

To: CN=Noriko Akagi/OU=AP/O=LLY@Lilly; CN=Anne Bille/OU=AP/O=LLY@Lilly; CN=Anne M Goebel NONLILLY/OU=AM/O=LLY@Lilly; CN=Jared G Kerr/OU=AM/O=LLY@Lilly; CN=Mark D Millikan/OU=AM/O=LLY@Lilly; CN=Shelli A Reckert/OU=AM/O=LLY@Lilly; CN=Yoko X1 Tanaka/OU=AM/O=LLY@Lilly

CC: CN=Noriko Akagi/OU=AP/O=LLY@Lilly; CN=Anne Bille/OU=AP/O=LLY@Lilly; CN=Patrizia Cavazzoni/OU=AM/O=LLY@Lilly; CN=Keiichi Enomoto/OU=AP/O=LLY@Lilly; CN=James L Gahimer/OU=AM/O=LLY@Lilly; CN=Namie Hara/OU=AP/O=LLY@Lilly; CN=Tetsu Kawade/OU=AP/O=LLY@Lilly; CN=Yumi Kinoshita/OU=AP/O=LLY@Lilly; CN=Yasuko Kojima/OU=AP/O=LLY@Lilly; CN=Akira Kokan/OU=AP/O=LLY@Lilly; CN=Sachiko Konaka/OU=AP/O=LLY@Lilly; CN=Mikihito Kosuge/OU=AP/O=LLY@Lilly; CN=Mark Lakshmanan/OU=AP/O=LLY@Lilly; CN=Rie Nagashiro/OU=AP/O=LLY@Lilly; CN=Kenji Nobuhara/OU=AP/O=LLY@Lilly; CN=Ichiro Obi/OU=AP/O=LLY@Lilly; CN=Hiromasa Tara/OU=AP/O=LLY@Lilly; CN=Anna R Thornton/OU=AM/O=LLY@Lilly; CN=Chisato Toma NONLILLY/OU=AP/O=LLY@Lilly; CN=Andrew J Wood/OU=AP/O=LLY@Lilly; CN=Michael L Zeckel/OU=AM/O=LLY@Lilly

Date: 03/20/2002 07:04:46 PM

From: CN=Jared G Kerr/OU=AM/O=LLY

Subject: Re: <Priority A> MHLW Inquiry for hyperglycemic/diabetic SAE of ZYP - PLAN

To all:

Let me outline the plan for handling the response to the MHLW regarding hyperglycemia. This has been **extensively** discussed by Noriko Akagi, Patrizia Cavazzoni, Jared Kerr, Jim Gahimer, Mark Millikan, and Yoko Tanaka.

Please note that the Global Zyprexa Product Team does NOT agree with inclusion of diabetes language in the "Precautions" or "Warnings" section (not present at this time) of the Japan label or release a letter to Japanese physicians.

1. **Key People**
Japan: Bille-sensei, Akagi-san (co-lead), and Obi-san (co-lead)
Indy: Jared Kerr (lead for Indy), Patrizia Cavazzoni, Jim Gahimer, Mark Millikan
2. **Project Outline**

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Request: Inquiry for hyperglycemic/diabetic SAE
Timeline: Data from Indy due to Japan Friday, March 22, 2002
Meet with MHLW Monday, March 25, 2002
Objective: Prevent inclusion of terminology in Japan PI for olanzapine inconsistent with the Core Data Sheet
Format: Bullet-points and tables
Responsibilities:

PV-Japan:

Noriko Akagi/Ichiro Obi: Japan coordination

PhV-Indy:

Jim Gahimer: Japan case reports summaries (text of 13 cases and tabulation (template provided by Noriko

Akagi))

Event

Related Unrelated

ZPT:

Jared Kerr: Project Coordination
Mark Millikan: Foreign Data Preparation
Yoko Tanaka: Foreign Data Analysis
Shelli Reckert/Anne Goebel: Editing and Formatting

Necessary Products:

Patient Exposures (from IMS data)- Jared Kerr through Ralph Robinson
Japan and Global

Japan Case reports (All expedited reports concerning hyperglycemia)
Case summaries, table, and numbers for each category (Jim Gahimer)
- Serious, related (Deaths)
- Serious, unknown (Deaths)

Foreign hyperglycemia SAE case line-listing (Japan cases excluded)
Time Period (cut-off: Sept. 30th, 2001 (reference Glucose 4 data))

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- Total time
- From Japan launch (June 1, 2001)

[Note: If MHLW provides time extension Indy can increase data capture for Global case to March 22,

2002]

Data Categories

Categories: Serious (Related and Unknown), Serious (Unrelated), Non-serious

(Related/Unknown/Unrelated)

Example (not absolute): Dose, Dosage Dates, Event(s) Date(s), MeDRA terms, actual term, Reporting Outcome, Relatedness, and Confounding factors

Country,

Analysis of Serious Case Data (Japan and Global)

- Number of Serious (Related and Unknown) and Serious (Unrelated)
- %(number) of patients with >= 1 Risk Factor(s) for diabetes (see *Risk Factor description*)

Baseline glucose >= 126 (random or fasting)

Age >= 45 years old

BMI >= 27 (Non-Japanese)

BMI >= 25 (Japanese)

Dyslipidemia

- %(n) of patients on other medications that may cause an increase in glucose
- %(n) of patients with a medical event that may cause an increase in glucose
- %(n) of patients have history of diabetes

		Reporting Period Dates			
		Global		Japan	
Relatedness Category		1996 - 9/30/2001	6/1/2001-9/30/2001	6/1/2001 - 3/22/2001	6/1/2001 - 9/30/2001
ALL	Related/Unknown				
	Unrelated				
Serious	Related/Unknown				
	Unrelated				
Death	Related/Unknown				
	Unrelated				

4. **Literature Review**

Japan PV: Request Japan Medical Information Services to search literature on issue
Recommend use of Diabetes GRD (OLO54) which summarizes current data for antipsychotics. Please note PCS and
HGIM data.

Please note that Noriko Akagi is flying back to Kobe on March 28, 2002. Please let me know if you have any questions.

Sincerely,

Jared Kerr
Critical Issues-Customer Response Team
Zyprexa Product Team

O/F: (317)-433-7216/5101
jkerr@lilly.com

Anne Bille

03/20/2002 08:10 AM

To: Ichiro Obi/AP/LLY@Lilly
cc: Akira Kokan/AP/LLY@Lilly, Andrew J Wood/AP/LLY@Lilly, Hiromasa Tara/AP/LLY@Lilly, Mark
Lakshmanan/AP/LLY@Lilly, Anne Bille/AP/LLY, Akira Kokan/AP/LLY@Lilly, Noriko Akagi/AP/LLY@Lilly,
Yasutomo Senoo/AP/LLY@Lilly, Keiichi Enomoto/AP/LLY@Lilly, Kenji Nobuhara/AP/LLY@Lilly, Mark
Lakshmanan/AP/LLY@Lilly, Mikihito Kosuge/AP/LLY@Lilly, Namie Hara/AP/LLY@Lilly, Rie
Nagashiro/AP/LLY@Lilly, Sachiko Konaka/AP/LLY@Lilly, Anna R Thornton/AM/LLY, James L Gahimer/AM/LLY,
Jared G Kerr/AM/LLY, Michael L Zeckel/AM/LLY, Patrizia Cavazzoni/AM/LLY@Lilly, Yasuko Kojima/AP/LLY@Lilly,
Yumi Kinoshita/AP/LLY@Lilly
Subject: Re: <Priority A> MHLW Inquiry for hyperglycemic/diabetic SAE of ZYP

It had to come. Are there any possibilities of showing data on it is not only olanzapine that causes this but other drugs do too - and moreover that
there are a higher incidence of diabetes among mentally ill?
Anne Bille

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Ichiro Obi

03/20/02 09:23 PM

To: JP_Zyprexa_Safety, US_Zyprexa_Japan Safety List, Kenji Nobuhara/AP/LLY@Lilly, Andrew J Wood/AP/LLY@Lilly
cc: Keiichi Enomoto/AP/LLY@Lilly, Namie Hara/AP/LLY@Lilly, Yumi Kinoshita/AP/LLY@Lilly, Yasuko Kojima/AP/LLY@Lilly, Akira Kokan/AP/LLY@Lilly, Sachiko Konaka/AP/LLY@Lilly, Mikihiro Kosuge/AP/LLY@Lilly, Rie Nagashiro/AP/LLY@Lilly, Hiromasa Tara/AP/LLY@Lilly, Anne Bille/AP/LLY@Lilly, Mark Lakshmanan/AP/LLY@Lilly
Subject: <Priority A> MHLW Inquiry for hyperglycemic/diabetic SAE of ZYP

Dear all,

We, Japan PV team for ZYP, have received MHLW inquiry for hyperglycemic/diabetic SAE today PM8:00.

They request us the all expedite reports concernig hyperglycemia (Japan Case reports). They also request to submitt the freeign hyperglycemia SAE case reports or line-listing, which we need not to report to MHLW because these events have already labeled.

We have to visit MHLW on 25 March and discuss this issue with the officers of MHLW.

Regards,

Ichiro,
PV Kobe

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