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**MONOAMINE OXIDASE INHIBITORS (MAOIs)**

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**FOR PATIENTS AND FAMILIES**

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- **Isocarboxazid (Marplan)**
  - **Phenelzine (Nardil)**
  - **Tranlycypromine (Parnate)**
  - **Selegiline (Eldepryl)**
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**Monoamine oxidase inhibitors (MAOIs)** represent an older class of antidepressants that have essentially been replaced by safer agents for treatment of depression. Physicians generally do not initiate MAOIs as first-line antidepressants because of their serious side effects, involving potentially dangerous interactions with certain foods and medications.

MAOIs are indicated for treatment of severe forms of depression, such as **atypical depression**, that have not responded to other antidepressants. In atypical depression, the patient is overly sensitive to rejection, has difficulty with expressing emotions, is prone to labile or fragile moods, oversleeps and overeats, feels extreme fatigue or “leaden paralysis,” and is highly emotional and reactive to daily events. When patients with atypical depression do not respond to a selective serotonin reuptake inhibitor (SSRI) antidepressant, such as fluoxetine (Prozac), an MAOI may be indicated and often may be effective. MAOIs may also be efficacious, when other antidepressants have not been effective, in treating anxiety and panic attacks, agoraphobia, and eating disorders such as bulimia.

Monoamine oxidases are enzymes distributed throughout the body, including the brain. These enzymes are responsible for breaking down specific chemicals in the body, including two important neurotransmitters in the brain: **norepinephrine** and **serotonin**. Norepinephrine and serotonin are just a few of many neurotransmitters in the central nervous system. Decreased concentrations of neurotransmitters in the brain may be associated with depression and the aforementioned disorders. *Monoamine oxidase inhibitors*, as the term implies, work by inhibiting, or “blocking,” this enzyme system, thus increasing the levels of neurotransmitters, including norepinephrine and serotonin. As more neurotransmitters are made available, the brain undergoes changes that ultimately relieve depression. The lag time for the brain to normalize may explain why antidepressants, including MAOIs, may take weeks before achieving their full effects.

Three MAOIs—**phenelzine** (Nardil), **tranlycypromine** (Parnate), and **isocarboxazid** (Marplan)—are approved by the U.S. Food and Drug Administration (FDA) for treatment of depression. Another MAOI—**selegiline** (Eldepryl)—is approved for treatment of **Parkinson’s disease** (a neurologic disorder that affects movement). When selegiline is used for treatment of depression, higher doses than those used for treatment of Parkinson’s disease are necessary.

Phenelzine, tranlycypromine, and isocarboxazid are available only under their brands. Selegiline is available under the trade names **Eldepryl** and **Carbex**, as well as from different generic manufacturers. MAOIs are available only in the following strengths: phenelzine, 15 mg; tranlycypromine and isocarboxazid, 10 mg; and selegiline, 5 mg.

## HOW MAOIS ARE PRESCRIBED

MAOIs should not be taken concomitantly with other antidepressants. The combination is hazardous and may precipitate a severe reaction. MAOIs should not be taken within 14 days after stopping another antidepressant, which allows sufficient time for it to be eliminated from the body. Also, at least 2 weeks must be allowed after stopping an MAOI before another antidepressant may be started.

The dosages for MAOIs are carefully individualized to the patient's clinical response and tolerability to the medication. Physicians usually start slowly with low doses and increase the dose gradually to allow patients to adapt to the side effects. It may take several weeks before the patient feels a significant response. The dosage ranges for MAOIs are as follows: phenelzine, 45 to 90 mg/day; tranylcypromine, 30 to 60 mg/day; isocarboxazid, 40–60 mg/day; and selegiline, 20–50 mg/day. The total daily doses are usually administered in two or three divided doses.

## PROPER USE OF YOUR MEDICATION

### Storing Your Medication

- Keep your medication in a tamper-resistant vial and out of reach of children.
- Store your medication so as to keep it from excessive heat, moisture, and direct light.
- Keep your medication in its original prescription vial with the label intact to prevent others from taking the medication inadvertently.

### Taking Your Medication

- Take your medication exactly as instructed by your physician. Do not abruptly stop taking your medication without consulting your physician. Abrupt discontinuation of your medication may result in unpleasant withdrawal symptoms and relapse of symptoms. MAOI antidepressants need to be decreased gradually before stopping the medication.
- An MAOI antidepressant, like all antidepressants, may take several weeks to achieve full effect.
- If you missed a dose, take it as soon as possible. However, if it is near the time of your next dose, skip the dose you missed and go back to your regular dosing schedule, but do not double-up the dose.
- Your antidepressant may be taken with food or without food. If it upsets your stomach, take it at mealtime.

### Avoid Tyramine-Containing Foods

Certain foods and beverages are rich in **tyramine**. Tyramine is a naturally occurring substance generally derived from the aging process of food and alcohol. Tyramine is broken down in the intestines by monoamine oxidase enzymes before any significant amount is absorbed and distributed in the body. However, when an MAOI is present, the enzyme system is blocked throughout the body, including in the patient's intestines. As foods high in tyramine are consumed, large amounts of tyramine are absorbed and distributed unchecked. High levels of tyramine can cause blood vessels to constrict, thus elevating blood pressure. When blood pressure becomes dangerously elevated and goes untreated, a **hypertensive crisis** ensues. Patients taking MAOI antidepressants minimize the risks of a hypertensive reaction by avoiding certain foods and beverages high in tyramine (see Table 1).

<b>Table 1. Dietary Restrictions When Taking Monoamine Oxidase Inhibitors (MAOIs)</b>
<b>Tyramine-Containing Foods That Must Be Avoided</b>
<ul style="list-style-type: none"> <li>• Cheese and cheese-containing foods (present in Italian dishes, salad dressings, and sauces) <i>Cream cheese, cottage cheese, and ricotta are safe.</i></li> <li>• Beer (including some nonalcoholic), ale, red wine (especially Chianti), sherry, cognac, and Vermouth</li> <li>• Aged meats (e.g., corned beef), processed meats, and nonfresh meats</li> <li>• Sausages, including salami, pepperoni, bologna, and summer sausages</li> <li>• Fermented or aged fish (e.g., pickled herring)</li> <li>• Beef liver or chicken liver, including liverwurst</li> <li>• Fava or broad bean pods</li> <li>• Meat extracts or yeast extracts (e.g., Marmite) <i>Yeasts in baked goods are safe.</i></li> <li>• Tofu, fermented bean curd (in miso soup and soybean curd), and shrimp paste</li> <li>• Sauerkraut</li> </ul>
<b>Foods That Should Be Consumed in Moderation</b>
<ul style="list-style-type: none"> <li>• Caffeine-containing beverages, including coffee, cola, and tea</li> <li>• Chocolate</li> <li>• Yogurt</li> <li>• Sour cream</li> <li>• Soy sauce</li> <li>• Distilled spirits, including vodka, gin, and whiskey</li> <li>• Smoked fish, including salmon and whitefish</li> <li>• Ripe avocados and bananas</li> <li>• Dried fruits, including figs and raisins</li> </ul>

### **Use of Alcohol and Other Medications**

Patients taking MAOIs should not drink alcohol. Beer and red wine must definitely be avoided because the combination may cause a sudden rise in blood pressure and a hypertensive crisis.

Certain medications, including over-the-counter medicines, may interact with MAOI antidepressants and must be avoided (see Table 2). The drug interaction can precipitate a potentially fatal hypertensive crisis. Before taking any medications, including over-the-counter medicines and herbal supplements, the patient should always consult with his or her physician or pharmacist. The patient should be sure to inform other physicians that he or she is taking an MAOI.

**Table 2. Drug Restrictions When Taking Monoamine Oxidase Inhibitors (MAOIs)****Drugs That Must Be Avoided**

- Other antidepressants (e.g., Prozac, Elavil, Effexor, Remeron)
- Meperidine (e.g., Demerol)
- Levodopa (e.g., Sinemet) for Parkinson’s disease
- L-Tryptophan (an over-the-counter amino acid promoted for insomnia)
- Methylphenidate (e.g., Ritalin)
- Decongestants in cold/sinus and allergy/hay fever medications
- Bronchodilator inhalants for breathing (e.g., Alupent, Ventolin)
- Epinephrine in local anesthetics, emergency bee-sting kits, injections for treatment of acute asthma (Sus-phrine), and nasal inhalers and solution for nebulizers
- Amphetamines (e.g., Dexedrine)
- Diet pills
- Cocaine

*Note.* The table lists the common drugs that must be avoided with MAOIs. There may be other medications not listed that can interact with MAOIs. Always consult your physician or pharmacist before taking any medication with an MAOI.

**POSSIBLE SIDE EFFECTS**

The patient may experience some bothersome side effects from the MAOI antidepressant, especially shortly after beginning therapy, but should not become unduly alarmed. These common side effects usually subside as the individual becomes adjusted to the medication. If the side effect is intolerable or persists, the patient should consult with the physician to reduce the dosage. The patient, however, should understand and recognize the signs and symptoms of more serious reactions (discussed later under “Possible Adverse Reactions”) with MAOIs.

- *Orthostatic hypotension.* Low blood pressure due to a postural change is known as **orthostatic hypotension**. MAOIs may oppose the body’s ability to raise blood pressure when there is a change in position. If the blood pressure cannot elevate in time to compensate for the change in position as the individual rises from a lying or sitting position, **orthostatic hypotension** ensues. As a result, the individual feels light-headed and dizzy, has a rapid heart rate, and may faint and fall. By learning to rise slowly to allow the blood pressure to adjust, the patient may avoid or minimize orthostatic hypotension. Elderly patients and patients taking larger doses may be more susceptible to this side effect.
- *Insomnia and daytime sleepiness.* For some people, MAOIs may cause sleeping difficulties. Insomnia may be minimized by taking a larger portion of the divided doses in the morning. Other patients, paradoxically, may experience daytime sleepiness. When daytime sleepiness becomes a problem, the larger dose may be taken at night.
- *Gastrointestinal side effects.* Constipation, nausea, dry mouth, diarrhea, heartburn, and abdominal pain can occur.
- *Sexual dysfunction.* MAOIs may induce sexual dysfunction, including impotence, delayed ejaculation, diminished libido, and anorgasmia (inability to achieve orgasm). Although many patients may be hesitant to discuss their sexual problems, they are encouraged to express their concerns to their doctor. The physician may suggest switching to another antidepressant with lower incidences of inducing sexual dysfunction.
- *Withdrawal symptoms.* Abrupt withdrawal of MAOIs may be associated with nausea, vomiting, and flu-like symptoms. These symptoms may be prevented by gradually decreasing the dose before discontinuation.

- *Other possible side effects:* Dizziness, headaches, tremors, muscle twitching, confusion, nervousness, weight gain, urinary retention, and urinary hesitancy can occur. If any of the side effects persist or are intolerable, discuss the symptoms with your physician.

**Warning:** MAOIs may cause drowsiness and dizziness. Patients must exercise caution when engaging in activities that require mental alertness, such as operating a motor vehicle. It is recommended that patients do not engage in hazardous tasks until they are reasonably certain that their medication does not adversely affect their performance or impair their judgment.

### POSSIBLE ADVERSE REACTIONS

- *Hypertensive crisis.* The major—and the most worrisome—adverse reaction with MAOIs is sudden and dramatic elevation of blood pressure. High blood pressure, or **hypertension**, usually occurs several hours after ingestion of a contraindicated food or medication. Dangerously high blood pressure may cause strokes and other serious cardiovascular sequelae. This kind of malignant high blood pressure is known as a **hypertensive crisis**.

Patients should learn to recognize the signs and symptoms of high blood pressure. Patients should also learn to take their blood pressure and monitor it on a regular basis. A severe headache is usually the first sign of high blood pressure. Early signs of a hypertensive crisis may include rapid heartbeat (palpitations), sweating, nausea, vomiting, fever, cold and clammy skin, and dilated pupils. When these symptoms occur, discontinue all medications immediately and contact your physician and seek immediate medical attention.

- *Serotonin syndrome.* When two or more drugs that increase serotonin levels are taken together, excessive stimulation of the serotonergic system in the brain may result in a reaction called **serotonin syndrome**. Drugs that increase serotonin include MAOIs; L-tryptophan; amphetamines; SSRIs, such as fluoxetine (Prozac); tricyclic antidepressants, such as amitriptyline (Elavil); and even over-the-counter herbal supplements such as St. John's wort. The combination of an MAOI and an SSRI is especially hazardous and should be avoided. Symptoms of serotonin syndrome include restlessness, confusion, tremors, muscle jerks, and loss of coordination. If the medications are not stopped immediately, the complications of serotonin syndrome may include high fever, muscle rigidity, clotting disorders, and loss of consciousness. In a severe case that goes untreated, the syndrome can be fatal. Patients taking MAOIs should never self-medicate without first consulting with their physician or pharmacist.

### PREGNANCY AND BREAST FEEDING

The MAOIs are in **Category C** of the U.S. Food and Drug Administration (FDA) Pregnancy Risk Categories. The MAOIs are given this classification because there are no clinical studies, or there is inadequate information, on MAOI use in women to determine the risk during pregnancy. Animal studies have found some abnormalities in the fetus during maternal exposure to MAOIs. However, interpretation of animal studies in regard to human risks is unclear. The risk of these agents to the fetus cannot be ruled out, and MAOIs should be prescribed during pregnancy only if the benefits outweigh the potential risk.

Tranlycypromine is excreted in breastmilk, but it is not known if the other MAOIs are. Women taking MAOIs should not breastfeed.

**If you have any questions about this handout, please consult your physician.**