PASS Study Report Synopsis

Drug Substance	quetiapine fumarate
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Assessment of Physician Behaviour Regarding Metabolic Monitoring of Patients Treated with SEROQUEL® (quetiapine fumarate) Tablets and SEROQUEL® (quetiapine fumarate) Extended-Release Tablets in Selected Countries in the European Union (EU)

Study dates: Start of data collection: 19 June 2013
End of data collection: 27 September 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)

A total of 800 healthcare providers in 8 European Union (EU) countries (Austria, Germany, Hungary, Italy, Romania, Spain, Sweden, and the United Kingdom [UK]) took part in an online survey to assess the receipt of previously distributed educational materials and to assess the monitoring of metabolic parameters for patients treated with quetiapine fumarate and quetiapine fumarate extended release (XR).

Publications

Not applicable.

Research question

AstraZeneca was requested by the Medicines Evaluation Board to distribute educational materials on the importance of metabolic monitoring of patients receiving quetiapine fumarate to prescribing physicians in all EU member states. These educational materials were distributed as part of the EU risk minimisation management plan. The effectiveness of the risk minimisation measure was evaluated using a physician survey, which included questions to appraise 2 measures: outcome indicators (assessment of metabolic monitoring activities) and process indicators (assessment of receipt of the materials). An additional process indicator was added to the study for interpretive purposes. A description of the 3 measures is presented in Table S1.

Table S1 Summary of outcome and process indicators

Measures	Description
Outcome indicator	The proportion of physicians who: 1. monitored the patient's weight at initiation and during continuing treatment 2. ordered or reviewed lipid panel tests 3. observed patients for signs or symptoms associated with hyperglycaemia 4. ordered or reviewed blood glucose tests in patients with diabetes mellitus or in patients with risk factors for diabetes mellitus for worsening of glycaemic control 5. counselled patients on healthy lifestyle
Process indicator	The proportion of physicians who received the educational materials and the proportion of physicians who read the educational materials
Additional process indicator (for interpretive purposes)	The proportion of patients treated with quetiapine fumarate and quetiapine fumarate XR who were monitored within the respondent's practice or by another healthcare provider. This indicator was considered to represent an awareness of metabolic monitoring.

Study design

This research study used a cross-sectional quasi-experimental design. The assessments utilised a self-administered online survey questionnaire accessed via a secure website.

Target subject population and sample size

A random sample of healthcare providers who were targeted to receive quetiapine fumarate/quetiapine fumarate XR educational materials was invited to participate in the physician survey. The physician specialties targeted in this study were those considered to be likely prescribers of quetiapine fumarate, namely, general practitioners, psychiatrists, and neurologists.

The designated sample size was 100 completed questionnaires from healthcare providers in each of the 8 selected countries. The size of the sample was determined based on both practical and statistical considerations, and was calculated to allow estimation of the rate of effectiveness of risk minimisation with a moderate degree of precision (within 6-10 percentage points, regardless of the actual level of the process or outcome measure).

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

Active substance: quetiapine fumarate (an 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

Summary measures included response rates to all survey questions, physician estimates of patients monitored within and outside of the respondent's practice, and the specific types of metabolic monitoring activities occurring within the practice. For each survey query, the frequency distribution of the responses were reported, as well as their corresponding mean, median, minimum and maximum values, standard deviation, inter-quartile range, and 2-sided 95% confidence intervals. In addition, the monitoring of physician behaviour was also assessed using a summary rating.

All results were reported as descriptive statistics. Binomial confidence intervals were calculated using the Clopper-Pearson ("exact") method.

Additional subgroup analyses were conducted. Certain questions in the survey were broken out by specialty and some responses were stratified according to thresholds of ≥50%, 67%, 80%, 90%, and 95% monitoring rates. Finally, response rates to applicable questions were examined by whether responding physicians reported receipt of the distributed educational materials.

Subject population

A total of 800 healthcare providers from 8 EU countries participated in this research. Each of the 8 countries had 100 participants who met inclusion criteria, completed the monitoring survey, and were included in the analysis. The specialties of the physician population consisted of 574 psychiatrists (72%), 123 general practitioners (15%), and 87 neurologists (11%). The remaining 16 participants (2%) were other healthcare providers.

Summary of outcome indicator results

The primary outcome was to assess the monitoring of metabolic parameters by healthcare providers.

Survey responses across the 8 countries studied indicated that the monitoring rates of patients' weight at initiation of treatment and on a regular basis after initiating treatment were similar: 67% (95% CI [63.6, 70.3]) and 71% (95% CI [67.2, 73.6]) of practices, respectively.

Across all physicians surveyed within the 8 countries, the proportion of physician practices that reported monitoring of weight at any time (either at initiation or regularly) was 82% (95% CI [79, 84]). Individually, physicians from Romania reported the highest rate of monitoring weight at initiation of treatment (82%, 95% CI [73.1, 89.0]), and physicians from Spain reported the highest rate of monitoring weight both on a regular basis (81%, 95% CI [71.9, 88.2]) and at any time (91%, 95% CI [84, 96]). Physicians in Italy reported the lowest rates of monitoring weight at initiation of treatment (42%, 95% CI [32.3, 52.3]), regularly during treatment (60%, 95% CI [49.7, 69.7]), or at any time (72%, 95% CI [62, 81]).

The proportion of physician practices reporting monitoring tests for hyperlipidaemia was 69% (95% CI [66.1, 72.6]). General practice physicians in the UK reported the highest rates of monitoring tests for hyperlipidaemia (85%, 95% CI [76.5, 91.4]), and physicians from Hungary reported the lowest rates (45%, 95% CI [35.0, 55.3]).

The proportion of physician practices reporting monitoring tests for signs and symptoms of hyperglycaemia was 71% (95% CI [68.0, 74.4]). The highest rates of monitoring signs and symptoms of hyperglycaemia were reported by physicians in Romania (81%, 95% CI [71.9, 88.2]), and the lowest rates were both reported by Austria and Italy (58%, 95% CI [47.7, 67.8]).

The proportion of physician practices reporting monitoring tests for worsening of glucose control among patients with diabetes mellitus or with risk factors for diabetes mellitus was 77% (95% CI [74.1, 80.0]). General practice physicians in the UK reported the highest rates of monitoring tests for worsening of glucose control among patients with diabetes mellitus or with risk factors for diabetes mellitus (89%, 95% CI [81.2, 94.4]), while physicians from Hungary reported the lowest rates (63%, 95% CI [52.8, 72.4]).

Across all physicians surveyed within the 8 countries, the proportion of physician practices who reported counselling patients on making healthy lifestyle improvements was 86%,

ranging from a low of 71% (95% CI [61.1, 79.6]) in Germany to a high of 98% (95% CI [93.0, 99.8]) in Romania.

Eighty-seven percent of physicians in the UK reported performance of 3 or more monitoring activities; rates for other countries were 80% for Romania, 77% for Spain, 70% for Austria, 69% for Italy, 64% for Germany, and 58% for both Hungary and Sweden.

General practitioners (GPs) reported the highest mean monitoring rates (79%), with neurologists and psychiatrists both estimating somewhat lower proportions (70% and 67%, respectively).

Summary of process indicator results

The secondary outcome was to assess the receipt of previously distributed educational materials and reading of the educational material by physicians.

Thirty-seven percent (95% CI [34.0, 40.8] of all participating physicians surveyed in the 8 countries reported having received the materials, 28% reported not receiving the materials, and 35% reported being uncertain of having received the materials. Of those reporting receiving the materials (n=299), 91% (95% CI [86.8, 93.7]) indicated that they had read the educational materials. The proportion of physicians who indicated that they had not read the materials was 4%, and those who did not know if they had read the materials was 5%.

Physicians in Romania reported the highest rate of having received the educational materials (69%, 95% CI [59.0, 77.9]), while physicians in Germany reported the lowest (16%, 95% CI [9.4, 24.7]). Physicians within the remaining countries of Spain, Hungary, Italy, Sweden, UK, and Austria reported reception rates of 61%, 44%, 36%, 26%, 24%, and 23%, respectively.

Among those physicians who reported receipt of the materials, the proportion of physicians reporting having read the educational material ranged from 69% (Sweden) to 98% (Hungary).

Psychiatrists reported receiving the educational materials most often (44%), with a substantial margin over both GPs (25%) and neurologists (14%); however, some degree of uncertainty was reported among all 3 specialties (31%, 41% and 45%, respectively). Reading rates were 84% for GPs, and 92% for both the other 2 specialties among the providers who indicated receiving the materials.

Summary of additional process indicator results

This additional process indicator assessed whether patients treated with quetiapine fumarate and quetiapine fumarate XR were monitored by physicians within their practice or by another healthcare provider.

Physicians reported that 65% (95% CI [62.1, 66.8]) of patients receiving quetiapine fumarate or quetiapine fumarate XR were monitored either within their medical practice or were monitored by providers outside of their practice. The proportion of patients monitored by

another healthcare provider outside of the respondent's medical practice was 36% (95% CI [31.2, 35.9]).

The proportion of patients reported to be monitored by the responding physician, by others in their practice, or by another healthcare provider varied by country. The reported mean proportion of patients monitored by a healthcare provider ranged from a low of 40% (95% CI [34.0, 46.8]) in Hungary to a high of 83% (95% CI [77.5, 88.3]) in the UK. The reported mean proportion of patients monitored by another healthcare provider outside of the respondent's practice ranged from 23% in Sweden to 43% in Germany.