

EXHIBIT 29

DEAR DOCTOR LETTER

- EMERGENCY SAFETY INFORMATION -

November 2002

NO. 02-5

Dear Dr. Letter

Diabetic ketoacidosis and diabetic coma due to an increase in blood glucose level during administration of Seroquel[®] 25mg, 100mg tablets (quetiapine), an antipsychotic drug

Since February 2001 when Seroquel was started to be marketed, 12 serious cases (including 1 death) of hyperglycaemia, diabetic ketoacidosis, and diabetic coma where causality with the drug could not be ruled out have been reported (estimated number of patients who used Seroquel of the end of September 2002 was approximately 130,000). Hyperglycaemia was added in the "Precautions for use" to call attention in July 2002; however, based on the discussion of serious cases, "Contraindication" and "Precautions for use" were revised, and "Warning" was added to the package leaflet. This drug should be cautiously administered with strict attention to the following instructions. If Adverse reaction as above is confirmed, please contact the person in charge of Drug Information of Fujisawa which is the marketing company for Japan.

Manufacturing company: AstraZeneca K.K.

Marketing company: Fujisawa Pharmaceutical Co. Ltd.

1. **Seroquel must not be administered to patients with diabetes or a history of diabetes.**

In diabetic patients or patients having a history of diabetes, blood glucose levels may elevate, which may rapidly aggravate metabolic conditions. This drug must not be given to such patients.

2. **During administration of Seroquel, the patient should be monitored carefully including measurement of blood glucose levels.**

During administration of this drug, the patient must be carefully observed, and blood glucose levels should be measured, because marked elevation of blood glucose after administration of the drug may cause serious adverse reactions such as diabetic ketoacidosis and diabetic coma, and in some cases, death may occur.

3. Information on the adverse reactions and action to be taken must be fully explained to the patient and the family.

Prior to administration of the drug, sufficient explanation should be provided to the patient and the family that significant adverse reactions including diabetic ketoacidosis and diabetic coma may occur. They should be instructed to stop administration of the drug and visit hospital if any symptoms such as thirst, polydipsia, polyuria, increased urinary frequency or others appear.

“Warning”, “Contraindication” and “Precautions for use” were revised on the underside of the leaflet.

Contact : Post-Marketing Surveillance 1, Fujisawa Pharmaceutical Co., LTD.

1-6, Kashima 2-Chome, Yodogawa-ku, Osaka, Japan, 532-8514

Phone: +81-6-6390-5266

Fax: +81-6-6304-1319

(Narratives)

Not fixed

No.	Sex, age, reason for use [Complication]	Clinical course and treatment
1		
	Concomitant drugs:	
2		
	Concomitant drugs:	
3		
	Concomitant drugs:	
4		
	Concomitant drugs:	

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“Warning”, “Contraindication” and “Precautions for use”

“Warning”, “Contraindication” and “Precautions for use” were revised as follows:

This revision is based on the post-marketing incidence of hyperglycaemia.

[Warning]

1. During administration of this drug, the patient must be carefully observed, and blood glucose levels should be measured, because marked elevation of blood glucose after administration may cause significant side effects such as diabetic ketoacidosis and diabetic coma, and in some cases, death may occur.
2. Prior to administration of the drug, sufficient explanation should be provided to the patient and the family to notify that the above side effects may occur. They should be advised to note abnormalities such as thirst, polydipsia, polyuria, and increased urinary frequency and also instructed to stop administration of the drug and visit hospital if any of these symptoms appear. [See “Important basic precautions”]

[Contraindication] The drug must not be given to the following patients.

5. Patients with diabetes or a history of diabetes.

[Precautions for use]

1. Careful administration (The drug should be given with particular caution in the following patients.)
 - (6) Patients with a family history of diabetes, or those having diabetes risk factors such as hyperglycaemia or obesity [See “Important basic precautions”]
2. Important basic precautions
 - (1) Administration of the drug may markedly increase blood glucose, in some patients, leading to life-threatening clinical courses including diabetic ketoacidosis or

diabetic coma. During administration of the drug, blood glucose levels should be measured, and thirst, polydipsia, polyuria, increased urinary frequency and others should be fully monitored. Especially for the patients with diabetes risk factors such as hyperglycaemia or obesity, increased blood glucose may rapidly aggravate metabolic conditions.

- (2) Prior to administration of the drug, sufficient explanation should be provided to the patient and the family to notify that the above serious side effects may occur. They should be advised to note abnormalities such as thirst, polydipsia, polyuria, and increased urinary frequency, and also instructed to stop administration of the drug if such a symptom may appear, and visit hospital.
- (3) Administration of the drug may increase body weight. Pay attention to obesity, and if a sign of obesity is observed, appropriate action including diet therapy or exercise therapy should be taken.

3. Adverse Reactions

(1) Clinically significant adverse reactions

- 1) Hyperglycaemia, diabetic ketoacidosis, and diabetic coma: Hyperglycaemia may appear, and occurrence of diabetic ketoacidosis or diabetic coma may lead to life-threatening clinical courses. Measurement of blood glucose and observation of thirst, polydipsia, polyuria, and increased urinary frequency should be fully carried out. If any abnormalities are found, administration should be stopped, and appropriate action such as administration of insulin preparations should be taken.

(Only revised parts are described.)