

Marplan[®] (isocarboxazid) Facts

IDENTIFYING TREATMENT RESISTANT DEPRESSION

Among who, despite treatment, continue to suffer from Treatment-Resistant Depression (TRD), approximately 22%-30% will achieve remission. TRD is not consistently defined, and variations in this definition used across treatment centers may complicate discussion of treatments. Here are two common definitions:

- Failure to respond to 3 or more adequate trials is frequently considered to be the standard for categorizing a patient as Treatment-Resistant.

USE OF MAO-INHIBITORS IN TREATMENT-RESISTANT DEPRESSION

The treatment of depression that has not responded to multiple treatment trials has rarely been systematically studied.

- ECT has long been considered the primary option for treatment-resistant depression, but high rates of relapse, cognitive side effects, and poor acceptability make this option problematic.
- Monoamine oxidase inhibitors (MAOIs), such as Marplan, have been used as an alternative to ECT for treatment-resistant depression.
- **Marplan is unique among the irreversible MAOIs in having the largest body of placebo-controlled clinical trial data supporting the safety and efficacy of its use for the treatment of depression.**

MARPLAN[®] (ISOCARBOXAZID) TITRATION

Marplan[®] (isocarboxazid) is supplied in bottles of 100 peach-colored, scored tablets each containing 10 mg of isocarboxazid.

- For maximum therapeutic effect, the dosage of Marplan must be individually adjusted on the basis of careful observation of the patient.
- Dosage should be started with one tablet (10 mg) of Marplan twice daily.
- If tolerated, dosage may be increased by increments of one tablet (10 mg) every 2 to 4 days to achieve a dosage of four tablets daily (40 mg) by the end of the first week of treatment.
- Dosage can then be increased by increments of up to 10 mg/week, if needed and tolerated, to a maximum recommended dosage of 60 mg/day. Daily dosage should be divided into two to four dosages.
- After maximum clinical response is achieved, an attempt should be made to reduce the dosage slowly over a period of several weeks without jeopardizing the therapeutic response.
- Beneficial effect may not be seen in some patients for 3 to 6 weeks. If no response is obtained by then, continued administration is unlikely to help.

IMPORTANCE OF FOOD CHOICES WHEN TAKING MARPLAN[®] (ISOCARBOXAZID)

Since serum levels of MAO-Inhibitors in the presence of tyramine may yield a pressor effect, there is a potential risk of hypertension among MAO-I-treated patients who consume tyramine containing foods or beverages. However, the most recent nutritional findings about tyramine levels in foods show that patients can consume nearly all of the foods and beverages that they like.

NEWER FINDINGS = LESS RESTRICTIVE DIETARY GUIDELINES

While there still are some foods and drinks patients should avoid—or consume only in moderation—the most recent studies have shown that many foods which had once been restricted are, in actuality, very low in tyramine and now considered safe to consume by patients taking Marplan.

THE KEY IS FRESH FOODS

When instructing your patients, the key is to emphasize that they eat fresh foods. Fresh dairy, fresh poultry, fresh fish, and fresh packaged or processed meats are all safe food choices for patients taking Marplan. So they can go right ahead and enjoy a burger or a hot dog at the barbecue. And nearly all fruits and vegetables are OK too.

However, you'll want to counsel patients to avoid any aged cheeses, fermented/dry/aged meats such as salami, most soy products, and any foods that haven't been stored properly or have gone beyond their expiration dates.

IT IS BEST TO AVOID ALCOHOL

Patients on MAOI's should not drink alcoholic beverages, especially those containing high amounts of tyramine (including white wine and tap beer). The Menu for a new beginning lists alcoholic beverages to avoid. As with all antidepressants, it is unwise to drink any alcohol, since it may aggravate the symptoms of depression.

The good news is that patients can benefit from MAO-Inhibiting medications like Marplan while consuming most of the foods and beverages that they like-including a number of foods that were incorrectly thought to be 'off-limits'.

DRUG INTERACTIONS

Because some medications can interact with Marplan and cause adverse reactions, you'll want to encourage your patients to fully report all medications they are taking, including OTC medications and herbal supplements before prescribing Marplan.

Medication combinations that should be avoided:

- Marplan should be administered with caution to patients receiving Antabuse[®] (disulfiram)
- The use of Marplan in combination with other psychotropic agents is not recommended because one product can potentially magnify the effects of the other.
- The MAO-Inhibiting effects of Marplan can persist for a substantial period after it has been discontinued, so it is best for patients to wait at least 10 days before taking any other psychotropic medication

Marplan should not be used with:

- other MAO-Inhibitors, tri-cyclic medications (dibenzazepine-related and other); Wellbutrin[®] (bupropion); SSRI antidepressants; Buspar[®] (buspirone);
- sympathomimetic drugs, including amphetamines, and over-the-counter cold, hay fever or weight-reducing preparations containing vasoconstrictors (decongestants); tryptophan; Demerol[®] (meperidine); the cough-preventive dextromethorphan;
- anesthetic agents; blood pressure drugs, including thiazide diuretics; excessive amounts of caffeine; central nervous system depressants such as narcotics, barbiturates, and alcohol.

META-ANALYSES OF MARPLAN CLINICAL TRIALS

- In 1995 **Thase, et al**¹, conducted a meta-analysis of 12 randomized controlled trials in 434 depressed patients, comparing FDA-approved MAO-I drugs. Using the Intent-To-Treat sample method, the authors concluded that Marplan exhibited a 41.3% average difference vs. placebo in the number of patients randomized to treatment who demonstrated improvement.
- Intent-to-treat samples in five of these 12 studies revealed a Marplan efficacy rate of 60.1%.
- The 1984 study of **Giller, et al**², one of seven placebo-controlled studies in the meta-analysis, out-patients who were crossed over from placebo (due to lack of response) achieved a 69% response rate with Marplan treatment.

Please see Full Prescribing Information including **BOXED WARNINGS regarding increased risk of suicidality in children and adolescents. MAO-Inhibitors are contraindicated with certain drugs. Potential hypertensive crises may occur with foods that contain tyramine. As with all antidepressants, patients should be observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of treatment.**

1. Thase, ME, et al. (1995): MAOIs in the Contemporary Treatment of Depression. *Neuropsychopharmacology* 12(3):202-203.

2. Giller, E, et al. (1984): Assessing Treatment Response to the Monoamine Oxidase Inhibitor Isocarboxazid. *Journal of Clinical Psychiatry* 45:44-48.