Now it’s time for...

Teva Clozapine®
(Clozapine, USP Tablets and Orally Disintegrating Tablets)

Patient & Family Guide to Teva Clozapine Therapy
This is a very important time in your life

You and your family have been working hard to deal with your schizophrenia, and you’ve been taking medication to help—but your schizophrenia has not been completely under control for some time now. With your doctor’s help you’ve switched medications a couple of times, but you still haven’t experienced the additional improvement you’ve been hoping for. Now it’s time to see if a different medication can help.

Clozapine may work when other medications don’t

Doctors prescribe Clozapine for the treatment of severely ill patients with schizophrenia after they’ve tried other medications for schizophrenia and have not been helped by these medications (a condition called treatment-resistant schizophrenia).

Clozapine is indicated for the treatment of severely ill patients with schizophrenia who fail to respond adequately to standard antipsychotic treatment.

• Clozapine is also used for reducing the risk of suicide in patients with schizophrenia or schizoaffective disorder who have attempted suicide in the past and may be at risk of suicidal behavior again.
• Clozapine was the first of a class of treatments called atypical antipsychotic agents and, over the years, studies have shown that Clozapine is an effective treatment option for some patients.

You and your doctor can decide if Clozapine is right for you.
How this guide can help
This guide is designed to help you understand your illness and learn how you can do your part to take your medication safely. Clozapine is reserved for use only by those patients whose previous medications have not provided adequate relief.

Risks of Clozapine
• A possibly life-threatening blood disorder called agranulocytosis can occur
  - In this disorder not enough white blood cells are made, which could lead to a serious infection
  - That’s why you’ll need to get regular blood testing
• Other serious side effects may occur, such as:
  - seizures
  - fainting
  - breathing problems
  - heart problems
• You may experience drowsiness or drooling
• Some patients gain weight or have abnormal lipids or cholesterol levels while taking Clozapine. There is also a risk of developing high blood sugar or diabetes while taking Clozapine.

Your doctor will help you evaluate these risks.

Important Information
You should NOT take Clozapine if you:

• Have had blood problems called agranulocytosis or severe granulocytopenia after taking Clozapine.
• Are allergic or had an allergic reaction (photosensitivity, vasculitis, erythema multiforme, or Stevens-Johnson syndrome) to Clozapine or any of the ingredients of Clozapine.

Let your doctor know if you or any family members have diabetes, or if you find that you are often very thirsty, urinate very frequently, feel very hungry, blurry vision or feel weak. Clozapine is not approved for use in elderly patients with dementia-related psychosis.
What is schizophrenia?
Schizophrenia is a mental illness that medical researchers believe comes about when the brain develops a chemical imbalance or structural change. It can affect the way people think, their personal feelings, or even how they deal with other people. For some, schizophrenia can be disabling or even life-threatening. About 2.4 million Americans are affected by the disease. That’s about 1.1% of the population age 18 and older. The illness affects equal numbers of men and women, but it typically begins earlier in men. The average onset of symptoms in men occurs in the late teens or early 20s, and in women in the 20s or 30s.

How Clozapine works
Scientists have made major breakthroughs in their understanding of the chemistry of the brain and how medications can help rebalance that chemistry. Prior to those breakthroughs, we had little knowledge of the role of the chemical messengers in the brain (called neurotransmitters) that affect our moods and our thought processes. Now, based on discoveries about the brain’s use of the neurotransmitter chemical dopamine, scientists have learned how to treat many of the disturbing manifestations of schizophrenia, thereby enabling many previously unresponsive patients to lead more normal lives. [See neurotransmitter illustrations on the next page.]

Important Information
Common Side Effects. The most common side effects of Clozapine are feeling drowsy or sleepy, feeling dizzy or lightheaded, headache, trembling, fast heart rate, low blood pressure, fainting, excess salivation, sweating, dry mouth, vision changes, constipation, nausea, and fever. Tell your doctor if you are pregnant or plan to become pregnant.

Tell your doctor right away if you experience high fever, stiff muscles, confusion, sweating, changes in your pulse, heart rate, or blood pressure; or severe constipation.
**Getting the most from your treatment**

To get the most from your Clozapine therapy: 1) closely follow the treatment plan prescribed by your doctor, 2) tell your doctor if you experience any side effects, such as tiredness, dizziness, neck muscle spasm, seizures, or fever, and 3) regularly come in for your Clozapine-monitoring blood tests (see page 6 for more information). Your lab tests are very important because they help your doctor identify possibly life-threatening side effects. That’s also the reason why your pharmacy can’t dispense your next Clozapine refill until it gets a favorable update on your blood test results.

**Important Information**

Clozapine can cause a rapid fall in blood pressure, which makes you feel dizzy or lightheaded and can lead to fainting when you suddenly change position.

**How Clozapine can help you**

Clinical studies have proven that Clozapine therapy enables patients with schizophrenia to experience significant relief. However, please keep in mind that it may take several weeks or months for the medication to start to have its full effect. For Clozapine to help relieve your schizophrenia you’ll need to take it exactly as your doctor directs. And, to get maximum benefit from Clozapine, you may have to take the medication throughout your life—just as a diabetic patient has to take insulin every day. So, please do not stop taking your medication without first talking with your doctor.

**Clozapine blocks a chemical called dopamine**

![Artist’s conception of the chemical messenger dopamine (shown as blue spheres) leaving one nerve cell and traveling to the adjacent nerve cell to occupy one of five possible dopamine receptors (D1, D2, D3, D4, or D5).](image1)

![Clozapine (shown as orange spheres) is believed to relieve symptoms of schizophrenia by temporarily occupying these same receptors and blocking the dopamine from having its usual effect.](image2)
Your need for blood tests and monitoring
When you first start taking Clozapine, your doctor will enroll you in the Teva Clozapine Patient Registry to help you monitor your white blood cell count (WBC) and absolute neutrophil count (ANC). In the beginning you’ll be tested every week. Then, after six months—if your blood test results are acceptable—your doctor may decide that you need testing only every two weeks. After another six months of acceptable test results, your doctor may decide to further reduce your monitoring schedule to just once every four weeks.

The important work you have to do to get good results from your new medication is:
1) closely follow your doctor’s instructions, 2) regularly return for your blood monitoring, and 3) tell your doctor if you miss a dose, especially if you miss your Clozapine dose for more than two days. If you make it a priority to follow these three steps, you’ll be helping your doctor to help you.

Months 1-6
Every week

Months 7-12
Every 2 weeks*

Months 12+
Every 4 weeks*

* with acceptable blood test results

Potential Clozapine side effects you need to know about
As with any medication, Clozapine can produce unwanted side effects. Some of these side effects disappear as you continue taking your medication and others may go away as your doctor adjusts your dosage.

Treatment-Resistant Schizophrenia is a serious mental illness with serious symptoms, and the potent medications that are required to treat these symptoms can have significant side effects as well. As mentioned earlier, agranulocytosis is a possibly life-threatening side effect associated with Clozapine therapy and it causes a severe decrease in a patient’s white blood cell count. That’s why your doctor has enrolled you in a Clozapine Patient Registry, and you are required to have blood tests on a regular basis as long as you are taking this medication.

PLEASE SEE IMPORTANT SAFETY INFORMATION ON PAGES 7-10 AND ENCLOSED PRESCRIBING INFORMATION, INCLUDING BOXED WARNINGS
**Important Safety Information**

• **Agranulocytosis.** Clozapine therapy can cause a severe decrease in white blood cells, called agranulocytosis which could lead to a serious infection and death. You should report any signs or symptoms to your doctor that may be associated with agranulocytosis or infection such as fever; mouth sores; skin, throat, vaginal, kidney, bladder or lung infection. Because of the risk of agranulocytosis, Clozapine is available only through a restricted program called the Clozapine Patient Registry. Prescribers, patients, and pharmacies must enroll in the program. Your doctor will schedule frequent blood tests while you are taking Clozapine so that he/she can monitor and make sure you are not developing agranulocytosis. You must have your blood tested before beginning treatment with Clozapine. If your results are acceptable after weekly blood tests for the first 6 months of treatment, you may be able to have your blood tested every other week for the next 6 months. After that, testing once each month might be possible. Your doctor will determine how often you will need testing. When stopping treatment with Clozapine for any reason, blood tests will continue on a weekly basis for 4 weeks.

• **Orthostatic Hypotension, Bradycardia, and Syncope:** Clozapine can cause your blood pressure to drop suddenly, called orthostatic hypotension, which can make you feel dizzy or lightheaded and can lead to fainting (syncope) when you change position, such as standing or sitting up after lying down. This can also cause you to stop breathing or your heart to stop beating. Tell your doctor if you have heart disease or any other cardiovascular or cerebrovascular problems or are taking medicine for hypertension, or high blood pressure or have experienced dehydration. Follow your doctor’s instructions for dosage and administration. Contact your doctor immediately if you feel faint, lose consciousness, or have any signs or symptoms suggestive of low heart rate or abnormal heart beat.

• **Seizures.** There is a high risk of having seizures during Clozapine treatment. Tell your doctor if you have a history of seizures or are at risk for seizures. Alcohol abuse while taking Clozapine may increase the risk of seizures. You should avoid driving or doing any other dangerous activity while taking Clozapine.

• **Myocarditis and Cardiomyopathy.** Clozapine can cause an inflammation of the heart muscle, known as cardiomyopathy and myocarditis, which can be life-threatening. Tell your doctor if you experience any chest pain, difficulty breathing, an increase in heart rate, palpitations, fever, flu-like symptoms, or low blood pressure. Patients with Clozapine-related myocarditis or cardiomyopathy should not take Clozapine again.

**Indications**

Clozapine is a prescription medicine for the treatment of severely ill patients with schizophrenia, a serious mental illness, who are not helped by other medicines for schizophrenia (treatment-resistant schizophrenia). It should be used only after at least two standard drugs for schizophrenia have either failed or caused serious side effects. Clozapine is also used for reducing the risk of suicide in patients with schizophrenia or schizoaffective disorder who have attempted suicide in the past and may be at risk of suicidal behavior again.
Important Safety Information (continued)

• Elderly patients with a mental illness called dementia-related psychosis and who are taking antipsychotic drugs, such as Clozapine, are at a higher risk of death. Clozapine is not approved for use in these patients.

• You should not take Clozapine if you:
  - Have had blood problems called agranulocytosis or severe granulocytopenia after taking Clozapine.
  - Are allergic or had an allergic reaction (photosensitivity, vasculitis, erythema multiforme, or Stevens-Johnson syndrome) to Clozapine or any of the ingredients of Clozapine.

• Eosinophilia. Clozapine treatment can cause eosinophilia, or an increase in the number of white blood cells. This usually occurs during the first month of treatment and has been associated with inflammation of the heart, pancreas, liver, colon and kidneys. If it is suspected, Clozapine should be discontinued immediately.

• QT Prolongation. Clozapine treatment is associated with abnormal heartbeat that can become life-threatening. Tell your doctor if you, or anyone in your family, have had any heart problems. You should not use Clozapine with other medicines that are known to cause any heart problems. Notify your doctor if you feel faint, lose consciousness or have abnormal heartbeat.

• Neuroleptic Malignant Syndrome (NMS). Clozapine can cause NMS, a condition that can be life-threatening. Tell your doctor right away if you have high fever, stiff muscles, confusion, sweating, or changes in your heart rate or blood pressure.

• Pulmonary Embolism. Pulmonary embolism (blood clot in the lungs) and deep vein thrombosis have occurred in patients treated with Clozapine. Patients should report pain in their legs (deep vein thrombosis), shortness of breath, chest pain or other respiratory signs and symptoms to their doctor.

• Anticholinergic Toxicity. Clozapine should be used with caution in patients who have narrow-angle glaucoma, are taking other anticholinergic medications, or have enlarged prostates. Clozapine can result in gastrointestinal adverse reactions, which may be fatal, including constipation, fecal impaction, or paralytic ileus. Tell your doctor if you have ever had any eye, prostate or colon problems and about all of the medications you are taking.

• Tardive Dyskinesia (TD). Clozapine can cause TD, a serious, sometimes permanent, condition in which you have uncontrolled movements of the face or other parts of the body. The risk for developing TD can increase over time with more medicine, but can also develop within a short time and at low doses. There is no known treatment for TD, but it may go away partially or completely if the medicine is stopped.
• **Metabolic Changes (hyperglycemia and diabetes mellitus, dyslipidemia, weight gain).** Clozapine is associated with metabolic changes that require specific monitoring. The risks include hyperglycemia and diabetes mellitus, dyslipidemia, weight gain, and cardiovascular reactions. Clozapine can cause an increase in the amount of glucose, or sugar, in your blood, called hyperglycemia. Your doctor may check your blood sugar level before you start taking Clozapine and periodically during treatment. Tell your Doctor right away if you have any of the following symptoms while taking Clozapine: you are very thirsty, urinate very often, are very hungry, have blurry vision, or feel weak. Tell your doctor if you have diabetes or if you are at risk for diabetes (because of obesity or because someone in your family has diabetes). Abnormal lipids or cholesterol levels have occurred in patients treated with Clozapine. Weight gain has also occurred with the use of Clozapine. Monitoring of weight and cholesterol levels at baseline and during Clozapine therapy is recommended.

• **Effect on Behavior and/or Physical Abilities.** Clozapine can affect how you think or behave and/or your physical abilities, and may make you feel sleepy and less alert, especially during the first few days of treatment. Do not drive or operate heavy machinery until you know how Clozapine affects you. Ask your doctor when it would be okay to do these activities.

• **Missed Doses and Re-initiating Treatment.** Tell your doctor if you miss a dose of Clozapine for more than two days. You should not restart your medication, and contact your doctor for dosing instructions.

• **Pregnancy and Nursing.** Clozapine should be used in pregnancy only if the potential benefit is greater than the potential risk to the fetus. Tell your doctor if you are pregnant or plan to become pregnant. You should not breastfeed while taking Clozapine.

• **Use with Other Medications.** Tell your doctor about all the medicines you are taking, including over-the-counter medicines. There is a potential that the drugs could interact with each other.

• **Clozapine, USP Orally Disintegrating Tablets contain phenylalanine (a component of aspartame).**

• **Common Side Effects.** The most common side effects of Clozapine are feeling drowsy or sleepy, feeling dizzy or lightheaded, headache, trembling, fast heart rate, low blood pressure, fainting, excess salivation, sweating, dry mouth, vision changes, constipation, nausea, and fever.

This does not discuss all of the risks associated with Clozapine. Please see the accompanying full Prescribing Information, including Boxed Warnings, for the complete risks associated with Clozapine use. If you would like more information, talk with your doctor or pharmacist.
Important Safety Information (continued)
You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 800.FDA.1088.

Tips for Success
1. Mark your calendar so you’ll remember when to take your medication, and when to come in for your regular blood tests.
2. Follow your doctor’s dosing instructions exactly.
3. Don’t skip any doses—and, if you forget to take your Clozapine, tell your doctor right away.
4. If drooling occurs, wrap a towel around your pillow at night.
5. Exercise regularly and eat right to help maintain a healthy weight.

Doing Your Part
Are you willing to do your part?
☑ Yes, I’m willing to follow a schedule on my calendar.
☑ Yes, I’m willing to have blood tests regularly.
☑ Yes, there are people who will help me.

Isn’t Clozapine worth a little extra effort?

This booklet does not discuss all of the risks associated with Clozapine. Please see the Important Safety Information on pages 7-10 and the enclosed full Prescribing Information, including Boxed Warnings, for the complete risks associated with Clozapine use.
Look inside this pocket for useful items that will help you be successful with **Teva Clozapine®**

(Clozapine, USP Tablets and Orally Disintegrating Tablets)

A handy reference card for use in recording your starting dosage schedule and other helpful information

**Dosing Schedule**

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<thead>
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<th>Date</th>
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Wallet-sized folding calendar so you can mark the days when you need to come in for your blood tests

**Patient Nutrition Guide**

**Patient Nutrition Guide**

A handy reference card for use in recording your starting dosage schedule and other helpful information

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Wallet-sized folding calendar so you can mark the days when you need to come in for your blood tests

**LAB VISIT CALENDAR**

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Clozapine requires a little extra effort, but it’s worth it

For more information and support, please consult the following resources:

National Alliance on Mental Illness (NAMI)
3803 N. Fairfax Dr., Suite 100
Arlington, VA 22203
Phone: 703.524.7600
Fax: 703.524.9094
Help Line: 800.950.NAMI (6264)
Email: info@nami.org
Website: www.nami.org

Brain and Behavior Research Foundation
90 Park Avenue, 16th Floor
New York, NY 10016
Phone: 800.829.8289
Email: info@bbrfoundation.org
Website: www.bbrfoundation.org

National Institute of Mental Health (NIMH)
6001 Executive Blvd., Room 6200, MSC 9663
Bethesda, MD 20892
Phone: 301.443.4513
Toll Free: 866.615.6464
TTY: 301.443.8431
TTY Toll Free: 866.415.8051
Email: nimhinfo@nih.gov
Website: www.nimh.nih.gov

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