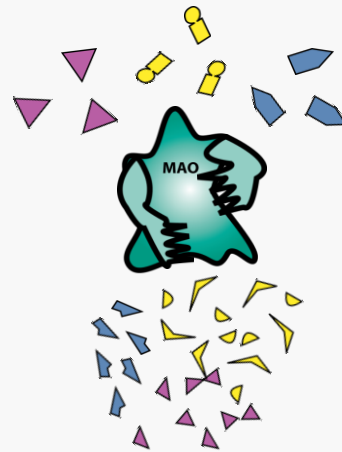


Handout for the Neuroscience Education Institute (NEI) online activity:

Practical Guide to Using MAOs



Learning Objectives

- Identify foods and medications that interact with MAO inhibitors
- Implement safe management strategies when switching between MAO inhibitors and serotonin reuptake inhibitors
- Integrate MAO inhibitors into clinical practice according to best practices standards

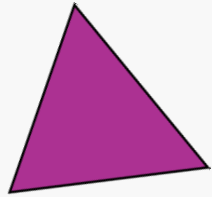


MAO Inhibitors

Name	MAO-A Inhibition	MAO-B Inhibition	Amphetamine Properties
phenelzine	+	+	
tranylcypromine	+	+	+
isocarboxazid	+	+	
amphetamines (high-dose)	+	+	+
selegiline (transdermal)			
brain	+	+	+
gut	+/-	+	+
selegiline (oral low-dose)	-	+	+
selegiline (oral high-dose)	+	+	+
rasagiline (Europe, Israel)	-	+	-
moclobemide (not in U.S.)	+	-	-
CX 157	+	-	-

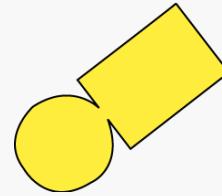


Two Major Interactions With MAOIs



Noradrenergic

- Dietary: tyramine
- Drug: norepinephrine (NE) reuptake inhibitors and other NE-boosting drugs



Serotonergic

- Drug: serotonin (5HT) reuptake inhibitors

Noradrenergic Interactions

Dietary: Tyramine

Myth #1: The Tyramine Interaction

You can't eat cheese, drink wine or beer, or eat lots of foods that contain tyramine, or else you will develop hypertensive crisis...

...so if you go to pizza parties or wine and cheese receptions, eat in restaurants, or follow a normal diet, you can't take an MAOI.

Myth #1: The Tyramine Interaction

The Truth

There are a few things to avoid (which are easy to remember), but in practice, diet is not really a problem...

...unless you plan to drink a gallon of blue cheese.

Myth #1: The Tyramine Interaction

The Pharmacology

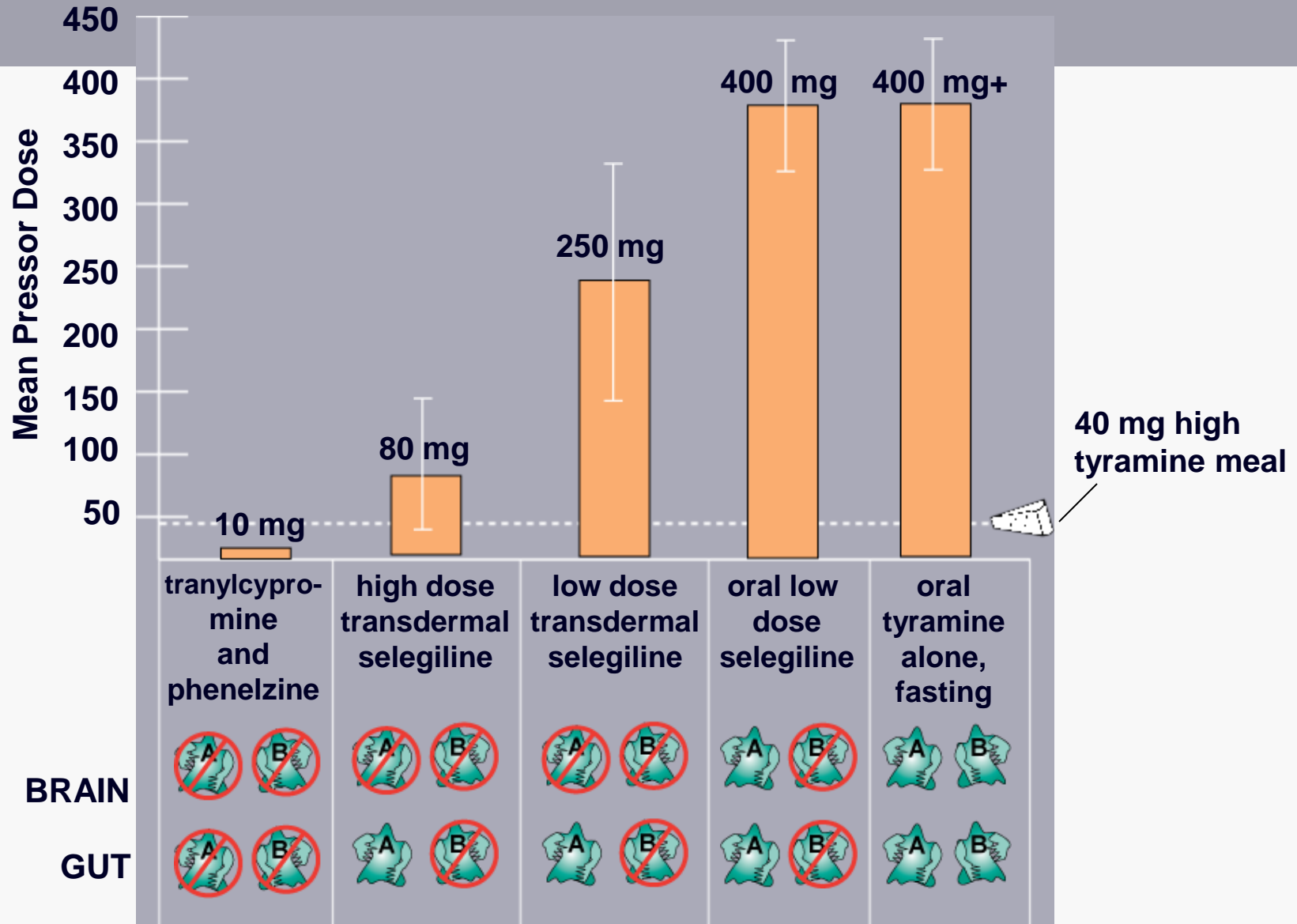
You should be cautious when combining an MAOI with anything that boosts NE because this can raise blood pressure.

Hypertensive Crisis

- Diastolic blood pressure >120 mm Hg
- Potentially fatal reaction characterized by:
 - Occipital headache that may radiate frontally
 - Palpitation
 - Neck stiffness or soreness
 - Nausea
 - Vomiting
 - Sweating (sometimes with fever)
 - Dilated pupils, photophobia
 - Tachycardia or bradycardia, which can be associated with constricting chest pain



How Much Tyramine Is Dangerous With Irreversible MAO-A Inhibitors?



Stahl SM. Stahl's Essential Psychopharmacology. 3rd ed. 2008.

Myth #1: The Tyramine Interaction

The Owner's Manual

Foods to Avoid*

Dried, aged, smoked, fermented, spoiled, or improperly stored meat, poultry, and fish

Broad bean pods

Aged cheeses

Tap and unpasteurized beer

Marmite

Soy products/tofu

Sauerkraut, kimchee

Banana peel

Tyramine-containing nutritional supplement

Foods Allowed

Fresh or processed meat, poultry, and fish; properly stored pickled or smoked fish

All other vegetables

Processed cheese slices, cottage cheese, ricotta cheese, yogurt, cream cheese

Canned or bottled beer and alcohol

Brewer's and baker's yeast

Peanuts

Bananas, avocados, raspberries

*Not necessary for 6 mg transdermal or low-dose oral selegiline

Wimbiscus et al. Curr Drug Ther 2010;77(2):859-82; Grady MM, Stahl SM. CNS Spectr 2012;In press.

Copyright © 2012 Neuroscience Education Institute. All rights reserved.



Noradrenergic Interactions

Cold Medications,
Stimulants, and Anesthetics

Myths #2 and #3: The Cold Medication/Stimulant Interaction

If you're taking an MAOI, you can't take anything with NE reuptake inhibition, which means:

You can't take cold medications, such as decongestants, antihistamines, or cough medicines, so patients who get colds cannot take MAOIs.

You can't take stimulants, so patients who need stimulants cannot take MAOIs.

Myths #2 and #3: The Cold Medication/Stimulant Interaction

The Truth

Sympathomimetic decongestants and stimulants should be used with caution while monitoring blood pressure in patients for which the benefits are greater than the risks and should be avoided only in high-risk/low-benefit populations.

Myths #2 and #3: The Cold Medication/Stimulant Interaction

The Pharmacology

You should be cautious when combining an MAOI with anything that boosts NE because this can raise blood pressure.

Some cold medications also inhibit 5HT reuptake; you should completely avoid combining an MAOI with anything that blocks 5HT reuptake because this can cause dangerous or fatal serotonin toxicity.

Transdermal Selegiline Drug Interaction Trial: Pseudoephedrine (PSE)

Mean SBP and DBP (mm Hg) and HR (bpm) before and during multiple-dose treatment with PSE and/or selegiline 6 mg/24 hr

Parameter	Baseline		End of PSE Treatment	
	Untreated Control	selegiline	PSE	selegiline+PSE
SBP (mm Hg)	118.4	109.1	122.9	122.2
DBP (mm Hg)	71.0	63.2	68.9	67.9
HR (bpm)	62.7	59.4	73.5	75.5

N=10 healthy volunteers

Pseudoephedrine dose: 60 mg TID for 2 days

Azzaro AJ et al. J Clin Pharmacol 2007;47:978-90.

Copyright © 2012 Neuroscience Education Institute. All rights reserved.



Transdermal Selegiline Drug Interaction Trial: Phenylpropanolamine (PPA)

Mean SBP and DBP (mm Hg) and HR (bpm) before and during multiple-dose treatment with PSE and/or selegiline 6 mg/24 hr

Parameter	Baseline		End of PPA Treatment	
	Untreated Control	selegiline	PPA	selegiline+PPA
SBP (mm Hg)	120.2	123.5	121.2	125.1
DBP (mm Hg)	72.3	71.2	71.9	74.0
HR (bpm)	64.7	64.3	62.2	64.1

N=10 healthy volunteers

Pseudoephedrine dose: 60 mg TID for 2 days

Azzaro AJ et al. J Clin Pharmacol 2007;47:978-90.

Copyright © 2012 Neuroscience Education Institute. All rights reserved.



Myth #2: The Cold Medication Interaction

The Owner's Manual

- Probably best to use antihistamines, which are safe except for two that are also 5HT reuptake inhibitors (i.e., brompheniramine and chlorpheniramine)
- Cough medicines with expectorants or codeine are safe, but avoid dextromethorphan, a weak serotonin reuptake inhibitor

Sun-Edelstein C et al. Expert Opinion Drug Safety 2008;7(5):587-96;
Grady MM, Stahl SM. CNS Spectr 2012;In press.



Availability of Cough and Cold Medications (Active Ingredient)

Over-the-counter	Behind-the-counter	Prescription	Off the market (U.S.)
phenylephrine	pseudoephedrine	diphenhydramine (injection)	phenyl-propranolamine
diphenhydramine		dextromethorphan	
dextromethorphan			

Available at: www.accessdata.fda.gov

Copyright © 2012 Neuroscience Education Institute. All rights reserved.



Myth #3: The Stimulant Interaction

The Owner's Manual

- Stimulants are useful as bridging medications when starting or stopping MAOIs and as augmenting medications to boost partial response to MAOIs
 - Don't use an MAOI in a known cocaine/methamphetamine/stimulant abuser

Sun-Edelstein C et al. Expert Opinion Drug Safety 2008;7(5):587-96;
Feinberg SS. J Clin Psychiatry 2004;65(11):1520-4;
Grady MM, Stahl SM. CNS Spectr 2012;In press.



Myth #4: The Anesthetic Interaction

If you're taking an MAOI, you can't take anything with NE reuptake inhibition, which means:
You can't have a local or general anesthetic, so patients who need dental work, sutures, or surgery cannot take an MAOI.

Myth #4: The Anesthetic Interaction

The Truth

Be careful using local anesthetics that contain epinephrine and general anesthesia, as both can cause blood pressure changes.

Myth #4: The Anesthetic Interaction

The Pharmacology

Pressor agents inadvertently injected intravenously can raise blood pressure; inhalation anesthetics can cause blood pressure changes.

Myth #4: The Anesthetic Interaction

The Owner's Manual

If Your Patient Needs:

Local anesthetic

Elective surgery

Urgent or elective surgery while on an MAOI

Choose an agent that does not contain vasoconstrictors

Wash out the MAOI 10 days prior to surgery (if possible)

Cautiously use a benzodiazepine, mivacurium, rapacuronium, morphine, or codeine



Summary: Noradrenergic Drug Interactions

Use With Caution:

Decongestants	Stimulants	Antidepressants With NRIs	Other
Phenylephrine	Amphetamine	Most TCAs	Phentermine
Pseudoephedrine	Methylphenidate	NRIs	Local anesthetics containing vasoconstrictors
	Modafinil	SNRIs	Tramadol, tapentadol
	Armodafinil	NDRIs	Cocaine, meth- amphetamine

Sun-Edelstein C et al. Expert Opinion Drug Safety 2008;7(5):587-96;
Wimbiscus et al. Curr Drug Ther 2010;77(2):859-82;
Grady MM, Stahl SM. CNS Spectr 2012;In press.



Serotonergic Interactions

A yellow arrow with a black outline, pointing to the right, is positioned behind the main title text.

Tricyclic Antidepressants (TCAs),
Pain Medications, and Other
Psychotropic Medications

Myth #5: The Tricyclic Interaction

Tricyclic antidepressants are so dangerous that patients on MAO inhibitors cannot take them or anything that resembles them, including carbamazepine and cyclobenzaprine.

Myth #5: The Tricyclic Interaction

The Truth

Other than clomipramine, tricyclic antidepressants and related agents can be used with caution in patients taking MAO inhibitors.

Myth #5: The Tricyclic Interaction

The Pharmacology

You should completely avoid combining an MAOI with anything that blocks 5HT reuptake because this can cause dangerous or fatal serotonin toxicity.

****Some TCAs also increase NE:**

You should be cautious when combining an MAOI with anything that boosts NE because this can raise blood pressure.

Myth #5: The Tricyclic Interaction

The Owner's Manual

- Contraindicated: clomipramine
- Other TCAs can be used with caution for severe TRD
- If an MAOI and a TCA are combined:
 - DO NOT START THE MAOI FIRST!
 - Start the MAOI at the same time as the TCA (both at low doses) after an appropriate drug washout
 - Alternately increase the doses of these agents every few days to a week as tolerated
- Cyclobenzaprine, carbamazepine, and oxcarbazepine can be used with caution because they do not block 5HT or NE reuptake



Myth #6: The Painkiller Interaction

You can't take painkillers with MAOIs because they will kill you, so patients who have sprained ankles, sore muscles, dental extractions, or surgeries cannot take MAOIs, as they must avoid all opiate and non-opiate painkillers.

Myth #6: The Painkiller Interaction

The Truth

There are a few things to avoid (which are easy to remember), and in practice, this is not really a problem.

Myth #6: The Painkiller Interaction

The Pharmacology

There is no interaction of MAOIs with opiate mechanisms.

Meperidine is a potent 5HT reuptake inhibitor and should be avoided.

Fentanyl, methadone, and tramadol are weak 5HT reuptake inhibitors and should be avoided.

Tapentadol is an NE reuptake inhibitor and should be avoided.

Myth #6: The Painkiller Interaction

The Owner's Manual

Use With MAOIs Should Be Cautious	Use With MAOIs May Sometimes Be Done By Experts	Use With MAOIs Strictly Prohibited
acetaminophen	hydromorphone	fentanyl
aspirin	morphine*	meperidine
buprenorphine	oxycodone*	methadone
butorphanol	oxymorphone	tapentadol
codeine		tramadol
hydrocodone		
nalbuphine		
NSAIDs		
pentazocine		

*Not all experts agree that these drugs require more caution than those in the left-hand column.
Grady MM, Stahl SM. CNS Spectr 2012;In press; Gillman PK. Br J Anaesth 2005;95(4):434-41.



Myth #7: The Psychotropic Medication Interaction

You can't take any medications that block 5HT reuptake, which means you can't take any psychotropic medications. Since all patients who are candidates for an MAOI need concomitant medications, no one can take an MAOI.

Besides, in order to start an MAOI, you have to stop all other medications for 2 weeks after taper. And if you have to stop an MAOI to go back to a psychotropic medication, you have to go without all medications for another 2 weeks. This is an unacceptable risk and a hassle.

Myth #7: The Psychotropic Medication Interaction

The Truth

You must completely avoid only agents that block serotonin reuptake. There are many options for not only bridging between serotonin reuptake inhibitors and MAOIs, but also augmenting MAOIs.

Myth #7: The Psychotropic Medication Interaction

The Pharmacology

You should completely avoid combining an MAOI with anything that blocks 5HT reuptake because this can cause dangerous or fatal serotonin toxicity.

You should be cautious when combining an MAOI with anything that boosts NE because this can raise blood pressure.

Serotonin Syndrome/Toxicity*

Neuromuscular hyperactivity

Akathisia

Tremor

Clonus

Myoclonus

Hyperreflexia

Rigidity

Nystagmus

Autonomic hyperactivity

Diaphoresis

Fever

Tachycardia

Tachypnea

Altered mental status

Agitation

Excitement

Confusion

*Presents abruptly and can progress quickly



Hunter Criteria for Serotonin Toxicity

In the Presence of a Serotonergic Agent:

spontaneous clonus OR

inducible clonus and agitation OR

inducible clonus and diaphoresis OR

ocular clonus and agitation OR

ocular clonus and diaphoresis OR

tremor and hyperreflexia OR

hypertonia, temperature $>38^{\circ}\text{C}$,
and ocular clonus OR

hypertonia, temperature $>38^{\circ}\text{C}$,
and inducible clonus



Myth #7: The Psychotropic Medication Interaction

The Owner's Manual: Drugs to Avoid Due to Risk of Serotonin Toxicity

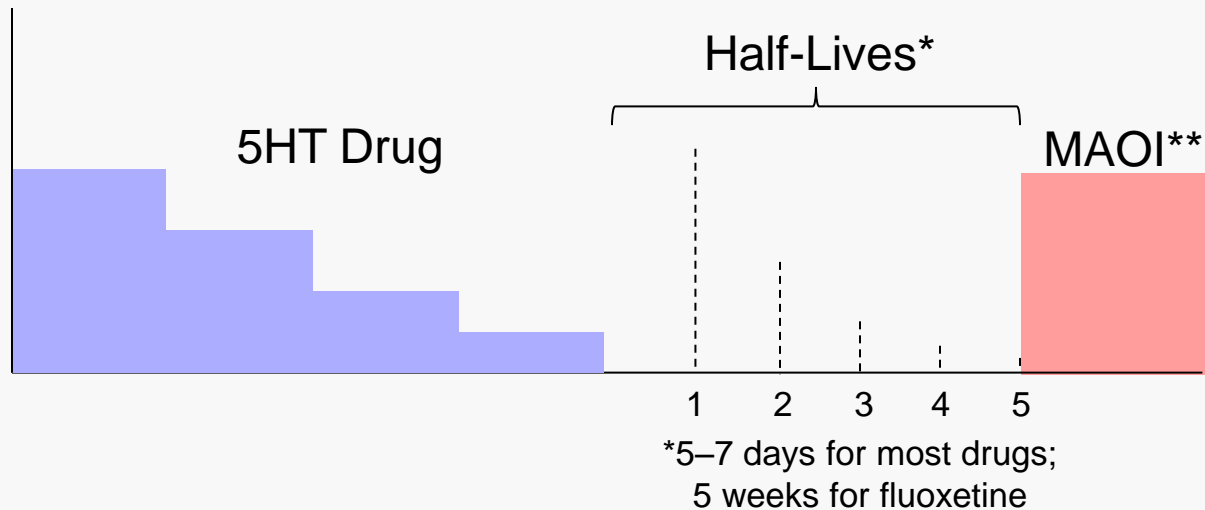
Antidepressants	Drugs of Abuse	Opioids	Other
SSRIs	MDMA (ecstasy)	meperidine	non-subcutaneous sumatriptan
SNRIs	cocaine	tramadol	chlorpheniramine
clomipramine	methamphetamine	methadone	brompheniramine
St. John's wort	High-dose or injected amphetamine		dextromethorphan
		fentanyl	procarbazine?

Wimbiscus et al. Curr Drug Ther 2010;77(2):859-82;
Grady MM, Stahl SM. CNS Spectr 2012;In press.



Myth #7: The Psychotropic Medication Interaction

The Owner's Manual: Switching From a Serotonergic Drug to an MAOI

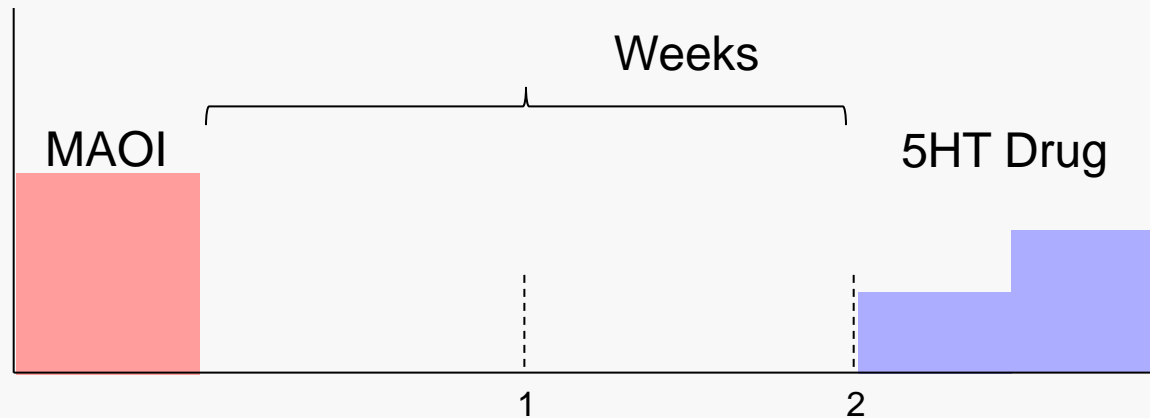


**Titration schedule for MAOI may differ depending on the individual agent

Stahl SM. Prescriber's Guide. 4th ed. Cambridge University Press; 2011.

Myth #7: The Psychotropic Medication Interaction

The Owner's Manual: Switching From an MAOI to a Serotonergic Drug



**Titration schedule for 5HT drug may differ depending on the individual agent

Stahl SM. Prescriber's Guide. 4th ed. Cambridge University Press; 2011.

Myth #7: The Psychotropic Medication Interaction

The Owner's Manual: How to Bridge Use These Drugs While Waiting to Start an MAOI or When Discontinuing an MAOI

- Benzodiazepines, Z-drug hypnotics, trazodone
- Lamotrigine, valproate, lithium
- Gabapentin, pregabalin, topiramate, carbamazepine, oxcarbazepine
- Stimulants
- Atypical antipsychotics



Summary

- MAOIs still have a role in modern psychopharmacology
- Distinct and understandable pharmacological mechanisms account for MAOIs and their therapeutic, drug, and dietary interactions
- Bottom line:
 - Be cautious when combining an MAOI with anything that boosts NE because this can raise blood pressure
 - Completely avoid combining an MAOI with anything that blocks 5HT reuptake because this can cause dangerous or fatal serotonin toxicity

