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To: DDSO Directors
Executive Directors of Voluntary Agencies . . .

From: *PK* Kathy Keating and Elaine Czerw *el*

Re.: Medication Alert

Date: July 15, 2003

**Suggested
Distribution:** RNs, MDs, Investigative staff, QA staff

Attached are findings of a recent death investigation involving a 49-year old woman who expired due to Prozac intoxication.

The information contained in the alert is relatively new information about an enzyme (P450[CYP]2D6), which if deficient, causes impaired metabolism and clearance of some medications.

A reference to a case report (Sallee, Floyd R., DeVane, C. Lindsay, Ferrell, Robert E.) is also included which describes a similar event with a 9-year old boy who was taking several medications including Prozac. The Medical Examiner in this case concluded the child's death was a result of Prozac toxicity.

It is important to monitor consumers for toxicity if they are taking medications metabolized by CYP 2D6. This information is being shared with you due to the importance of these new findings and the potential to assist you with consumers under your care.

Please feel free to contact me (518-474-4376) if you have any questions.

cc: Central Office Leadership Team

Encl.

ESC/lm



A 49-year-old Caucasian woman with a diagnosis of mild mental retardation and schizophrenia with major depression, of average height and weight was prescribed the following medications:

Fluoxetine (Prozac)	20 mg.	2 caplets	po/qd
Risperdal	0.5 mg.	1 tablet	po/qd
Claritin D	5 mg.	1 tablet	po/qd
Lipitor	10 mg.	1 tablet	po/qd

The woman was discovered in the bedroom of her apartment deceased. An autopsy was performed and the cause of death was fluoxetine intoxication. The manner of death was undetermined.

An investigation was conducted relative to the circumstance of the death. The blood levels of the fluoxetine and norfluoxetine, its metabolite, show concentrations were significantly higher than would be expected with chronic administration. Reports did not suggest an acute overdose.

Medication administration records did not suggest any major discrepancies.

Fluoxetine is metabolized by liver cytochrome enzyme P450[CYP]2D6. If this enzyme is deficient, an impaired metabolism results as well as impaired clearance. This may cause blood and tissue concentrations of fluoxetine and norfluoxetine to increase, thereby resulting in a lethal intoxication and death. It is reasonable to conclude that this was the case scenario based on the available data.

Scientific literature also suggests that some herbal products such as St. John's Wort may inhibit various P450 isoenzymes.

A deficiency of this CYP2D6 isoenzyme is an inherited trait. Five to ten percent of the Caucasian population may have a mutation of this enzyme, which could cause the build up of medication in the blood and tissue.

It is therefore imperative that consumers be monitored carefully for side effects of toxicity when they are taking medications. Monotherapy would be a best practice and starting at a low dose would be prudent. After 4-6 weeks, when a steady state is reached, a blood level of the medication could be drawn to insure the medication is being metabolized. This result would have to be clinically interpreted to determine if the medication should be continued.

The following medications are also metabolized by 2D6:

"Table 2. Selected Drugs with Metabolism Mediated by CYP2D6"	
Antidepressants	Fluoxetine, paroxetine, venlafaxine, desipramine, nortriptyline
Antipsychotics	Clozapine, haloperidol, risperidone
Others	Promethazine, chlorpheniramine, codeine, dextromethorphan, propranolol, fenfluramine, encainide, flecainide, propafenone, mexiletene ^{1*}

¹Sallee, Floyd R., DeVane, C. Lindsay, Ferrell, Robert E.: Case Report – Fluoxetine-Related Death in a Child with Cytochrome P-450 2D6 Genetic Deficiency. Journal of Child and Adolescent Psychopharmacology 10(1):37-34, 2000.

For additional information, or if you have any questions, contact Elaine Czerw, R. N., Investigator, at the Office of Internal Affairs 518-474-4376 or czerw@omrdd.state.ny.us.