

**PSYCHIATRIC MEDICATIONS AND  
HIV ANTIRETROVIRALS  
ADULT MANAGEMENT  
Winter 2013**

**A DRUG INTERACTION GUIDE FOR CLINICIANS**

# Psychiatric Medications and HIV Antiretrovirals: A Drug Interaction Guide for Clinicians ADULT MANAGEMENT 2013

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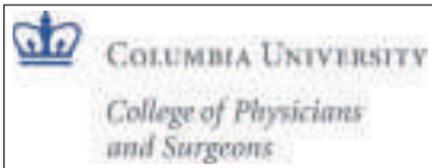
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## Disclaimer:

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 were compiled through February 2013. The NY/NJ AETC would like to acknowledge Ewald Horwath, MD and Christine Kubin, PharmD for their initial development work on this guide.

## Pregnancy Category Definitions:

Within the Black Box Warnings/Caution sections of each medication category, medications that are Category D or X are noted. Category D medications are defined by the FDA as medications with positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. Category X medications are defined as medications where studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.



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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	Intelence™	CYP 3A4 inducer, inhibitor of 2C9, 2C19
Rilpivirine, RPV	Edurant®	CYP 3A4 inducer

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

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

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

COMBINATION PRODUCTS, SINGLE TABLET REGIMENS		
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
Elvitegravir/cobicistat/tenofovir, and emtricitabine	Stribild®	See individual medications
Rilpivirine, tenofovir, and emtricitabine	Complera®	See individual medications
Tenofovir and emtricitabine	Truvada®	See individual medications
Zidovudine and lamivudine	Combivir®	See individual medications

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
Elvitegravir EVG (available as combination with cobicistat, tenofovir, emtricitabine)	Stribild®	Metabolized by CYP3A4. Cobicistat is a potent CYP3A4 inhibitor used to boost levels of elvitegravir. See individual medications.

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

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

Black Box Warnings and medications which are Pregnancy Category D or X 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)\*\*, vilazodone (Viibryd)\*\*\*

#### Tricyclics (TCAs)

nortriptyline (Pamelor), desipramine (Norpramin), amitriptyline (Elavil), imipramine (Tofranil), doxepin (Sinequan, Adapin, Silenor), clomipramine (Anafranil)\*\*, protriptyline (Vivactil), maprotiline (Ludiomil)\*\*\*\*, amoxapine (Asenden)\*\*\*\*, trimipramine (Surmontil)

#### 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. Citalopram is associated with increased risk of sudden cardiac death. **Paroxetine is Pregnancy Category D.**

##### 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. Nortriptyline is associated with increased risk of sudden cardiac death. **Imipramine and nortriptyline are Pregnancy Category D.**

#### 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.  
Vilazodone: Metabolized mainly via CYP3A4, minor contribution from CYP2C19 and CYP2D6

Metabolized by CYP 2D6

\* 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.

\*\*\* vilazodone (Viibryd) is also a serotonin 1A receptor partial agonist

\*\*\*\* maprotiline and amoxapine are classified as a tetracyclic, and heterocyclic antidepressant, respectively

## 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.



<b>CATEGORY</b> <i>(Continued)</i>	<b>Selective serotonin reuptake inhibitors (SSRIs)</b> fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Pexeva, Paxil), citalopram (Celexa), escitalopram (Lexapro), fluvoxamine (Luvox)**, vilazodone (Viibryd) ***	<b>Tricyclics (TCAs)</b> nortriptyline (Pamelor), desipramine (Norpramin), amitriptyline (Elavil), imipramine (Tofranil), doxepin (Sinequan, Adapin, Silenor), clomipramine (Anafranil)**, protriptyline (Vivactil), maprotiline (Ludiumil) ****, amoxapine (Asenden)****, trimipramine (Surmontil)
<b>NNRTIs</b>	Fluoxetine increased trough levels of delavirdine ~ 50% Efavirenz and Nevirapine may reduce drug levels of vilazodone Efavirenz reduces sertraline levels by 39% No effect when efavirenz or etravirine are used with paroxetine	No published data about drug interactions specific to this combination.
<b>NNRTIs</b>	No published data about drug interactions specific to this combination.	No published data about drug interactions specific to this combination.
<b>PIs</b>	Ritonavir may increase levels of SSRIs and can lead to serotonin syndrome. Fluvoxamine increases levels of all PIs. Darunavir/ritonavir decreases sertraline levels by ~49% and decreases paroxetine levels by ~39%; 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. All protease inhibitors may increase drug levels of vilazodone. Vilazodone dosage should be reduced to 20mg if used with strong CYP3A4 inhibitors.	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 boosted protease inhibitors, caution is required. Reduced dosages may be required; monitor EKG and serum TCA levels. Use lowest dose of TCA and titrate based upon clinical assessment.

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

\*\*\*vilazodone (Viibryd) is also a serotonin 1A receptor partial agonist

\*\*\*\*maprotiline and amoxapine are classified as a tetracyclic, and heterocyclic antidepressant, respectively.

# 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.



<b>CATEGORY</b> <i>(Continued)</i>	<b>Selective serotonin reuptake inhibitors (SSRIs)</b> fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Pexeva, Paxil), citalopram (Celexa), escitalopram (Lexapro), fluvoxamine (Luvox)**, vilazodone (Viibryd) ***	<b>Tricyclics (TCAs)</b> nortriptyline (Pamelor), desipramine (Norpramin), amitriptyline (Elavil), imipramine (Tofranil), doxepin (Sinequan, Adapin, Silenor), clomipramine (Anafranil)**, protriptyline (Vivactil), maprotiline (Ludiomil) ****, amoxapine (Asenden)****, trimipramine (Surmontil)
<b>CCRSI</b>	No published data about drug interactions specific to this combination	No published data about drug interactions specific to this combination
II	Elvitegravir/cobicistat/tenofovir/emtricitabine may increase paroxetine levels and levels of other SSRIs. Use lowest dose.	Elvitegravir/cobicistat/tenofovir/emtricitabine increased desipramine levels 65%. May also increase amitriptyline, imipramine and nortriptyline levels. Reduced dosages may be required; monitor EKG and serum TCA levels.

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

\*\*\*vilazodone (Viibryd) is also a serotonin 1A receptor partial agonist

\*\*\*\*maprotiline and amoxapine are classified as a tetracyclic, and heterocyclic antidepressant, respectively.

## CLASS

### Antidepressants

## INDICATIONS

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CATEGORY	Other Bupropion (Buproban, Forfivo XL, Wellbutrin, Wellbutrin SR/XL, Zyban)	Other nefazodone
<b>BLACK BOX WARNINGS/ CAUTIONS</b>	<b>Increased suicide risk in &lt;24 years old. *</b> 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.	<b>Increased suicide risk in &lt;24 years old. *</b> <b>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.</b> This drug is usually avoided. Associated with somnolence and dizziness, especially at higher doses.
<b>PK</b>	Metabolized by CYP 2D6, 3A4, 2B6.	Metabolized by and potent inhibitor of CYP 3A4
<b>NNRTIs</b>	Efavirenz reduces bupropion levels by 55%, titrate bupropion based upon response.	No published data about drug interactions specific to this combination (See Cautions).
<b>NRTIs</b>	No published data about drug interactions specific to this combination.	No published data about drug interactions specific to this combination. (See Cautions).
<b>PIs</b>	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 57%. Avoid with high dose ritonavir. Tipranavir/ritonavir reduces bupropion levels 46%.	Caution advised; combination of PI's and nefazodone may increase levels of both drugs. Nefazodone dosage reduction may be required with protease inhibitors.
<b>CCRSI</b>	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.
<b>II</b>	Elvitegravir/cobicistat/tenofovir/emtricitabine may increase bupropion levels.	Elvitegravir/cobicistat/tenofovir/emtricitabine may increase nefazodone levels.

**\*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	Serotonin norepinephrine reuptake inhibitors (SNRIs) mirtazapine (Remeron)**, venlafaxine (Effexor, Effexor XR), duloxetine (Cymbalta), desvenlafaxine (Pristiq)	Other trazodone (Desyrel, Oleptro)
<b>BLACK BOX WARNINGS/ CAUTIONS</b>	<b>Increased suicide risk in &lt;24 years old.*</b> Mirtazapine: Orthostatic hypotension, drowsiness. Venlafaxine: Hypertension.	<b>Increased suicide risk in &lt;24 years old.*</b> Increased plasma levels may cause nausea, hypotension, syncope and drowsiness. Trazodone has been associated with increased incidence of priapism and arrhythmias.
<b>PK</b>	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.	Trazodone: substrate of CYP 3A4
<b>NNRTIs</b>	No published data about drug interactions specific to this combination.	No published data about drug interactions specific to this combination.
<b>NRTIs</b>	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.

\*\* Mirtazapine (remeron) is also classified as a tetracyclic compound

## 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.



<b>CATEGORY</b> <i>(Continued)</i>	<b>Serotonin norepinephrine reuptake inhibitors (SNRIs)</b> mirtazapine (Remeron), venlafaxine (Effexor, Effexor XR), duloxetine (Cymbalta), desvenlafaxine (Pristiq)	<b>Other</b> trazodone (Desyrel)
	<p><b>PIs</b> 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. 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>
<b>CCRS1</b>	No published data about drug interactions specific to this combination	No published data about drug interactions specific to this combination.
<b>II</b>	No published data about drug interactions specific to this combination.	Elvitegravir/cobicistat/tenofovir/emtricitabine likely to increase trazodone levels. If using concurrently, initiate trazodone at lowest available dosage and monitor for adverse effects.

## 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.**

# 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 buspirone (BuSpar), diphenhydramine (Benadryl) eszopiclone (Lunesta), ramelteon (Rozerem), zaleplon (Sonata), zolpidem (Ambien, Ambien CR, Edluar, Intermezzo, Zolpimist)
<b>BLACK BOX WARNINGS/ CAUTIONS</b>	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. <b>Alprazolam, clonazepam, clorazepate, diazepam and lorazepam are Pregnancy Category D. Temazepam and Triazolam are Pregnancy Category X.</b>	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.
<b>PK</b>	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 see PI section for contraindications and caution with use.	Buspirone: Substrate for CYP 3A4 Diphenhydramine: CYP2D6 Eszopiclone: Metabolized by CYP 3A4 and 2E1 Ramelteon: CYP 1A2, minor contribution from CYP 2C and CYP 3A4 Zaleplon: Metabolized by aldehyde oxidase and CYP 3A4. Zolpidem: CYP 3A4 substrate
<b>NNRTIs</b>	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.
<b>NRTIs</b>	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  
and sleep  
disorders.*



<b>CATEGORY</b> <i>(Continued)</i>	<b>Benzodiazepines</b> alprazolam (Niravam, Xanax), chlordiazepoxide (Librium), clonazepam (Klonopin), clorazepate (Tranxene), diazepam (Valium), flurazepam (Dalmene), lorazepam (Ativan), midazolam (Versed)*, oxazepam, temazepam (Restoril), triazolam (Halcion)	<b>Non-Benzodiazepine sedative/hypnotics</b> buspirone (BuSpar), diphenhydramine (Benadryl), eszopiclone (Lunesta), ramelteon (Rozerem), zaleplon (Sonata), zolpidem (Ambien, Ambien CR, Edluar, Intermezzo, Zolpimist)
	<p><b>Pls</b> Oral midazolam and triazolam are metabolized by CYP 3A4, and are <b>CONTRAINDICATED</b> in combination with Pls 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. Flurazepam and clonazepam are also metabolized by CYP 3A4, and should be used with caution in combination with Pls due to the potential for serious reactions such as prolonged or severe sedation or respiratory depression. Alprazolam and diazepam likely to be increased by Pls, consider alternatives such as lorazepam, oxazepam or temazepam. Lorazepam, temazepam, and oxazepam are metabolized by glucuronidation and are free of interactions with Pls.</p>	<p>Use zolpidem and zaleplon with caution in combination with Pls due to potential for serious reactions such as prolonged or severe sedation or respiratory depression. With ritonavir-boosted Pls, use lowest dosage available and monitor for excess CNS depression. Avoid with other CNS-depressants. Use eszopiclone and Pls with caution, if at all. Monitor for excess sedation and/or respiratory depression. Ketoconazole increases eszopiclone levels by 2.2-fold; similar interactions with Pls and ritonavir -boosted Pls would be expected. Avoid concurrent use if possible. Buspirone is a substrate of CYP 3A4 - Concurrent use with Pls is likely to increase buspirone drug levels.</p>
<p><b>CCR5I</b></p>	<p>No published data about drug interactions specific to this combination</p>	<p>No published data about drug interactions specific to this combination.</p>
	<p><b>II</b> Oral midazolam and triazolam contraindicated with elvitegravir/cobicistat/tenofovir/emtricitabine due to potential for prolonged sedation or respiratory depression. Other benzodiazepines such as diazepam, clonazepam, flurazepam may be increased. Lorazepam, temazepam, and oxazepam unlikely to interact.</p>	<p>Elvitegravir/cobicistat/tenofovir/emtricitabine likely to increase levels of buspirone and zolpidem. Monitor for excess sedation.</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, Equetro), divalproex sodium (Depakote, Depakote ER, Stavzor), gabapentin (Neurontin, Gabarone and Gralise), lamotrigine (Lamictal), levetiracetam (Keppra), oxcarbazepine (Trileptal), phenobarbital, phenytoin (Dilantin), pregabalin (Lyrica), tiagabine (Gabitril), valproic acid (Depakene)
<b>BLACK BOX WARNINGS/ CAUTIONS</b>	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. <b>Lithium is Pregnancy Category D</b>	<b>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.</b> Lamotrigine has a black box warning for life threatening rashes, including Stevens-Johnson Syndrome, toxic epidermal necrolysis, and rash related fatalities. Carbamazepine, divalproex sodium, phenobarbital and valproic acid are Pregnancy Category D. 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.
<b>PK</b>	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
<b>NNRTIs</b>	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 and rilpivirine 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, Equetro), divalproex sodium (Depakote, Depakote ER, Stavzor), gabapentin (Neurontin, Gabarone and Gralise), lamotrigine (Lamictal), levetiracetam (Keppra), oxcarbazepine (Trileptal), phenobarbital, 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 with phenytoin. 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 600mg twice daily when combined with carbamazepine, phenobarbital or phenytoin in the absence of a strong CYP3A4 inhibitor.

#### II

No published data about drug interactions specific to this combination.

Carbamazepine, oxcarbazepine, phenobarbital and phenytoin may significantly reduce elvitegravir concentrations and should be avoided.

## 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), asenapine (Saphris), clozapine (Clozaril, FazaClo), iloperidone (Fanapt), olanzapine (Zyprexa), lurasidone (Latuda), 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), asenapine (Saphris), clozapine (Clozaril, FazaClo), iloperidone (Fanapt), olanzapine (Zyprexa), lurasidone (Latuda), 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. Iloperidone: Metabolized by CYP2D6, CYP3A4 Clozapine: Metabolized by CYP 3A4, 2D6, 1A2, 2C19. Lurasidone: Metabolized by CYP3A4 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.  Asenapine: Metabolized by CYP1A2
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.

\*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), pimozone (Orap)*, thioridazine (Mellaril), thiothixene (Navane), trifluoperazine (Stelazine)	Atypical Antipsychotics aripiprazole (Abilify), asenapine (Saphris), clozapine (Clozaril, FazaClo), iloperidone (Fanapt), olanzapine (Zyprexa), lurasidone (Latuda), paliperidone (Invega), quetiapine (Seroquel), risperidone (Risperdal), ziprasidone (Geodon)
	<p><b>PIs</b> 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 &amp; increase the risk for seizures &amp; 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. Iloperidone: CYP3A4 inhibitors may increase active metabolite of iloperidone. Decrease iloperidone by 50% with strong CYP3A4 or CYP2D6 inhibitors. Risperidone: Dosage reductions may be required with RTV boosted protease inhibitors. Lurasidone: CYP3A4 inhibitors likely to increase lurasidone levels, CYP3A4 inducers may reduce lurasidone levels. Ziprasidone: caution is indicated when ziprasidone is co-administered with drugs that inhibit CYP 3A4, such as ritonavir.</p>
<p><b>CCRS1</b></p>	<p>No published data about drug interactions specific to this combination</p>	<p>No published data about drug interactions specific to this combination.</p>
<p><b>II</b></p>	<p>Elvitegravir/cobicistat/tenofovir/emtricitabine may increase perphenazine and thioridazine levels. Use lowest dose.</p>	<p>Elvitegravir/cobicistat/tenofovir/emtricitabine may increase risperidone levels. Use lowest dose.</p>

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

## 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), armodafinil (Nuvigil), atomoxetine (Strattera), dexamethylphenidate (Focalin), dextroamphetamine (Dexadrene, ProCentra), lisdexamfetamine (Vyvanse), methamphetamine (Desoxyn), methylphenidate (Concerta, Metadate, Methylin, Ritalin), methylphenidate transdermal (Daytrana), modafinil (Provigil)

### 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

May reduce levels of elvitegravir and cobicistat. Do not co-administer with elvitegravir/cobicistat/tenofovir/emtricitabine

## 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: 1-888-448-4911**

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](http://www.aidsetc.org)

**NY/NJ AIDS Education and Training Center**

[www.nynjaetc.org](http://www.nynjaetc.org)

**U.S. DHHS AIDS Info and Treatment Guidelines**

[www.aidsinfo.nih.gov](http://www.aidsinfo.nih.gov)

**NYSDOH AIDS Institute Clinical Resources**

[www.hivguidelines.org](http://www.hivguidelines.org)

**Substance Abuse and Mental Health Services Administration**

[www.samhsa.gov](http://www.samhsa.gov)

**Addiction Technology Transfer Center**

[www.nattc.org](http://www.nattc.org)

**Harm Reduction Coalition**

[www.harmreduction.org](http://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, February 2013. Available at [www.aidsinfo.nih.gov](http://www.aidsinfo.nih.gov). Accessed February 14, 2013.**

**Facts and Comparisons 4.0®**

**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.