



Macfadden
EXHIBIT NO. 4
A. M. MITCHELL

IMPORTANT DRUG INFORMATION

January 30, 2004

Dear Health Care Provider,

AstraZeneca Pharmaceuticals LP would like to inform you of important labeling changes regarding SEROQUEL® (quetiapine fumarate). The FDA has asked all manufacturers of atypical antipsychotic medications, including AstraZeneca, to add a Warnings statement describing the increased risk of hyperglycemia and diabetes in patients taking these medications, including SEROQUEL. Accordingly, the SEROQUEL Prescribing Information has been updated with the addition of the following information:

WARNINGS

Hyperglycemia and Diabetes Mellitus

Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics, including Seroquel. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available.

Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (eg, obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

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AstraZeneca remains committed to providing you with the most current product information available for the management of your patients. You may immediately review the Warnings statement about hyperglycemia and diabetes mellitus in the SEROQUEL Prescribing Information by visiting the web site www.Seroquel.com. Updated package inserts containing the additional hyperglycemia and diabetes mellitus information will accompany the medication in the near future and you should, of course, refer to the insert for full Prescribing Information.

As always, we request that serious adverse events be reported to AstraZeneca at 1-800-236-9933 or to the FDA MedWatch program at 1-800-FDA-1088, by fax at 1-800-FDA-0178, or by email at www.fda.gov/medwatch. For additional medical information about SEROQUEL, please call 1-800-236-9933 from 9:00 am to 5:00 pm EST, Monday through Friday.

Sincerely,



Wayne Macfadden
Senior Director/Clinical Research

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