

**To:** CN=Felix Aguado/OU=EMA/O=LLY@Lilly; CN=Ernie Anand/OU=EMA/O=LLY@Lilly; CN=Neil G Archer/OU=EMA/O=LLY@Lilly; CN=Eric Baclet/OU=EMA/O=LLY@Lilly; CN=John P Bamforth/OU=EMA/O=LLY@Lilly; CN=Michael E Bandick/OU=AM/O=LLY@Lilly; CN=Suzanne F Clifford/OU=AM/O=LLY@Lilly; CN=Giuliano Delfino/OU=EMA/O=LLY@Lilly; CN=Eric Edgell/OU=AM/O=LLY@Lilly; CN=Nadia Fontaine/OU=AM/O=LLY@Lilly; CN=Eugen Greco/OU=EMA/O=LLY@Lilly; CN=James B Gregory/OU=AM/O=LLY@Lilly; CN=Patrick Jonsson/OU=EMA/O=LLY@Lilly; CN=Tetsu Kawade/OU=AP/O=LLY@Lilly; CN=Ian Knowlton/OU=EMA/O=LLY@Lilly; CN=Andreas Kohler/OU=EMA/O=LLY@Lilly; CN=Antonio Leao/OU=EMA/O=LLY@Lilly; CN=Kenneth R Linke/OU=AP/O=LLY@Lilly; CN=Daniel Lucas/OU=EMA/O=LLY@Lilly; CN=Eugenia Montilla/OU=EMA/O=LLY@Lilly; CN=Jacques Mosseri/OU=EMA/O=LLY@Lilly; CN=Mark Pemberton/OU=AM/O=LLY@Lilly; CN=Valerie Pichot/OU=EMA/O=LLY@Lilly; CN=Matthew R Pike/OU=AM/O=LLY@LILLY; PM\_ONLY\_CC@Lilly; CN=Eric L Prouty/OU=AM/O=LLY@Lilly; CN=Joel Raskin/OU=AM/O=LLY@Lilly; CN=John R Richards/OU=AM/O=LLY@Lilly; CN=Mark R Russom/OU=AM/O=LLY@Lilly; CN=Robert P Schmid/OU=AM/O=LLY@Lilly; CN=Robert Schnitzler/OU=EMA/O=LLY@Lilly; CN=Jason Steele/OU=AM/O=LLY@Lilly; CN=Giovanni Stropoli/OU=EMA/O=LLY@Lilly; CN=Ian M Thompson/OU=AP/O=LLY@Lilly; CN=Lewis L Truex/OU=AM/O=LLY@Lilly; CN=Jill R Welch/OU=AM/O=LLY@Lilly; CN=Padraig Wright/OU=EMA/O=LLY@Lilly; ZELDOX\_C@Lilly; CN=Charl Van Zyl/OU=AM/O=LLY@Lilly

**CC:** CN=Darren Alcock/OU=AM/O=LLY@Lilly; CN=Hector Baerga/OU=AM/O=LLY@Lilly; CN=Albertus VanDenBergh/OU=EMA/O=LLY@Lilly; CN=Kristin Webb/OU=AM/O=LLY@Lilly; CN=Thomas G Wellner/OU=AM/O=LLY@Lilly; CN=Doug Williamson/OU=AM/O=LLY@Lilly; CN=Robert W Baker/OU=AM/O=LLY@Lilly; CN=Jennifer J Beaulieu/OU=AM/O=LLY@Lilly; CN=Alan Breier/OU=AM/O=LLY@Lilly; CN=Patrizia Cavazzoni/OU=AM/O=LLY@Lilly; CN=Enrique A Conterno/OU=AM/O=LLY@Lilly; CN=Gaetano Crupi/OU=AM/O=LLY@Lilly; CN=Javier Ellena/OU=EMA/O=LLY@Lilly; CN=Ali Gumus/OU=AM/O=LLY@Lilly; CN=Jonnetta L Hardin/OU=AM/O=LLY@Lilly; CN=Simon Harford/OU=AM/O=LLY@Lilly; CN=James A Harper/OU=AM/O=LLY@Lilly; CN=William Hess/OU=AM/O=LLY@Lilly; CN=Rolf Hoffmann/OU=AM/O=LLY@Lilly; CN=Andrew T Hotchkiss/OU=EMA/O=LLY@Lilly; CN=Abbas Hussain/OU=EMA/O=LLY@Lilly; CN=Barry Jones/OU=AM/O=LLY@Lilly; CN=Jack E Jordan/OU=AM/O=LLY@Lilly; CN=Sun Keeling/OU=AM/O=LLY@LILLY; CN=John S Kennedy/OU=AM/O=LLY@Lilly; CN=Mark C Kershnik/OU=AM/O=LLY@Lilly; CN=Bruce

Kinon/OU=AM/O=LLY@Lilly; CN=John J Kody/OU=AM/O=LLY@Lilly; CN=John C Lechleiter/OU=AM/O=LLY@Lilly; CN=Nancy Lilly/OU=AP/O=LLY@Lilly; CN=Eberhard Ludewigs/OU=EMA/O=LLY@Lilly; CN=Lorrie Mamlin/OU=AM/O=LLY@Lilly; CN=Andrew Mascarenhas/OU=AP/O=LLY@Lilly; CN=Gerhard Mayr/OU=AM/O=LLY@Lilly; CN=Ronald K McPherson/OU=AP/O=LLY@Lilly; CN=Jason R Nawrocki/OU=AM/O=LLY@Lilly; CN=Jorg Ostertag/OU=AP/O=LLY@Lilly; CN=Yiannos Palate/OU=AP/O=LLY@Lilly; CN=Jorge Velasquez Parodi/OU=AM/O=LLY@Lilly; CN=Timothy F Parshall/OU=AM/O=LLY@Lilly; CN=Richard D Pilnik/OU=AM/O=LLY@Lilly; CN=Theodore J Planje/OU=AM/O=LLY@Lilly; CN=Pascal Prigent/OU=EMA/O=LLY@Lilly; CN=Alvin H Rampey Jr/OU=AM/O=LLY@Lilly; CN=Vivian Wong/OU=AM/O=LLY@Lilly; CN=Jeffrey T Ramsey/OU=AM/O=LLY@Lilly; CN=Derica W Rice/OU=EMA/O=LLY@Lilly; CN=Viktor K Riedl/OU=AM/O=LLY@Lilly; CN=James A Ringer/OU=AM/O=LLY@Lilly; CN=Bill Robinson/OU=AM/O=LLY@Lilly; CN=Ralph Robinson/OU=AM/O=LLY@Lilly; CN=Michael R Sale/OU=AM/O=LLY@Lilly; CN=Gino Santini/OU=AM/O=LLY@Lilly; CN=Richard A Smith/OU=AP/O=LLY@Lilly; CN=Rob B Smith/OU=AP/O=LLY@Lilly; CN=Robert Lee Smith/OU=AM/O=LLY@Lilly; CN=Lorenzo Tallarigo/OU=AM/O=LLY@Lilly; CN=Jacques Tapiero/OU=EMA/O=LLY@Lilly; CN=Mauricio F Tohen/OU=AM/O=LLY@Lilly; CN=Gary D Tollefson/OU=AM/O=LLY@Lilly; CN=Paula T Trzepacz/OU=AM/O=LLY@Lilly

**Date:** 02/07/2001 09:01:01 AM  
**From:** CN=Roland Powell/OU=AM/O=LLY  
**Subject:** Ziprasidone FDA approval and update - important  
**Attachments:** zapraisidone.doc

Ziprasidone approval was announced by the FDA on the afternoon of Monday February 5 2001. This has been anticipated but will no doubt generate much internal email. The following is 5 minutes of recommended reading even if ziprasidone launch in your market is not imminent. Consistent internal communication is the first step to consistent external communication and implementation.

Many thanks.  
Roland Powell

=====

**Contents**

Breaking news and current status  
Ziprasidone US label - key points  
Zeldox Sweden - key learning points and actions  
Pfizer position - Lilly position  
Affiliate/region expectations

In summary...

### 1. Breaking news and current status

Food and Drug Administration (FDA) announced approval of ziprasidone oral in the USA (5 February pm)

This product has had its problems achieving approval in the US. It was first submitted in March '98 and has taken until now to gain approval in a process that generally takes 12-14 months. We still do not know the full extent of label restrictions. This product is far from achieving a 'global' launch status and is today only marketed in Sweden

Currently, only half the label is available.

Ziprasidone was withdrawn from the European Union mutual recognition process (of the Swedish Zeldox approval) pending submission of additional ziprasidone data from Pfizer - additional EU approvals not anticipated until the end of 2001

Lilly Zyprexa RAIM FDA hearing February 14, Pfizer ziprasidone IM FDA hearing February 15

Much learning to date - read on!

### 2. Ziprasidone US label - key points

In general, much more severe warning language than the Swedish label

Unprecedented 10 paragraph bolded warning on QTc and safety concerns, including dose related QTc

The label states an unfavourable cardiac profile comparison to Zyprexa, risperidone, thioridazine, haloperidol etc

Indications section - *'When deciding among alternative treatments available for this condition, the prescriber should consider the finding of ziprasidone's greater capacity to prolong the QT/QTc interval compared to several other antipsychotic drugs (see Warnings). Prolongation of the QTc interval is associated in some other drugs with the ability to cause torsades de pointes arrhythmia, a potentially fatal polymorph ventricular tachycardia, and sudden death. In many cases, this would lead to the conclusion that other drugs should be tried first'*

This supports our positioning for ziprasidone that it should not be a drug for routine use

Recommendations for baseline monitoring, both metabolic and cardiovascular

Multiple warnings eg certain patient types, concomitant medications etc

Schizophrenia indication including maintenance of response labelling



ziprasidone.doc

Pfizer press statement refers to a March US launch and ongoing negotiations with the FDA regarding the ziprasidone trademark (known possibilities are Zeldox and Geodon - FDA known to have objections to Zeldox)

A more thorough analysis will follow with specific verbatims related to patient types in the next few days.

### 3. Zeldox Sweden - key learning points and actions

Page: 3 of 5

### *Learnings*

Despite blunting planning and initial implementation, Pfizer surprised us and launched with 2x the detail power of Lilly (use of multiple sales forces). Be prepared and flexible in planning so that you can act quickly

Lilly Sweden Zyprexa message (core message and blunting message) was too broad

Inadequate cardiology OL support to independently raise the cardiac safety concern. The QTc issue is more effectively driven by opinion leaders vs Lilly

Lilly Sweden was effective in increasing the importance of cardiac safety as an issue amongst customers - it takes time and needs to be linked to Zeldox. Pfizer detail time is being taken up handling QTc objections

Lilly Sweden increased its DTP programmes (symposia etc) causing the cancellation of 3 out of 4 Pfizer launch symposia - lack of delegates - impacting Zeldox message delivery

Zeldox launch is accelerating conversion from typicals (market currently 35% converted) and where prescriptions are coming from atypicals early indicators suggest that this is in equal proportions from Zyprexa and Risperdal

Zeldox market share progression from launch has been approximately 50% of the uptake of Zyprexa

Legal challenges are a predictable Pfizer strategy and affiliates need to be prepared

### *Actions*

Pre-trained Lilly Sweden retail sales force will be deployed behind Zyprexa to increase detail SOV

Zyprexa message focus has been tightened: efficacy in core symptoms, safety - EPS/TD and QTc, weight gain

Anticipate sales force vacancies (and have contingencies)

Incentive programme aligned to strategy

Increase CRP and medical liaison heads

Continued emphasis on high non-sales force spend (full marketing mix)

Fast turn around of clinical studies and case reports

### **4. Pfizer ziprasidone position - Lilly ziprasidone position**

*Pfizer - ziprasidone - atypical efficacy without weight gain*

positive and negative symptom efficacy including maintenance of response

good tolerability (weight neutral, low EPS and mild QTc prolongation lacking clinical importance)

*Lilly - ziprasidone - nominal response rates (efficacy) and dose-related side effect and safety concerns (EPS, cardiovascular) make ziprasidone an undesirable choice as a first line agent*

efficacy - in their respective clinical trials, Zyprexa demonstrated consistently higher response rates than that of ziprasidone

cardiac safety - QTc prolongation can lead cardiac arrhythmias and is associated with drugs like sertindole and ziprasidone

EPS - Zyprexa's EPS profile is comparable to placebo. This is unlike risperidone and ziprasidone, which have dose-dependent EPS

Patient selection criteria for ziprasidone registration studies have been questioned. It remains to be seen how QTc prolongation, EPS and 'weight neutrality' claims are supported by broader clinical use. Case reports of weight gain, EPS and QTc effects are already surfacing. Pfizer will draw comparison between what they may present as a theoretical QTc risk versus a visibly clinical issue of weight gain.

**Our focus must be to drive home the efficacy of Zyprexa** - especially at the sales force level. Safety concerns around EPS and QTc with competitor products need to be elevated while we responsibly manage weight gain objections with data, perspective and interventions.

**5. Affiliate/region expectations**

*Several previous communications have documented the well established Pfizer method of launching new products. The Sales and Marketing Executive Committee has made clear policy statements about our competitive response.*

*We must place a stake in the ground in terms of our full marketing mix competitiveness. So far, we have increased total spend by 50% in expected Pfizer launch countries*

*We need to increase sales force size to match the expected Pfizer sales force size*

*If this is not enough, we need to quickly upgrade. Contingency plans should contain training of retail sales forces as back up SOV that could be redeployed on specialist customers and/or use of contract sales forces. Affiliates are expected to raise any resourcing concerns through geographical and regional management*

*Early experience from Sweden shows that despite increased resourcing, we can still be very surprised.*

**In summary.....**

Throughout last year, emphasis on Zyprexa brand strategy development has been combined with aggressive increases in sales force, marketing and medical investment for what is now our #1 product.

We are ready and confident for this challenge - we have had plenty of time to anticipate it

We have the best Brand, let's go out and lead and set the rules of the game for our competitors

This competitive encounter gives us a great opportunity to show how we're capitalizing on our medical, regulatory, marketing, product development and sales capabilities to address customer needs.

At the end of the day, we are talking here about treating serious illnesses. Zyprexa's efficacy helps patients and their carers achieve goals which we may take for granted. This is supported by Zyprexa being used in approaching 6 million patients. Zyprexa is really providing an answer that matters.

Please continue to use the product team as the central point for market intelligence and information. We will continue to issue regular updates and request that all 'news' and requests are routed to Nadia Fontaine, Zyprexa Product Team marketing.