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A Better Way to Health

Caremark Inc.
2211 Sanders Road, NBT8
Northbrook, Illinois 60062

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Dr. <<First>><<Last Name>>
<<Address Line 1>>
<<Address Line 2>>
<<Address Line 3>>

Dear Dr. <<Last Name>>:

Caremark manages the prescription drug benefit plan for one or more of your patients. Caremark is committed to providing physicians with the most current information on the management of various mental health topics. As part of this commitment, we are pleased to provide you the enclosed information on ZYPREXA[®] (olanzapine) to review at your convenience.

ZYPREXA is a psychotropic agent that belongs to the thienobenzodiazepine class. Recent reports on the incidence of hyperglycemia induced by atypical antipsychotics have raised concern among physicians. This is especially important because **patients with schizophrenia, regardless of treatment, have been reported to have a higher rate of diabetes than the general population.**¹⁻² In a recent study looking at the association of diabetes mellitus with use of the atypical antipsychotics, clozapine, olanzapine, quetiapine and risperidone were all associated with similarly increased rates of hyperglycemia.³ It is important to note that elevated blood glucose levels were observed in the placebo-treated patients as well. Due to an increased incidence of diabetes mellitus in people with schizophrenia compared to the general population, occasional monitoring of blood sugar levels in the schizophrenic population may be a consideration, irrespective of the type of antipsychotic prescribed. It is important when treating people with schizophrenia or other mental illnesses to acknowledge the risk of diabetes and analyze the risk factors.

ZYPREXA (olanzapine) is a therapeutic option available on the Caremark National Formulary. *ZYPREXA is the first of the atypical antipsychotics to be approved for long-term therapy in schizophrenia and also the first approved for the short-term treatment of acute mania associated with bipolar disorder. ZYPREXA offers the following benefits and features:*⁴⁻⁵

- ZYPREXA is beneficial in controlling both the positive (hallucinations, delusions) and negative (apathy, social withdrawal) symptoms of schizophrenia.
- ZYPREXA may be dosed once daily without regard to meals.
- The recommended daily starting dose for schizophrenia is 5 to 10 mg with a target dose of 10 mg per day. Further dosage adjustments may be made in increments or decrements of 5 mg/day at intervals of 1 week.
- For bipolar mania, ZYPREXA is initiated at daily doses of 10 or 15 mg. Dosing adjustments in bipolar mania, if indicated, should generally occur at intervals of no less than 24 hours.
- ZYPREXA[®] ZYDIS (olanzapine orally disintegrating tablets) disintegrate rapidly in saliva and can be easily swallowed with or without liquid.
- Use of ZYPREXA does not require routine WBC monitoring.
- ZYPREXA use was associated with a low incidence of treatment-emergent extrapyramidal symptoms (EPS). EPS was not significantly higher with ZYPREXA compared with placebo and generally did not lead to discontinuation.

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To assist you in the management of your patients with schizophrenia or bipolar mania, we have enclosed the following items:

- ⇒ An **Atypical Antipsychotic Dosing Card** - A double-sided educational tool containing information about the dosing of atypical antipsychotics on side one and information to consider when prescribing antipsychotics on side two.
- ⇒ A business reply card to obtain additional **Atypical Antipsychotic Dosing Cards** and other services related to this mailing.
- ⇒ Full prescribing information for ZYPREXA.

We hope you find this information helpful in your practice and we thank you for considering ZYPREXA as a treatment option for your patients who receive their prescription benefit through Caremark. **If you have any questions or comments, please do not hesitate to contact us by mail at the above address or by email at clinical.services@caremark.com.**

Sincerely,

Audrey A. Moyna

Audrey A. Moyna, Pharm. D., R.Ph.
Pharmaceutical Services

A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with administration of antipsychotic drugs, including olanzapine. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis and cardiac dysrhythmia). Additional signs may include elevated creatinine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.

A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown.

Olanzapine may induce orthostatic hypotension associated with dizziness, tachycardia, and in some patients, syncope, especially during the initial dose-titration period, probably reflecting its α_1 -adrenergic antagonistic properties. The risk of orthostatic hypotension and syncope may be minimized by initiating therapy with 5 mg QD. A more gradual titration to the target dose should be considered if hypotension occurs. **Olanzapine should be used with particular caution in patients with known cardiovascular disease (history of myocardial infarction or ischemia, heart failure, or conduction abnormalities), cerebrovascular disease, and conditions which would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications).**⁴

References:

1. Dixon L, Weiden P, Delahanty J et al. Prevalence and correlates of diabetes in national schizophrenia samples. *Schizophr Bull.* 2000; 26:903-12.
2. Mukherjee S, Decina P, Bocola V et al. Diabetes mellitus in schizophrenic patients. *Compr Psychiatry.* 1996; 37:68-73.
3. Sernyak MJ, Leslie DL, Alarcon RD et al. Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia. *Am J Psychiatry.* 2002; 159:561-66.
4. Zyprexa package insert. Indianapolis, IN: Eli Lilly and Company. 2001 November.
5. Data on file. Eli Lilly and Company. 2002.

For a complete discussion of the indications, contraindications, warnings, precautions, adverse reactions, drug interactions, dosing and administration information for Zyprexa, please consult the enclosed full prescribing information.

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