CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-152/ S-031

MEDICAL REVIEW

Review and Evaluation of Clinical Data

NDA: 20-639; 20-152
Sponsor: Astra-Zeneca; Bristol Myers Squibb
Drugs: quetiapine (Seroquel); nefazodone (Serzone)
Subject: name confusion
Date Review Completed: 4-4-02

Background:

In a separate document, Dr. David Gan, safety reviewer in DNDP, presented the findings of an Office of Drug Safety (formerly OPDRA) Medical Errors staff consult describing 23 reports of name confusion between Seroquel (quetiapine) and Serzone (nefazodone).

The Division's initial response to these concerning reports was to ask Astra-Zeneca to change Seroquel, the proprietary name of quetiapine, as the drug product was approved more recently than BMS's Serzone (nefazodone). Simultaneously, the Division requested that BMS initiate an educational campaign among pharmacists and physicians to raise their awareness of the name similarity problem.

BMS agreed to initiate an educational program, but their proposal was limited in scope. Essentially they submitted a "Dear Pharmacist Letter" and offered changes to the packaging/container labeling to minimize the confusion between the two medications.

Astra-Zeneca declined to change the proprietary name of quetiapine. In a counterproposal, they offered an educational campaign. The components of the proposed campaign are laid out below:

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As this is the third occurrence of name confusion involving Division drug products within two years (previously, Lamictal- Lamisil [and others] and Sarafem-Serophene), it would be useful for the Division to have a consistent approach to name confusion that should address the following elements:

- General Interventions by Sponsor

- Drug Product
- Activities for Pharmacists
- Activities for Physicians
- Activities for Patients

Specific Proposals:

General Interventions by Sponsor

Drug Product

Activities for Pharmacists

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Activities for Physicians

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Activities for Patients

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Discussion

Name confusion leading to prescribing and dispensing errors has become a more frequent problem involving Division products over the last few years. GlaxoSmithKline, Lilly, BMS, and Astra-Zeneca have each proposed programs to disseminate the message regarding the name confusion with their respective products, as well as initiated ways to minimize future name confusion. The line items in the above proposal draw on each company's ideas to produce a program with the optimal likelihood of eliminating prescribing and dispensing errors in the future. As cases of name confusion arise, we can

use these proposals as a starting point for a discussion with the sponsor to craft an appropriate education program.

The programs submitted by BMS for Serzone and Astra-Zeneca for Seroquel make a start to alert mainly pharmacists to the potential for dispensing mix-ups. In each case, however, more can be done to ensure that the message widely disseminated to physicians and patients, as well, and to institute strategies to combat the problem.

Recommendation:

1. Present proposals outlined herein to the Seroquel and Serzone review teams to discuss what should be recommended to the sponsors as the next course of action.
2. Following the internal divisional discussion, communicate with Astra-Zeneca and BMS regarding a broadening of their educational programs to combat the name confusion issue with Seroquel and Serzone.

Judith A. Racoosin, MD, MPH
Safety Team Leader
Division of Neuropharmacological
Drug Products

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/s/

Judith Racoosin
4/5/02 09:57:50 AM
MEDICAL OFFICER

Review of Clinical Data

Drug: Serzone®
Bristol-Myers Squibb
NDA#: 20-152

Seroquel®
AstraZeneca
NDA#: 20-639

Topic: Medication Error Review

Reviewer: David Gan, M.D., Dr.PH

Review Completion Date: 3/27/02

I. Introduction

On September 13, 2001, DNDP received a copy of a Medication Error Review from the Office of Postmarking Drug Risk Assessment (OPDRA [now Office of Drug Safety]) regarding medication error reports involving Serzone and Seroquel.

As of September 13, 2001, OPDRA received twenty-three (23) medication error reports involving Serzone and Seroquel. Between December 2001 and January 2002, AstraZeneca reported eight more cases of potential or actual medication errors between Serzone and Seroquel.

Serzone® (nefazodone hydrochloride), an antidepressant for oral administration, was approved on December 22, 1994. Serzone® tablets are hexagonal in shape and are available as 50, 100, 150, 200, and 250 mg tablets.

Seroquel® (quetiapine fumarate), an "atypical" antipsychotic drug was approved on Setember 26, 1997. Seroquel tablets are round in shape and are available as 25, 100, and 200 mg tablets.

II. OPDRA's Risk Assessment

A. AERS Database Searches

OPDRA searched the FDA Adverse Event Reporting System (AERS) database on August 28, 2001 in order to identify any post-marketing safety reports of medication errors associated with Serzone and Seroquel. The search terms included Meddra

Preferred Term (PT), "Drug Maladministration", and the drug names. OPDRA retrieved and reviewed all reports from the AERS search and the USP. There were 23 accounts of Serzone and Seroquel name confusion.

Between December 2001 and January 2002, AstraZeneca reported eight more cases of potential or actual medication errors with these two products.

B. OPDRA's Risk Evaluation

As of September 13, 2001, OPDRA received twenty-three medication error reports of name confusion between Serzone and Seroquel. In total, all except two prescriptions were actually administered to patients. Various adverse events were reported. OPDRA provided a table in their review that describes the events in detail. (Appendix 1).

OPDRA observed that frequency of these medication error reports is increasing since the approval of Seroquel in 1997. Of the 23 medication error reports, 14 were received in 2001 alone.

Thirteen of the reports indicated that Seroquel was mistakenly filled for Serzone. Of the ten patients for whom exposure was described, two patients did not actually ingest the Seroquel, six patients had exposure ≤ 3days, one patient had exposure for 42 days, and one had exposure for 90 days. For mistaken Seroquel ingestion, the primary adverse events noted in the reports included GI pain, nausea, diarrhea, muscle weakness, vomiting, dizziness, sleepiness, hallucination and paranoia, loss of coordination and anxiety. Three patients visited emergency room. One patient was hospitalized. One patient died of respiratory arrest[1].

Ten of the reports involved misfilling of Serzone for Seroquel. Of the seven patients for whom exposure was described, the median exposure time was 5 days (range 1 to 30 days). For mistaken Serzone ingestion, the primary adverse events noted in the reports included mental status deterioration, lethargy, confusion, disorientation, nausea, vomiting, cold and hot sweats. Two patients were hospitalized, and one patient required emergency room visit.

Risk factors contributing to the medication errors included:

1). Trade name similarity: Both Serzone and Seroquel start with the same prefix, "Ser". They tend to be stored next to each other on pharmacy shelves. As a result of the similar sounding names, prescriptions were incorrectly interpreted from written and verbal prescriptions, labeled incorrectly, and/or filled incorrectly.

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[1] This patient is a 25 year-old female patient inadvertently started on Seroquel 100 mg PO TID for 3 days instead of Serzone. The patient developed increased fever and respiratory arrest and died. The patient has a history of COPD, asthma, depression, suicide attempts, and allergy to seafood, apples, and coconut. Concomitant medications were antipsychotics, Depakote, Cogentin, Atrovent, Dilaudid, and Clozaril

2). Overlapping strengths (100 mg and 200 mg), identical dosage (tablets), and dosing interval (BID).

III. OPDRA's Recommendations:

A. OPDRA suggests that both manufacturers provide to OPDRA all existing reports of potential or actual errors involving Serzone and Seroquel that have not been submitted to FDA.
B. OPDRA suggests that the manufacturers disseminate appropriate educational materials, such as Dear Pharmacist and/or Doctor Letter(s), to inform healthcare professionals about the potential medication errors between Seroquel and Serzone and possible interventions.
C. OPDRA has reviewed the current labeling of Seroquel and Serzone. They recommend both manufacturers to highlight the different portions of their proprietary names (e.g., serZONE, seroQUEL).
D. OPDRA recommends that AstraZeneca be requested to change the name of Seroquel if a proprietary name change is considered since it was approved after Serzone.

IV. DNDP Reviewer's Assessment of the Initial Submission

After reviewing the initial submission, I made the following comments:
1). There is a probable risk of medication errors due to same prefix, "Ser" and overlapping dosage strengths.
2). It is difficult to attribute the non-fatal adverse events, serious adverse events, and death to the reported medication error. However, every effort must be made to protect public health.
3). I concurred with OPDRA's recommendations.

V. DNDP Response

Following internal discussions within the Division and with the Medication Errors staff from OPDRA, DNDP has requested that AstraZeneca Pharmaceuticals LP do the following:

1). Submit an alternative proprietary name.
2). Submit all existing reports of potential or actual errors involing Seroquel and Serzone that have not been submitted to the Agency.
3). Disseminate appropriate educational materials, such as a "Dear Health Practitioner" letter, to inform healthcare professionals about the potential medication errors between Serzone and Seroquel and possible interventions.
4). The supplement should be submitted within 30 days.

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B. Response From Bristol-Myers Squibb Company

In response to DNDP's letter of December 13, 2001 regarding medication errors between Serzone and Seroquel, the Bristol-Myers Squibb Company submitted a "Special Supplement – Changes Being Effected" on January 29, 2002. This submission contained a "Dear Pharmacist Letter" and changes to the packaging/container labeling to minimize the confusion between the two medications.

VII. Reviewer's Comments

1). There is a probable risk of medication errors due to same prefix, "Ser" and overlapping dosage strengths.
2). It is difficult to attribute the non-fatal adverse events, serious adverse events and death to the reported medication error. However, every effort must be made to protect public health.
3). Both companies should submit all existing reports of potential or actual errors involving Seroquel and Serzone that have not been submitted to the Agency.
4). Both companies should disseminate appropriate educational materials, such as a "Dear Health Practitioner" letter, to inform healthcare professionals about the potential for medication errors with Serzone and Seroquel, and possible interventions.
5). Both companies should place educational/reminder ads in pharmacy AND medical journals. We recommend both companies place journal ads in medical journals with broad readership as well as prominent psychiatry journals in addition to the journals geared towards pharmacists proposed by AstraZeneca.
6). Both companies should advise chain pharmacies to implement a computer screen message that will appear whenever the Serzone or Seroquel NDC codes are entered into the system that will alert the pharmacist to the potential for dispensing errors.
7). Both companies are requested to conduct a survey to evaluate the effectiveness of the Seroquel/Serzone name confusion education campaign. (See sample of survey questionnaire in Appendix 2).

8). If the Seroquel/Serzone name confusion education campaign fails to prevent Seroquel/Serzone dispensing errors, one of the two companies should change its proprietary name.

David Gan, MD, Dr.PH
Safety Reviewer

Appendix 1

Adverse Events Associated with Seroquel and Serzone.

[redacted]	[redacted]	[redacted]
3094873-5 (USP 51166)	5/06/98	Two nurses incorrectly transcribed verbal order of Seroquel as Serzone. The patients ingested one wrong dose each, but suffered no adverse event.
3116782-5 (USP 51438)	6/11/98	A pharmacist dispensed Seroquel 100 mg instead of Serzone 100 mg. The patient took the wrong medication for 15 days and experienced mental status deterioration. According to the reporter, the error occurred because both drugs are "dosed twice day, are packaged in 60's, and sit next to each other in white square packages."
3149099-3	*7/98*	*The pharmacist misinterpreted a phone order for Seroquel as Serzone. Serzone was dispensed for* 1 month before the pharmacy realized that the prescriber wanted Seroquel. The patient was hospitalized again.
3176408-1	12/08/98	A 56-year-old male patient reported that he received Seroquel 100 mg tablets instead of Serzone tablets. After taking one Seroquel 100 mg tablet, he went to the ER, because "all of his body systems had shut down." He thought he was having a stroke, but stroke and MI were ruled out. Since December 1998, he suffers from short-term memory loss.
3588613-0 (USP 53327)	9/19/00	A 39-year-old female patient with Bipolar disorder received Serzone 100 mg instead of Seroquel 100 mg from pharmacy. The patient experienced "decompensation of mental health."
3613500-9	11/20/00	A 37-year-old female patient reported that she ingested Seroquel 600 mg for six weeks. The patient incorrectly received samples of Seroquel 600 mg daily instead of Serzone. She experienced "extreme gastrointestinal pains, nausea, vomiting, and diarrhea. She also had 'zero muscle strength' and had to go the Emergency room."
3676433-8 (USP 81363)	2/16/01	A pharmacist placed Seroquel 100 mg tablets in a pharmacy bottle labeled Serzone. The patient took 4 tablets at bedtime and experienced nausea and vomiting. The doctor discovered the error and reported the pharmacist to the board of pharmacy. The pharmacist explained that the error occurred "at a very busy time." In addition, the two bottles are placed right next to each other on the shelf.
3717444-3	4/03/01	A consumer reported that his 12 year-old stepson received Serzone instead of Seroquel. The patient ingested Serzone 200 mg in the morning and 200 mg at 4 pm for about 4 days and became "extremely lethargic, confused, disoriented, and more difficult to arouse." He went to the emergency room, where it was discovered that the bottle, which was labeled Seroquel, contained Serzone. He was hospitalized for observation purpose only. According to the stepfather, the patient has been "severely depressed since, cries daily, eating poorly, and not himself."
3705988-X (USP 53909)	4/05/01	A pharmacy technician at a nursing home pharmacy filled card for Serzone 100 mg with Seroquel 100 mg for a 52-year-old male patient with psychosis and depression. A pharmacist failed to catch the error. The patient experienced no known adverse event.
3707906-7	4/17/01	Due to the similar trade names, Seroquel was inadvertently ordered for Serzone into the hospital computer system. No adverse events occurred, because the error was identified prior to patient receiving it.
3710667-9 (USP 53973)	4/17/01	A pharmacist dispensed Seroquel 200 mg instead of Serzone 200 mg to a patient with depression and anxiety. The patient took one dose prior to the discovery of the error by his mother. He slept for 3 hours and experienced dizziness. He was unable to do his homework. According to the reporter, this is the third time this pharmacy has made an error in a year and a half, and this was the most serious.
3720123-X (USP 54029)	4/30/01	On three occasions, three different pharmacists have misread Seroquel for Serzone. The patients ingested the wrong medication, but experienced "no adverse sequelae." The facility educated the staff and entered computer prompts to flash during the order entry.
3724376-3 (USP 54065)	5/11/01	A pharmacist filled Serzone instead of Seroquel during the evening with one technician on duty. The patient experienced nausea and "rapid heart beat." In order to prevent future errors, Serzone and Seroquel were separated on stock shelf.
3739895-3 (USP 81445)	5/31/01	A pharmacist at a retail community pharmacy selected the incorrect bottle from the shelf and dispensed Serzone 100 mg for Seroquel 100 mg. The patient discovered the error prior to

		ingestion; it was a refill. According to the pharmacist, the error occurred, because of the failure to check NDC numbers and rushing.
3750750-5	1/30/01	A patient reported that a pharmacist incorrectly filled Seroquel for Serzone. On a follow-up call on 8/3/01, the patient ingested the wrong medication for 3 months. She experienced hallucination and paranoia. According to the patient, the pharmacy placed Seroquel tablets in a pharmacy bottle labeled Serzone.
3765462-1 (USP 54186)	7/26/01	A 14-year male with schizoaffective disorder received Serzone 100 mg instead of Seroquel 100 mg. The patient took the wrong medication for 1 week. According to the reporter, it was mislabeled. In order to prevent future errors, the reporter recommends making the names more different. (i.e., SerZone, SeroqueLL)
3762591-3 (USP 54170)	7/23/01	A patient received Serzone 200 mg instead of Seroquel 200 mg. This patient took one dose of 5 tablets at bedtime. The patient experienced nausea, vomiting, cold, and hot sweats; she went to the emergency room. According to the reporter, the error occurred due to similar sounding names. In order to prevent future errors, the reporter recommends double checking labels and NDC numbers and looking inside of the bottle.
3771981-4	8/3/01	A pharmacist reported that a 25 year-old female patient inadvertently started on Seroquel 100 mg po TID for 3 days instead of Serzone. The patient developed increased fever and respiratory arrest. The patient died. The patient has a history of COPD, asthma, depression, suicide attempts, and allergy to seafood, apples and coconut. Concomitant medications were antipsychotics, Depakote, Cogentin, Atrovent, Dilaudid, and Clozaril.
(USP 54368)	8/28/01	A pharmacist grabbed the stock bottle of Seroquel 200 mg instead of Serzone 200 mg. She placed the pharmacy label of Serzone on the stock bottle of Seroquel. The patient, 40-year-old female, took Seroquel 400 mg at bedtime and required emergency room visit. The patient experienced loss of coordination and anxiety. The patient discovered the error when she noticed that the drug was not what she had been taking and realized that name on the bottle was different. To prevent future errors, the reporter recommended double checking "every thing before dispensing."
(USP 54351)	8/30/01	Serzone was dispensed instead of Seroquel. The reporter had severe reaction; she was transported to the hospital by ambulance. While being transferred, it was discovered that her Seroquel bottle contained Serzone 200 mg tablets. The reporter stated that the pharmacist told her that she took Serzone in the past. She does not remember taking Serzone, but has taken many medications, which caused reactions. She was finally able to take Seroquel. The reporter feels that the pharmacist did not take the error seriously. The reporter trusted that the right medication was in the container. The reporter has seizures and this error caused her to have many more.

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David Gan
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Judith Racoosin
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MEDICAL OFFICER

Review and Evaluation of Clinical Data

NDA: 20-152
Sponsor: Bristol Myers Squibb
Drugs: nefazodone (Serzone)
Subject: medication errors: response to 8/29/02 approvable letter (#251); revised patient information leaflet (#256)
Date of submission: 10/29/02; 12/31/02

Background

In an approvable letter dated 8/29/02, the Division requested additional information regarding BMS' plan for responding to the medication error reports that described name confusion between Serzone (nefazodone) and Seroquel (quetiapine). This document reviews BMS' responses, including their amended patient information leaflet.

BMS' response

I will address the sponsor's response to each of the Division's requests. (The Division's requests are in italics.)

1. *The statement you intend to add to pharmacy print-outs (point #4 under "Sponsor-Generated Actions") is not adequate because reading the drug name on the label does not ensure that the pills in the bottle match the name on the bottle label. It would be preferable if the statement said something like "Before taking this medication, check the pills in the bottle to make sure that they match the picture of the medication on the patient brochure."*

BMS has addressed this issue by inserting a statement at the beginning of the Patient Information Leaflet that, by law, is affixed to each bottle of Serzone (unit of use packaging). The statement reads, "Before taking this medication be sure to check the tablets in the bottle to make sure that they match one of the following descriptions:". A description of the appearance of each pill strength follows.

> Reviewer comment: Other than the dose strength, the factor that distinguishes the appearance of the tablets is the color. On the next label printing, the color of each tablet strength and the number on the tablet corresponding to the dose should be bolded or underlined. For example, "**50 mg** tablets are six-sided light pink tablets imprinted with "BMS" and "50" on one face of the tablet."

2. *Please update us on the status of the incorporation of the message about Serzone-Seroquel name confusion into a pharmacy computer screen alert.*

BMS reports that this message has been incorporated since September 30, 2002.

3. *We note that you have disseminated the "Dear Pharmacist" letter. We request that you send the letter to physicians/health care providers as well, as some of the medication errors stemmed from physician (or physician office) actions. We have attached a version of the "Dear Pharmacist" letter edited for health care providers.*

BMS attached a "Dear Health Care Provider" letter for our comment. This letter is attached to this review as Appendix 1. It was distributed on December 23, 2002.

4. *Please clarify the use of the patient brochure. Is your intent/expectation that this brochure be distributed to all patients who are initiated on Seroquel? How do these brochures get to the patients (e.g., from the physician or the pharmacist)?*

BMS reports that the patient brochure is given to patients at the physician's discretion. However, because Serzone is distributed in unit of use packaging, every patient should receive a patient information leaflet that emphasizes checking to make sure that the appearance of the pills in the bottle matches the description in the patient information leaflet.

5. *Surveillance for new instances of prescribing and dispensing errors should be conducted on an ongoing basis, with updates to us provided on a monthly basis.*

BMS agrees to provide periodic updates of medication errors with nefazodone; however, they plan to provide them quarterly, rather than monthly (as we requested).

Reviewer comment: Quarterly updates on the medication error reports are acceptable.

6. *The USP Medication Errors Reporting Program is not designed to address the effectiveness of educational programs aimed at raising awareness of specific name confusion pairs. We request that you conduct your own survey to determine the effect of your educational campaign on the awareness of the name confusion issue with Serzone and Seroquel.*

BMS agrees to conduct their own survey to determine the impact of their educational campaign on the awareness of the name confusion issue with Serzone and Seroquel. They proposed to conduct the survey after the "Dear Health Care Provider" letter has been disseminated.

Reviewer comment: The sponsor should provide the survey questionnaire to the Division for review. Because the survey is only being conducted following the dissemination of the educational program and the packaging change, a baseline awareness will not be obtainable.

Conclusion/Recommendations

BMS has responded adequately to the Division's questions, but there are some issues that will need to be addressed in an ongoing fashion, including an evaluative survey of the educational plan and quarterly updates on newly occurring medication errors.

1. In the next printed labeling, in the Patient information leaflet section where the appearance of the pill strengths are listed, the color of each tablet strength and the number on the tablet corresponding to the dose should be bolded or underlined. For example, "**50 mg** tablets are six-sided light pink tablets imprinted with "BMS" and "50" on one face of the tablet."

2. The sponsor should provide the quarterly updates of medication errors with Serzone in a timely fashion.

3. The sponsor should provide the Division with the survey they plan to use to measure prescriber awareness of the Serzone-Seroquel name confusion issue with some time allowed for the Division to provide comment

Appendix 1- Dear Healthcare Provider letter

Bristol-Myers Squibb Company
U.S. Medicines Group
P.O. Box 4500 Princeton, NJ 08543-4500

December 9, 2002

IMMEDIATE ATTENTION REQUIRED
DISPENSING ERROR ALERT

Dear Health Care Provider,

Bristol-Myers Squibb and AstraZeneca have received reports of prescription dispensing errors involving **SERZONE® (nefazodone HCl) Tablets** and **SEROQUEL® (quetiapine fumarate) Tablets**.

According to the medication error reports, verbal and written prescriptions were incorrectly interpreted, labeled, and/or filled due to the similar names between **SERZONE** and **SEROQUEL**. Furthermore, the overlapping strengths (100 mg and 200 mg), the dosage form (tablets), the dosing interval (BID), and the fact that these two products are stocked close together in pharmacies were also critical in causing medication errors. Additionally, both drugs are generally titrated in similar increments to overlapping target ranges (see prescribing information).

The error reports involve dispensing **SERZONE** Tablets when **SEROQUEL** Tablets were prescribed and the reverse scenario. Patients erroneously receiving either medication would be inadequately treated; control of schizophrenia symptoms may deteriorate in patients erroneously receiving **SERZONE**, while depression may worsen in patients inappropriately receiving **SEROQUEL**. In addition, patients may be placed at risk for adverse events.

SERZONE is an antidepressant drug marketed as ***hexagonal*** tablets imprinted with "BMS" and the strength on one side and the identification code number on the other. The 100 mg (white) and 150 mg (peach) tablets are bisect scored on both tablet faces; the 50 mg (light pink), 200 mg (light yellow), and 250 mg (white) tablets are not scored.

SEROQUEL is an antipsychotic drug marketed as ***round***, biconvex film coated tablets identified with "SEROQUEL" and the strength on one side and plain on the other. The 25 mg tablets are peach-colored, the 100 mg tablets are yellow, and the 200 mg tablets are white.

Bristol-Myers Squibb has developed a patient-information leaflet about **SERZONE**, which is being given to patients when prescriptions are filled. These leaflets will facilitate communication between you and your patients and help ensure that patients receive the correct medication. Please encourage your patients to make sure that the medication dispensed by the pharmacist matches the **SERZONE** picture card enclosed with this letter and the description of **SERZONE** tablets in the patient-information leaflet. Also, encourage your patients to be certain that the tablets they receive are imprinted with "BMS".

Additionally, certain packaging changes to both products have been implemented that highlight the endings of the product names. The revised **SERZONE (nefazodone HCl)** logo appears at the end of this letter. This should assist the dispenser in distinguishing the products.

Recommended actions to help prevent dispensing errors

If you become aware of a prescription dispensing error involving **SERZONE** or **SEROQUEL**, please contact one of the following:

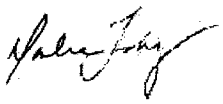
- USP Medication Errors Reporting Program (1-800-233-7767 or www.usp.org)
- Institute for Safe Medicines Practice (www.ismp.org)
- FDA MEDWATCH program (phone 1-800-FDA-1088, FAX 1-800-FDA-0178, Internet: www.fda.gov/medwatch or www.fda.gov/medwatch, or mail: FDA Safety Information and Adverse Event Reporting Program, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852-9787)
- Bristol-Myers Squibb Company at 1 (609) 818-3737 **[SERZONE]**
- AstraZeneca at 1 (800) 236-9933 **[SEROQUEL]**

For additional information please contact:

- Bristol-Myers Squibb Drug Information Department at 1 (800) 321-1335
- AstraZeneca Information Center at 1 (800) 236-9933

Thank you.

Sincerely,



Darlene Jody, M.D.
Vice President Global Medical Marketing
Bristol-Myers Squibb Company

PLEASE CONSULT THE ENCLOSED COMPLETE PRESCRIBING INFORMATION FOR **SERZONE**, INCLUDING **BOXED WARNING REGARDING HEPATOTOXICITY**.

serZone®
(nefazodone HCl)

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/s/

Judith Racoosin
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MEDICAL OFFICER