of CYP 3A4
NNRTIs	Efavirenz inhibits CYP 2B6; may increase bupropion levels.	No published data about drug interactions specific to this combination (See Cautions).
NNRTIs	No published data about drug interactions specific to this combination.	No published data about drug interactions specific to this combination. (See Cautions).
PIs	Nelfinavir and ritonavir inhibit 2B6 and may increase bupropion levels, increasing risk of drug-induced seizures. Lopinavir/ritonavir has been demonstrated to reduce bupropion levels by ~ 60%. Avoid with high dose ritonavir. Tipranavir/ritonavir reduces bupropion levels by 46%.	Caution advised; combination of PI's and nefazodone may increase levels of both drugs. Nefazodone dosage reduction may be required with protease inhibitors.

*Patients with major depressive disorder (MDD) may experience worsening of depression and/or emergence of suicidal ideation/behavior and/or unusual changes in behavior.

CLASS

Antidepressants

INDICATIONS

Many antidepressants can be used to treat both depressive and anxiety disorders. Antianxiety drugs, such as benzodiazepines, however, are not a treatment for depression.



CATEGORY	Other bupropion (Wellbutrin, Wellbutrin SR/XL, Zyban, Aplenzin)	Other nefazodone
CCR5I	No published data about drug interactions specific to this combination	When nefazodone is used in combination with maraviroc, the maraviroc dosage should be reduced to 150mg twice daily. No change in nefazodone dosage is necessary.
II	No published data about drug interactions specific to this combination.	No published data about drug interactions specific to this combination.

CLASS

Antidepressants

INDICATIONS

Many antidepressants can be used to treat both depressive and anxiety disorders. Antianxiety drugs, such as benzodiazepines, however, are not a treatment for depression.



CATEGORY	Serotonin norepinephrine reuptake inhibitors (SNRIs) mirtazapine (Remeron), venlafaxine (Effexor), duloxetine (Cymbalta), desvenlafaxine (Pristiq)	Other trazodone (Desyrel)
BLACK BOX WARNINGS/ CAUTIONS	<p>Increased suicide risk in <24 years old.* Mirtazapine: Orthostatic hypotension, drowsiness. Venlafaxine: Hypertension.</p>	<p>Increased suicide risk in <24 years old.* Increased plasma levels may cause nausea, hypotension, syncope and drowsiness. Trazodone has been associated with increased incidence of priapism and arrhythmias.</p>
PK	<p>Duloxetine: Metabolized by CYP 2D6, 1A2 Mirtazapine: Metabolized by CYP 2D6, 1A2, 3A4. Venlafaxine: Metabolized by CYP 2D6, 3A4. Desvenlafaxine: Metabolized primarily by conjugation and to a minor extent, oxidation via CYP 3A4 pathway. CYP 2D6 is not involved with desvenlafaxine metabolism.</p>	<p>Trazodone: substrate of CYP 3A4</p>
NNRTIs	<p>No published data about drug interactions specific to this combination.</p>	<p>No published data about drug interactions specific to this combination.</p>
NRTIs	<p>No published data about drug interactions specific to this combination.</p>	<p>No published data about drug interactions specific to this combination.</p>

***Patients with major depressive disorder (MDD) may experience worsening of depression and/or emergence of suicidal ideation/behavior and/or unusual changes in behavior.**

CLASS

Antidepressants

INDICATIONS

Many antidepressants can be used to treat both depressive and anxiety disorders. Antianxiety drugs, such as benzodiazepines, however, are not a treatment for depression.



CATEGORY <i>(Continued)</i>	Serotonin norepinephrine reuptake inhibitors (SNRIs) mirtazapine (Remeron), venlafaxine (Effexor), duloxetine (Cymbalta), desvenlafaxine (Pristiq)	Other trazodone (Desyrel)
	<p>PIs Venlafaxine may decrease indinavir levels. An in vivo study (n=9) showed a 28% decrease in AUC and a 36% decrease in the Cmax of indinavir. The clinical significance of this interaction is unknown. Protease inhibitors may increase levels of venlafaxine or desvenlafaxine; monitor closely for adverse events when combining.</p>	<p>Short-term administration of ritonavir (200 mg twice daily, 4 doses) increased the Cmax of trazodone by 34%, AUC increased 2.4 - fold, half-life increased by 2.2-fold, trazodone clearance decreased by 52%. Lopinavir/ritonavir increased trazodone levels 2.4 fold. Potential for drug interactions when trazodone is co-administered with PIs, especially ritonavir boosted PIs. If trazodone is used with CYP 3A4 inhibitor, a lower dose of trazodone should be considered. Use caution when combining; if using concurrently, initiate trazodone at lowest available dosage and monitor for adverse effects as listed in the cautions section.</p>
CCR5I	No published data about drug interactions specific to this combination	No published data about drug interactions specific to this combination.
II	No published data about drug interactions specific to this combination.	No published data about drug interactions specific to this combination.

CLASS

Antidepressants

INDICATIONS

Many antidepressants can be used to treat both depressive and anxiety disorders. Antianxiety drugs, such as benzodiazepines, however, are not a treatment for depression.



CATEGORY

Monoamine oxidase inhibitors (MAOIs) isocarboxide (Marplan), tranylcypamine (Parnate), phenelzine (Nardil), selegiline transdermal (Emsam)**

BLACK BOX WARNINGS/CAUTIONS **Increased suicide risk in <24 years old.*** Other antidepressants, meperidine, tramadol, sumatriptan, dextromethorphan and linezolid should be avoided during concurrent MAOI treatment due to potential for serotonin syndrome or hypertensive crisis. Patients should also be counseled to avoid tyramine containing foods and beverages. **Consult additional references for a complete list of medications and foods to be avoided with concurrent MAOI use.** A 14 day washout period is recommended after discontinuation of an MAOI before initiating any therapy that may interact. Also a 14 day washout is required before initiating an MAOI when patients are discontinuing medications likely to interact.

PK Isocarboxide: Hepatic metabolism by oxidation via monoamine oxidase
Phenelzine: Hepatic metabolism by oxidation via monoamine oxidase
Selegiline: Metabolism via various CYP450 isoenzymes
Tranylcypamine: Hepatic metabolism by oxidation via monoamine oxidase

NNRTIs No published data about drug interactions specific to this combination

NRTIs No published data about drug interactions specific to this combination

PIs No published data about drug interactions specific to this combination. Data with ketoconazole (a potent CYP 3A4 inhibitor) and transdermal selegiline demonstrated no effect on ketoconazole or selegiline levels.

CCRSI No published data about drug interactions specific to this combination

II No published data about drug interactions specific to this combination

* Patients with major depressive disorder (MDD) may experience worsening of depression and/or emergence of suicidal ideation/behavior and/or unusual changes in behavior.

** Selegiline (Emsam) transdermal is not FDA approved for the management of depression.

CLASS

Anxiolytics and Sedative- Hypnotics

INDICATIONS

*Anxiolytics
and Sedative-
Hypnotics
can be used
to treat
anxiety
and sleep
disorders.*



CATEGORY	Benzodiazepines alprazolam (Niravam, Xanax), chlordiazepoxide (Librium), clonazepam (Klonopin), clorazepate (Tranxene), diazepam (Valium), flurazepam (Dalmene), lorazepam (Ativan), midazolam (Versed)*, oxazepam, temazepam (Restoril), triazolam (Halcion)	Non-Benzodiazepine sedative/hypnotics zolpidem (Ambien), zaleplon (Sonata), eszopiclone (Lunesta), buspirone (Buspar), ramelteon (Rozerem)
BLACK BOX WARNINGS/ CAUTIONS	Some caution advised in patients with history of drug dependence, in order to avoid additional dependency. Note: CNS side effects are more prominent in patients with advanced AIDS. In these patients, start with lower doses and titrate slowly.	Should be only used after sleep hygiene has been established and proves insufficient. Use with caution in patients receiving other CNS depressants or psychoactive medication; effects with other sedative drugs or ethanol may be potentiated.
PK	Alprazolam, flurazepam, clonazepam, and diazepam are metabolized by CYP 3A4 Midazolam, triazolam extensively metabolized by CYP 3A4 Clorazepate, lorazepam, oxazepam, temazepam are metabolized by glucuronidation and are free of drug interactions with inhibitors of CYP 3A4. Please look below in the PI section for contraindications and caution with use.	Buspirone: Substrate for CYP 3A4 Eszopiclone: Metabolized by CYP 3A4 and 2E1 Ramelteon: CYP 1A2, minor contribution from CYP 2C family and CYP 3A4 Zaleplon: Metabolized by aldehyde oxidase and CYP 3A4. Zolpidem: CYP 3A4 substrate
NNRTIs	Concurrent etravirine and diazepam may increase diazepam plasma concentrations. A decrease in diazepam dosage may be needed when using with etravirine	No published data about drug interactions specific to this combination.
NRTIs	No published data about drug interactions specific to this combination.	No published data about drug interactions specific to this combination.

*Midazolam is used for pre-procedural sedation or for use in ICU settings

CLASS

Anxiolytics and Sedative- Hypnotics

INDICATIONS

*Anxiolytics
and Sedative-
Hypnotics
can be used
to treat
anxiety
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disorders.*



CATEGORY <i>(Continued)</i>	Benzodiazepines alprazolam (Niravam, Xanax), chlordiazepoxide (Librium), clonazepam (Klonopin), clorazepate (Tranxene), diazepam (Valium), flurazepam (Dalmene), lorazepam (Ativan), midazolam (Versed)*, oxazepam, temazepam (Restoril), triazolam (Halcion)	Non-Benzodiazepine sedative/hypnotics zolpidem (Ambien), zaleplon (Sonata), eszopiclone (Lunesta), buspirone (Buspar), ramelteon (Rozerem)
	<p>PIs Oral midazolam and triazolam are metabolized by CYP 3A4, and are CONTRAINDICATED in combination with PIs due to the potential for serious and life-threatening reactions such as prolonged or severe sedation or respiratory depression. Single dose IV midazolam in controlled settings for sedation is acceptable. Alprazolam, flurazepam, clonazepam, and diazepam are also metabolized by CYP 3A4, and should be used with caution in combination with PIs due to the potential for serious reactions such as prolonged or severe sedation or respiratory depression. Lorazepam, temazepam, and oxazepam are metabolized by glucuronidation and are free of the serious interactions with PIs.</p>	<p>Use zolpidem and zaleplon with caution in combination with PIs due to potential for serious reactions such as prolonged or severe sedation or respiratory depression. With CYP 3A4 inhibitors, such as ritonavir -boosted PIs, use lowest dosage available and monitor for excess CNS depression. Avoid with other CNS-depressants.</p> <p>Use eszopiclone and PIs with caution, if at all. Monitor for excess sedation and/or respiratory depression. Ketoconazole increases eszopiclone levels by 2.2-fold; similar interactions with PIs and ritonavir -boosted PIs would be expected. Avoid concurrent use if possible. Buspirone is a substrate of CYP 3A4 - Concurrent use with PIs is likely to increase buspirone drug levels.</p>
	<p>CCR5I No published data about drug interactions specific to this combination</p>	<p>No published data about drug interactions specific to this combination.</p>
	<p>II No published data about drug interactions specific to this combination.</p>	<p>No published data about drug interactions specific to this combination.</p>

*Midazolam is used for pre-procedural sedation or for use in ICU settings

CLASS

Mood Stabilizers and Anticonvulsants

INDICATIONS

Mood Stabilizers (lithium, anticonvulsants) are used as monotherapy and in combination with other drugs (ie atypical antipsychotics) for the treatment of acute mania and as maintenance treatment for bipolar disorder



CATEGORY	Lithium carbonate (Eskalith, Lithobid)	Anticonvulsants carbamazepine (Tegretol), divalproex sodium (Depakote), gabapentin (Neurontin), lamotrigine (Lamictal), levetiracetam (Keppra), oxcarbazepine (Trileptal), phenobarbital (Luminal), phenytoin (Dilantin), pregabalin (Lyrica), tiagabine (Gabitril), valproic acid (Depakene)
BLACK BOX WARNINGS/ CAUTIONS	Lithium toxicity occurs above therapeutic serum levels. Long-term use can impair renal or thyroid function: regularly monitor serum lithium levels, creatinine, electrolytes and thyroid function tests.	Divalproex sodium and valproic acid have three black box warnings: hepatotoxicity (including fatalities) can occur usually within the first 6 months of therapy; teratogenicity, including neural tube defects; and life threatening pancreatitis. Lamotrigine has a black box warning for life threatening rashes, including Stevens-Johnson Syndrome, toxic epidermal necrolysis, and rash related fatalities. Carbamazepine has two black box warnings: bone marrow suppression including aplastic anemia and agranulocytosis; and serious dermatologic reactions including severe and fatal cases of Stevens-Johnson Syndrome and toxic epidermal necrolysis. Monitor LFTs and CBC, and use caution when prescribing medications with overlapping toxicities.
PK	Lithium is cleared exclusively by the kidneys; renal impairment requires lower doses to avoid toxicity.	Carbamazepine: CYP 3A4 enzyme inducer Gabapentin: renal elimination. Lamotrigine: undergoes glucuronidation Phenobarbital: CYP 450 inducer Phenytoin: metabolised by and induces CYP 2C9, CYP 2C19; also inducer CYP 2D6 and CYP 3A4 Topiramate: inhibits CPY 2C19 Valproic acid: inhibitor of glucuronidation
NNRTIs	No published data about drug interactions specific to this combination.	Carbamazepine, phenobarbital, phenytoin: CYP 3A4 inducers, may decrease levels of PIs and NNRTIs. Avoid if possible. Carbamazepine, phenobarbital, and phenytoin may decrease etravirine drug levels and should not be used together.

CLASS

Mood Stabilizers and Anticonvulsants

INDICATIONS

Mood Stabilizers (lithium, anticonvulsants) are used as monotherapy and in combination with other drugs (ie atypical antipsychotics) for the treatment of acute mania and as maintenance treatment for bipolar disorder



CATEGORY	Lithium carbonate (Eskalith, Lithobid)	Anticonvulsants carbamazepine (Tegretol), divalproex sodium (Depakote), gabapentin (Neurontin), lamotrigine (Lamictal), levetiracetam (Keppra), oxcarbazepine (Trileptal), phenobarbital (Luminal), phenytoin (Dilantin), pregabalin (Lyrica), tiagabine (Gabitril), valproic acid (Depakene)
NRTIs	No published data about drug interactions specific to this combination.	Valproic acid: inhibitor of glucuronidation; study showed 100% increase in AUC of zidovudine, but dosage adjustment not recommended; monitor for zidovudine toxicity.
PIs	No published data about drug interactions specific to this combination.	Carbamazepine: may decrease levels of PIs; decreases indinavir levels resulting in virologic failure. Ritonavir increases carbamazepine levels. Avoid with PIs if possible. Phenytoin: Co-administration of LPV/r and phenytoin results in a 2-way drug interaction whereby both LPV/r and phenytoin concentrations are decreased ~ 30%. Once daily Kaletra not recommended. Co-administration of nelfinavir (NFV) with phenytoin resulted in a 30% reduction in the phenytoin AUC and a 20% reduction in the AUC of the major NFV metabolite, M8, but had no effect on the NFV AUC. Lamotrigine: When combined with LPV/r, lamotrigine levels were markedly decreased; increased lamotrigine dosage may be required.
CCR5I	No published data about drug interactions specific to this combination	Increase maraviroc dosage to 600 mg twice daily when combined with carbamazepine, phenobarbital or phenytoin. No change in carbamazepine, phenobarbital or phenytoin required.
II	No published data about drug interactions specific to this combination.	No published data about drug interactions specific to this combination.

CLASS

Antipsychotics

INDICATIONS

Antipsychotics can be used to treat psychotic disorders, mania, and behavioral disturbances, such as agitation, associated with dementia.



CATEGORY

First Generation - Typical chlorpromazine (Thorazine), fluphenazine (Prolixin), haloperidol (Haldol), loxapine (Loxitane), mesoridazine (Serentil), molindone (Moban), perphenazine (Trilafon), pimozone (Orap)*, thioridazine (Mellaril), thiothixene (Navane), trifluoperazine (Stelazine)

Atypical Antipsychotics aripiprazole (Abilify), clozapine (Clozaril), olanzapine (Zyprexa), olanzapine/fluoxetine (Symbyax), paliperidone (Invega), quetiapine (Seroquel), risperidone (Risperdal), ziprasidone (Geodon)

BLACK BOX WARNINGS/ CAUTIONS

Pimozide side-effects are prominent in patients with HIV illness. In these patients, start with low doses and titrate slowly.

Pimozide prolongs the QT interval on EKG, and is CONTRAINDICATED in combination with protease inhibitors.

Mesoridazine and thioridazine should not be used in individuals who have known cardiac conduction defects (e.g. AV block, bundle-branch block, cardiac arrhythmia, QT prolongation)

Elderly patients with dementia-related behavioral disorders are at increased risk of death compared to placebo.

All drugs in class: Elderly patients with dementia-related behavioral disorders are at increased risk of death compared to placebo. Clozapine contains 5 black box warnings, which include seizures, myocarditis, cardiovascular effects, respiratory effects, and the risk of life-threatening agranulocytosis; avoid with other medications that suppress bone marrow function. Inhibitors of CYP 3A4 and 2D6 may increase plasma levels of clozapine & increase the risks for seizures, orthostatic hypotension & other adverse effects. Ziprasidone: 1) Causes a dose-related prolongation of the QT interval, and is CONTRAINDICATED with prolongation of the QT interval, recent acute myocardial infarction, or uncompensated heart failure. Also CONTRAINDICATED in combination with other drugs that prolong the QT interval, such as pentamidine, mesoridazine, thioridazine, chlorpromazine, droperidol, or pimozide (not a complete list). 2) An in vivo study showed a 35-40% increase in the AUC and Cmax of ziprasidone when co-administered with ketoconazole, a potent inhibitor of CYP 3A4; caution is indicated when ziprasidone is co-administered with drugs that inhibit CYP 3A4

*Pimozide (Orap) is indicated for severe Tourette's syndrome.

CLASS

Antipsychotics

INDICATIONS

Antipsychotics can be used to treat psychotic disorders, mania, and behavioral disturbances, such as agitation, associated with dementia.



CATEGORY (Continued)	First Generation - Typical chlorpromazine (Thorazine), fluphenazine (Prolixin), haloperidol (Haldol), loxapine (Loxitane), mesoridazine (Serentil), molindone (Moban), perphenazine (Trilafon), pimozide (Orap), thioridazine (Mellaril), thiothixene (Navane), trifluoperazine (Stelazine)	Atypical Antipsychotics aripiprazole (Abilify), clozapine (Clozaril), olanzapine (Zyprexa), olanzapine/fluoxetine (Symbyax), paliperidone (Invega), quetiapine (Seroquel), risperidone (Risperdal), ziprasidone (Geodon)
	PK Chlorpromazine: Metabolized by CYP 1A2, 2D6, 3A4; inhibits CYP 2D6. Fluphenazine: Metabolized by CYP 2D6; inhibits CYP 2D6. Haloperidol: Metabolized by CYP 2D6; inhibits CYP 2D6. Loxapine: metabolized via glucuronidation Mesoridazine: renal elimination. Molindone: Metabolized by CYP 2D6. Perphenazine: Metabolized by CYP 2D6; inhibits CYP 2D6. Pimozide: metabolized via N-dealkylation. Thioridazine: Metabolized by CYP 1A2, 2D6; inhibits CYP 2D6. Trifluoperazine: Metabolized by CYP 1A2.	Aripiprazole: Metabolized by CYP 3A4 and 2D6. Clozapine: Metabolized by CYP 3A4, 2D6, 1A2, 2C19. Olanzapine: Metabolized by CYP 1A2, 2D6. Paliperidone: Not expected to effect CYP 450 in vivo Quetiapine: Metabolized by CYP 3A4. Risperidone: Metabolized by CYP 2D6, 3A4; inhibits CYP 2D6 Ziprasidone: Metabolized by CYP 3A4.
	NNRTIs No published data about drug interactions specific to this combination.	No published data about drug interactions specific to this combination.
	NRTIs No published data about drug interactions specific to this combination.	No published data about drug interactions specific to this combination.

CLASS

Antipsychotics

INDICATIONS

Antipsychotics can be used to treat psychotic disorders, mania, and behavioral disturbances, such as agitation, associated with dementia.



CATEGORY (Continued)	First Generation - Typical chlorpromazine (Thorazine), fluphenazine (Prolixin), haloperidol (Haldol), loxapine (Loxitane), mesoridazine (Serentil), molindone (Moban), perphenazine (Trilafon), pimozone (Orap), thioridazine (Mellaril), thiothixene (Navane), trifluoperazine (Stelazine)	Atypical Antipsychotics aripiprazole (Abilify), clozapine (Clozaril), olanzapine (Zyprexa), olanzapine/fluoxetine (Symbyax), paliperidone (Invega), quetiapine (Seroquel), risperidone (Risperdal) ziprasidone (Geodon)
	<p>PIs Pimozide: prolongs the QT interval on EKG, and is CONTRAINDICATED in combination with PIs due to potential for serious and life-threatening reactions, such as cardiac arrhythmia. Ritonavir may increase levels of antipsychotics; caution with other PIs and ritonavir- boosted PIs. Dosage reductions may be required.</p>	<p>PIs may inhibit CYP 3A4 and 2D6 and may increase plasma levels of clozapine & increase the risk for seizures & orthostatic hypotension. Olanzapine: one study showed an increased clearance of olanzapine, when used in combination with ritonavir, which induces CYP 1A2, but the clinical significance is unclear. Quetiapine: Drug levels may be increased by PIs. Caution when combining these medications. Consider using lower doses of quetiapine. Risperidone: Dosage reductions may be required with RTV boosted protease inhibitors. Ziprasidone: caution is indicated when ziprasidone is co-administered with drugs that inhibit CYP 3A4, such as ritonavir.</p>
CCRS1	No published data about drug interactions specific to this combination	No published data about drug interactions specific to this combination.
II	No published data about drug interactions specific to this combination.	No published data about drug interactions specific to this combination.

CLASS

Stimulants and Medications for attention deficit disorder

INDICATIONS

Stimulants can be used to treat attention deficit hyperactivity disorder, and as adjunctive/augmentation therapy in depression, cognitive disorders and fatigue.



CATEGORY

Stimulants amphetamine and dextroamphetamine (Adderall/Dexedrine), atomoxetine (Strattera), methylphenidate (Ritalin), modafinil (Provigil), armodafinil (Nuvigil), lisdexamfetamine (Vyvanse) and dexamethylphenidate (Focalin)

BLACK BOX WARNINGS/ CAUTIONS

All drugs in class except for armodafinil, modafinil: Potential for drug dependency exists; avoid abrupt discontinuation in patients who have received for prolonged periods. Adderall, Dexedrine: Use has been associated with serious cardiovascular events including sudden death in patients with pre-existing structural cardiac abnormalities or other serious heart problems (sudden death in children and adolescents; sudden death, stroke and MI in adults).

PK

Amphetamine, dextroamphetamine: CYP 2D6 substrate and weak inhibitor
Armodafinil: Metabolized via glucuronidation. Moderate induction of CYP 3A4 with chronic use.
Atomoxetine: Metabolized via CYP 2D6 and glucuronidation
Methylphenidate: CYP 2D6 inhibitor
Modafinil: Substrate for CYP 3A4

NNRTIs

No published data about drug interactions specific to this combination.

NRTIs

No published data about drug interactions specific to this combination.

PIs

Use of ritonavir may increase drug concentrations of modafinil, methylphenidate, amphetamine, and dextroamphetamine.

CCRSI

No published data about drug interactions specific to this combination.

II

No published data about drug interactions specific to this combination.

CLASS

Herbal Preparations

INDICATIONS

Self-prescribed by patients for multiple needs. Providers need to be aware of preparations used by their patients



CATEGORY

St. John's Wort (Hypericin, Hyperforin)
Derived from the plant, Hypericum perforatum.

BLACK BOX WARNINGS/ CAUTIONS

St. John's Wort is contraindicated with concurrent PI therapy.

PK

Inducer of CYP 3A4 and p-glycoprotein.

NNRTIs

May reduce blood levels of NNRTIs. Induces metabolism of nevirapine; increased clearance ~35%. Do not co-administer with NNRTIs.

NRTIs

No published data about drug interactions specific to this combination.

PIs

May reduce levels of PIs, Indinavir levels reduced by 50-80% in volunteers treated with St. Johns Wort and indinavir. Do not co-administer with PIs.

CCRSI

No published data about drug interactions specific to this combination.

II

No published data about drug interactions specific to this combination.

RESOURCES

The National AETC Program also includes the following services:

National HIV/AIDS Clinicians Consultation Center: 1-800-933-3413

Offering treating clinicians current HIV clinical and drug information and individualized, expert case consultation.

Post-Exposure Prophylaxis hotline: 1-888-HIV-4911

Providing consultation for occupational exposures.

Perinatal HIV Hotline: 1-888-448-8765

Providing consultation for perinatal exposure and treatment.

AETC HIV/AIDS National Resource Center: <http://www.aidsetc.org/>

Providing resources (including curricula and lecture slide sets) on HIV disease treatment, education and data.

The following websites may be helpful in managing HIV infected patients:

AETC HIV/AIDS National Resource Center

www.aidsetc.org

NY/NJ AIDS Education and Training Center

www.nynjaetc.org

U.S. DHHS AIDS Info and Treatment Guidelines

www.aidsinfo.nih.gov

NYSDOH AIDS Institute Clinical Resources

www.hivguidelines.org

Substance Abuse and Mental Health Services Administration

www.samhsa.gov

Addiction Technology Transfer Center

www.natfc.org

Harm Reduction Coalition

www.harmreduction.org

RESOURCES

Data supporting this guide was gathered from various sources including:

Micromedex® Health Care Series

Lexicomp® Online

Department of Health and Human Services Guidelines for the use of antiretroviral agents in HIV-1 infected adults and adolescents, December 1, 2009.

Facts and Comparisons 4.0® Available at www.aidsinfo.nih.gov

Food and Drug Administration Approved Product Labels

Various HIV related conference abstracts, posters and oral presentations

Additional Information

For detailed references, training requests, or to order additional guides, please contact the NY/NJ AETC Central Office: (212) 304-5530.