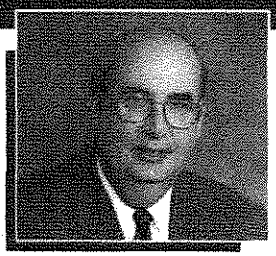
# Managing Weight Gain and Diabetes in Schizophrenia



A Patient Case Study

From the files of
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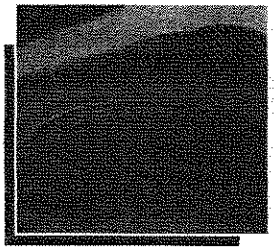



EXHIBIT 31
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DATE: 11-25-08
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## Patient Presentation

- A 49-year-old white male, unemployed, with a long history of psychiatric hospitalizations dating from age 25
- His various diagnoses include acute schizophrenic episode, paranoid schizophrenia, bipolar disorder, and schizoaffective disorder
- The patient also has a history of alcohol abuse

## Past Medical/ Psychiatric History

- The patient was first hospitalized in 1976 with religious delusions, auditory hallucinations, and withdrawal
- He was subsequently hospitalized on several different occasions and followed on an outpatient basis after each discharge

## Personal History

- There is no family history of psychiatric illness
- The patient was married with a son but has not had contact with either his wife or son for over 20 years
- He has not been gainfully employed for over 15 years
- He lives sporadically with either his mother or in homeless shelters

As with all antipsychotic medications, prescribing should be consistent with the need to minimize the risk of tardive dyskinesia. If its signs and symptoms appear, discontinuation should be considered.

Seroquel®
quetiapine fumarate 25 mg, 100 mg & 200 mg tablets

For a more normal life

Please see accompanying full prescribing information.

## Mental/Physical Evaluation

- At presentation, the patient was alert and oriented to time, place, and person, maintained good eye contact, and was stable and in a cooperative mood
- Intelligence appeared to be within normal range
- He denied any hallucinations or ideas of reference
- No EPS, rigidity, or ataxia; no suicidal or homicidal ideations were expressed
- Judgment and reality contact were impaired, he appeared to have no insight, and he frequently laughed inappropriately in response to internal stimuli
- The patient answered questions only after considerable pauses—very briefly and in a low tone and volunteered no information whatsoever
- Physical evaluation revealed a patient overweight by approximately 10 lb

Treatment with SEROQUEL, like other antipsychotics, may result in somnolence, especially during initial dose titration.

## Rationale for SEROQUEL Therapy

- Previous treatment with olanzapine 10 mg/day resulted in significant weight gain (10 lb) and subsequent development of type II diabetes (NIDDM)
- Accu-Chek™ was scheduled tid with sliding scale of Humulin® insulin

**"This patient demonstrated some classic negative symptoms—blunted affect, emotional withdrawal, poor rapport, lack of spontaneity. Negative symptoms can often be very difficult to treat. We chose SEROQUEL for this patient because in our experience it provides excellent results with negative psychotic symptoms, and weight gain with SEROQUEL hasn't been an issue."**

**—Michael J. Reinstein, MD**

## SEROQUEL Dosing Regimen

- Olanzapine therapy was discontinued due to weight gain and the development of diabetes
- SEROQUEL was initiated at 150 mg/day for 1 week
- The SEROQUEL dose was then increased to 300 mg/day where it remains

## Response to SEROQUEL

- The patient has shown a positive response to SEROQUEL, becoming more spontaneous, more interested in his surroundings, and has demonstrated improved interactions with others
- Blood glucose levels were brought under control, permitting the substitution of an oral hypoglycemic agent for insulin treatments
- Metabolic stability was maintained, allowing the patient to discontinue the hypoglycemic agent and return to a normal diet
- Not only did the patient not gain weight with SEROQUEL, he lost approximately 8 of the 10 lb gained while on olanzapine

**"Our laboratory data revealed a normalization of serum glucose levels which is valid proof of improvement of diabetes and metabolic stabilization. His psychotic symptoms were well controlled, including the negative symptoms. The patient lost weight (8 lb) and is very pleased about this. He is also relieved that he no longer has to take daily insulin injections."**

**—Michael J. Reinstein, MD**

## Follow Up

- After 7 months, the patient remains well on SEROQUEL 300 mg/day
- The patient is currently taking part in a research study, where he perceives himself as a partner in a joint endeavor. He has achieved clinical improvement and a better quality of life
- He denies having any side effects and is considered competent to handle his own funds and supervised self-medication

**"We have found SEROQUEL to be ideal in patients who have problems with weight gain and, due to this, the development of diabetes. In this patient, once olanzapine was discontinued and SEROQUEL was started, the weight was lost, the diabetes resolved, and the patient was able to stop taking hypoglycemic medication. In our experience, weight gain is not an issue with SEROQUEL, unlike some other antipsychotic medications."**

**—Michael J. Reinstein, MD**

As with all antipsychotic medications, a rare condition referred to as neuroleptic malignant syndrome (NMS) has been reported, and prescribing should be consistent with the need to minimize the risk.

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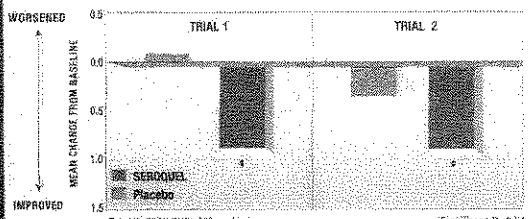
# The Strength to Control Both Positive and Negative Symptoms

*Across well-controlled trials*

## Consistent Efficacy in the Treatment of Positive Symptoms[1,2]...

### Mean Change in BPRS* Positive Symptom Cluster Scores (LOCF)[1,4†]




Trial 1: SEROQUEL 300 mg/day
Trial 2: SEROQUEL 500 mg/day (mean dose, high-dose group)

*Significant $P<0.01$

- **SEROQUEL significantly reduced positive symptom scores**

SEROQUEL was compared with placebo in the following well-controlled, 6-week, acute-phase, multicenter trials.

**Trial 1:** fixed doses of 75, 150, 300, 600, and 750 mg/day of SEROQUEL (n=255), placebo (n=51).

**Trial 2:** titrated doses up to 250 mg/day (low dose, n=94) and up to 750 mg/day (high dose, n=96) of SEROQUEL, placebo (n=96).

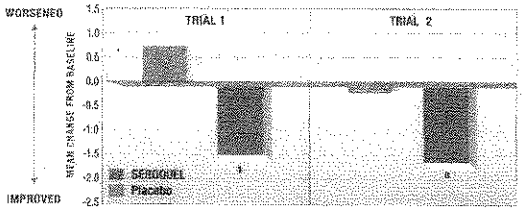
*BPRS: Brief Psychiatric Rating Scale is a clinical assessment tool that measures a combination of 18 individual positive, negative, and general symptom items. The BPRS positive symptom cluster score is the mean of 4 of the 18 individual symptom items for the clinical assessment of conceptual disorganization, suspiciousness, hallucinatory behavior, and unusual thought content.

†LOCF: Last Observation Carried Forward.

Precautions listed in the label include orthostatic hypotension and the risk of cataract development.

## ...and Consistent Efficacy in the Treatment of Negative Symptoms[1,2]

### Mean Change in SANS[5] Summary Scores (LOCF)[1,4]




Trial 1: SEROQUEL 300 mg/day
Trial 2: SEROQUEL 500 mg/day (mean dose, high-dose group)

*Significant $P<0.01$
†Significant $P=0.02$

- **SEROQUEL significantly reduced negative symptom scores**

[5]SANS: Modified Scale for the Assessment of Negative Symptoms is used to assess the negative symptoms associated with schizophrenia. The SANS summary score is a total of 5 global items: affective flattening or blunting, alogia, avolition/apathy, anhedonia/asociality, and attention.

The most common adverse events leading to treatment withdrawal were somnolence (0.8%) and hypotension (0.4%).

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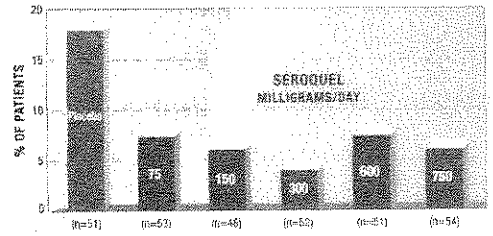
## Outstanding Overall Tolerability Across the Entire Dose Range

### Across the entire dose range,* an EPS† profile no different from placebo

EPS Adverse Events by Dose[‡]

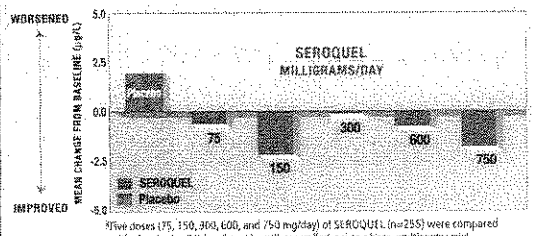



*In a 6-week, acute-phase, placebo-controlled trial.
†EPS: Extrapyramidal Symptoms were defined as dystonia, akathisia, and parkinsonism.
‡Five doses (75, 150, 300, 600, and 750 mg/day) of SEROQUEL (n=255) were compared with placebo (n=51) in a 6-week, well-controlled, acute-phase, multicenter trial.

- No dose-related EPS were associated with treatment with SEROQUEL® (quetiapine fumarate)[5]

### Across the entire dose range, plasma prolactin levels no different from placebo[5]

Mean Change in Plasma Prolactin Levels[‡]




‡Five doses (75, 150, 300, 600, and 750 mg/day) of SEROQUEL (n=255) were compared with placebo (n=51) in a 6-week, well-controlled, acute-phase, multicenter trial.

- There were no statistically significant differences in plasma prolactin levels between any group taking SEROQUEL and the placebo group[1]

## Minimal Weight Gain

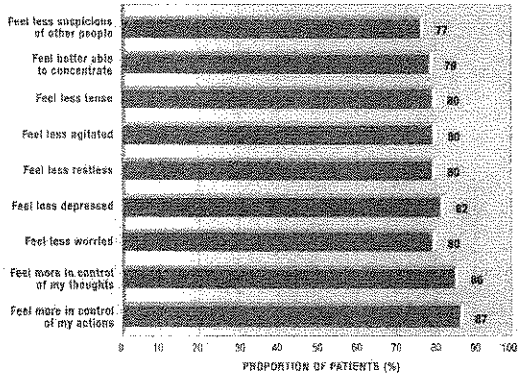
- In a recent open-label study, only 2.5% of patients treated with SEROQUEL (n=553) reported weight gain[6]

## Patient Preferred

In a survey of patients (n=129) using SEROQUEL[7]

- 97% reported that they preferred SEROQUEL to previous medications
  - —Two reasons for preferring SEROQUEL were efficacy (29%) and tolerability (41%)[7]
- Benefits noticed in the last 6 months by patients using SEROQUEL

Efficacy-Related Benefits[7]




As with other antipsychotic agents, SEROQUEL has been associated with weight gain. However, in all placebo-controlled clinical trials, weight gain was approximately 5 lb, which occurred mainly during the early weeks of treatment.[5]

Please see accompanying full prescribing information.