Patient & Family Guide

How to make the most of its benefits

Why it works so well
This Patient & Family Guide is designed to help you get the best possible results from your medication.

Your doctor has given you a prescription for Marplan® (isocarboxazid) tablets to help relieve your symptoms of Treatment-Resistant Depression.

In the next few pages you’ll learn how Treatment-Resistant Depression is different from other types of depression, and how Marplan is different from other types of antidepressant medications.

This Guide also will point out important safety guidelines to follow when you take Marplan tablets, including certain beverages and foods that you should avoid.
On the back cover you’ll find an area where you can jot down important instructions your doctor has given to you. There’s also information about a unique new web site that opens the door to a special community of patients and families like your own. When you join this special site, you’ll have the opportunity to share in the support and encouragement of many other patients and families who —day by day— are taking steps toward recovery from their Treatment-Resistant Depression.
Why Marplan® (isocarboxazid) works so well in depression

Marplan works differently¹

- **Antidepressant drugs are thought to elevate a person’s mood by raising the levels of chemical messengers in the brain called neurotransmitters.**

  The chemical names of the neurotransmitters are **norepinephrine, serotonin, and dopamine.**

  Scientists believe that some antidepressant medications may work by raising the amount of serotonin in the brain. Others may work by raising norepinephrine levels, and still others by raising levels of dopamine. In addition, some antidepressant medications raise the levels of two of these neurotransmitters.

- **Marplan is different from more widely prescribed antidepressant medications because it is an MAO-Inhibitor (MAO-I).** That means it blocks the action of an important enzyme called **Mono-Amine Oxidase** which is found concentrated in the tissues of the brain and the digestive system.

  **Only MAO-Inhibiting medications like Marplan elevate the levels of all three of the key neurotransmitters that can relieve depression symptoms.**

  **This difference may explain why Marplan therapy is often successful in alleviating the symptoms associated with Treatment-Resistant Depression.**

* Images on page 5 are an artist’s conception.
Marplan is different:

Marplan elevates the levels of all three key neurotransmitters in the brain.

**BEFORE MARPLAN TREATMENT**
One of the many places where the brain uses chemical messengers called neurotransmitters to carry signals from one nerve cell to another.*

**DURING MARPLAN THERAPY**
Marplan elevating the levels of all 3 key neurotransmitters to lift a patient’s mood.*
In recent years our understanding of depression has vastly improved. We’ve learned that clinical depression is not a personal weakness, and it is not a lack of mental toughness in dealing with life’s difficulties. Clinical depression is simply a disease caused by an imbalance in the chemistry of the brain.

**What clinical depression feels like**

Everyone goes through periods when they feel sad or “down” or have “the blues”. For most of us these moods just disappear in a few days. But for some people, the sadness of depression can be overwhelming — even emotionally paralyzing. They begin to feel a sense of hopelessness that can cause them to withdraw from their daily routine and avoid the very people who care about them. Often, no matter how hard they try, they cannot break free from these “blue” feelings.

The symptoms of clinical depression are listed on the next page.
Symptoms of Clinical Depression

- Persistent sad, anxious, or “empty” feelings
- Feelings of hopelessness and/or pessimism
- Feelings of guilt, worthlessness, and/or helplessness
- Irritability, restlessness
- Loss of interest in activities or hobbies once pleasurable, including sex
- Fatigue and decreased energy
- Difficulty concentrating, remembering details, and making decisions
- Insomnia, early-morning wakefulness, or excessive sleeping
- Overeating, or appetite loss
- Thoughts of suicide, suicide attempts
- Persistent aches or pains, headaches, cramps, or digestive problems that do not ease even with treatment

When a person has several of these symptoms of depression for a period of two weeks or more, they usually have clinical depression and require antidepressant medication and the help of a trained healthcare professional.
What Makes Treatment-Resistant Depression So Different

For some people with clinical depression, a prescription for an antidepressant medication and their doctor’s therapy are all that’s needed for their lives to return to normal. In a reasonable period of time, antidepressant medications are able to relieve the depression symptoms by correcting the temporary imbalance in their brain chemistry.

For other people the symptoms of clinical depression are not brought into balance with the antidepressants prescribed. When a patient has been prescribed several antidepressants that have resulted in little or no relief of their symptoms, this condition may be due to Treatment-Resistant Depression.

Marplan tablets can often help people with Treatment-Resistant Depression. Because it is an MAO-Inhibitor, Marplan works differently from other antidepressant medications. The MAO-Inhibiting action of Marplan is able to elevate all three of the brain’s neurotransmitter chemicals—and that is why Marplan has proven to be effective in many patients with Treatment-Resistant Depression.

How to take Marplan

To avoid the possibility of interactions between medications, your doctor will ask you to stop taking your current antidepressant for two weeks before starting you on Marplan. This is called a “wash-out” period, because it allows your body to be cleansed of your previous medication.

Your doctor then will prescribe gradually increasing dosages of Marplan while monitoring your improvement. Marplan is supplied in 10mg tablets that are scored on one side so it is easy to break them in half to suit the dosage your doctor believes is most appropriate for you.
Important Marplan Safety Information

Because Marplan works by inhibiting an important enzyme in the body called Mono-Amine Oxidase (see page 5) it can potentially affect other medications you are taking; it can also interact with the chemical tyramine which is found in the digestive tract as well as in some foods and beverages that are aged or fermented.

Avoiding medication interactions

Some medications can interact with Marplan and cause unwanted effects. To avoid these effects, be sure to tell your doctor about ALL of the other medications you are taking, including herbal supplements.

Here is a list of 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 without your doctor’s knowledge, 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 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® (buproprion); 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.
The importance of food choices

In the gut, MAO-Inhibitors can cause an increase in levels of a chemical called tyramine. Tyramine is also present in foods and beverages, particularly when those foods and beverages are aged or fermented.

If there is too much tyramine in the body, a dangerous rise in blood pressure may occur and possibly lead to a stroke. That’s why it is important that you minimize the tyramine you consume while you are taking Marplan.

Years ago, when Marplan was first introduced, nutritionists didn’t have advanced ways to measure tyramine in foods and beverages. So, to be as safe as possible, a diet restricting foods containing tyramine was developed, but that old diet was difficult to follow because so many foods were incorrectly thought to be “off limits”.

Fortunately — based on newer scientific studies — things have changed! While there still are some foods and drinks you should avoid — or have only in moderation, we now know that most foods that were once restricted are very low in tyramine and are now considered safe to consume when you are taking Marplan.
The Good News about the many foods you can enjoy

The most contemporary diet guidance is that you can take Marplan while enjoying almost all of the foods and beverages that you like.

Look at the *Menu for a New Beginning* on the following pages and you’ll see that *freshness is key* — *fresh* dairy, *fresh* poultry, *fresh* fish, and *fresh* packaged or processed meats are safe food choices when you are taking Marplan.

So go right ahead and enjoy a burger or a hot dog at the barbecue. Nearly all fruits and vegetables are OK too.

**However, you’ll want 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.**

*Don’t drink alcoholic beverages, especially those containing high amounts of tyramine* (including white wine and tap beer). The *Menu for a New Beginning* on the next pages lists alcoholic beverages to avoid. As with all antidepressants, it is unwise to drink any alcohol because it may aggravate the symptoms of depression.

For additional information about safely consuming dairy products or alcoholic beverages check with your doctor.

Now take a “fresh” look at the following diet guidelines and envision a bright future where you can enjoy a healthy, varied diet along with the symptom relief that Marplan offers.
Menu for a New Beginning

Dietary Guidelines
**Foods to AVOID**

*Based on abridged Sunnybrook MAO-I Diet*

**Meat, Poultry & Fish**
- Fermented / dry sausage (salami, mortadella, summer sausage, etc)

**Beverages**
- All tap beers**

**Cheese**
- All matured or aged cheese

**Fruits & Vegetables**
- Fava or broad bean pods (not beans)

**Miscellaneous**
- Marmite concentrated yeast extract
- Sauerkraut
- Soy sauce and other soy bean condiments

* Based on abridged Sunnybrook MAO-I Diet
** No more than two domestic or canned beers, or 4 fl.-oz glasses of red wine per day; this applies to non-alcoholic beer, also. Please note that red wine may produce headache unrelated to a rise in blood pressure.
Based on abridged Sunnybrook MAO-I Diet

**No more than two domestic or canned beers, or 4 fl.-oz glasses of red wine per day; this applies to non-alcoholic beer, also. Please note that red wine may produce headache unrelated to a rise in blood pressure.

*Foods to ENJOY*

**Meat, Poultry & Fish**
- All Fresh packaged or processed meat (eg, chicken loaf, hot dogs), fish or poultry

**Beverages**
- Alcohol**

**Cheese**
- Fresh cheeses; fresh milk products that have been stored properly

**Fruits & Vegetables**
- Banana pulp
- All others

**Miscellaneous**
- Other yeast extract (eg, Brewer’s yeast)
- Pizza without aged cheeses added
- Soy milk, tofu

* Based on abridged Sunnybrook MAO-I Diet

** No more than two domestic or canned beers, or 4 fl.-oz glasses of red wine per day; this applies to non-alcoholic beer, also. Please note that red wine may produce headache unrelated to a rise in blood pressure.
My Marplan Resources

My first day to take Marplan will be________________________
My dosage is_________________________________________
My doctor’s phone number is________________________________

For more information about Marplan please log on to www.MARPLAN.com

You’re invited to JOIN our special MARPLAN FORUM on-line community of patients, caregivers, and families.

There you can express your thoughts about the challenges presented by Treatment-Resistant Depression. Get info and support while you get to know other people who’ll share stories about their progress, and insights about their treatment. They will also provide encouragement and support.

To JOIN the Forum, log on to www.MARPLAN.com/forum.

SEE FULL PRESCRIBING INFORMATION, INCLUDING BOXED WARNINGS REGARDING INCREASED RISK OF SUICIDALITY IN CHILDREN AND ADOLESCENTS.

MAO-Inhibitors are contraindicated with certain drugs, and 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 therapy.

References:
1. Data on file, Validus Pharmaceuticals, Inc.