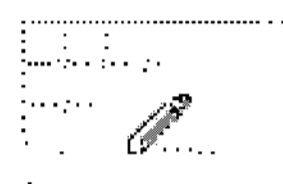


**To:** CN=Christopher C Bomba/OU=AM/O=LLY@LILLY; CN=Suzanne F Clifford/OU=AM/O=LLY@Lilly;  
CN=Charles R Feehan/OU=AM/O=LLY@Lilly; CN=James B Gregory/OU=AM/O=LLY@Lilly;  
CN=Samuel Maloy/OU=AM/O=LLY@LILLY; CN=John R Richards/OU=AM/O=LLY@Lilly; CN=Jill R  
Welch/OU=AM/O=LLY@Lilly  
**Date:** 11/29/1999 10:07:38 AM  
**From:** CN=Jack E Jordan/OU=AM/O=LLY  
**Subject:** Olanzapine-associated Weight Changes (OWC)

FYI....

----- Forwarded by Jack E Jordan/AM/LLY on 11/29/99 10:04 AM -----



Newton F Crenshaw  
11/28/99 09:41 PM

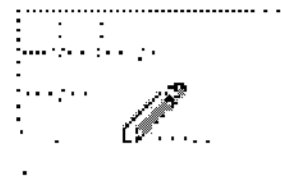
To: Gerhard Mayr/AM/LLY@Lilly  
cc: Jack E Jordan/AM/LLY@Lilly, Gino Santini/AM/LLY@Lilly  
Subject: Olanzapine-associated Weight Changes (OWC)

gerhard,  
thanks for forwarding alan's email on weight change with zyprexa. i will not comment further on this email, other than to state that we recognize this as a critical issue that must be addressed appropriately with our customers.

i will be reviewing a multi-faceted strategy with my neuroscience lead team on monday, december 6th. we are working in conjunction with the product team as the scientific data must provide our foundation. i am confident that we can significantly improve our current position in the market, but not without significant effort.

regards,  
newt

----- Forwarded by Newton F Crenshaw/AM/LLY on 11/28/99 09:22 PM -----



Gerhard Mayr  
11/26/99 07:48 AM

To: Newton F Crenshaw/AM/LLY@Lilly, Rolf Hoffmann/EMA/LLY@Lilly, Cameron G Marshall/EMA/LLY@Lilly  
cc:  
Subject: Olanzapine-associated Weight Changes (OWC)

▶ **Alan Breier**  
24/11/99 19:12

\*\*\*\*\*

To: Gerhard Mayr/AM/LLY@Lilly, Gino Santini/AM/LLY@Lilly, Lorenzo Tallarigo/EMA/LLY@Lilly, Albertus VanDenBergh/EMA/LLY@Lilly  
cc: Alan Breier/AM/LLY@Lilly, John C Lechleiter/AM/LLY@Lilly, Roland Powell/AM/LLY@Lilly, Gary D Tollefson/AM/LLY@Lilly  
Subject: Olanzapine-associated Weight Changes (OWC)

John asked me to overview the topic of olanzapine-associated weight changes (OWC). I want to emphasize to you that OWC has been and continues to be a top priority for the Zyprexa Product Team. Although it is a significant issue for us, perhaps our only/major clinical Achilles heel, and our competitors have robustly focused on it (redacted) the fact is Zyprexa offers the best combination of efficacy, safety and ease of use of any available treatment for psychosis and acute mania. The most critical immediate issue is to keep the focus where it belongs - superior treatment and outcome - an arena where we have no peer. What follows is a high level review. Please contact me for more information and your thoughts/recommendations.

**Market Research**

- OWC is seen as a greater issue for less severely ill patients; e.g. more impactful to bipolar patients than schizophrenics
- Females more concerned than males (**Fact:** weight changes are equal among males and females)
- OWC is not an age-related issue (although weight gain in the elderly is often viewed favorably)
- Cosmetic concerns is a far greater issue than long-term health implications
- "Outliers" are the main concern for physicians; 20 lb increase is viewed as threshold for concern (**Fact:** two-thirds of olanzapine-treated

patients gain less than 20 lbs)

Olanzapine is viewed to have more associated weight gain than risperidone, seroquel, and traditional neuroleptics (**Fact:** the order of weight gain among antipsychotics is: Clozapine>olanzapine>seroquel>risperidone> traditional neuroleptics)

In US, when patients are switched because of weight gain, they tend to be switched to risperidone

The plateauing of weight gain is not appreciated (**Fact:** weight gain plateaus after 6 to 9 months of treatment)

Physicians view EPS as something they can address with dose adjustment but not OWC (**Fact:** OWC is not dose dependent)

Physicians want more data

Blanket detailing will be damaging since many physicians do not see OWC as an issue

### Scientific Data

All antipsychotic drugs and mood stabilizers are associated with weight gain; mechanism is not known

Mean weight change associated with olanzapine at 36 months of treatment is 6.73 kg

OWC plateaus between 6 to 9 months

22% of patients lose weight; another 22% gain less than 5kgs

Low baseline weight, good clinical response and increase in appetite predict OWC

As noted above, doses between 5mg and 20mg do not predict OWC

When olanzapine is stopped, weight change returns to baseline levels

Behavioral interventions (exercise and diet considerations) work to reduce weight gain even in the severely ill schizophrenic patient

Prozac does not prevent OWC

### Actions To Date

In June 1999, a full OWC package compiled by Roland including verbatims, slide set, speaker notes, OWC facts, sent to major affiliates

More market research under way, quantify SOM impact

Two publications under review at American Journal of Psychiatry

Numerous presentations at congresses, scientific venues, medical letter

Two cross-functional action teams formed: one scientific which is addressing the mechanism of OWC and effective treatments (Steering Committee: S. Paul, R. DiMarchi, G. Tollefson, C. Fibiger, J. Caro, G. Probst); the other marketing (organized by Roland) which is focusing on immediate issues, strategy

Dedicated market research associate on ZPT and in US Affiliate

Axid intervention study started (preliminary data suggests H-2 blockers may attenuate OWC; N=150, LPV December 2000, interim analysis summer 2000)

Approximately seven IIT intervention studies funded (examining behavioral and pharmacological interventions)



**To:** CN=Suzanne F Clifford/OU=AM/O=LLY@Lilly  
**Date:** 05/02/2000 05:52:28 PM  
**From:** CN=Lara A Jensen/OU=AM/O=LLY  
**Subject:** LTC Expansion Analysis  
**Attachments:** Zyprexa\_Wishlist.xls

Suzanne,

the LTC expansion is the second tab.



Zyprexa\_Wishlist.xls