PASS Study Report Synopsis

Drug Substance	quetiapine fumarate
Study Code	D1443C00128
Edition Number	1
Date	05 March 2015

Objective Assessment of Metabolic Monitoring in Patients Treated with SEROQUEL® or SEROQUEL® XL/XR (Quetiapine Fumarate): Use of IMS Disease Analyzer to Assess Physician Behaviour in the UK and Germany

Study dates: Start of data collection: 04 April 2013
End of data collection: 20 June 2013

Phase of development: Phase IV

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

Study centre(s)

Ninety-three general practitioner (GP) practices in the United Kingdom (UK), and 42 psychiatry and 145 neurology practices in Germany were involved in this research study.

Publications

Not applicable.

Objectives

This study supported activities to assess the effectiveness of educational materials in scope of the European Union (EU) Risk Management Plan and Summary of Product Characteristics (SmPC) for SEROQUEL® (quetiapine fumarate) tablets and SEROQUEL® extended release (XL/XR) tablets with respect to evaluation and monitoring for hyperglycaemia and other metabolic parameters for patients treated with these medications. The assessment proposed in this program involved the evaluation of outcome indicators (evaluation and monitoring of metabolic parameters) by physicians prescribing quetiapine fumarate. An Electronic Medical Records (EMR) database was utilised as a potential means to assess the monitoring of patients.

The primary objective was to document whether entries in electronic medical records provided an objective source of physician monitoring of patients treated with SEROQUEL® or SEROQUEL® XL/XR or with quetiapine fumarate during the observation period, which included: recording patient weight at initiation and during treatment, monitoring of lipids, signs and symptoms of hyperglycaemia, blood glucose in patients diagnosed or at risk for diabetes mellitus (DM), and counselling patients on healthy lifestyle improvement. A summary of the primary outcome indicator and the metabolic monitoring parameters recorded by physicians during the research study are described in Table S1.

Table S1 Summary of Outcome Indicators

Objective		Metabolic monitoring parameters
Priority	**Description**	**Description**
Primary outcome indicator	The primary objective was to document whether physicians in the UK and Germany performed metabolic monitoring of patients treated with quetiapine.	The frequency range among physicians was recorded for the following metabolic monitoring parameters: 1. Recording patient weight at initiation of treatment 2. Monitoring of weight of patients receiving on-going treatment 3. Monitoring for elevated cholesterol 4. Monitoring for signs and symptoms of hyperglycaemia 5. Monitoring of blood glucose in patients with DM 6. Monitoring of blood glucose in patients with risk factors for DM for worsening of glycaemic control 7. Counselling patients on healthy eating, exercise, and healthy lifestyle improvements In order to understand the impact of distribution of the educational material upon patients, the proportion of patients monitored for each of the metabolic parameters listed above was also documented.

Study design

This was a cross-sectional assessment of retrospectively collected EMR data from UK GPs and German psychiatrists and neurologists regarding patient management following the distribution of metabolic educational materials on quetiapine fumarate.

Target subject population and sample size

The main inclusion criteria for this study included male or female patients aged ≥18 years who were prescribed SEROQUEL®, SEROQUEL® XL/XR, or quetiapine fumarate between 11 January 2012 and 31 July 2012 in the UK and between 13 February 2012 and 31 August 2012 in Germany and had a prior diagnosed condition (schizophrenia, bipolar disorder, or major depressive disorder) appropriate for use of quetiapine.
Given that the study was descriptive in nature and retrospective, all patients meeting the study inclusion criteria were considered for analyses.

Investigational product and comparator(s): dosage, mode of administration and batch numbers

Active substance: quetiapine fumarate (antipsychotic drug).
Medicinal product: SEROQUEL® 25, 100, 150, 200, and 300 mg film-coated tablets and SEROQUEL® XL/XR 50, 150, 200, 300, and 400 mg prolonged release tablets.

Duration of treatment

Not applicable.

Statistical methods

Data sets were created for each of the 3 physician practice groups (UK GPs, German psychiatrists, and German neurologists) and their respective patients. Results were reported separately for each data set.
Means, percentiles, maxima, and minima where obtained using PROC MEANS. Frequencies and proportions were calculated using PROC FREQ. The odds ratio (OR) for risk factors and the confidence interval (CI) were calculated by exponentiation of the coefficient from a fitted mixed-logistic regression model.

Subject population

A total of 887 patients in 93 GP practices in the UK from the IMS Disease Analyzer (DA) database as of January 2013 met the eligibility criteria for the study. In Germany, 1451 patients in 42 psychiatry practices and 4702 patients in 145 neurology practices from the IMS DA database as of January 2013 met the eligibility criteria for the study.

Summary of outcome indicators by country and practice

General Practitioners (UK)

1. Monitoring of weight for patients newly initiated on quetiapine

Out of a total of 72 practices (77% of total practices included in the analysis) that had patients newly initiated on quetiapine, only 2 practices (3%) monitored weight on the date of initial prescription for ≥50% of their patients.
As the number of patients monitored was very small, a full analysis of monitoring activities according to patient risk factors was not performed.

2. Monitoring of weight for patients receiving treatment with quetiapine

Overall, 33 practices (35% of the total) monitored weight at least once during the study period for ≥50% of their patients and 7 practices (8% of the total) monitored weight for ≥80% of patients.
Factors associated with reduced odds of monitoring of weight during on-going treatment included having been prescribed antidepressants in the prior 12 months (OR=0.55; 95% CI [0.40, 0.77]) and being within the age ranges of either 50 to 64 years or >64 years as compared to the youngest age group (18 to 39 years) (OR=0.48 and 0.61, respectively).
Factors associated with higher odds of having weight monitored during at least 1 visit during the observation period included having a body mass index (BMI) >25 kg/m^2 (OR=1.93; 95% CI [1.42, 2.64]), having either elevated cholesterol (OR=1.71; 95% CI [1.21, 2.61]) or prior lipid testing (OR=2.26; 95% CI [1.64, 3.12]) during the 12 months prior to the study period, or having a diagnosis of DM (OR=1.81; 95% CI [1.07, 3.06]).

3. Monitoring for elevated cholesterol for patients receiving treatment with quetiapine

Overall (without regard to number of eligible patients in the practice), 15 practices (16%) performed monitoring of cholesterol with lipid panel testing for ≥50% of their patients and only 2 practices (2%) performed such testing for ≥80% of patients at least once during the study period.
Factors associated with higher odds of being monitored for elevated cholesterol included having either elevated cholesterol (OR=1.81; 95% CI [1.16, 2.81]) or prior lipid testing (OR=1.78; 95% CI [1.24, 2.54]) during the 12 months prior to the study period, having DM

(OR=2.48; 95% CI [1.43, 4.30]), and being within the age ranges of 40 to 49 years or 50 to 64 years compared to patients in the age range of 18 to 39 years (OR=3.19; 95% CI [1.90, 5.33] [for both former age ranges] and OR=4.55; 95% CI [2.73, 7.58], respectively).

4. Monitoring for signs and symptoms of hyperglycaemia for patients receiving treatment with quetiapine

Among the practices included in the analysis (n=93), 21 practices (23%) monitored for signs and symptoms of hyperglycaemia for ≥50% of their patients and only 2 practices (2%) monitored for signs and symptoms of hyperglycaemia for ≥80% of patients at least once during the study period.
The risk factor associated with reduced odds of a patient being monitored for signs and symptoms of hyperglycaemia was receipt of a prescription for antidepressants in the prior 6 months (OR=0.69; 95% CI [0.49, 0.97]). Factors associated with increased odds of being monitored for signs and symptoms of hyperglycaemia included having BMI >25 kg/m^2 (OR=1.60; 95% CI [1.16, 2.21]), having elevated cholesterol in the prior 12 months (OR=2.08; 95% CI [1.42, 3.06]), having DM (OR=1.26; 95% CI [0.75, 2.11]), and having testing of glucose in the prior 12 months (OR=1.76; 95% CI [1.28, 2.41]).

5. Monitoring for signs and symptoms of hyperglycaemia among patients with DM receiving treatment with quetiapine

Thirty-two (67%) of 48 practices monitored for signs and symptoms of hyperglycaemia for ≥50% of their diabetic patients and only 18 practices (38%) monitored for signs and symptoms of hyperglycaemia for ≥80% of their diabetic patients at least once during the study period.
Patients had nearly 4 times the odds of being monitored for hyperglycaemia if they had a history of blood glucose testing in comparison to those who did not have a recording of such a test (OR=3.90; 95% CI [1.14, 13.31]).

6. Monitoring for signs and symptoms of hyperglycaemia among those at risk of DM

Twenty-seven (30%) of 89 practices monitored for signs and symptoms of hyperglycaemia in patients at risk of DM for ≥50% of their patients and 7 practices (8%) monitored for signs and symptoms of hyperglycaemia in patients at risk of DM for ≥80% of patients at least once during the study period.
Prescriptions of antidepressants during the 6 months prior to the beginning of the study period reduced the odds of having a glucose monitoring during the study period (OR=0.63; 95% CI [0.40, 0.98]). Patients possessing other risk factors, including having BMI >25 kg/m^2 (OR=0.84; 95% CI [0.18, 4.04]) and a history of cardiovascular disease (OR=0.60, 95% CI [0.19, 1.88]), demonstrated reduced odds of monitoring, but these results did not reach statistical significance.
Factors associated with increased odds for patients at risk of diabetes being monitored for signs and symptoms of hyperglycaemia included having elevated cholesterol in the prior 12 months (OR=1.98; 95% CI [1.18, 3.32]) or being within the age ranges of 40 to 49 years and 50 to 64 years compared to age range of 18 to 39 years (OR=1.80; 95% CIs [1.03, 3.15] for all age ranges). Similarly, higher odds of monitoring with glucose testing in the prior 12 months and patients of older age (≥65 years) as compared to the youngest age group (18 to 39 years) were not statistically significant.

7. Monitoring for healthy lifestyle counselling

Overall, 27 practices (29% of all practices) provided counselling to ≥50% of their patients and 8 practices (9% of total practices) provided counselling to ≥80% of patients at least once during the study period. The proportion of practices providing health/lifestyle counselling to ≥50% of their patients during the study period decreased with increasing number of eligible patients in the practice.
The odds of counselling was 1.5-fold higher among patients hospitalised in the year prior to the observation period (OR=1.46; 95% CI [1.02, 2.10]). All other demographic and tested risk factors were not found to be associated with the performance of counselling at a significant level.

Psychiatrists and Neurologists (Germany)
The performance and/or recording of metabolic monitoring among patients treated with quetiapine in psychiatry and neurology practices in Germany were very low. Due to the low number of patients monitored, modelling of factors predictive of monitoring was not conducted for the patients seen in psychiatry or neurology practices in Germany.